C

Caisson Disease3

Caldwell-Luc Approach

Caldwell-Luc Puncture

Canal Dehiscence

Canal Wall Down Mastoidectomy

Joe Walter Kutz Jr.[1], Brandon Isaacson[1] and Peter Sargent Roland[2]
[1]Otolaryngology-Head and Neck Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA
[2]Department of Otolaryngology-Head and Neck Surgery, UT - Southwestern Medical Center, University of Texas Southwestern, Dallas, TX, USA

Definition

Removal of the posterior external auditory canal resulting in a common cavity consisting of the mastoid and external auditory canal.

Cross-References

▶ Mastoidectomy

Canal Wall Reconstruction

Canal Wall Up Mastoidectomy

Joe Walter Kutz Jr.[1], Brandon Isaacson[1] and
Peter Sargent Roland[2]
[1]Otolaryngology-Head and Neck Surgery, University
of Texas Southwestern Medical Center, Dallas,
TX, USA
[2]Department of Otolaryngology-Head and Neck
Surgery, UT - Southwestern Medical Center,
University of Texas Southwestern, Dallas, TX, USA

Definition

Complete mastoidectomy removing the air cells along
the tegmen mastoideum, sigmoid sinus plate, and
posterior external auditory canal. The posterior
external auditory canal is preserved.

Cross-References

▶ Mastoidectomy

Canalplasty

▶ Surgery for Congenital Aural Atresia

Canal-Wall Down Mastoidectomy

▶ Mastoidectomy

Canal-Wall Up Mastoidectomy

▶ Mastoidectomy

Cancer

▶ Skull Base Neoplasms

Cancer of Ear

▶ Squamous Cell Carcinoma of Ear

Cancer of External Auditory Canal

▶ Squamous Cell Carcinoma of Ear

Cancer of Nasopharynx

▶ Nasopharyngeal Carcinoma

Canker Sore

▶ Oral Mucosal Lesions

Canthal Positions

Michael M. Kim
Division of Facial Plastic & Reconstructive Surgery,
Department of Otolaryngology-Head and Neck
Surgery, Oregon Health & Science University,
Portland, OR, USA

Definition

The canthal tendons attach to the eyelids at the lateral
and medial orbital rims. They are extensions of
orbicularis oculi muscle that attach to the periorbita
overlying the bone. The lateral canthal tendon is typi-
cally positioned 2 mm higher than medial canthus in
the horizontal plane.

The pretarsal and preseptal portions of the
orbicularis oculi muscle taper to form the superior
and inferior limb of the lateral canthal tendon. These
superior and inferior limbs coalesce to form the lateral
canthal tendon, which attaches to the inner aspect of
the lateral orbital rim on Whitnall's tubercle. Attenua-
tion of this tendon is often the cause of lower lid laxity
and can be surgically restored by procedures such as
the lateral tarsal strip operation.

Similarly, the medial pretarsal and preseptal por-
tions of the orbicularis oculi muscle form the two limbs
of the medial canthal tendon. The anterior limb
attaches to the frontal process of the maxilla along

the anterior lacrimal crest while the posterior limb attaches at the posterior lacrimal crest and is also known as Horner's muscle. These two limbs envelop the lacrimal sac and can function as a "pump" for the lacrimal drainage system. Laxity of the medial canthal tendon is uncommon in the atraumatic lid.

Canthoplasty

Michael M. Kim
Division of Facial Plastic & Reconstructive Surgery, Department of Otolaryngology-Head and Neck Surgery, Oregon Health & Science University, Portland, OR, USA

Definition

A procedure typically performed to change the position of either the medial or lateral canthus. It may be done for aesthetic or functional purposes. Because medial canthal position and laxity rarely change with age, the majority of canthoplasty procedures are performed on the lateral canthus. Examples include canthopexy, retinacular suspension, and lateral tarsal strip procedures.

Carotid Artery Pseudoaneurysm

▶ Imaging for Parapharyngeal Space Masses, Carotid Artery Pseudoaneurysm

Carotid Body Tumor

▶ Osteoradionecrosis of Skull Base (Benign Neoplasia-Paragangliomas)

Carotid Transposition

▶ Imaging for Parapharyngeal Space Masses, Ectatic Internal Carotid Artery

Cartilage Tympanoplasty

John L. Dornhoffer and Jennings R. Boyette
Department of Otolaryngology-Head and Neck Surgery, University of Arkansas for Medical Sciences, Little Rock, AR, USA

Synonyms

Tympanoplasty

Definition

▶ Tympanoplasty is the reconstruction of the tympanic membrane (TM) in such a manner that specific middle ear pathology, such as ▶ cholesteatoma, ▶ chronic otitis media, or an ossicular chain defect, is also addressed. Cartilage tympanoplasty refers to the use of autogenous cartilage as graft material to reconstruct or reinforce portions of the TM.

Purpose

Techniques utilizing cartilage are typically reserved for persistent perforations, severe retractions, cholesteatoma, and revision surgery; however, cartilage is also employed by many for primary tympanoplasty.

For more information on tympanoplasty and middle ear surgery please refer to: ▶ Tympanoplasty, and ▶ Ossiculoplasty.

Principle

Background
Cartilage has long been used as a graft material in middle ear surgery. Utech was the first to begin using it in the 1950s. Others, such as Salen and Goodhill, began using cartilage for repairing portions of the TM; however, Heermann was the first to establish the use of cartilage and the palisade technique for chronic middle ear disease (Tos 2009). Recently it has also been employed to reconstruct large portions of the TM. The use of cartilage to reconstruct the pars tensa

in cases of perforation, atelectasis, and cholesteatoma has expanded the indications and utilization of cartilage in tympanoplasty. While cartilage has classically been implemented for ▶ ossiculoplasty, this entry specifically addresses the use of cartilage in type I tympanoplasty.

Cartilage differs from traditional graft material, such as fascia and perichondrium, primarily due to its increased thickness. This might suggest an increased rigidity, with resulting conductive hearing loss; however, several studies have demonstrated that hearing results are no different than with fascia (Tos 2009; Milewski 1993; Amedee et al. 1989). Moreover, it is precisely this increased thickness and rigidity that makes cartilage an ideal graft material capable of resisting the resorptive and retracting forces of continuous ▶ eustachian tube dysfunction.

Many variations exist regarding the shape and placement of cartilage grafts. Most of these fall under two distinct techniques: the cartilage/perichondrium island flap and the palisade technique. The choice of technique is generally dictated by the specific otologic pathology. For example, the cartilage island flap is preferred for the repair of high-risk perforations and the atelectatic ear while the palisade technique is preferred in cases of cholesteatoma when ossiculoplasty is needed around an intact malleus.

Fate of Graft Material

Cartilage grafts are largely nourished by diffusion. While degeneration of the chondrocytes occurs, the cartilage retains its framework of lacunae and, thus, its rigid quality. In both experimental and clinical studies, cartilage has been shown to be well tolerated by the middle ear, and long-term survival should be expected (Kerr et al. 1973; Don and Linthicum 1975).

Surgical Technique

The surgical approaches for cartilage tympanoplasty are no different than those for traditional tympanoplasty and middle ear surgery. In general, a postauricular approach provides good visualization and access. This is the most commonly used approach due to the tendency of surgical candidates to have more extensive middle ear disease. However, for small postauricular perforations or retraction pockets, a transcanal or endaural approach may be utilized. The specifics of these approaches with regard to the TM and middle ear are detailed elsewhere in this text,

see ▶ Tympanoplasty for more information. While many surgeons may place their graft material on the lateral surface of the TM in an onlay technique, the underlay technique of placing the graft on the medial surface of the TM is preferable and will be described herein.

Harvesting of Cartilage

Cartilage may be obtained from the tragus (most commonly) or the conchae (cymba or cavum). Tragal cartilage is ideal because it is thinner and flatter than conchal cartilage. In order to harvest tragal cartilage, the initial incision is made on the medial surface of the cartilage and extending through the medial skin, medial perichondrium, cartilage, and lateral perichondrium. A 2-mm strip of cartilage at the dome is preserved for cosmesis. Scissors are then used to dissect in the plane between the skin and the perichondrium. Dissection is extended as far as possible in each direction in order to deliver the largest piece of cartilage possible (typically 15 mm × 10 mm in children and slightly larger in adults).

Cymba cartilage is slightly curved and is more suitable for use in the palisade technique. If a postauricular approach is utilized, cymba cartilage can be readily obtained by extending dissection anteriorly in the plane along the perichondrium of the posterior auricle.

Cartilage thickness does not appear to differ between children and adults. However, there is a tendency for the perichondrium to be more adherent in children. In patients over 65 years, the cartilage may be slightly brittle and gentle handling of the graft is advised.

The Cartilage/perichondrium Island Flap

Creation of a cartilage/perichondrium island flap begins with the harvesting of tragal cartilage. The perichondrium on one side of the graft is preserved. A round knife is then used to create a disk that measures 7–9 mm in diameter, which can be used for total TM reconstruction. A 2-mm strip of cartilage is then removed centrally (while preserving the perichondrium) to accommodate the malleus handle. A triangle of cartilage may also be removed from the posterior-superior portion of the graft in cases where the incus is still present. The graft is now composed of two cartilage islands that can flex at the malleus to conform to the normal, conical shape of the native TM.

An underlay technique is used to place the graft, with a tail of perichondrium extending along the posterior canal wall. The malleus fits into the carved central groove of the cartilage islands. Some surgeons have reported additional scarring and fixation if the perichondrium is placed on the side facing the middle ear; therefore, it is recommended that the graft is placed in such a fashion that the perichondrium is facing the ear canal (Tos 2009). Gelfoam (Upjohn Laboratories, Kalamazoo, MI) is packed into the middle ear anteriorly and posteriorly to support the graft. A single pieced of Gelfoam is placed lateral to the graft, and the ear canal is filled with water-soluble antibiotic ointment.

The Palisade Technique

Instead of using a single piece of cartilage, as with the cartilage/perichondrium island flap, the palisade technique generally refers to using individual pieces of cartilage to reconstruct the TM. This technique has been preferred in cases of chronic eustachian tube dysfunction and cholesteatoma and when precise cartilage placement is needed around an intact malleus. It has also been suggested that palisade reconstruction allows for better detection of residual cholesteatoma growth postoperatively because the palisades enable the reconstruction to bulge outward when cholesteatoma recurs (Uzun et al. 2005).

Heermann's palisade technique entailed the use of several narrow strips of cartilage that were carefully inset and layered across the defect (Tos 2009). This technique has subsequently been modified in multiple ways, including the use of a variety of cartilage shapes and thicknesses as well as changes to the inset and placement with utilization of modern ossicular prostheses. The use of several semicircular shapes of cartilage to reconstruct the TM, often referred to as the "mosaic" technique, is preferred as this method allows for more exact graft coverage and placement. The graft can be modified in a "cut as you go" fashion for a precise fit between the reconstructed TM, the remaining malleus or ossicular prosthesis, and the canal wall.

Cartilage can be harvested from either the cymba or the tragus. The perichondrium is removed from one side of the cartilage and is used to reinforce the reconstruction after graft placement. In the traditional palisade technique, the cartilage is sliced into several rectangular strips measuring approximately 1–2 mm. These strips are then placed side by side to create the new TM. This technique has been criticized due to the space left between the strips of cartilage. Therefore, many surgeons prefer to layer the palisades similar to the tiles on a roof. Perichondrium is then placed over the grafts to encourage epithelialization.

With the mosaic technique, a single semilunar-shaped piece is placed against the malleus and on top of the prosthesis in order to reconstruct a major portion of the posterior TM initially. Once this piece has been positioned, a second semilunar piece is placed between the first piece and the canal wall to reconstruct the scutum precisely. The remaining spaces are then carefully filled with small slivers of cartilage in a jigsaw-puzzle fashion. The entire reconstruction is then covered with a large piece of perichondrium that further drapes over the posterior wall.

Postoperative Care

The patient is typically seen in the clinic 1–2 weeks postoperatively. Ear wicks or other packing materials are removed at this time, and residual ointment is suctioned from the ear canal. Antibiotic ear drops are prescribed if any additional residue remains. At 2–3 weeks from the day of surgery, the patient is instructed to begin Valsalva maneuvers to inflate the middle ear. A postoperative audiogram is usually obtained at 6–8 weeks post-surgery. The development of a conductive hearing loss should prompt the examination for middle ear effusion or residual cholesteatoma.

Complications

Proper graft sizing and placement intraoperatively are key to preventing postoperative complications. Island grafts that are too small can be rectified by using cartilage slivers, as in the palisade technique, to ensure complete coverage. Grafts that are too large should be trimmed to fit precisely at the bony annulus. An intact chain with a medially rotated malleus may alter the position of the graft. This can be remedied by either modifying the manubrium for a better fit or by removing a larger strip of cartilage from the island graft. Further manipulation or displacement of the chain is discouraged due to the risk of acoustic trauma.

The most commonly encountered postoperative complications of cartilage tympanoplasty generally stem from the inability to examine the status of the middle ear through the opaque cartilage graft. Persistent middle ear effusion with resultant

conductive hearing loss is seen in about 7–10% of cases (Brackmann et al. 2010), and tympanograms are unreliable as they will frequently exhibit a low-volume type B tympanogram. Therefore, if a conductive hearing loss is found, a CT scan may be needed to assess the middle ear.

Placement of a ▶ tympanostomy tube is often difficult following cartilage tympanoplasty and typically necessitates taking the patient to the operating room. Silastic t-tubes or titanium tubes specifically designed for cartilage tympanoplasty (Razrbac Tube, Grace Medical Inc., Memphis, TN) are used in lieu of grommet tubes as these will not fit properly due to the thickness of the cartilage graft. It is also often necessary to remove an ellipse of cartilage to accommodate the tube. In patients with severe and pervasive eustachian tube dysfunction (such as in those with craniofacial abnormalities or a history of radiation therapy or multiple otologic surgeries), it is advisable to consider tube placement at the time of the initial tympanoplasty.

Surveillance of the middle ear following cholesteatoma is also made difficult by the opaque cartilage graft. Therefore, if major spillage of the cholesteatoma sac occurs during the initial removal, a second-look surgery should be considered. However, because residual cholesteatoma in the epitympanum is often hidden from view in traditional tympanoplasty reconstructions, many surgeons utilize surveillance CT scans to detect recidivistic disease after either traditional or cartilage reconstruction. Ultimately, residual cholesteatoma typically manifests as a ▶ conductive hearing loss, which may prompt CT imaging.

Indications

The use of cartilage as a graft material for tympanoplasty should generally be considered in any ear thought to be at a high risk for failure using traditional graft materials, such as fascia or perichondrium. These high-risk situations are commonly encountered with the atelectatic ear, ▶ cholesteatoma, revision surgery, perforations anterior to the annulus, draining perforations at the time of surgery, perforations larger than 50% of the TM, and bilateral perforations. Cartilage has been particularly useful in the case of the atelectatic ear as the increased rigidity of the cartilage helps to resist the negative

pressure forces of ▶ eustachian tube dysfunction, and its efficacy over fascia has been extensively reported (Sheehy 1985; Glasscock and Hart 1992; Levinson 1987). Furthermore, cartilage has also proven useful in reinforcing the scutum and preventing recurrent retraction pockets in cholesteatoma surgery.

Cartilage tympanoplasty is applicable in both adult and pediatric patients; however, success in pediatric patients requires careful patient selection. In general, tympanoplasty is avoided during the otitis-prone years (<3 years) and in cases where contralateral ear disease is present. With a normal contralateral ear, cartilage tympanoplasty is typically performed around age 4. When contralateral ear disease is present, ▶ adenoidectomy is considered, and the tympanoplasty is performed around age 7 (Brackmann et al. 2010).

In both adult and pediatric patients, an effort is made preoperatively to optimize middle ear aeration and resolve otorrhea. Thus, performing the Valsalva maneuver is encouraged (or use of the Otovent in young children). Those unable to insufflate the middle ear space or those with concomitant sinonasal disease are treated with nasal steroid sprays. Otorrhea is treated with antibiotic- and steroid-containing topical solutions and aural cleaning for 6–8 weeks preoperatively. Smoking cessation is also strongly encouraged.

Contraindications

While the indications for cartilage tympanoplasty have broadened, the contraindications have been narrowed. Efforts to optimize the middle ear environment are advised in all patients, and, therefore, eustachian tube dysfunction and otorrhea should be maximally treated prior to surgery. While a draining ear at the time of surgery has classically been associated with graft failure, it should not necessarily be considered a contraindication to cartilage tympanoplasty. However, due to the opaque nature of the reconstructed TM postoperatively, if surveillance via audiometry or CT is not available, traditional fascia tympanoplasty should be considered.

Advantage/Disadvantage

Cartilage tympanoplasty has the primary advantage of a more rigid reconstruction that can resist the

resorption and retraction associated with chronic middle ear dysfunction. Cartilage is well tolerated in the middle ear environment and exhibits long-term survival, and successful graft take can be expected in over 95% of patients (Brackmann et al. 2010; Dornhoffer 1997, 1999, 2003). Therefore, in patients with chronic middle ear disease or cholesteatoma, cartilage techniques can provide a more stable, long-lasting repair.

Given the increased thickness of cartilage grafts compared to the native TM, it would be expected that the acoustic properties and postoperative hearing results would differ from traditional fascia tympanoplasty. However, multiple studies have demonstrated good closure of the air-bone gap with cartilage tympanoplasty (Brackmann et al. 2010; Demirpehlivan et al. 2011; Dornhoffer 1997, 1999, 2003). It appears that, compared to fascia, cartilage grafts can be expected to provide equivalent hearing results with an increased efficacy and durability of repair.

The major disadvantage associated with cartilage reconstruction of the TM is that the TM is essentially opaque following the surgery. Therefore, assessment of the middle ear can be challenging as middle ear effusions or residual cholesteatoma cannot be visualized with otoscopy. Furthermore, following cartilage tympanoplasty, tympanograms are unreliable and usually will reveal a low-volume type B curve regardless of middle ear status. Therefore, the hearing result is the best indicator of middle ear status. In some cases a CT scan may ultimately be needed to examine the middle ear space. If it is determined that a ventilation tube is necessary, intubation through the cartilage is often difficult and usually requires a general anesthetic. Fortunately, revision surgery following cartilage tympanoplasty is relatively straightforward. The tympanomeatal flap can be raised easily in the standard fashion, and adhesions and scarring appear to be less common than with other graft materials.

Cross-References

References

Amedee RG, Mann WJ, Riechelmann H (1989) Cartilage palisade tympanoplasty. Am J Otol 10:447–450

Brackmann DE, Shelton C, Arriaga MA (2010) Otologic surgery. WB Saunders/Elsevier, Philadelphia

Demirpehlivan IA, Onal K, Arslanoglu S et al (2011) Comparison of different tympanic membrane reconstruction techniques in type I tympanoplasty. Eur Arch Otorhinolaryngol 268:471–474

Don A, Linthicum FH (1975) The fate of cartilage grafts for ossicular reconstruction in tympanoplasty. Ann Otol Rhinol Laryngol 84:187–191

Dornhoffer JL (1997) Hearing results with cartilage tympanoplasty. Laryngoscope 1107:1094–1099

Dornhoffer JL (1999) Surgical modification of the difficult mastoid cavity. Otolaryngol Head Neck Surg 120:361–367

Dornhoffer J (2003) Cartilage tympanoplasty: indications, techniques, and outcomes in a 1,000 patient series. Laryngoscope 113(11):1844–1856

Glasscock ME 3rd, Hart MJ (1992) Surgical treatment of the atelectatic ear. In: Friedman M (ed) Operative techniques in otolaryngology–head and neck surgery. WB Saunders, Philadelphia, pp 15–20

Kerr AG, Byrne JE, Smyth GD (1973) Cartilage homografts in the middle ear: a long-term histological study. J Laryngol Otol 87:1193–1199

Levinson RM (1987) Cartilage-perichondrial composite graft tympanoplasty in the treatment of posterior marginal and attic retraction pockets. Laryngoscope 197:1069–1074

Milewski C (1993) Composite graft tympanoplasty in the treatment of ears with advanced middle ear pathology. Laryngoscope 103:1352–1356

Sheehy JL (1985) Surgery of chronic otitis media. In: English G (ed) Otolaryngology. Harper and Row, Philadelphia, pp 1–86

Tos M (2009) Cartilage tympanoplasty: classification of methods, techniques, results. Thieme, Stuttgart

Uzun C, Yagiz R, Tas A et al (2005) Combined Heerman and Tos (CHAT) technique in cholesteatoma surgery: surgical technique and preliminary results. J Laryngol Otol 119:429–435

Cavernous Sinus Thrombosis

Cellular Immunity

Cellulitis

Central Auditory Processing Disorder – [(C)APD]

Central Auditory System, Anatomy

Hinrich Staecker[1] and Jennifer Thompson[2]
[1]Department of Otolaryngology-Head and Neck Surgery, University of Kansas Medical Center, Kansas City, KS, USA
[2]University of Kansas Medical Center, Kansas City, KS, USA

Synonyms

Acoustic nerve; Auditory brainstem response (ABR); Auditory nerve; Brainstem audio-evoked response; Cochlear nerve; Heschl's gyrus; Transverse temporal gyri

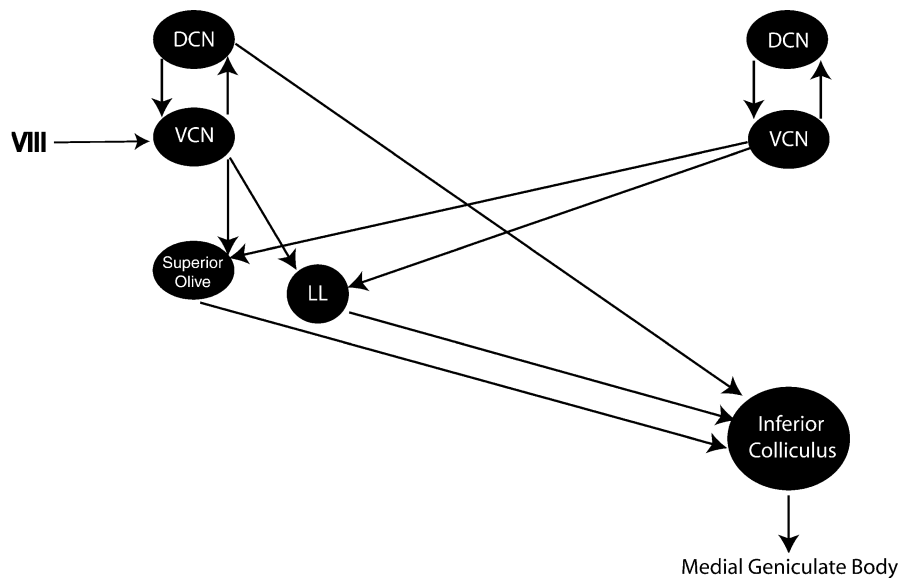### Summary of the Central Auditory System

The central auditory system begins as the cochlear nerve ascends from the cochlea to higher order auditory structures in the brainstem and functions to process information from the organ of Corti in the cochlea. Besides recognition of sounds, the central auditory system is responsible for localization of sound and discrimination of sound. The inner hair cells of the cochlea are innervated by the type I bipolar ganglion cells in the spiral ganglion, and the outer hair cells are innervated by the type II bipolar ganglion cells. The first point of information transfer in the central auditory system is to the cochlear nuclei. The cochlear nuclei are located at the pontomedullary junction, with the ventral cochlear nucleus extending laterally into the middle cerebellar peduncle and the dorsal cochlear nucleus lying lateral and dorsal to the inferior cerebellar peduncle.

From the cochlear nuclei, auditory information is further processed into the superior olivary complex that sits in the trapezoid body where the ability to localize sounds based upon interaural differences is first delineated. Auditory fibers continue from the superior olivary complex and form a flattened fiber track ascending in the lateral lemniscus of the upper pons. Fibers from the lateral lemniscus converge on the mesencephalic inferior colliculus. The commissure of the inferior colliculus, located just dorsal to the aqueduct, crosses the midline and serves to carry information bidirectionally and contains ascending fibers of the crossed pathway from the colliculus. Fibers project from the inferior colliculus to the diencephalic medial geniculate body located in the dorsal thalamus. Finally, auditory nerve fibers converge on the auditory cortex located in the upper surface of the temporal lobe. Figure 1 illustrates the connections of the central auditory pathway between the auditory nerve and the geniculate body.

Auditory Nerve

The cochlear branch of the vestibulocochlear nerve leaves the cochleae and enters the brainstem at the pontomedullary junction where it terminates on the cochlear nuclei. More specifically, the auditory nerve enters the anteroventral cochlear nucleus on its ventromedial surface. Axons from the basal end of the cochlea carry high-frequency sound information and project dorsally and medially, supplying the dorsal part of all cochlear nuclei divisions. Conversely, axons from the apical part of the cochlea carry low-frequency sound information and project ventrally ending in the venterolateral part of all cochlear nuclei divisions (Malmierca and Smith 2009). The auditory nerve fibers on entering the cochlear nucleus bifurcate into an ascending branch that supplies the anteroventral

Central Auditory System, Anatomy, Fig. 1 Simplified illustration of the brainstem auditory pathway. The auditory nerve makes synaptic contacts in the ventral cochlear nucleus. From there, auditory information is passed through the superior olivary complex that sits in the trapezoid body where the ability to localize sounds based upon interaural differences is first delineated. Auditory fibers continue from the superior olivary complex and form a flattened fiber track ascending in the lateral lemniscus of the upper pons. Fibers from the lateral lemniscus converge on the mesencephalic inferior colliculus. Fibers project from the inferior colliculus to the diencephalic medial geniculate and from there converge on the auditory cortex located in the upper surface of the temporal lobe

cochlear nucleus and a descending branch that primarily supplies the posteroventral cochlear nucleus and the dorsal cochlear nucleus.

Two types of afferent auditory nerve fibers exist. Type I thick myelinated axons carry auditory information from the cochlear inner hair cells. They form large, axosomatic endings termed "bulbs of Held" and supply most parts of the cochlear nucleus except the periphery and granule cell areas. Type II thin unmyelinated axons carry information from outer hair cells. These axons appear to supply primarily the marginal shell of the ventral cochlear nucleus and areas rich in granule cells (Malmierca and Smith 2009). Both type I and type II fibers originate from the high-frequency base and the low-frequency apex of the cochlea.

Cochlear Nucleus

The cochlear nuclei are the first destination for all afferent auditory nerve fibers continuing from the cochlea. The cochlear nuclei are located bilaterally at the pontomedullary junction and lateral to the course of the auditory nerve. There are two primary cochlear nuclei, termed the ventral cochlear nucleus and the dorsal cochlear nucleus. The ventral cochlear nucleus extends laterally along the edge of the middle cerebellar peduncle and contains five main cell types, each converting auditory nerve information into a unique response: spherical bushy, globular bushy, octopus, multipolar, and small cells. The ventral cochlear nucleus is divided into the anteroventral cochlear nucleus and the posteroventral cochlear nucleus. The anteroventral cochlear nucleus is further subdivided into both an anterior and a posterior division. The anterior division of the anteroventral cochlear nucleus contains spherical bushy cells, and the posterior division of the anteroventral cochlear nucleus contains globular bushy cells. The bushy cells of the anteroventral cochlear nucleus receive afferents from the cochlear nerve via the synaptic endings termed "bulbs of Held." Anterior division spherical bushy cells are innervated by larger and more complex end bulbs (Cummings et al. 2005). The posteroventral cochlear nucleus contains octopus cells. The multipolar and small cells are dispersed throughout the ventral cochlear nucleus. The bifurcating type I fibers form

dorsoventrally arranged sheets with low-frequency fibers from the apical spiral ganglion terminating ventrally and high-frequency fibers from the basal spiral ganglion terminating dorsally (Nieuwenhuys et al. 2008).

The dorsal cochlear nucleus is a flat structure containing five primary layers that curves around the inferior cerebellar peduncle on the dorsolateral surface of the brainstem and contains pyramidal (fusiform) cells and granule cells. The dorsal cochlear nucleus is much more sparsely innervated than the ventral cochlear nucleus. It receives afferent fibers from the posteroventral cochlear nucleus and sends projections to the anteroventral cochlear nucleus. The major projection neurons of the dorsal cochlear nucleus are the pyramidal cells that send fibers to the contralateral inferior colliculus through the dorsal acoustic stria.

Acoustic Striae

The acoustic striae are composed of three bundles of second-order neuron projections from the cochlear nucleus to higher auditory structures. The three acoustic striae include the ventral acoustic stria (also called the trapezoid body), intermediate acoustic stria, and the dorsal acoustic stria. The spheric and globular bushy cells of the anteroventral cochlear nucleus form the ventral acoustic stria that projects to the lateral superior olive, medial superior olive, medial nucleus of the trapezoid body, and the inferior colliculus. The intermediate acoustic starts with the octopus cells of the posteroventral cochlear nucleus and projects to the ventral nucleus of the trapezoid body, lateral superior olive, and periolivary region. The dorsal acoustic stria projects to the lateral lemniscus and the central nucleus of the inferior colliculus. It joins the ventral stria as it nears the superior olivary complex.

Superior Olivary Complex

The superior olivary complex located in the caudal pons is comprised of the first neurons that receive binaural input and display responsiveness to interaural stimuli disparities. The superior olivary complex consists of the medial nucleus of the superior olive, lateral nucleus of the superior olive, and the periolivary nuclei, all embedded in the trapezoid body. The medial

superior olive is the most prominent part of the olivary complex consisting of 10,000–11,000 bipolar neurons (Moore 2004). Projections from the cochlear nucleus are tonotopic, with lower frequencies concentrated in the dorsal part and higher frequencies in the ventral part of the medial superior olive, although still biased to low-frequency range bipolar neurons. The medial superior olive receives bilateral fibers from the ventral cochlear nucleus via the ventral acoustic stria. More specifically, lateral dendrites of the bipolar neurons receive fibers from the ipsilateral anteroventral cochlear nucleus, and medial dendrites receive fibers from the contralateral anteroventral cochlear nucleus. Projections from the medial superior olive target the ipsilateral central nucleus of the inferior colliculus. While a few medial superior olive cells use GABA or glycine neurotransmitters, the majority use an excitatory neurotransmitter (Schofield 2005).

The lateral nucleus of the superior olive is a smaller nucleus comprised of multipolar neurons. Projections from the cochlea are tonotopic with lower frequency fibers targeting the lateral part of the nucleus and higher frequency fibers targeting the medial part, although the majority of fibers are high frequency ones (Nieuwenhuys et al. 2008). The major excitatory input to the lateral superior olive originates from the ipsilateral spherical bushy cells from all divisions of the ventral cochlear nucleus via the medial nucleus of the trapezoid body. The major inhibitory input originates from the globular bushy cells of the contralateral posterior part of the anteroventral cochlear nucleus and the posteroventral cochlear nucleus via the medial nucleus of the trapezoid body. Projections from the lateral superior olive extend bilaterally, with an excitatory contralateral projection and a glycinergic inhibitory ipsilateral projection. These crossed and uncrossed projections allow for the "acoustic chiasm," holding that most cells above the level of the midbrain respond to sounds in the contralateral sound field (Schofield 2005).

The periolivary nucleus is an additional component of the periolivary complex surrounding the medial and lateral olivary nuclei and consisting of three cell groups termed dorsomedial preolivary nucleus, dorsal preolivary nucleus, and dorsolateral preolivary nucleus. All three acoustic striae send afferent input to the periolivary nuclei. It also receives descending inputs from the inferior colliculus and collateral fibers that project to the medial nucleus of the trapezoid

body. There are three main projections from the periolivary nucleus. All nuclei send ascending projections to the ipsilateral inferior colliculus, primarily synapsing in the central nucleus of the inferior colliculus, with a smaller projection to the contralateral inferior colliculus. The periolivary nucleus also projects bilaterally to the cochlear nuclei. Finally, the periolivary nucleus sends axons to the cochlea itself through the olivocochlear system.

The olivocochlear system contains descending axons that cross the brainstem, enter the vestibular nerve, and join the cochlear nerve through a vestibulocochlear anastomosis (Nieuwenhuys et al. 2008). There is both a medial and lateral efferent subdivision of the olivocochlear system that terminates on two types of hair cells in the organ of Corti. The medial olivocochlear system contains large multipolar cells in the medial nucleus of the trapezoid body that send bilateral cholinergic projections to the outer hair cells in the cochlea. Additionally, this system sends collateral fibers to the ventral cochlear nuclei. The medial system exhibits the olivocochlear reflex whereby it can restrict the cochlear gain by acting upon the inner hair cells. The interneurons in the posteroventral cochlear nucleus activated by a tone stimulus are connected to neurons in the medial olivocochlear system. Through a frequency-dependent process, this system decreases the outer hair cell contribution to cochlear amplification of the inner hair cell's processing of auditory information. Therefore, the olivocochlear reflex can act as a protective mechanism to the cochlear hair cells, lessen the cochlea response to environmental noise, and minimize damage to auditory receptors during intense sound exposure. There are separate sets of fibers comprising the ipsilateral and contralateral olivocochlear reflex (Nieuwenhuys et al. 2008). The medial olivocochlear system forms an intricate process in which the brain influences the actions of the input into the central auditory system.

The lateral olivocochlear system contains small cells in and around the lateral olivary nucleus that project to the ipsilateral cochlea to the peripheral processes of ganglion cells near their synapse with the inner hair cells. Additionally, there are collateral fibers that project to the ventral cochlear nuclei. The projections of the lateral olivocochlear bundle consist of both cholinergic neurons and neurons that primarily use GABA as the neurotransmitter.

Lateral Lemniscus

The lateral lemniscus is located in the dorsolateral part of the pons and the caudal part of the midbrain. Specifically, it is a flattened band of auditory fibers that ascend through the pontine tegmentum to the midbrain. The lateral lemniscus, near the lateral surface of the brainstem, bridges the connection between the superior olivary nucleus and the inferior colliculus. The three major nuclei of the lateral lemniscus have a tonotopic organization such that low frequencies are located dorsally and high frequencies are located ventrally. The major efferent target of all nuclei is to the central nucleus of the mesencephalic inferior colliculus.

The three major nuclei of the lateral lemniscus include the ventral lateral lemniscus, intermediate lateral lemniscus, and the dorsal lateral lemniscus. The ventral lateral lemniscus receives bilateral fibers from the ventral cochlear nucleus (largely contralateral) and ipsilateral fibers from the medial nucleus of the trapezoid body. The majority of cells are excited by stimulation in the contralateral ear. Most cells in the ventral lateral lemniscus use glycine or GABA as the neurotransmitter, suggesting that the afferent projections to the inferior colliculus are primarily inhibitory. Furthermore, the ventral lateral lemniscus is the largest single source of inhibition to the inferior colliculus (Schofield 2005). The projections are widespread and diffuse, terminating on the ipsilateral central nucleus and the dorsal cortex of the inferior colliculus.

The intermediate lateral lemniscus receives fibers from the contralateral ventral cochlear nucleus and the ipsilateral medial nucleus of the trapezoid body. It is excited by contralateral stimulation and remains excited throughout the duration of the stimulus. A minority of cells use GABA or glycine neurotransmitters, while the rest use an excitatory neurotransmitter. This tonotopically organized projection to the inferior colliculus is largely ipsilateral and terminates diffusely in the central nucleus and the dorsal cortex.

The dorsal lateral lemniscus is the most prominent lemniscal nucleus in humans. It receives all projections that ascend to the inferior colliculus. This includes afferent fibers from the ipsilateral medial nucleus of the superior olive and bilateral fibers from the lateral nucleus of the superior olive. Additional inputs include a limited amount of fibers from the contralateral ventral cochlear nucleus as well as some inputs from the

intermediate and ventral lateral lemnisci. The dorsal lateral lemnisci on each side of the brain share information via the commissure of Probst. The cells of the dorsal lateral lemniscus are largely GABAergic, binaural, excited by the contralateral ear, and inhibited by the ipsilateral ear (Schofield 2005). In addition to ascending projections continuing onto the inferior colliculus, the dorsal lateral lemniscus also sends a smaller set of fibers bilaterally to the superior colliculi and descending fibers to the superior olivary complex.

Inferior Colliculus

The inferior colliculus is a bilateral mesencephalic structure that forms the tectum of the brainstem with the superior colliculi. It is a major relay station for both ascending and descending auditory projections. Almost all the fibers from the lateral lemniscus terminate in the inferior colliculus, specifically in the central nucleus of the inferior colliculus. The commissure of the inferior colliculus is a transverse fiber tract consisting of thin fascicles forming the upper border of the recess of the fourth ventricle. The commissure contains axons of inferior colliculus neurons that carry information bidirectionally between the right and left inferior colliculus (Saldana and Merchan 2005).

The three major nuclei of the inferior colliculus include the central nucleus, external nucleus, and the pericentral nucleus. The central nucleus of the inferior colliculus is the largest and most prominent with a laminar organization containing parallel layers of cells with flat dendritic fields. The tonotopic organization is preserved with high frequencies located ventrally and low frequencies located dorsally. There is both a dorsomedial and a ventrolateral aspect to the central nucleus. The central nucleus receives almost all of the ascending information from the lower brainstem. It receives bilateral input from the cochlear nucleus. Although the dorsal cochlear nucleus projects directly to the central nucleus, the ventral cochlear nucleus projects first to the superior olive and to the lateral lemniscus. The central nucleus receives ipsilateral and contralateral input from the medial and lateral superior olivary nucleus. Additionally, it receives ipsilateral projections from the medial nucleus of the trapezoid body and periolivary nucleus. The dorsal lateral lemnisci project bilaterally to the central nucleus of the inferior colliculus, while the ventral lateral lemnisci project ipsilaterally to the venterolateral part of the inferior colliculus. The majority of descending projections from the primary auditory cortex target the dorsomedial portion of the inferior colliculus.

The external nucleus of the inferior colliculus (also termed the lateral or dorsal cortex) is located ventral and caudal to the central nucleus and receives input from the cochlear nuclei and the dorsal and ventral nucleus of the lateral lemniscus. Unlike the central nucleus, no fibers from the superior olivary complex synapse on the external nucleus of the inferior colliculus. Additionally, the external nucleus receives collaterals from fibers of the central nucleus.

The third nucleus of the inferior colliculus, the pericentral nucleus, completely surrounds the central nucleus of the inferior colliculus. Descending projections from the auditory cortex, lateral tegmental system, and the dorsal nuclei of the lateral lemniscus synapse on the pericentral nucleus. Efferents of all inferior colliculi nuclei travel via the brachium of the inferior colliculus to the medial geniculate nucleus in the thalamus.

Medial Geniculate Body

The medial geniculate body is the major relay to follow the brachium of the inferior colliculus in the ascending path of auditory information. It is located in the thalamus, medial to the lateral geniculate body and ventral to the pulvinar. The three parts of the medial geniculate body include the ventral, medial, and dorsal nuclei. All three divisions receive ascending axons from the inferior colliculus and descending fibers from the auditory cortex. The ventral division is located in the ventrolateral quadrant of the medial geniculate body and is tonotopically organized. It serves as the major input to the auditory cortex. The ventral division of the medial geniculate body contains Golgi type I and type II cells. Golgi type I cells are the main neurons, and Golgi type II cells are interneuronal cells that synapse on the dendrites of the principal cells. Both cell types receive afferent fibers from the brachium of the superior colliculus, but only the principal neurons send axons to the auditory cortex. The ventral division of the medial geniculate body receives axons running parallel to the laminae.

The medial division of the medial geniculate body is located in the ventromedial aspect, extending from the caudal to rostral pole. It contains the most heterogeneous neurons of the medial geniculate body. Although auditory information is the main type of information supplying the medial division, axons from the fastigial nucleus, superior colliculus, and vestibular system also converge on the medial division of the medial geniculate body. In the medial division, there exists no frequency map and no architectural subdivisions. It projects to subcortical, auditory cortical, and non-auditory cortical regions.

The dorsal division is the largest of the three divisions and occupies the entire caudal portion of the medial geniculate body. It has the most subdivisions, greatest neuronal diversity though predominantly stellate cells, and two types of interneurons. The large neuron diversity includes highly tufted cells with giant dendritic fields adding to the complexity by disrupting any sort of laminar pattern. Many nuclei comprise the caudal, dorsal, dorsomedial, and anterodorsal subdivisions. Afferent fibers from the lateral tegmental system target the dorsal division.

Auditory Cortex

The final processing unit of sound in the human brain is the auditory cortex. It comprises the ultimate destination of the central auditory system ascending fiber tracks. It is composed of primary auditory cortex (core) and associated auditory belt regions. The primary auditory cortex (A1) is located in the upper bank of the temporal lobe and surrounded by specific auditory and nonspecific association areas. It corresponds to the transverse gyrus of Heschl. The association areas connect the primary auditory cortex to the frontal and temperoparietal regions involved in language, speech, and vision. The major input to the auditory cortex is from the ventral division of the medial geniculate body in the thalamus.

The primary auditory cortex has a tonotopic and binaural organization serving as a map of the cochlea. High frequencies are localized rostrally in the middle ectosylvian gyrus, and low frequencies are localized caudally in the dorsal part of the ectosylvian gyrus. Orthogonal to the primary auditory cortex tonotopic map of the cochlea is an alternating linear arrangement serving binaural traits. The neurons in the first stripe are excited by both ears and referred to as the EE cells,

while the neurons (EI cells) in the next stripe are inhibited by one ear and excited by the other ear (Purves et al. 2001).

The cortical association fibers connect the primary auditory cortex with the belt. The koniocortex of the primary auditory cortex is centered on Heschl's transverse gyrus and forms area 41 of Brodmann. The belt areas include the cortex medial to the transverse gyrus, sections of the planum temporale, and part of area 42 of Brodmann. The lateral parabelt comprises the rostral half of area 22 of Brodmann (Nieuwenhuys et al. 2008). The lateral parabelt interconnects the associated belt areas but not the primary auditory cortical areas. These afferents initiate from belt areas, with thalamic afferents arising from the medial and dorsal nuclei of the medial geniculate body rather than the ventral nuclei of the medial geniculate body. Therefore, the parabelt neurons are entirely dependent on the belt inputs rather than primary auditory cortex inputs (Nieuwenhuys et al. 2008).

There are three major descending pathways from the auditory cortex targeting the thalamus, midbrain, and the pons. The primary auditory cortex also projects bilaterally to the central nucleus of the inferior colliculus, ipsilaterally to the pericentral nucleus of the inferior colliculus, and to the corpus striatum. The corticothalamic and thalamocortical connections of the medial geniculate body are reciprocal. The primary auditory cortex areas project to the ventral and medial nuclei of the medial geniculate body. They also project tonotopically to the central nucleus of the inferior colliculus. Alternatively, the belt areas project to the dorsal and medial nuclei of the medial geniculate body as well as the suprageniculate nucleus and the nucleus limitans. The lateral parabelt projects to the medial pulvinar (Nieuwenhuys et al. 2008).

Auditory Brainstem Response Audiometry

The auditory brainstem response (ABR) (Fig. 2) audiometry is a procedure first described by Jewett and Williston in 1971. It is a neurologic test for the auditory brainstem function to monitor for cochlear hearing loss or deafness. It refers to an evoked potential generated by a brief click that is transmitted through an acoustic transducer such as an earphone and generates a response from the basilar region of the cochlea. These potentials are generated by the

Central Auditory System, Anatomy, Fig. 2 Example of an ABR recording. Waves I (eighth nerve), III (ipsilateral cochlear nucleus), IV (superior olivary nucleus), and V (lateral lemniscus/inferior colliculus) are marked. See text for detail
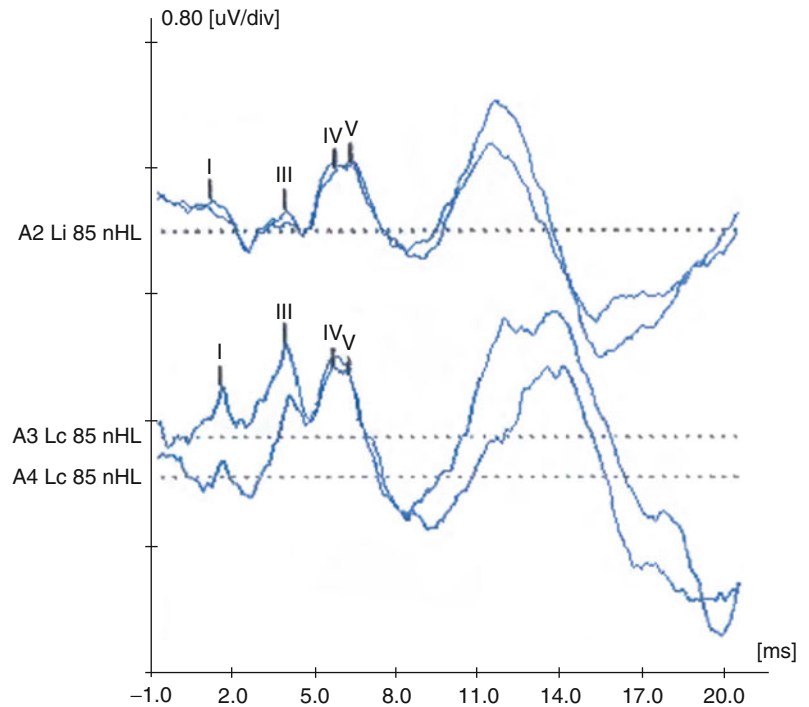
ear, the auditory nerve, and fiber tracts and nuclei of the ascending auditory pathways traversing the brainstem (Moller 2004). The elicited action potentials are then measured by surface electrodes that are placed on the patient's vertex, earlobes, and forehead. The amplitude of the resulting signal is in microvoltage. It is averaged and charted against the time in milliseconds. These responses produce 5–7 characteristic waves generated at particular latencies. If cochlear hearing loss is present, there will be an alteration in the pattern of waves I-V. Auditory brainstem responses can lead to a localization of the central pathology through identification of dissociations between the early brainstem response and the middle latency response (Griffiths 2002).

Normally the first five peaks are relatively constant, while peaks VI and VII have a tendency to vary. The auditory nerve generates peaks I and II, with the distal part of the auditory nerve corresponding to peak I and the more proximal part of the auditory nerve as it enters the brainstem corresponding to peak II. Peak III is predominantly generated by the ipsilateral cochlear nucleus. Peak IV is a less constant peak, and therefore is harder to identify. The superior olivary colliculus is the most likely anatomical generator of peak IV. The sharp vertex

is of peak V is generated by the lateral lemniscus as it terminates in the inferior colliculus, while the slow portion of this peak is generated by the inferior colliculus (Moller 2004). In this manner, second-order neuron activity may contribute to peak V. The amplitude of peak V can be used to measure the threshold in cochlear hearing loss (Griffiths 2002). The anatomical site of generation of peak VI and VII is not certain, although ascertained to be the thalamic medial geniculate body.

Conclusion

Increased understanding of the central auditory system is leading to a better understanding of a variety of clinical disorders in which central hearing is impaired. The central auditory system is responsible for complex processing tasks such as sound localization. Recognition of these roles has led to the development of diverse interventions such as bilateral cochlear implantation and auditory brainstem implantation. An appreciation of the physiology of the brainstem auditory nuclei is additionally increasing our understanding of phenomena such as tinnitus. Advances in physiology and

functional imaging further increase our ability to encompass the central auditory system into day-to-day otolaryngologic practice.

References

Eshraghi A, King J, Hodges A, Balkany T (2006) Cochlear implants. In: Johnson FE, Virgo KS (eds) The bionic human. Human Press, Totowa, pp 379–403

Griffiths T (2002) Central auditory pathologies. Br Med Bull 63:107–120

Malmierca M, Smith P (2009) Cochlear nucleus. In: Binder MD, Hirokawa N, Windhorst U (eds) Encyclopedia of neuroscience. Springer, Heidelberg

Moller A (2004) Physiology of the ear and the auditory nervous system. In: Jackler R, Brackmann D (eds) Neurotology. Mosby, St Louis, pp 19–36

Moore J (2004) The human brainstem auditory pathway. In: Jackler R, Brackmann D (eds) Neurotology. Mosby, St Louis, pp 5–15

Nieuwenhuys R, Voogd J, Van Huijzen C (2008) Auditory system. In: Nieuwenhuys R, Voogd J, van Huijzen C (eds) The human central nervous system, 4th edn. Germany, Heidelberg, pp 733–750

Purves D, Augustine GJ, Fitzpatrick D, Katz L, LaMantia A, McNamara J, Williams S (2001) Neuroscience. The auditory cortex. Sinauer Associates, Sunderland

Saldana E, Merchan M (2005) Intrinsic and commissural connections of the inferior colliculus. In: Winer JA, Schreiner C (eds) Inferior colliculus. Springer, New York, pp 155–181

Schofield B (2005) Superior olivary complex and lateral lemniscal connections of the auditory midbrain. In: Winer JA, Schreiner C (eds) Inferior colliculus. Springer, New York, pp 132–154

Central Neck Dissection

▶ Neck Dissection Anatomy

Central Neurofibromatosis

▶ Benign Neoplasia-Schwannoma-Neurofibromatosis Type 2

Central Pathways

▶ Vestibular and Central Nervous System, Anatomy

Cephalocele

▶ Temporal Bone Meningocele/Encephalocele

Cerebellopontine Angle Meningiomas

▶ Temporal Bone Meningiomas

Cerebrospinal Fluid Fistula

▶ Cerebrospinal Fluid Rhinorrhea, Evaluation and Management

Cerebrospinal Fluid Leak

Randal Leung
The Royal Victorian Eye and Ear Hospital, The University of Melbourne, Melbourne, VIC, Australia

Definition

Cerebrospinal fluid leak is the escape of cerebrospinal fluid from the normally closed fluid-filled space bounded by the meninges into an adjacent compartment.

Cross-References

▶ Temporal Bone Encephaloceles, Meningoceles, and CSF Leak, Repair of

Cerebrospinal Fluid Rhinorrhea

▶ Cerebrospinal Fluid Rhinorrhea, Evaluation and Management

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management

Seth Isaacs[1], Samer Fakhri[2,3], Amber Luong[2,3] and Martin J. Citardi[2,3]
[1]Cincinnati Sinus Institute, Group Health Associates, Cincinnati, OH, USA
[2]Department of Otorhinolaryngology-Head and Neck Surgery, University of Texas Medical School at Houston, Houston, TX, USA
[3]Texas Skull Base Physicians and Texas Sinus Institute, Houston, TX, USA

Synonyms

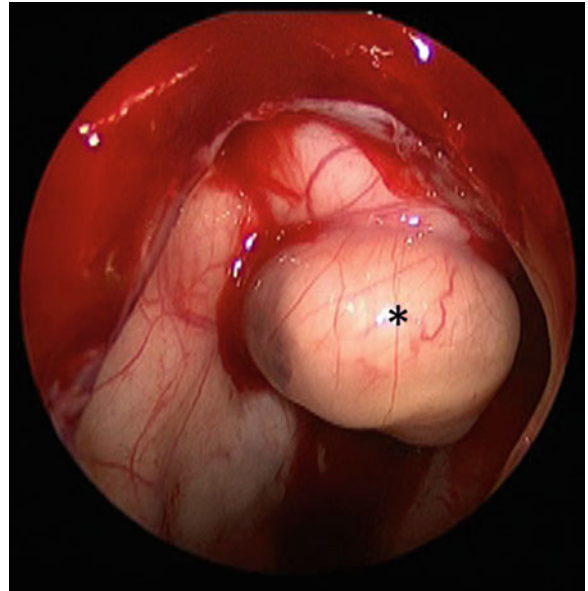Cerebrospinal fluid fistula; Cerebrospinal fluid rhinorrhea; CSF leak; Spinal fluid leak

Definitions

Cerebrospinal fluid rhinorrhea refers to the clear nasal drainage that results from an abnormal communication between the subarachnoid space and the air-containing space of the nose and paranasal sinuses.

Clinical Features and History

A patient with CSF rhinorrhea typically describes profuse, unilateral, clear drainage with a unique taste that the patient will characterize as salty or metallic. The volume of drainage is positional, often increasing in flow when the patient bends or leans the head forward. A history of any antecedent trauma is important in identifying a presumed skull base defect. Symptoms of anosmia or hyposmia may indicate a fracture or defect through the cribriform plate.

A detailed history of inflammatory sinus disease and allergies is warranted in patients with suspected CSF rhinorrhea. Other rhinopathies including allergic rhinitis, vasomotor rhinitis, and chronic sinusitis may mimic the symptoms associated with a CSF leak. It is also important to consider prior sinus surgery that may have resulted in unrecognized skull base defects that manifest as CSF rhinorrhea at any point in the postoperative course (see ▶ Sinus Surgery, Complications.)

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 1 Endoscopic visualization into the sphenoid sinus reveals evidence of a meningoencephalocele (*asterisk*) penetrating through a defect of the sphenoid roof

A history of headaches must be evaluated. Often patients with nontraumatic or spontaneous CSF rhinorrhea describe headaches that fluctuate. The severity of the headache worsens as the ICP increases and then improves at times of CSF rhinorrhea as the elevated ICP is relieved. Headaches may also be associated with bacterial meningitis or an unrecognized intracranial neoplasm.

The physical examination should include reproduction of the unilateral clear rhinorrhea. This can be accomplished by having the patient lean forward and perform a Valsalva maneuver. Anterior rhinoscopy or nasal endoscopy may demonstrate glistening nasal mucosa or even evidence of an active leak. Nasal endoscopy permits a more comprehensive evaluation of the sinuses and nasal cavity. Identification of soft tissue mass at the site of a suspected leak may represent a meningoencephalocele (Fig. 1).

In cases of suspected BIH, an ophthalmologic examination may reveal papilledema. In fact, all patients with CSF rhinorrhea in the absence of trauma should undergo a full ophthalmologic examination.

Diagnostic Tests

In certain circumstances, the CSF leak can be obvious as in patients who suffer a head trauma with an identifiable skull base fracture. However, the diagnosis of CSF rhinorrhea and the precise localization of the skull base defect can often be a challenge. Another dilemma is that the leak can often be intermittent – yielding a high false-negative rate of diagnosis. The primary goals of diagnosing CSF rhinorrhea include identification of extradural CSF and the exact location of the skull base defect.

The halo sign was a traditional marker of CSF rhinorrhea after head trauma. Collection of bloody nasal discharge on a white towel demonstrates a clear ring around a central spot of blood. The limitation of this test is the reproduction of the halo sign with both tears and saliva. The presence of glucose in nasal secretions was once thought to be an adequate marker of CSF. However, a high false-positive rate was described due to the reactivity of tears and normal nasal secretions with glucose oxidase strips (Katz and Kaplan 1985).

B2 transferrin is a protein present only in CSF, perilymph, and aqueous humor. It has become the preferred biochemical marker for CSF. Several studies have demonstrated both high sensitivity and specificity for this test (Nandapalan et al. 1996). Limitations of this study include the volume of specimen required and the availability of the test. Patients with intermittent or low flow leaks may not obtain adequate specimens. Degradation of the sample during transportation may also yield false-negative results. Beta-trace protein is another common protein found in CSF that can serve as a reliable marker, with nearly 100% sensitivity and specificity (Arrer et al. 2002).

Intrathecal agents may confirm the presence of a CSF rhinorrhea but also provide information about the location of the leak. They may be classified as visible dyes or radionuclide markers. These tests are invasive however as a lumbar puncture is required to introduce the agent into the subarachnoid space. Intrathecal fluorescein is the most common visible agent. It has a characteristic green color which allows endoscopic identification within the nose and sinuses. Blue light filters may permit better visualization of the fluorescein but often are not required. Serious complications have been linked to the intrathecal application of fluorescein including seizures and even death.
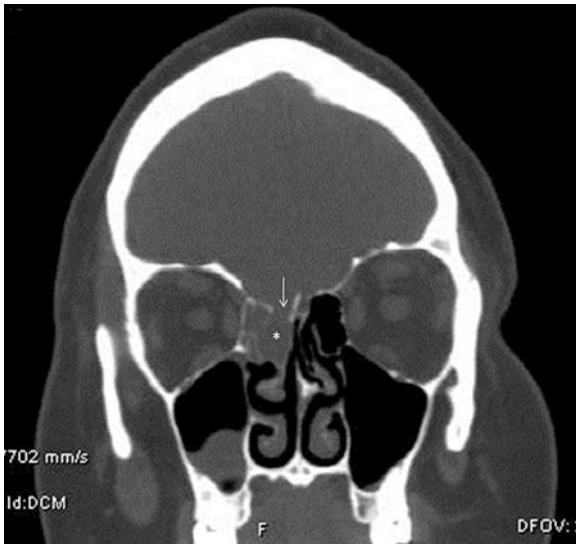

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 2 Endoscopic visualization of the right nasal cavity demonstrates the presence of fluorescein within the middle meatus (which has been obliterated by meningoencephalocele and polypoid mucosa) and olfactory groove region

A large study by Keerl et al. showed that low-dose fluorescein is safe and that the incidence of complications is dose related (Keerl et al. 2004). The use of fluorescein is not FDA-approved, and therefore, its use is an off-label use of the agent. The recommended dose is 0.1 mL of 10% intravenous fluorescein in 10 mL of the patient's CSF (Lanza et al. 1996). This is infused over 30 min (Fig. 2).

Radionuclide cisternography involves the intrathecal administration of a radionuclide tracer followed by identification within the nose using pledgets or a scintillation camera. The amount of radioactivity on the pledgets is assayed using a gamma probe. The major limitations of these studies include a high rate of indeterminate results and ineffectiveness at identifying the location of the leak.

Computed tomography (CT) cisternography involves CT imaging after the intrathecal administration of radiopaque contrast (metrizamide). As many as 80% of CSF leaks can be confirmed with the used of CT cisternography. Magnetic resonance imaging (MRI) cisternography is a noninvasive technique that permits the identification of a leak in patients with active CSF rhinorrhea. The characteristic signal of the CSF is identified using a T2-weighted image with
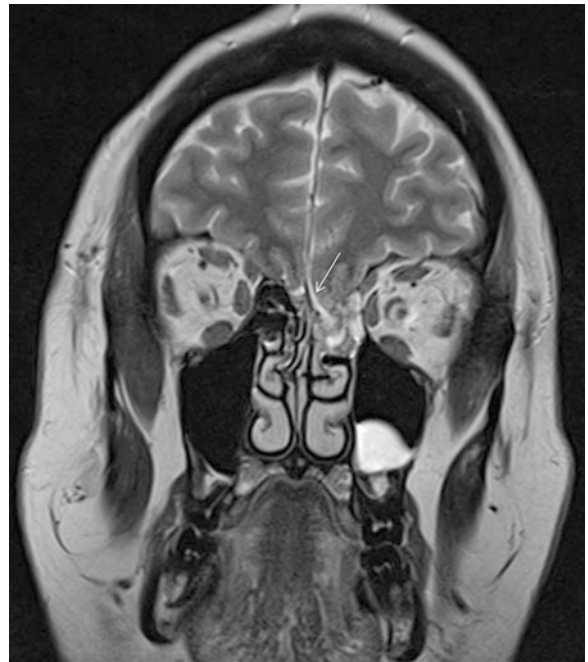
Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 3 The coronal CT image demonstrates a bony dehiscence at the lateral lamella of cribriform plate on the right (*arrow*). There is evidence of a soft tissue density within the right ethmoid cavity, which may represent a meningoencephalocele and/or swollen mucosa (*asterisk*)

fat suppression and video reversal (Sillers et al. 1997). These studies may also be used to localize the site of the skull base defect causing the CSF leak. Limitations of these imaging modalities include the poor resolution and high false-negative rates in patients with low flow or intermittent leaks.

After confirmation of a beta-2 transferrin in the nasal secretions, accurate localization of the skull base defect is critical for the development of a strategy for the surgical repair of a CSF leak. High-resolution CT and MRI of the skull base may demonstrate areas of dehiscence along the skull base. Thus, these imaging modalities should be considered complementary. The CT provides an image of the bony architecture of the skull base, and the MRI defines the soft tissue anatomy including any meningoencephaloceles or intracranial masses (Figs. 3 and 4).

Differential Diagnosis

CSF rhinorrhea is a rare condition compared to other rhinopathies including allergic rhinitis, vasomotor rhinitis, and rhinosinusitis (Table 1). In most instances, rhinorrhea due to these other conditions is bilateral,

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 4 Magnetic resonance imaging (MRI) provides excellent visualization of intracranial and paranasal sinus soft tissue structures. The T2-weighted coronal image demonstrates evidence of a meningoencephalocele penetrating through a defect in the lateral lamella of the cribriform plate on the *left*. The *arrow* indicates an area of high intensity which represents CSF on this T2 image

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Table 1 Differential diagnosis

Allergic rhinitis
Seasonal
Perennial
Vasomotor rhinitis
Sinonasal saline irrigations
CSF otorrhea (skull base defect with intact tympanic membrane)

and it is rarely positional. In contrast, CSF rhinorrhea is generally unilateral and positional. CSF rhinorrhea that is bilateral only results from severe disruption of skull base integrity. In fact, the presence of unilateral, watery rhinorrhea that is clearly positional must be fully evaluated to exclude the diagnosis of CSF leak.

A CSF leak into the middle ear space also may produce CSF rhinorrhea, if the CSF drains from the middle ear space through the Eustachian tube to the nasopharynx.

Etiology and Epidemiology

Cerebrospinal fluid (CSF), produced by the choroid plexus, circulates through the ventricular system to subarachnoid space, and is resorbed by the arachnoid villi. It is produced at a rate of 15–20 mL an hour in adults. The total CSF volume is 140 mL with pressures ranging from 40 mm H_2O in infants to 140 mm H_2O in adults. This pressure may vary with the patient age, activity level, and cardiac cycles. The relative balance between CSF production and resorption sets the CSF pressure. Since production is felt to be relatively constant, the main determinant of CSF pressure is the CSF resorption. Processes that interfere with CSF resorption can lead to increased intracranial pressure (ICP). At pressures greater than 150–200 mm H_2O, neurologic symptoms may develop (Daube and Sandok 1986).

CSF rhinorrhea occurs when a direct communication exists between the CSF-containing subarachnoid space and the paranasal sinuses. The leak incorporates defects of the dura mater, paranasal sinus mucosa, and the intervening bone. The defect provides a path for the intracranial spread of pathogens, which may lead to meningitis or cerebritis. Pneumocephalus may develop with secondary brain compression. The skull base defect also permits the development of a meningoencephalocele within the sinonasal cavity.

Thinning or weakening of the bony architecture of the skull base plays a role in the development of CSF rhinorrhea. Sites of weakness include the lateral lamella of the cribriform plate and a congenital dehiscence in the lateral sphenoid roof (Castelnuovo et al. 2007). Pressure from the overlying parenchyma and dural pulsations further weaken the bone at these locations. In addition, direct disruption of the skull base due to trauma or surgery also may create a site for CSF fistula.

Another major factor in the pathogenesis of CSF rhinorrhea is elevated ICP. Etiologies of increased ICP include intracranial mass, hydrocephalus, strong cough, and Valsalva. It has been postulated that an elevated ICP may play a role in the development of idiopathic or spontaneous CSF rhinorrhea (Schlosser and Bolger 2003a, b). Furthermore, patients with apparent idiopathic CSF rhinorrhea fulfill the diagnostic criteria for benign intracranial hypertension (BIH, also known as pseudotumor cerebri or idiopathic intracranial hypertension), which is characterized by

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Table 2 Classification of cerebrospinal fluid rhinorrhea

I. Traumatic
  A. Accidental
    1. Immediate
    2. Delayed
  B. Surgical
    1. Complication of neurosurgical procedures
      a. Transphenoidal hypophysectomy
      b. Frontal craniotomy
      c. Other skull base procedures
    2. Complication of rhinological procedures
      a. Sinus surgery
      b. Septoplasty
      c. Other combined skull base procedures
II. Nontraumatic
  A. Elevated intracranial pressure
    1. Intracranial neoplasm
    2. Hydrocephalus
      a. Noncommunicating
      b. Obstructive
    3. Benign intracranial hypertension
  B. Normal intracranial pressure
    1. Congenital anomaly
    2. Skull base neoplasm
      a. Nasopharyngeal carcinoma
      b. Sinonasal malignancy
    3. Skull base erosive process
      a. Sinus mucocele
      b. Osteomyelitis
    4. Idiopathic

increased intracranial pressure in the absence of specific causes (Badia et al. 2001). Patients with spontaneous CSF rhinorrhea and patients with BIH share very similar demographics in that the typical patient for each condition is an obese, middle-aged woman. In addition, the clinical and radiological manifestations of spontaneous CSF rhinorrhea and empty sella syndrome (ESS) are remarkably similar, suggesting a common pathophysiological mechanism for both conditions (Schlosser and Bolger 2003a; Silver et al. 2007). Because of these relationships with BIH and ESS, consideration must be given to them in the evaluation of any patient with an apparent idiopathic CSF leak.

CSF rhinorrhea may be broadly classified into traumatic and nontraumatic groups (Table 2) in a classification approach that serves to guide definitive management. The traumatic group includes accidental trauma and surgical complications. The nontraumatic group may be divided into cases with elevated ICP and normal ICP.

Accidental trauma in the form of closed head injuries accounts for 80% of all cases of CSF rhinorrhea. Conversely, CSF rhinorrhea is present in only 2–3% of patients with serious head trauma. Skull base fractures are associated with CSF fistulae in 12–30% of the cases, with 50% of these fractures occurring along the anterior skull base and cribriform plate (Leow et al. 1984). The majority of traumatic CSF leaks present within 48 h of the accident and resolve with conservative treatment including bed rest and lumbar drain. In some cases, a traumatic CSF leak may present days, weeks, months, or even years later, when the skull base injury site weakens to the point of CSF fistula formation.

Traumatic CSF leaks include complications of intracranial and paranasal sinus surgery. Inadvertent injury to the skull base during routine endoscopic sinus surgery may result in CSF fistula. Though this complication is rare, the increased frequency of sinus surgery makes it an important etiology of CSF rhinorrhea (Stankiewicz 1989; Kennedy et. al 1994). The lateral lamella of the cribriform plate is the weakest portion of the anterior skull base and therefore at the greatest risk of injury during sinus surgery. Fractures may occur at this location secondary to inadvertent pressure from instrumentation and overly aggressive middle turbinate resection (Fig. 5). The posterior ethmoid roof is another common location of inadvertent skull base injury during functional endoscopic sinus surgery, since the position of the ethmoid roof will vary with differences in ethmoid pneumatization. Powered endoscopic instrumentation increases the risk of more extensive injury to the skull base, dura, and even brain parenchyma. Neurosurgical procedures can also result in CSF rhinorrhea. This may include frontal craniotomies or subcranial approaches to the skull base. CSF leaks may occur during pituitary surgery as a result of injury to the sellar diaphragm or inadvertent penetration through the sphenoid roof.

Intracranial or skull base neoplasms can lead to CSF leaks directly or indirectly. Direct tumor extension across the skull base may result in large defects secondary to bone erosion. Intracranial tumors may indirectly result in CSF leaks by obstructing the ventricles and increasing the ICP. In these cases, resection of the lesion is required to alleviate the pressure prior to CSF leak repair.

Nontraumatic CSF leaks associated with normal ICP may be caused by a skull base neoplasm that
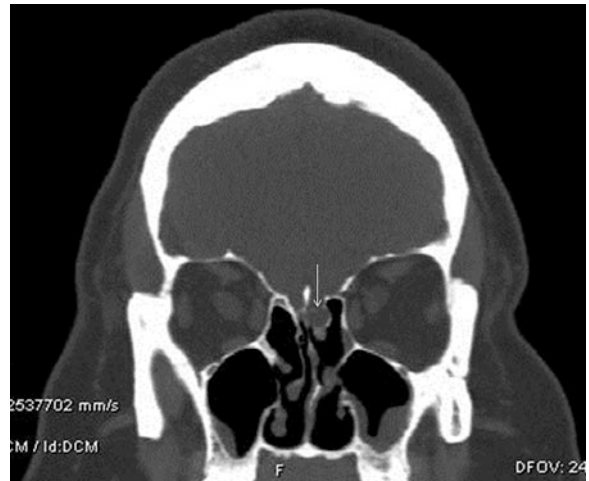
Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 5 Computed tomography (CT) provides adequate visualization of the bony anatomy of the paranasal sinuses and skull base. The *arrow* indicates a skull base defect located at the superior attachment of the middle turbinate. A partial middle turbinate resection is evident

directly destroys the skull base and thereby creates the CSF fistula. Other nonneoplastic processes, including skull base osteomyelitis, may also disrupt skull base integrity. Finally, congenital anomalies may predispose to the formation of CSF fistula.

Elevated ICP from a wide variety of causes also may result in CSF rhinorrhea. Intracranial masses may increase ICP and ultimately lead to a CSF leak. Similarly, both obstructive and noncommunicating hydrocephalus may lead to a sufficient increase in ICP that a CSF leak occurs. Finally, BIH is a risk factor for CSF rhinorrhea.

In many circumstances, the exact etiology of the CSF leak is unknown. This is commonly classified as nontraumatic or spontaneous CSF rhinorrhea. These spontaneous leaks have been associated with BIH – thus, in many instances, the so-called spontaneous or idiopathic CSF rhinorrhea may best be ascribed to a nontraumatic etiology associated with elevated ICP. The features of BIH and spontaneous CSF leak share remarkable similarities. BIH is a syndrome of increased ICP without any identifiable intracranial cause. It is manifested as headache, pulsatile tinnitus, and papilledema. MRI will demonstrate an empty sella in most BIH patients. Radiographically, most patients with spontaneous CSF leaks have empty sella, arachnoid pits, and often multiple skull base dehiscences

(Keerl et al. 2004). Schlosser et al. have demonstrated that a large proportion of patients with spontaneous CSF rhinorrhea fulfill the diagnostic criteria of BIH (Schlosser et al. 2006). These patients typically have the highest incidence of associate meningoence-phaloceles and the highest recurrence rates after surgical repair. See Table 2 for the classification of CSF rhinorrhea.

Treatment

Strategy

The optimal management of CSF rhinorrhea requires a multidisciplinary approach including otolaryngologists, neurosurgeons, and neuroradiologists. Specific indications for CSF leak repair include idiopathic (also known as "spontaneous" leaks), large skull base defects (especially when associated with pneumocephalus), intraoperative recognition of a CSF leak (during neurosurgical or otorhinolaryngic procedures), and open traumatic head wounds with CSF leakage. Ideally, the treatment strategy for each CSF leak should be directed at the presumed underlying mechanism that created the CSF leak. Thus, it is appropriate to consider the optimal approach in four clinical scenarios: traumatic, nonsurgical etiology; intraoperative injury with immediate recognition; operative injury with delayed recognition/onset; and nontraumatic etiology.

Traumatic, Nonsurgical Etiology

CSF rhinorrhea after head trauma should be managed conservatively with measures that reduce ICP, since such steps will favor spontaneous resolution of the CSF leak. In most instances of traumatic CSF leak (approximately 90% of cases), the CSF leak will heal without operative intervention. The addition of a lumbar drain during the first few days after injury may facilitate the natural process of healing by reducing the pressure and flow through the defect site. If the CSF rhinorrhea does not resolve spontaneously, then operative intervention will be required. Often, an endoscopic technique will suffice, but in some instances, transcranial techniques may be required.

The extent of the head injury will often determine the initial treatment. Massive head injuries will require exploratory craniotomy for management of the

neurosurgical injury. In addition, open head injuries with violation of the skull and dura will undergo immediate operative repair. In these instances, repair of the CSF leak may be accomplished during the primary surgery typically via a transcranial route. Traumatic CSF leak may also occur with significant maxillofacial injury. For these patients, operative repair of the facial skeleton may inadvertently disrupt the traumatized skull base integrity and create a CSF leak (or worsen a small leak). Thus, these patients need to be monitored postoperatively for a CSF leak. If a CSF leak is found, then it may typically be managed conservatively with bed rest and lumbar drainage; surgery would be reserved for failure of these measures.

Traumatic pneumocephalus must be recognized and managed quickly, since rapid air accumulation may lead to a neurosurgical catastrophe. Rarely, pneumocephalus may occur with an active CSF rhinorrhea shortly after the initial trauma or in a delayed fashion. In either case, this is a neurosurgical emergency, and prompt neurosurgical consultation is required. In general, these patients will require operative repair of the skull base defect. Traditionally, these procedures were done via external or transcranial approaches, but endoscopic techniques have been successfully applied even for large defects with major pneumocephalus (Clark et al. 2010).

Intraoperative Injury with Immediate Recognition

If CSF rhinorrhea is noted at the time of surgery, then an attempt should be made to repair the defect during that surgical procedure. In the situation where the surgeon suspects a CSF leak during sinus surgery, the surgeon should confirm the presence or absence of a leak via direct inspection. The endoscopic repair may be tailored to the extent of the injury. For instance, a small leak with a tiny 1–2 mm crack in the bone may be repaired with mucosal graft and tissue sealant, while a larger defect with 4–5 mm gaping hole through bone and dura will require layered reconstruction. Anecdotal reports suggest that skull base violations caused by the application of the tissue shaver to the skull base are associated with larger defects and even intracranial injury. Because of the risk of intracranial injury associated with larger defects, postoperative head CT should be considered. In all instances of inadvertent skull base injury during sinus surgery, neurosurgical consultation should be obtained. Some patients will benefit from a lumbar drain for a few days

postoperatively, and postoperative intravenous antibiotics with CSF penetration should be considered.

During transnasal/transsinus skull base procedures, planned violation of skull base integrity is intrinsic to the procedure. During transcranial skull base procedures, inadvertent injury to the skull base may occur. In either case, it is incumbent upon the surgeon to perform a robust repair of the defect before the conclusion of the procedure.

Operative Injury with Delayed Recognition/Onset

On occasion, CSF rhinorrhea may present itself days, weeks, months, or even years after a prior surgical procedure. In this instance, it may be reasonable to consider a trial of conservative measures, but it is likely that these measures may fail, especially if CSF leak has been active for a prolonged period of time (i.e., more than a few weeks). For most patients with a late presentation of CSF rhinorrhea, early surgical intervention is warranted.

Nontraumatic Etiology

CSF rhinorrhea due to a nontraumatic etiology will require surgical intervention. Specific etiologies, including the presence of hydrocephalus, neoplasm, etc., should be directly addressed. In many instances, the etiology for the CSF rhinorrhea appears idiopathic; as outlined above, these so-called spontaneous CSF leaks have been associated with altered CSF dynamics (mainly elevated ICP). For these patients, operative repair is warranted. Because of their high prevalence, these patients should be evaluated for both elevated ICP and BIH.

Patient Counseling

Prior to definitive treatment or surgical intervention, counseling the patient about the pathophysiology of CSF rhinorrhea is critical. Patients must understand the early signs and symptoms of meningitis as well as the importance of preventing maneuvers that increase ICP.

Conservative Treatment

Conservative treatment is based on the premise that decompression of the ICP may allow the leak to seal at the defect site. It involves a 2-week period of strict bed rest with head elevation coupled with several initial days of lumbar drainage. The patients are instructed to avoid measures that may increase the ICP, including coughing, sneezing, and straining. Stool softeners are often suggested.

Decompression of the subarachnoid through a lumbar drain typically occurs at a rate of 10 ml per hour. Higher rates of decompression may lead to an abnormally low ICP and intractable headaches. CSF studies including cell counts, protein, and glucose should be evaluated each day. Complications of lumbar drainage include meningitis.

The reported incidence of meningitis in patients with posttraumatic CSF rhinorrhea varies between 2% and 50% (Leech and Paterson 1973). Factors, including the location and duration of the leak, affect the risk of meningitis. Patients with posttraumatic CSF leaks lasting more than 7 days have an eight- to tenfold increase in the risks of meningitis (Brodie 1997). Thus, patients with a traumatic CSF leak may benefit from prophylactic antibiotics, but CSF leaks with other etiologies may not require prophylactic antibiotics. Although prophylactic antibiotics are not required in most situations, they may reduce the risk of cellulitis at the drain site. Typically, a first-generation cephalosporin is adequate for prophylaxis against cellulitis at the drain site.

Transcranial Techniques

Transcranial techniques for CSF leak repair require a frontal craniotomy. The defect is closed with fascia lata or pedicled galeal flaps. Potential morbidities include brain compression, hematoma, seizures, and anosmia. Failure rates of these techniques are high (25%) (Ray and Bergland 1969).

Extracranial Techniques

Extracranial techniques have advanced over the last several decades. Initially, the skull base defect was approached through an external incision such as a lateral rhinotomy or midface degloving. These procedures were considered transnasal or transsinus. Since the 1980s, endoscopic transnasal approaches have become the accepted approach to CSF leak repair (Senior et. al 2001). Reported outcomes of the endoscopic approach are excellent with successful repair of 85–90% of primary procedures (Lanza et al. 1996; Sethi et al. 1996; Kelley et al. 1996).
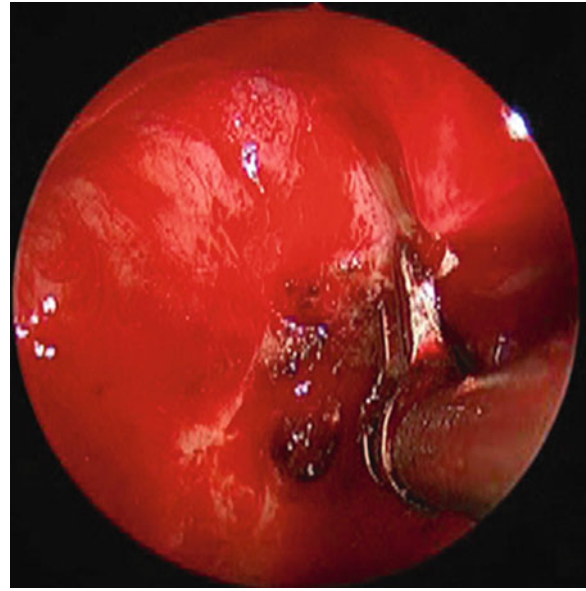
The endoscopic repair of CSF leaks begins with a standard endoscopic dissection to identify the defect site. The identification of the skull base dehiscence can often be assisted by intrathecal fluorescein
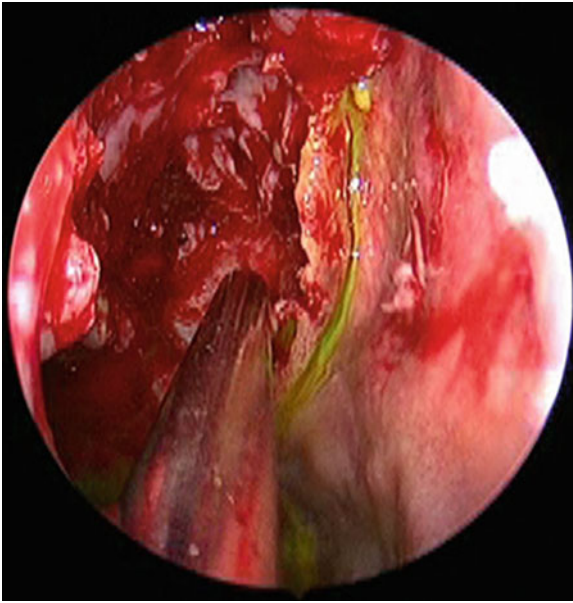
Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 6 The intraoperative endoscopic image demonstrates the presence of fluorescein medial to partially resected middle turbinate on the right side. This finding assisted with the localization of the skull base dehiscence and operative repair of the CSF leak

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 7 Bipolar cautery is used to fulgurate or reduce the meningoencephalocele and prepare the surrounding sinonasal mucosa prior to the graft placement

intraoperatively (Fig. 6). Leaks involving the cribriform and anterior ethmoid roof regions typically require a maxillary antrostomy and ethmoidectomy. Often, a frontal sinusotomy is performed to prevent the formation of iatrogenic mucoceles. Defects of the sphenoid can be approached through a transnasal or transethmoid approach. Often, bilateral sphenoidotomies and posterior septectomy are required for broad exposure. The lateral recess of the sphenoid sinus is a difficult location to access but can be approached through a transpterygoid dissection (Bolger and Osenbach 1999). Defects of the frontal recess and frontal sinus proper may require a combined above-and-below procedure or even an osteoplastic flap.

If there is a large defect or if there is high flow of CSF through a small defect, endoscopic identification of the CSF leak is simple. In other instances, precise localization of the CSF leak site may be problematic. Intrathecal fluorescein may be used to assist with the identification of the defect, and thus, many surgeons incorporate lumbar drain placement at the beginning of the surgical procedure. The lumbar

drain allows a route for intrathecal fluorescein administration and then postoperatively, the lumbar drain may be used to decompress the intrathecal space.

Bipolar cautery, potassium-titanyl-phosphate (KTP) laser, or coblation may be used to prepare the defect site for grafting (Isaacs et al. 2010). This includes fulgurating the meningoencephalocele if present and removing a margin of mucosa to expose the bony margins of the defect (Fig. 7). Hemostasis is critical when reducing the meningoencephalocele to prevent intracranial hemorrhage.

Graft selection remains controversial but largely depends on the size of the defect and preference of the surgeon. Potential grafts include temporalis fascia, fascia lata, pedicled middle turbinate flaps, free mucosal grafts (nasal septum or nasal floor), autogenous fat (Fig. 8), free cartilage grafts, and free bone grafts. The use of collagen dural substitutes has increased. An important benefit of this graft material is the avoidance of donor site morbidity. The collagen implant provides a scaffold for the ingrowth of fibroblasts which eventually replace the implant. Examples of collagen dural substitutes include Durepair® Dural Regeneration Matrix (Medtronic Inc., Minneapolis, MN), DuraGen®
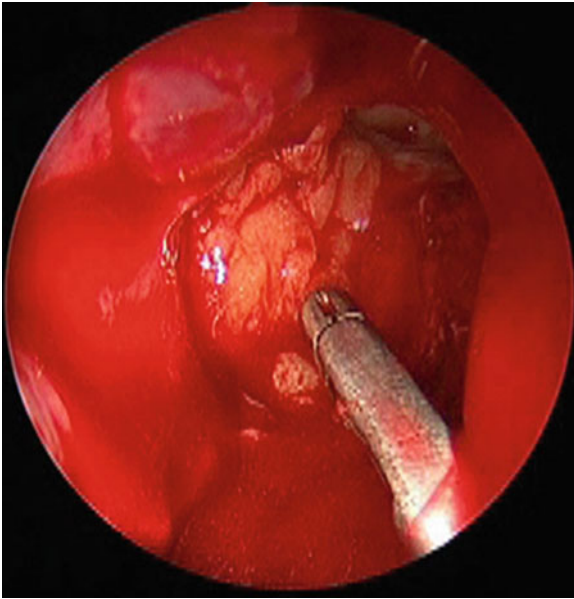
Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 8 Often autogenous fat can be used as a graft especially at locations not amenable to an underlay graft
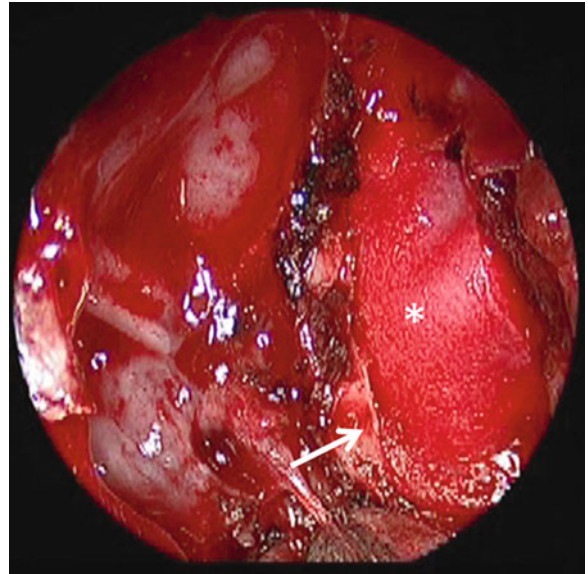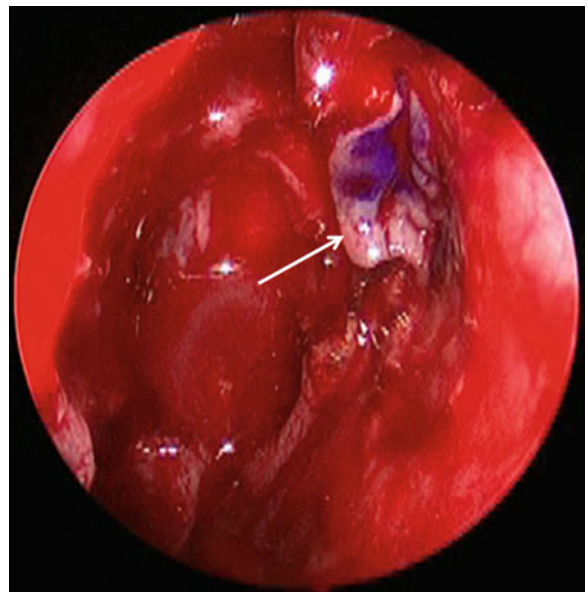

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 9 In this endoscopic image, collagen dural repair substitute has been placed in an underlay fashion (*asterisk*). The arrow shows the bony edge of the ethmoid roof on the lateral side of the defect. The defect was located along the lateral lamella of the cribriform plate on the *right*

Dermal Graft Matrix (Integra, Plainsboro, NJ), and DuraGuard® Dural Repair Patch (Synovis Surgical Innovations, St. Paul, MN). In an animal study comparing three dural substitutes (Durepair®, DuraGen®, and DuraGuard®), the three implants were found to be safe and effective in healing surgically created defects in the dura mater (Zerris et al. 2007).

The grafting technique depends on not only the defect size and location but also the CSF pressure gradient across the skull base defect. Ideally, an underlay reconstruction is preferred with all graft materials (except for the mucosal graft) placed intracranially (Fig. 9). Larger defects may require cartilage or bone grafts placed in the epidural space. This layered reconstruction provides more strength at the defect site to prevent the recurrence of meningoencephaloceles in patients with elevated ICP. Mucosal grafts should never be placed intracranially to avoid the risk of mucocele formation. A helpful technique at the time of repair is to mark the mucosal surface of the graft to ensure it remains on the sinonasal side of the reconstruction (Fig. 10).

After the grafts are placed, surgical sealants may be used to hold them in place (Fig. 11). Absorbable and

Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 10 Endoscopic view of a mucosal graft (*arrow*) used to cover a defect of the right cribriform plate. Notice the *purple ink* used to mark the mucosal surface. This prevents inadvertent placement of the mucosal surface along the intracranial defect and avoidance of a mucocele
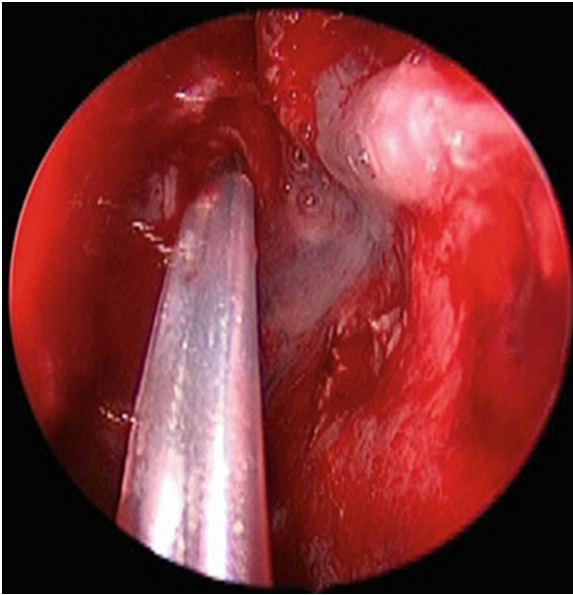
Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 11 A tissue sealant, in this case *fibrin glue*, is used to fix the graft to the surrounding mucosa
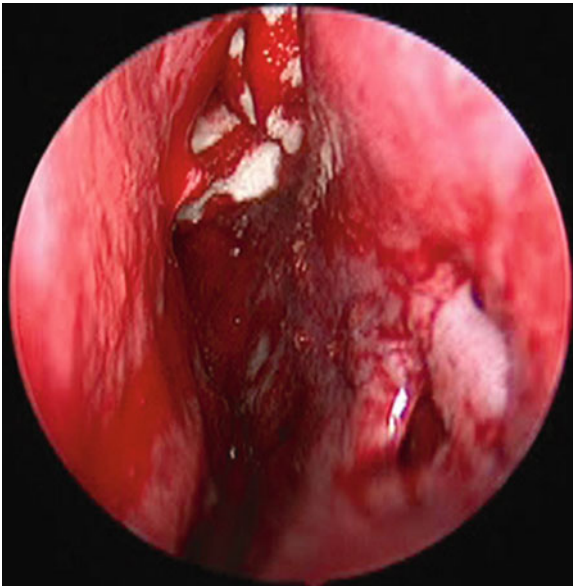
Cerebrospinal Fluid Rhinorrhea, Evaluation and Management, Fig. 12 Resorbable packing material has been placed over the tissue sealant as shown here. Permanent packing material, which is typically removed 2–4 days after surgery, is placed along the floor of the nasal cavity to provide support for the graft

nonabsorbable packing may be placed adjacent to the graft to provide support and hemostasis at the repair site (Fig. 12).

Postoperative care includes bed rest in a neurosurgical nursing unit that has personnel skilled in postoperative care of these patients. Typically, this is the neurosurgical intensive care unit or neurosurgical step-down unit. There, the patient can be monitored for intracranial complications. If a lumbar drain was placed at the time of surgery, the patient should be decompressed for at least 2–3 days after the procedure. Antistaphylococcal antibiotics are used while the nasal packing is in place. The packing can be removed 2–4 days after surgery.

Patients should be advised to avoid sneezing, coughing, or straining during the 6 weeks after surgery. Often, stool softeners are required. For those patients with elevated ICP, diuretic therapy or CSF diversion procedures should be considered.

Cross-References

► Sinus Surgery, Complications

References

Arrer E et al (2002) Beta-Trace protein as a marker for cerebrospinal fluid rhinorrhea. Clin Chem 48(6 Pt 1):939–941

Badia L, Loughran S, Lund V (2001) Primary spontaneous cerebrospinal fluid rhinorrhea and obesity. Am J Rhinol 15(2):117–119

Bolger WE, Osenbach R (1999) Endoscopic transpterygoid approach to the lateral sphenoid recess. Ear Nose Throat J 78:36–46

Brodie HA (1997) Prophylactic antibiotics for posttraumatic cerebrospinal fluid fistulae. A meta-analysis. Arch Otolaryngol Head Neck Surg 123(7):749–752

Castelnuovo P et al (2007) Endonasal endoscopic repair of Sternberg's canal cerebrospinal fluid leaks. Laryngoscope 117(2):345–349

Clark DW, Citardi MJ, Fakhri S (2010) Endoscopic management of skull base defects associated with persistent pneumocephalus following previous open repair: a preliminary report. Otolaryngol Head Neck Surg 142(6):820–826 Official Journal of American Academy of Otolaryngology-Head and Neck Surgery

Daube JR, Sandok BA (eds) (1986) Medical neurosciences: an approach to anatomy, pathology, and physiology by systems and levels, 2nd edn. Little, Brown, Boston, pp 93–111

Isaacs SJ, Luong A, Citardi MJ, Fakhri S (2010) Rhinologic applications of radiofrequency coblation. In: American rhinologic society spring meeting, Las Vegas

Katz RT, Kaplan PE (1985) Glucose oxidase sticks and cerebrospinal fluid rhinorrhea. Arch Phys Med Rehabil 66(6):391–393

Keerl R et al (2004) Use of sodium fluorescein solution for detection of cerebrospinal fluid fistulas: an analysis of 420 administrations and reported complications in Europe and the United States. Laryngoscope 114(2):266–272

Kelley TF et al (1996) Endoscopic closure of postsurgical anterior cranial fossa cerebrospinal fluid leaks. Neurosurgery 39(4):743–746

Kennedy DW et al (1994) Complications of ethmoidectomy: a survey of fellows of the American Academy of Otolaryngology-Head and Neck Surgery. Otolaryngol Head Neck Surg 111(5):589–599 Official Journal of American Academy of Otolaryngology-Head and Neck Surgery

Lanza DC, O'Brien DA, Kennedy DW (1996) Endoscopic repair of cerebrospinal fluid fistulae and encephaloceles. Laryngoscope 106(9 Pt 1):1119–1125

Leech PJ, Paterson A (1973) Conservative and operative management for cerebrospinal-fluid leakage after closed head injury. Lancet 1(7811):1013–1016

Loew F et al (1984) Traumatic, spontaneous and postoperative CSF rhinorrhea. Adv Tech Stand Neurosurg 11:169–207

Nandapalan V, Watson ID, Swift AC (1996) Beta-2-transferrin and cerebrospinal fluid rhinorrhoea. Clin Otolaryngol Allied Sci 21(3):259–264

Ray BS, Bergland RM (1969) Cerebrospinal fluid fistula: clinical aspects, techniques of localization, and methods of closure. J Neurosurg 30(4):399–405

Schlosser RJ, Bolger WE (2003a) Spontaneous nasal cerebrospinal fluid leaks and empty sella syndrome: a clinical association. Am J Rhinol 17(2):91–96

Schlosser RJ, Bolger WE (2003b) Significance of empty sella in cerebrospinal fluid leaks. Otolaryngol Head Neck Surg 128(1):32–38 Official journal of American Academy of Otolaryngology-Head and Neck Surgery

Schlosser RJ et al (2006) Spontaneous cerebrospinal fluid leaks: a variant of benign intracranial hypertension. Ann Otol Rhinol Laryngol 115(7):495–500

Senior BA, Jafri K, Benninger M (2001) Safety and efficacy of endoscopic repair of CSF leaks and encephaloceles: a survey of the members of the American Rhinologic Society. Am J Rhinol 15(1):21–25

Sethi DS, Chan C, Pillay PK (1996) Endoscopic management of cerebrospinal fluid fistulae and traumatic cephalocoele. Ann Acad Med Singapore 25(5):724–727

Sillers MJ, Morgan CE, el Gammal T (1997) Magnetic resonance cisternography and thin coronal computerized tomography in the evaluation of cerebrospinal fluid rhinorrhea. Am J Rhinol 11(5):387–392

Silver RI, Moonis G, Schlosser RJ, Bolger WE, Loevner LA (2007) Radiographic signs of elevated intracranial pressure in idiopathic cerebrospinal fluid leaks: a possible presentation of bliopathic intracranial hypertension. Am J Rhinol 21:257–261

Stankiewicz JA (1989) Complications of endoscopic sinus surgery. Otolaryngol Clin North Am 22(4):749–758

Zerris VA, James KS, Roberts JB, Bell E, Heilman CB et al (2007) Repair of the dura mater with processed collagen devices. J Biomed Mater Res B Appl Biomater 83(2):580–588

Ceruminous Adenocarcinoma

▶ Malignant Tumors of Ceruminous Glands

Ceruminous Adenoid Cystic Carcinoma

▶ Malignant Tumors of Ceruminous Glands

Ceruminousmucoepidermoidcarcinoma

▶ Malignant Tumors of Ceruminous Glands

Cervical Esophageal Squamous Cell Carcinoma

Vishal Gupta[1] and Todd Demmy[2]
[1]Head and Neck – Plastic reconstructive surgery, Roswell Park Cancer Institute, Buffalo, NY, USA
[2]Department of Thoracic Surgery, Roswell Park Cancer Institute, Buffalo, NY, USA

Synonyms

Squamous cell carcinoma of cervical esophagus

Definition

Cervical esophageal squamous cell cancers are the tumors involving the cervical part of esophagus. These tumors are generally aggressive and challenging in terms of surgical and nonsurgical management. Locoregional control is difficult to achieve because of advanced primary stage with frequent multicentricity, tendency toward submucosal spread, and nodal metastases. Cancers of this site mostly demonstrate squamous cell histology and usually invade nearby structures like the larynx and trachea (Pfister et al. 2004).

Cervical esophageal tumors are often compared with hypopharyngeal tumors because of similar

etiological factors, proximate anatomic relation, and similar signs and symptoms. Patients are usually older and malnourished from obstructive dysphagia. Heavy smoking and alcohol consumption histories are almost always present. Accordingly, these patients also sustain second primary malignancies, as well as recurrent disease and distant metastases.

Early symptoms of the disease are nonspecific like a vague swallowing difficulty. Unfortunately, most of these patients present at an advanced stage with symptoms like weight loss, debilitation, dysphonia, obstructive dysphagia, and neck mass.

Historically, both surgery and radiation have been used for the treatment of squamous esophageal cancers. Endoscopic resection of early stage Tis or T1a is appropriate treatment. However, for advanced disease (>T1b) chemoradiation is the treatment of choice (National comprehensive cancer network [NCCN] 2011). More extensive and radical surgery is considered for patients with persistent or recurrent disease.

Anatomy

The cervical esophagus is closely associated with the larynx and pharynx. It is located between the lower end of cricoid cartilage and the thoracic inlet and its wall is comprised of three layers. The innermost layer is non-keratinizing squamous epithelium overlying loose stromal tissue. Next, the muscular layer is made up of outer longitudinal and inner circular muscle fibers. The muscle in the cervical segment transitions from striated to completely smooth by the junction of the upper and middle third of the esophagus. Finally, an outer fascia covers these muscle layers and is derived from the buccopharyngeal fascia. Anteriorly, the cervical esophagus is related to the thyroid, larynx, trachea, and cricoid cartilage. Posteriorly, the outer fascial sheath separates it from the retroesophageal space (which courses above into retropharyngeal space and below into the posterior mediastinum). Laterally, the cervical esophagus is related to the recurrent laryngeal nerves, carotid sheath contents, and paratracheal lymph nodes. Thyroid lobes also lie in lateral relation to cervical esophagus and might be involved in neoplasms originating there. Superiorly, the cricopharyngeus marks the narrowest part of upper alimentary tract at the junction between the posterior cricoid and cervical esophagus.

The cervical esophagus derives its blood supply from the inferior thyroid artery and ascending thoracic esophageal vessels. The inferior thyroid vein provides the venous drainage. The nerve supply is provided by recurrent laryngeal nerves and sympathetic chain. The rich submucosal lymphatic network from the cervical esophagus drains into stations two, three, and six lymph nodes along the jugular vein, superior vena cava, and aortic vessels.

Physiology

Physiologically, the cervical esophagus actively participates in the swallowing process. The resting tone of the cricopharyngeus muscle helps prevent reflux of esophageal contents into the hypopharynx. Coordinated reflex dilation of cricopharyngeus helps initiate the esophageal peristalsis.

Epidemiology

The epidemiology of cervical esophageal cancer is influenced by sex, age, profession, and other risk factors. According to an estimate for 2010, about 16,640 (13,130 men and 3,150 women) new cases of esophageal cancer will be reported in the United States resulting in 14,500 deaths (11,650 men and 2,850 women) (NCCN 2011).

The average incidence of cervical esophageal cancer is about 1:100,000. Higher incidence rates are seen in developing countries like India and Brazil or those with lower social economic standards. These tumors typically present in individuals older than 50 with a male to female ratio of 193:16 (Triboulet et al. 2001). Hypopharyngeal along with cervical esophageal cancers account for about 10% of upper gastroesophageal tract tumors, far less than 1% of all cancers in the United States.

Like most head and neck cancers, cervical esophageal cancers are associated with excessive tobacco use and alcohol consumption which also lead to worse outcomes from associated comorbidities.

A 15 times higher mortality rate has been reported among smokers with esophageal cancers as compared to nonsmokers. Epidemiologic studies show type and volume of tobacco to be important. Black tobacco may be more dangerous than yellow tobacco. Twenty grams/day average consumption is seen in individuals with hypopharyngeal cancers (Popescu et al. 2010).

In a meta-analysis of 235 studies by Bagnardi et al. (2001), consumption of 25, 50, and 100 g of pure

alcohol per day was associated with pooled relative risk of 1.75, 2.85, and 6.01, respectively, of oropharyngeal cancer. In a study by Hayes et al. (1999), the relative risk of cancer declines only after 15–20 years of abstinence from alcohol consumption.

The relation between alcohol consumption and upper aerodigestive tract cancers is less consistent than smoking possibly because alcohol in itself is not considered to be carcinogenic. The primary breakdown product of ethanol, acetaldehyde, can cause DNA damage leading to carcinogenesis. Genetic mutation in alcohol dehydrogenase and aldehyde dehydrogenase can also cause neoplasia (Popescu et al. 2010). Alcohol may elute additional carcinogenic compounds out of tobacco products resulting in a synergistic effect.

Human papillomavirus (HPV) may also cause cervical esophageal cancer. Esophageal squamous cancer in condylomata-like lesions has been reported (Si et al. 2005). In order to prove the causative role of HPV in cervical esophageal squamous cancers, it is essential to find the integration of the viral genome in host DNA as is seen in uterine cervical cancers. During the integration process, there is selective disruption of viral E2 open reading frame. Because E2 negatively regulates E6/E7 promoters, the disruption leads to increased expression of E6/E7 viral oncoproteins. Si et al. (2005) studied HPV integration into the host genome by calculating the ratios of E2/E6 genes using a real-time quantitative PCR assay. In a sample of 35, they reported HPV integration in 32 (91.4%) esophageal squamous cell cancers showing that it is a common phenomenon in esophageal squamous cell cancers on par with uterine cervical cancers.

Occupational exposures to asbestos and sulfuric acid have long been blamed for causing pharyngoesophageal cancers; however, this is controversial because alcohol and tobacco use is common among such workers. Case control and cohort studies have associated asbestos with hypopharyngeal cancers.

Dietary factors may cause cervical esophageal cancer in specific geographical regions. The fungus Fusarium moniliforme may have a pathogenic role in human cervical esophageal cancer. Consumption of salted food and nitrosamine is also considered as one of etiologic factors of cervical esophageal cancer in China. Low blood selenium level has been found in South African black population affected with esophageal cancers (Popescu et al. 2010).

Genetic factors like polymorphism of enzymes involved in alcohol metabolism may predispose some populations to the carcinogenic metabolite aldehyde. Various experimental studies have shown a higher frequency of p53 mutations in smokers as compared with nonsmokers.

Natural History and Progression

Ninety-five percent of hypopharyngeal and cervical esophageal cancer have squamous histologies, predominantly poorly differentiated. Submucosal spread is very common in these tumors. Skip lesions from the postcricoid region to the cervical esophagus are very common. Squamous cell cancers of the cervical esophagus may spread intramurally and involve the trachea anteriorly and the thoracic inlet inferiorly.

Metastatic spread to cervical and mediastinal lymph nodes is very common in cervical esophageal cancer. The most common presenting finding is a neck mass. In a study of 67 patients, Kelley et al. (1995) found that the most common site of extension was the neck (18), followed by trachea (10), larynx (10), prevertebral fascia (6), and thyroid gland (4).

Clinical Presentation

An elderly male with history of significant alcohol and tobacco use is a typical patient. Patients usually present at an advanced stage with complaints of sore throat, dysphagia, odynophagia, neck mass, weight loss, and referred otalgia. The referred otalgia is due the overlying innervation of the glossopharyngeal and vagal nerve in this area. Progressive dysphagia begins with solid food and progresses to liquids (Pfister et al. 2004). Dysphagia is the hallmark symptom of cervical esophageal cancer (Table 1).

Globus sensation is another symptom which can be present at an early stage. Patients with nonspecific dysphagia are very commonly seen in clinic and their symptoms are usually attributed to gastroesophageal reflux disease or stress.

Dysphonia and hoarseness indicate involvement of a recurrent laryngeal nerve or direct extension to the larynx. Palpable cervical adenopathy is commonly symptomatic and can be seen in as many as 25% of patients as a presenting complaint (Pfister et al. 2004).

Cervical Esophageal Squamous Cell Carcinoma, Table 1 Presenting complaints in patients with cervical esophageal squamous cell cancer (Kelley et al. 1995)

Signs and symptoms	Percentage of patients
Dysphagia	86%
Odynophagia	12%
Hoarseness	6%
Weight loss	6%
Neck pain	6%
Neck mass	3%
Foreign body sensation	2%
Shortness of breath	2%

Diagnostic Evaluation and Clinical Staging

The following information is essential for proper patient evaluation for staging and treatment planning (▶ Diagnostic Hearing Evaluation):

1. Presence of distant metastasis
2. Location of primary tumor in relation to larynx and trachea
3. Involvement of surrounding structures
4. Histology
5. General health status of the patient

While indirect mirror examination might be able to detect hypopharyngeal tumors involving the posterior pharyngeal wall and piriform sinus, it often misses tumors involving the cervical esophagus. However, one finds pooling of secretions in hypopharynx from cervical esophageal obstruction. Fiberoptic laryngoscopic examination is essential to evaluate the status of the larynx and vocal cords. Involvement of these structures is seen in advanced stages of cervical esophageal cancers. Examination under anesthesia provides the most comprehensive assessment by viewing the entire upper aerodigestive tract including esophagus, trachea, and bronchus. Such "panendoscopy" shows macroscopic extent of disease and occasionally other primary tumors. At the same time, a ▶ tracheostomy might be required to treat an obstructed or unstable airway caused by laryngeal or tracheal involvement (Myers 2008).

As reported by Kelley et al. (1995), 56% of patients have unremarkable physical examinations. The most common physical finding on staging evaluation was the presence of a neck mass (21%) followed by vocal cord paralysis (11%), involvement of larynx or hypopharynx (9%), and Horner's syndrome (3%).

Imaging studies are essential to gauge local and locoregional involvement as well distant metastasis. A barium swallow can determine local disease extent as well as presence of second primaries. Most importantly, it can assess the invasion of retropharyngeal and retroesophageal spaces through the posterior esophageal wall (Myers 2008).

A CT scan is a rapid, common, and useful imaging modality for the assessment of cervical esophageal cancer. Preferably, it should be done before panendoscopy and biopsy to avoid any postoperative artifacts. MRI imaging can provide better soft tissue resolution but it takes long time and is not optimal for patients with compromised airways who cannot lie supine for long. It is also susceptible to motion artifacts. Whole body ▶ FDG-PET imaging is used preoperatively for staging purposes. It helps exclude distant metastasis and second primaries.

Ultrasonography can assess cervical lymph node metastases and can guide fine needle aspiration biopsy. Complete medical evaluation is also very important to determine the fitness of patients requiring extensive surgery like total laryngopharyngoesophagectomy. Many such patients have COPD from years of smoking. Severe COPD may exclude surgical options like reconstructions that require transthoracic dissections. Liver disease like cirrhosis from chronic alcohol consumption might prevent optimal neoadjuvant and adjuvant chemotherapy. Previous abdominal or cardiac surgery may also limit surgical options or increase risks.

Staging

The morphological extent of tumor is described by TNM (tumor, node, and metastasis) system. The current TNM staging of cervical esophageal cancer was published in the American Joint Commission on Cancer (AJCC) cancer staging manual and is similar to intrathoracic esophagus (2010).

Tis is carcinoma in situ. T1 indicates tumors that involve the lamina propria or submucosa. T1 is further divided into T1a and T1b. T1a represents invasion of lamina propria and muscularis mucosae, and T1b tumors invade the submucosa. T2 represents tumor which involves the muscularis propria. T3 tumors invade the adventitia and T4 indicates extraesophageal spread.

N0 indicates no clinically or pathologically involved nodes. N1 indicates metastasis in 1–2 regional lymph nodes. N2 is metastasis in 3–6 regional lymph nodes. N3 disease involves seven or more regional lymph nodes.

Treatment

Cancer control is the main goal of cervical esophageal tumor treatment. In early stage cancers, it may be possible to preserve speech and swallowing function. Aggressive treatments profoundly affect speech, swallowing, physical appearance, and employability.

Decision making is affected by tumor-related, patient-related, and physician-related factors. Important tumor-related factors are T-stage, nodal extension, circumferential involvement, involvement of larynx/trachea, and distant metastasis. Involvement of vertebral bodies, prevertebral fascia, and carotid encasement are contraindications for surgical disease management. Similarly, patients with chronic obstructive lung disease are poor operative candidates since their ability to tolerate aspiration is poor. Extensive involvement of thoracic inlet also rules out any meaningful resection. In patients with incurable cancer, efforts are directed at maintaining nutrition and prevention of aspiration. Nutrition can be maintained through enteral feeds.

The availability of a multidisciplinary team is one of the most important physician-related factors. Several types of surgical reconstructive techniques can be utilized depending upon physician preference and extent of the defect. This includes enteric procedures like gastric and colonic transposition, microvascular free flaps, and a combination of free flaps and regional flaps. Local flaps and pedicled myocutaneous flaps are not used anymore because of the need for multistaged reconstruction, high risk of anastomotic leak, and high incidence of stricture formation and flap necrosis.

The management of cervical esophageal cancer used to be dominated by surgical resection. Extensive resection was needed because often regional spread occurred even if not evident on staging evaluation. Given the critical location and extensive involvement of adjacent structures like larynx, oncologically sound operations require en bloc hypopharyngeal, laryngeal, and esophageal resections. This leaves a permanent tracheostoma resulting in poor quality of life. Because of high morbidity and mortality associated with surgical management, most comprehensive cancer centers recommend chemoradiation as the definitive treatment of choice for cervical esophageal cancers.

Chemotherapy and Radiation Therapy

In RTOG 85–01 trial (NCCN 2011), combined chemotherapy and radiotherapy was compared with radiotherapy alone for the patients with cancer of esophagus. The chemotherapy regimen utilized was 1,000 mg/m^2 of 5-fluorouracil administered as a continuous intravenous infusion for the first 4 days of weeks 1, 5, 8, and 11 along with 75 mg/m^2 cisplatin given on day 1, every 3 weeks for a total of four cycles. The radiation was given as 2 Gy/ fraction for 5 days a week for a total dose of 50 Gy in combined treatment group and 64 Gy in radiation treatment group.

The median survival was 8.9 months in radiation-only group and 12.5 months in chemoradiation group. The 12 and 24 months survival rates for chemoradiation group were 50% and 38%, respectively, as compared to 33% and 10% for the radiation-only group. This study concluded that concurrent treatment with cisplatin and fluorouracil and radiation is superior to radiation-alone treatment for patients with localized carcinoma of esophagus.

INT 0123 trial (NCCN 2011) compared higher dose radiation (64.8 Gy) with standard dose (50.4 Gy) given with a chemotherapy regimen of 5-fluorouracil and cisplatin. They failed to show any significant difference in median survival and 2-year survival.

These studies established primary chemotherapy with 5-fluorouracil and cisplatin with 50.4 Gy radiation as the definitive treatment of choice. In a pattern of practice study, 246 patients with squamous cell carcinoma of esophagus were retrospectively analyzed (Pfister et al. 2004). Combined cisplatin-based chemotherapy and RT (60 Gy over 6 weeks) was found to be the most frequent regimen used for the treatment of all stages of squamous esophageal cancers. The CRT regimen was compared with definitive RT alone and a 2-year survival rate of 39% and 20.6%, respectively, was noticed.

Although concurrent chemoradiation offers better organ preservation, whether it can produce comparable disease control and survival over radical surgical management is still being studied.

Induction Chemotherapy

RTOG 8911 (NCCN 2011) trial compared chemotherapy followed by surgery with surgery alone for localized esophageal cancer. They reviewed 467 patients from 123 institutions and found that 203 had squamous cell cancer of the esophagus. Out of the 203 patients, 110 patients were treated by surgery only and 103 with preoperative chemotherapy followed by surgery. Patients assigned to chemotherapy group received three cycles of cisplatin and fluorouracil. Clinical response to chemotherapy was evaluated by barium swallow and was scored as complete or partial response. They failed to show any improvement in overall survival by preoperative chemotherapy.

Role of Surgery

Surgery for cervical esophageal cancer can be performed for both curative as well as palliative intent. With the advent of organ preservation, surgery is now limited to early cervical esophageal cancer (T1b). Lymph node metastasis or microvascular permeation is unusual in patients with esophageal cancer limited to the epithelium or lamina propria.

These early esophageal cancers (<T1b) can be managed by endoscopic mucosal resection, the preferred minimally invasive technique for early SCC of cervical esophagus (NCCN 2011). It is extensively used in Japan and is gaining widespread acceptance in the United States. Technically, endoscopic resection of cervical esophageal cancer is more challenging because of its relation to the upper esophageal orifice.

Patients with localized and resectable recurrent tumors should also be considered for salvage surgery. Locoregional recurrence rates after chemoradiotherapy for esophageal cancer is as high as 40–60% (Chao et al. 2009). Salvage pharyngolaryngoesophagectomy after previous chemoradiation presents a formidable challenge. Operative morbidity and mortality is higher than standard surgery. Primary closure of the irradiated field carries a high risk of wound breakdown, anatomic leak, and fistula formation. Respiratory failure and wound infection from anastomotic leaks are major causes of postoperative death. It is crucial to provide adequate vascularized coverage to irradiated carotid arteries. Contamination of irradiated carotids by wound breakdown and leakage of salivary contents causes carotid hemorrhage.

Chao et al. (2009) investigated the survival benefit and preoperative risk factors for salvage surgery in 47 patients with locoregional residual or recurrent esophageal cancer after definitive chemoradiotherapy. The 5-year survival rate of 25.4% was noted in the salvage surgery group as compared to median survival of only 16.7 months noted in patients managed nonoperatively. They also noticed low albumin or hemoglobin levels as risk factors for high hospital mortality.

Urschel and Sellke (2003) proposed strict guidelines for patient selection for salvage surgery. This included conservative mediastinal dissection, use of cervical esophagogastric anastomosis for reestablishing the continuity of alimentary tract, preoperative enteral nutrition, and aggressive detection and treatment of postoperative complications.

Cervical esophageal cancers have high rates of lymph node metastases often involving local as well as upper mediastinal lymph node stations. Neck and upper mediastinal dissection is crucial for improving cure rate. However, lymph node dissection, especially upper mediastinal, increases postoperative morbidity and mortality. Hirano et al. (2007) reviewed 64 patients with hypopharyngeal and cervical esophageal cancer. Upper mediastinal nodal metastases occurred in 7.8% of hypopharyngeal and 33.3% of cervical esophageal tumors. Mediastinal lymph node involvement was even higher (55.6%) in cervical esophageal cancers extending to the upper thoracic esophagus. They reported excellent locoregional control of 77.7–94.1% following upper mediastinal dissection.

Surgical Technique

An apron neck flap incision is performed. Subplatysmal flaps are raised and the sternocleidomastoid (SCM) muscle is exposed. The SCM is then separated from the strap muscles and retracted laterally. The larynx is retracted medially and the carotid sheath is exposed. The prevertebral fascia is than palpated to rule out any disease involvement. If the retropharyngeal or retroesophageal spaces are involved, then surgery is terminated. Otherwise, surgery is continued with the removal of level 2, 3, 4, and 6 lymph nodes. Lymphatic metastases are an early event in squamous cell cancer of esophagus and removal of level 6 is important in all the cases.

Next, tracheal resection is performed depending upon its extent of involvement. In cases of limited disease, only 2–3 rings of trachea are resected. More extensive disease requires removal of a longer segment.

The pharynx is entered by performing an incision superior to the hyoid and is continued through the lateral and posterior wall to separate it from base of tongue. The specimen is then elevated from the prevertebral fascia by finger dissection in retropharyngeal and retroesophageal space. The dissection proceeds as necessary to the anterior mediastinum for remaining attachments to the cervical esophagus. Hemi- or total thyroidectomy may be required depending upon extent of the disease. In these cases, it is important to preserve at least one parathyroid gland to avoid postoperative hypocalcemia.

The stomach is then mobilized in the abdomen and delivered into the neck through blunt dissection in the posterior mediastinum. The esophagus is freed from the stomach by dividing below the gastroesophageal junction. Frozen sections are sent from the margins for microscopic tumor clearance.

Reconstruction

Choice of reconstruction depends upon the extirpative procedure extent including the type of remaining defect. Various parameters that need to be considered are amount of mucosa excised, circumferential versus partial defect, amount of external coverage required, and length of vascular pedicle for free flap. There are three different groups of reconstruction techniques available:

1. Visceral transposition
   (a) Gastric pull up
   (b) Colonic transposition
2. Free tissue transfer
   (a) Jejunal free flap
   (b) ▶ Fasciocutaneous flaps
3. Pedicled fasciocutaneous and ▶ myocutaneous flaps

Visceral Transposition

Gastric pull-up is most reliable method of circumferential reconstruction of pharyngoesophageal defects. This procedure can be utilized for the reconstruction of hypopharyngeal and upper cervical esophageal defects. The advantage of this method of reconstruction is immediate restoration of gastrointestinal continuity, reliable blood supply to flap, and low rate of stricture formation. The disadvantage is the need for abdominal and mediastinal dissection. The patient may experience gastric dumping syndrome and reflux because of loss of stomach filling capacity.

Colonic interposition is another method of visceral transposition which can be utilized in cases where free tissue transfer and gastric pull-up is not possible because of previous gastric surgery or vascular disease. However, presence of bacteria in colon puts abdominal and mediastinal cavities at risk in case of a leak.

Triboulet et al. (2001) reviewed 209 patients who underwent total pharyngolaryngectomy. Of these, 83 patients had advanced cervical esophageal cancer and 131 had hypopharyngeal cancer. Also, 127 patients had pharyngolaryngectomy and total esophagectomy with pharyngogastric anastomoses, 77 patients had pharyngolaryngectomy with cervical esophagectomy with free jejunal flap reconstruction, and five patients had phayngolaryngectomy with total esophagectomy with pharyngocolic anastomoses. In this study, they reported higher survival rates without dysphagia for gastric interposition (89%) as compared to (76%) with jejunal grafts. Necrosis and fistula rates for free jejunal transfers were significantly higher than rates for gastric interposition.

Free Tissue Transfer

For the pharyngeal defects not extending below thoracic inlet, microvascular free flap represents state-of-the-art reconstruction techniques for reestablishing the continuity of alimentary tract (▶ Free Tissue Transfer in Head and Neck). Murray et al. (2007) described the technique and functional outcome of using anterolateral thigh (ALT) flap with salivary bypass tube for circumferential reconstruction of the pharyngoesophageal defects in 14 patients. Twelve of these 14 patients recovered their swallowing function and the G-tube was removed in 11 cases. In a study by Yu et al. (2010) 91% of patients with ALT flap tolerated oral diet as compared to 65% with jejunal flap. ▶ Pharyngocutaneous fistulas and strictures were noted in 9% and 6% of patients, respectively. They also reported minimal donor site morbidity and quick postoperative recovery.

Radial forearm free flap is another fasciocutaneous free flap, which can be utilized in reconstruction of pharyngoesophageal defects. This flap offers thin flexible tissue and can be harvested simultaneously with oncologic resection. It has high tolerance to postoperative radiation and has the potential of sensory

innervation using the lateral antebrachial cutaneous nerve. The donor site morbidity is low and is well tolerated by elderly as compared to abdominal procedures. Its main disadvantages are a high fistula rate especially when it is tubed to reconstruct the circumferential defect. Pharyngocutaneous fistula rate as high as 67% has been reported.

Enteric Flaps

The jejunal free flap is the reconstruction method of choice for lesions involving the cervical esophagus (Triboulet et al. 2001). Since jejunum is already mucosa lined, it needs only two anastomoses in the neck, thereby decreasing the incidence of potential fistula formation and anastomotic leak. It can be easily tailored to the specific length of defect and can be used to reconstruct pharyngeal defects up to the nasopharynx. It is suited ideally for circumferential defects but can also be used to reconstruct subtotal defects simply by opening up the segment along its antimesenteric border. Its caliber is a good match with esophageal lumen. The jejunum tolerates full doses of postoperative radiation very well with less incidence of stricture formation (Pfister et al. 2004).

The major disadvantages are the three intestinal anastomoses needed to fashion the jejunal flap to appropriate length to avoid kinking and associated dysphagia and stasis. Besides, traditional jejunal free flaps can only be used for segmental repair.

Ascioti et al. (2005) described the supercharged jejunal flap for esophageal reconstruction. This involves augmentation of mesenteric circulation through an anastomosis with internal thoracic or cervical vessels. They reported an overall success rate of 92.3% in 26 patients reconstructed with this technique.

Pedicled Fasciocutaneous and Myocutaneous Flaps

These flaps are utilized rarely because of the need for two-staged reconstruction, limited length of reconstruction and high morbidity rates resulting from fistula formation, stricture, and flap necrosis. ▶ Pectoralis major myocutaneous flaps may be utilized for single stage reconstruction of subtotal defects where a posterior strip of mucosa has been preserved. However, the distal part of this flap receives an unreliable blood supply and hence has a higher chance of necrosis as compared to a free flap which homogeneous blood supply throughout.

Carlson et al. (1992) reported their experience in total reconstruction of hypopharynx and larynx in 148 patients. The functional failure rates (defined as inability to maintain adequate nutrition with tube feeding) with myocutaneous flaps, colon interposition, free jejunum, and gastric transposition were 40%, 42%, 20%, and 17%, respectively. They recommended microvascular free flaps as the method of choice for reconstruction of hypopharynx and cervical esophagus.

Prognosis

In spite of advances in multimodality treatment of patients with cervical esophageal cancer, overall survival at 5-year survival remains low at 10–30% (Herskovic et al. 1992; Pfister et al. 2004).

The most common cause of death is locoregional recurrence. Distant metastasis, second primaries, as well as intercurrent disease also contribute to the high mortality rate.

Wang et al. (1999) analyzed the clinicopathological and biological factors in patients with squamous esophageal cancer. In this study of 117 patients, every patient underwent en bloc esophagectomy with gastric conduit substitution. With careful patient selection, surgery-related complication and mortality rates were 25.6% and 6.4%, respectively. They noticed that patients with distant metastases to cervical lymph nodes and those with more than three diseased nodes had a poor prognosis.

Ishihara et al. (2010) studied the factors predictive of tumor recurrence and survival after achieving complete response to chemoradiotherapy therapy for squamous cell cancer of esophagus. They evaluated 110 patients of which 4 had disease in their cervical esophagus. All patients were treated with cisplatin- and fluorouracil-based chemotherapy. Concurrent radiation was given at a dose of 2 Gy per day, 5 days a week for a total dose of 60 Gy in 30 fractions. Local recurrence was seen in two of four cervical esophageal cancers. These patients were also found to be at increased risk of distant disease. In this study, cancers arising in upper esophagus were found to have higher prevalence of T4 and N1 disease as compared to middle and lower esophagus. These aggressive features of cervical esophageal cancer may be responsible for early microscopic metastases leading to high rates of regional and distant recurrence.

The timing of recurrence from starting date of chemoradiation was also noted as strong predictor of adverse outcome.

References

American Joint Committee on Cancer (2010) AJCC cancer staging manual, 7th edn. Springer, New York

Ascioti AJ, Hofstetter WL, Miller MJ, Rice DC, Swisher SG, Vaporciyan AA, Walsh GL (2005) Long-segment, supercharged, pedicled jejunal flap for total esophageal reconstruction. J Thorac Cardiovasc Surg 130(5):1391–1398. doi:10.1016/j.jtcvs.2005.06.032

Bagnardi V, Blangiardo M, La Vecchia C, Corrao G (2001) A meta-analysis of alcohol drinking and cancer risk. Br J Cancer 85(11):1700–1705

Carlson GW, Schusterman MA, Guillamondegui OM (1992) Total reconstruction of the hypopharynx and cervical esophagus: a 20-year experience. Ann Plast Surg 29(5):408–412

Chao YK, Chan SC, Chang HK, Liu YH, Wu YC, Hsieh MJ, Liu HP (2009) Salvage surgery after failed chemoradiotherapy in squamous cell carcinoma of the esophagus. Eur J Surg Oncol 35(3):289–294. doi:10.1016/j.ejso.2008.02.014

Hayes RB, Bravo-Otero E, Kleinman DV, Brown LM, Fraumeni JF Jr, Harty LC, Winn DM (1999) Tobacco and alcohol use and oral cancer in Puerto Rico. Cancer Causes Control 10(1):27–33

Herskovic A, Martz K, Al-Saraf M, Leichman L, Brindle J, Vaitkevicius V, Emami B (1992) Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. N Engl J Med 326(24):1593–1598

Hirano S, Nagahara K, Moritani S, Kitamura M, Takagita S (2007) Upper mediastinal node dissection for hypopharyngeal and cervical esophageal carcinomas. Ann Otol Rhinol Laryngol 116:290–296

Ishihara R, Yamamoto S, Iishi H, Takeuchi Y, Sugimoto N, Higashino K, Nishiyama K (2010) Factors predictive of tumor recurrence and survival after initial complete response of esophageal squamous cell carcinoma to definitive chemoradiotherapy. Int J Radiat Oncol Biol Phys 76(1):123–129. doi:10.1016/j.ijrobp. 2009.01.038

Kelley DJ, Wolf R, Shaha AR, Spiro RH, Bains MS, Kraus DH, Shah JP (1995) Impact of clinicopathologic parameters on patient survival in carcinoma of the cervical esophagus. Am J Surg 170(5):427–431

Murray DJ, Gilbert RW, Vesely MJ, Novak CB, Zaitlin-Gencher S, Clark JR, Neligan PC (2007) Functional outcomes and donor site morbidity following circumferential pharyngoesophgeal reconstruction using an anterolateral thigh flap and salivary bypass tube. Head Neck 29(2):147–154. doi:10.1002/hed.20489

Myers EN (2008) Cancer of the cervical esophagus. In: Myers EN (ed) Operative otolaryngology: head and neck surgery, 2nd edn. Saunders/Elsevier, Philadelphia, pp 473–484

National comprehensive cancer network (2011) Clinical practice guidelines in oncology. In: Esophageal and esophagogastric junction cancers (Version 1.2011, MS-14). http://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf

Pfister DG, Hu KS, Lefebvre JL (2004) Cancer of the hypopharynx and cervical esophagus. In: Harrison LB, Sessions RB, Hong WK (eds) Head and neck cancer, 2nd edn. Lippincott Williams & Wilkins, Philadelphia, pp 404–454

Popescu CR, Bertesteanu SV, Mirea D, Grigore R, Ionescu D, Popescu B (2010) The epidemiology of hypopharynx and cervical esophagus cancer. J Med Life 3(4):396–401

Si HX, Tsao SW, Poon CS, Wong YC, Cheung AL (2005) Physical status of HPV-16 in esophageal squamous cell carcinoma. J Clin Virol 32(1):19–23

Triboulet JP, Mariette C, Chevalier D, Amrouni H (2001) Surgical management of carcinoma of the hypopharynx and cervical esophagus. Arch Surg 136(10):1164–1170

Urschel JD, Sellke FW (2003) Complications of salvage esophagectomy. Med Sci Monit 9(7):RA173–RA180

Wang LS, Chow KC, Chi KH, Liu CC, Li WY, Chiu JH, Huang MH (1999) Prognosis of esophageal squamous cell carcinoma: analysis of clinicopathological and biological factors. Am J Gastroenterol 94(7):1933–1940

Yu P, Hanasono MM, Skoracki RJ, Baumann DP, Lewin JS, Weber RS, Robb GL (2010) Pharyngoesophageal reconstruction with the anterolateral thigh flap after laryngopharyngectomy. Cancer 116(7):1718–1724

Cervical Neck Metastasis

▶ Cervical Node Metastases from Squamous Cell Carcinomas, Patterns of

Cervical Node Metastases from Squamous Cell Carcinomas, Patterns of

Rodrigo Bayon and Scott McClintick
Department of Otolaryngology-Head and Neck Surgery, University of Iowa Hospitals & Clinics, Iowa City, IA, USA

Synonyms

Cervical neck metastasis; Locoregional metastasis

Definition

The dissemination of cancer of the upper aerodigestive tract to the lymph nodes located in the neck, a process which typically follows a predictable pattern of spread.

Introduction

Squamous cell carcinoma is the most common cancer of the upper aerodigestive tract, accounting for more than 90% of cancers. Its method of spread is through lymphatic channels, with a high propensity toward deposition in the regional lymph nodes. It is well known that the presence of cervical lymph node metastasis is the most important prognostic indicator, with a 50% reduction in 5-year survival compared to those without neck metastasis. Despite many common features, squamous cell carcinomas of the head and neck vary in their metastatic potential. Certain subsites such as the oropharynx and supraglottic larynx harbor a high risk of lymph node metastasis secondary to rich lymphatics of the area. Other sites such as the glottic larynx are much less likely to metastasize. Therefore, it is critical that head and neck surgeons understand the patterns with which these cancers spread if they are to successfully treat patients with squamous cell carcinoma of the head and neck.

History of Cervical Nodal Disease

Prior to the late nineteenth century, cancer of the upper aerodigestive tract with spread into the cervical lymphatics was considered incurable. Several surgeons including Kocher had described removal of cervical lymphatics for surgical exposure to primary cancers. However, Jawdynski is credited with describing the first radical neck dissection for the treatment of neck metastasis. The early twentieth century saw George Crile publishing a now landmark article describing the surgical treatment of neck metastasis with radical neck dissection. Half a century later, Hayes Martin became an outspoken proponent of radical neck dissection emphasizing the importance of sacrificing the sternocleidomastoid muscle, internal jugular vein and spinal accessory nerve. Many of his tenets of neck dissection lasted well into the twentieth century. However, other surgeons including Suarez and Bocca began advocating for modified techniques that reduced the morbidity associated with radical neck dissection by conserving structures not directly involved by cancer. These modified techniques, along with increased knowledge of patterns of nodal metastasis have allowed surgeons to start targeting lymphatic basins at highest risk for metastasis. Based on recognized

drainage patterns, most surgeons currently advocate selective neck dissection for the clinically negative neck with a greater than 20% risk of harboring microscopic disease. It allows not only for removal of this disease but also for more accurate staging, treatment planning, and determination of prognosis (Ferlito et al. 2006).

Anatomy

A discussion of patterns of cervical node metastasis would not be complete without an understanding of the lymphatic system and regional lymphatics. The lymphatic system is comprised of an intricate series of capillaries that gradually coalesce into larger vessels. Capillaries are avalvular with a lumen that is capable of expanding to twice its diameter. These capillaries drain into pre-collecting vessels found at the mucosa-submucosa junction and subsequently drain via peripheral collecting vessels into first echelon lymph nodes. Much like veins, these larger lymphatic channels have valves and permit only unidirectional flow. The afferent lymphatics drain into the marginal sinus of the lymph node before penetrating deeper into the medulla of the node. Lymph then exits the lymph node through efferent vessels and into lymphatic ducts that converge into larger jugular lymphatic trunks before emptying into the junction of the subclavian and internal jugular veins bilaterally (Werner et al. 2003).

The head and neck is rich in lymphatics and lymph nodes, with approximately 200–300 lymph nodes located in this region which are divided into superficial and deep systems. Each area of the head and neck drains along rather predictable pathways before entering the venous system in the lower neck. However, anatomic variation in the arrangement of lymph nodes can at time make predictions inaccurate. Advanced disease, infection, and history of prior radiation or surgery can also contribute to the dissemination of cancer to unlikely locations. This is thought to be due to alteration in lymphatic flow due to scarring or tumor emboli obstructing downstream lymphatics (Werner et al. 2003). Another critical consideration is the possibility of contralateral drainage which is more prevalent in certain subsites of the head and neck, and increases as one approaches the midline.

Because of the complexity of the lymphatics in the head and neck, a standardized system was developed to
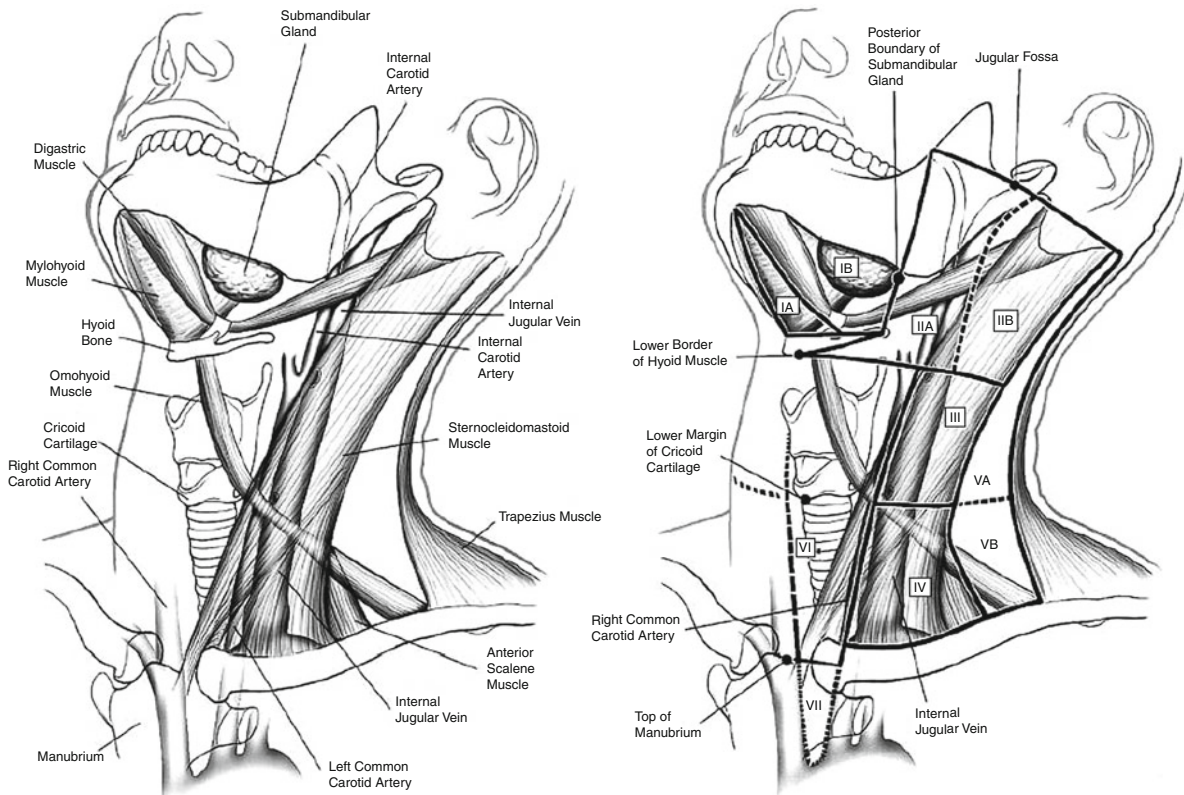
Cervical Node Metastases from Squamous Cell Carcinomas, Patterns of, Fig. 1 (**a**) Anatomic detail of neck with emphasis on structures important in nodal staging and neck dissection. (**b**) Division of neck into nodal stations I–VII

allow for consistency in describing the location of lymph node metastasis (Fig. 1). Level I is defined as the triangular space bounded by the mandible superiorly, the midline of the neck anteriorly, and the posterior belly of the digastric muscle posteriorly. This triangle can be further broken down into Ia (submental group), which is bounded by the midline, the anterior belly of the digastric muscle and hyoid bone, and Ib (submandibular group) which is bounded by the anterior belly of digastric, the mandible, and the stylohyoid muscle. Levels II, III, and IV constitute the jugular chain of lymph nodes and extend from the skull base to the clavicle. Level II is defined as the area from the skull base to the hyoid bone (clinical and radiographic landmark) or carotid bifurcation (surgical landmark) and is bounded anteriorly by the stylohyoid muscle and posteriorly by the posterior edge of the sternocleidomastoid muscle. The spinal accessory nerve divides this group into IIa (anterior to the nerve) and IIb (posterior to the nerve, also known as submuscular

triangle). Level III extends from the hyoid bone/ carotid bifurcation down to the level of the cricoid (clinical and radiographic landmark) or omohyoid muscle (surgical landmark). The anterior boundary is the sternohyoid muscle and the posterior boundary is the posterior edge of the sternocleidomastoid muscle. Level V extends from the bottom of level III to the clavicle and is bounded also by the sternohyoid muscle and posterior edge of the sternocleidomastoid muscle. Level V includes all lymph nodes within the posterior triangle of the neck, bounded by the posterior edge of the sternocleidomastoid muscle, the anterior edge of the trapezius muscle and the clavicle. Level V can be subdivided into Va and Vb by a horizontal line drawn from the cricoid cartilage. Level VI includes lymph nodes in the anterior compartment of the neck inferior to the hyoid bone and between the carotid sheath. This includes the paratracheal, perithyroidal, and precricoid (Delphian) nodes. Level VII includes superior mediastinal lymph nodes. Retropharyngeal nodes are divided

into medial and lateral chains, with the most superior of the lateral nodes referred to as the Nodes of Rouviere. Lastly, preauricular, postauricular, intraparotid, and suboccipital lymph nodes are not included within the triangles of the neck but are of importance in cutaneous malignancy (Robbins et al. 2010).

Pathophysiology of Lymphatic Spread of Tumor Cells

Lymphatics are located throughout the entire body, except the bone marrow and the central nervous system. The lymphatic system has four functions. It returns interstitial fluid back to the systemic circulation, it transports nutrients that are absorbed from intestines to the vascular space, it transports foreign antigens to lymph nodes, and it produces humoral antibodies or cell-mediated responses (Natarajan et al. 2005). Historically, breast cancer has been one of the earliest cancers where the importance of lymphatic tumor spread was recognized and studied. There have been differing theories regarding the mechanism of lymphatic spread of cancer cells. The earliest of these theories was known as a "lymphatic dominant" theory, as described by Handley and Halsted. This premise postulated that lymph nodes acted as mechanical barriers or filters to the spread of cancer cells. It was thought that by surgically ablating the lymphatic pathways, one could prevent the further spread of cancer cells. However, this theory was questioned by finding metastatic disease in distant sites in the absence of regional nodal metastases. Later, Fisher proposed a biologic theory that viewed cancer as a "systemic disease from the outset." The thought was that cancer cells escaped from the primary organ simultaneously through both lymphatics and the blood stream thereby creating distant metastases. However, it became apparent that "early" cancers had an excellent long-term survival and lacked distant metastases, thus questioning the "systemic disease from the outset" theory. The most recent theory, described by Hellman, is the "spectrum theory." This postulates that primary cancers exhibit a spectrum of biologic behavior, and some tumors display no capacity to create metastatic disease while others are more prone to regional or distant spread (Natarajan et al. 2005).

Most head and neck squamous cell cancers will progress from carcinoma in situ, to microinvasive carcinoma, to invasive carcinoma with invasion of the stroma, to a deeply invasive tumor with lymphatic metastasis. Multiple cellular events are involved in the development of metastases. These include the detachment of a malignant cell from the primary cancer, entry of the cancer cell into the lymphatic space and further local and distant dissemination (Natarajan et al. 2005). Cancer cells also can spread locally through direct infiltration into soft tissues. Although cancer cells carried in the blood can spread to essentially any location in the body, lymphatic spread follows a more stepwise fashion, moving through successive nodal stations.

Patterns of Drainage

Numerous studies have been performed to evaluate the pattern of spread of squamous cell carcinoma to cervical lymph node groups. These studies have aimed to retrospectively review the pathology of comprehensive neck dissections and correlate level of pathologic adenopathy and primary site. Most studies have been able to demonstrate a predictable pattern of spread that can be used to appropriately treat patients with a high risk of nodal metastasis without treatment of all nodal basins.

Oral Cavity – Cancers of the oral cavity most commonly drain to levels I–III of the ipsilateral neck. The majority of N0 patients are adequately treated by dissection of these three levels, with only 3–6% of patients having disease in level IV (Mukherji et al. 2001). Level V is almost always associated with clinical disease in other levels. Controversy exists regarding the necessity of removing level IV due to the risk of skip metastases in up to 16% of patients with no cancer in levels I–III (Byers et al. 1997). However, other studies have shown low risk with only 2% of all elective neck dissections demonstrating skip metastasis (Dias et al. 2006). Therefore, clinical judgment is critical in deciding whether the added morbidity of dissecting these levels is outweighed by the risk of leaving disease behind.

Oropharynx – The oropharynx has a significantly higher rate of occult metastasis, and therefore patients even with small primary tumors should have their neck

treated. The oropharynx most commonly drains to levels II through IV. Therefore, treatment of these levels in elective neck dissections is considered adequate to clear microscopic disease. Lesions that involve the soft palate are also at higher risk for developing contralateral metastasis, particularly in level II (Mukherji et al. 2001). Level I and V are rarely involved without other levels being involved as well. Another consideration in the treatment of oropharynx is the possibility of retropharyngeal node involvement. The retropharyngeal nodes are known to drain the soft palate, posterior pharyngeal wall, and less commonly the tonsillar fossae. Cancers that involve or approach these areas put the retropharyngeal nodes at risk.

Nasopharynx – Nasopharyngeal carcinoma, unlike other head and neck cancers, drains to the retropharyngeal nodes as its primary nodal basin. Drainage is primarily into the lateral retropharyngeal nodes and is commonly bilateral, placing both necks at risk for cervical metastasis. Palpable nodes are typically in upper level V and level II, with III and IV nodes less often involved. Rarely, the intraparotid lymph nodes may be involved, particularly with involvement of the Eustachian tube, tympanic membrane, or external auditory canal (Mukherji et al. 2001).

Hypopharynx and cervical esophagus – The hypopharynx, due to its rich lymphatic drainage, has a propensity for early lymphatic spread. In fact, nearly 70% of patients with hypopharyngeal malignancy present with palpable cervical adenopathy. Hypopharyngeal cancers most commonly drain to levels II through IV, with I and V rarely involved. There is also a propensity toward contralateral spread, particularly if there is ipsilateral palpable disease. Involvement of the medial wall of the pyriform sinus also increases risk of contralateral spread. The retropharyngeal and level VI nodes have also been shown to be at risk for metastasis in cancers of the hypopharynx. Some authors advocate routine inclusion of these nodal basins along with thyroidectomy to address this risk (Uppaluri and Sunwoo 2010).

Larynx – Due to its embryologic development, the larynx behaves as two separate compartments with distinct lymphatic drainage pathways. The supraglottic larynx is rich in lymphatics and therefore is at distinctly increased risk of lymph node metastasis than the glottis and subglottis. The lymphatic drainage follows the superior laryngeal vessels and drain into levels II and III bilaterally. Treatment of levels II through IV in the clinically N0 neck has been shown to be adequate for oncologic control of the neck. Because there is no embryologic fusion plane to prevent contralateral spread, it is critical to address both necks in the treatment of all supraglottic tumors. The glottis and subglottis, in contrast, drain inferiorly into the level VI compartment and level IV. The glottis has few lymphatics and tumors must infiltrate deeply prior to accessing the regional lymphatics. While less often involved with metastasis, addressing level II–IV without addressing the central neck compartment is at risk for leaving metastatic disease behind (Armstrong et al. 2010).

Unknown Primary – Carcinomas of unknown primary accounts for 3–5% of head and neck malignancies, 90% of which are squamous cell carcinoma. The predictable drainage patterns of the head and neck cervical lymphatics can prove useful in determining the likely site of the primary malignancy. The majority of these cancers arise within Waldeyer's ring in the nasopharynx and oropharynx. Tumors located within level V are most likely nasopharyngeal in origin. Those along the upper jugulodigastric chain are most likely to be tonsillar or tongue base. Cancers found low in the neck must raise suspicion for a malignancy arising below the clavicles.

Cutaneous – Squamous cell carcinoma of the skin represents a broad range of cancers with different patterns of behavior. The majority are considered low risk, with only a small risk of cervical metastasis. Therefore unlike squamous cell carcinomas of the upper aerodigestive tract, there is no standardized method for determining risk of regional metastasis. Selective neck dissection is not typically utilized in these cancers, but rather treatment of cervical nodal disease is performed as needed. Special attention must be paid to peri- and intraparotid lymph node metastasis as well as to superficial lymph nodes (perifacial, external jugular, suboccipital, and postauricular). Cutaneous SCCA of the head and neck most commonly affects the parotid and upper jugular lymph nodes. Patients presenting with parotid involvement have a high incidence of cervical metastasis, both clinically evident

(up to 26%) and occult (35%). Lesions found in the posterior scalp commonly have metastasis in level V (Vauterin et al. 2006).

Type of Neck Dissection

In an effort to standardize the terminology of neck dissections, a classification system was developed and published in 1991, by the Academy's Committee for Head and Neck Surgery and Oncology (Robbins et al. 1991). The different types of neck dissections were classified as follows: (1) Radical neck dissection (2) Modified radical neck dissection, (3) Selective Neck dissection, and (4) Extended radical neck dissection. The selective neck dissections were further subdivided into supraomohyoid neck dissection, posterolateral neck dissection, lateral neck dissection, and anterior compartment neck dissection.

Radical neck dissection refers to removal of all ipsilateral cervical lymph nodes in levels I through V. The spinal accessory nerve, the internal jugular vein, and sternocleidomastoid muscle are also removed. This procedure is of historical importance, but has largely been replaced by less morbid methods of removing cervical lymph nodes (Robbins et al. 1991).

Modified radical neck dissection is a variation of the classic radical neck dissection, and refers to the removal of all ipsilateral cervical lymph nodes in levels I through V while preserving one or all of the non-lymphatic structures in the neck, including the spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle (Robbins et al. 1991). Patients with N+ disease are still most commonly treated with modified radical neck dissection. The spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle are only sacrificed if involved or adjacent to cancer. However, there are some centers that perform selective neck dissection for N+ disease with no significant difference in recurrence rates. These studies do caution that patient selection is critical to success. Patients with N1, small N2 disease, and nodes contained within the upper aspect of the draining lymph node basins are most likely to have good outcomes (Ferlito et al. 2006).

Selective neck dissection refers to any type of cervical lymph node resection where there is preservation of one or more lymph node groups. There are four types of selective neck dissections:

Supraomohyoid neck dissection is designed to remove the lymphatic basins of levels I, II, and III. Consequently, it is used for cancers found in the oral cavity. As described previously, controversy exists regarding the necessity of removing level IV due to the risk of skip metastases in up to 16% of patients with no cancer in levels I–III (Byers et al. 1997). However, other studies have shown low risk with only 2% of all elective neck dissections demonstrating skip metastasis (Dias et al. 2006).

Posterolateral neck dissection refers to removal of the suboccipital and retroauricular lymph nodes along with nodes in levels II through V. This type of neck dissection is utilized in treating metastatic nodal disease typically from malignancies of the posterior scalp and neck (Robbins et al. 2010).

Lateral neck dissection is designed to remove the lymphatic tissue in levels II through IV. It is employed in cancers involving the oropharynx, larynx, and hypopharynx. Level IIb is typically included in the dissection except in laryngeal cancers.

Anterior compartment neck dissection refers to removal of lymph nodes surrounding the visceral structures of the anterior neck. Included are the pretracheal, paratracheal, perithyroidal, and the precricoid lymph nodes. This type of neck dissection is typically utilized in the treatment of thyroid cancer.

Extended radical neck dissection refers to the removal of one or more lymph node group or non-lymphatic structure that is not included in a standard radical neck dissection. Examples include the removal of parapharyngeal or upper mediastinal nodes, or removal of non-lymphatic structures such as the carotid artery, vagus nerve, or paraspinal muscles (Robbins et al. 1991).

Cross-References

▶ Lymphatic Spread from Cutaneous Neoplasms of Head and Neck
▶ Malignant Laryngeal Neoplasms
▶ Malignant Neoplasms of the Oral Cavity
▶ Nasopharyngeal Carcinoma
▶ Neck Dissection Anatomy

References

Armstrong WB, Vokes DE, Masel RH (2010) Malignant tumors of the larynx. In: Flint PW et al (eds) Cummings otolaryngology: head & neck surgery, 5th edn. Mosby Elsevier, Philadephia

Byers RM, Weber RS, Andrews T et al (1997) Frequency and therapeutic implications of "skip metastases" in the neck from squamous cell carcinoma of the oral tongue. Head Neck 19:14–19

Dias FL, Lima RA, Kingerman J et al (2006) Relevance of skip metastases for squamous cell carcinoma of the oral tongue and the floor of the mouth. Otolaryngol Head Neck Surg 134(3):460–465

Ferlito A, Rinaldo A, Silver CE et al (2006) Elective and therapeutic selective neck dissection. Oral Oncol 42:14–25

Harreus U (2010) Malignant neoplasms of the oropharynx. In: Flint PW et al (eds) Cummings otolaryngology: head & neck surgery, 5th edn. Mosby Elsevier, Philadephia

Mukherji SK, Armao D, Joshi VM (2001) Cervical nodal metastases in squamous cell carcinoma of the head and neck: what to expect. Head Neck 23(11):995–1005

Natarajan S, Taneja C, Cady B (2005) Evolution of lymphadenectomy in surgical oncology. Surg Oncol Clin N Am 14(3):447–459

Robbins KT, Samant S, Ronen O (2010) Neck dissection. In: Flint PW et al (eds) Cummings otolaryngology: head & neck surgery, 5th edn. Mosby Elsevier, Philadephia

Robbins KT, Medina JE, Wolfe GT et al (1991) Standardizing neck dissection terminology. Official report of the academy committee for head and neck surgery and oncology. Arch Otolaryngol Head Neck Surg 117:601–605

Tan L, Thomas L (2010) Benign and malignant tumors of the nasopharynx. In: Flint PW et al (eds) Cummings otolaryngology: head & neck surgery, 5th edn. Mosby Elsevier, Philadephia

Uppaluri R, Sunwoo JB (2010) Neoplasms of the hypopharynx and cervical esophagus. In: Flint PW et al (eds) Cummings otolaryngology: head & neck surgery, 5th edn. Mosby Elsevier, Philadephia

Vauterin TJ, Veness MJ, Morgan GJ et al (2006) Patterns of lymph node spread of cutaneous squamous cell carcinoma of the head and neck. Head Neck 28:785–791

Werner JA, Dunne AA, Meyers JN (2003) Functional anatomy of the lymphatic drainage system of the upper aerodigestive tract and its role in metastatic squamous cell carcinoma. Head Neck 25(4):322–332

Cervical Osteophytes

Julie A. Honaker and Amanda K. Wolfe
Department of Special Education and Communication Disorders, University of Nebraska-Lincoln, Lincoln, NE, USA

Definition

Abnormal bone growths or spurs on the cervical spine.

Cross-References

▶ Examination (Vestibular Dysfunction – Cervical Vertigo)

Cervicogenic Dizziness

Julie A. Honaker and Amanda K. Wolfe
Department of Special Education and Communication Disorders, University of Nebraska-Lincoln, Lincoln, NE, USA

Definition

Symptoms of dizziness, disequilibrium, or light-headedness due to neck afferent asymmetry.

Cross-References

▶ Examination (Vestibular Dysfunction – Cervical Vertigo)

Cervico-Ocular Reflex

Julie A. Honaker and Amanda K. Wolfe
Department of Special Education and Communication Disorders, University of Nebraska-Lincoln, Lincoln, NE, USA

Definition

Reflexive movement of the eyes due to changes in neck position.

Cross-References

Cheilioschisis

Cheiloplasty

Jonathan Mark[1] and Eric J. Dobratz[2]
[1]Department of Otolaryngology, Eastern Virginia Medical School, Norfolk, VA, USA
[2]Department of Otolaryngology, Eastern Virginia Medical School, Norfolk, VA, USA

Synonyms

Lip augmentation; Lip enhancement surgery; Lip reduction surgery

Definition

Chelioplasty: In general, chelioplasty refers to surgical modification of the lip or lips. Modifications performed may include the reconstruction of acquired or congenital deformities and lip reduction or lip augmentation procedures for cosmetic and/or functional purposes.

Basic Characteristics

Chelioplasty is defined as surgical modification of the lips. Modifications may include reconstruction of acquired or congenital deformities of the lip. Many of these reconstructive techniques are detailed in other entries including ▶ Cleft Lip, ▶ Cleft Lip and Palate, ▶ Abbe Flap, ▶ Estlander Flap, and ▶ Lip Reconstruction. Other modifications made to the lips are performed to reduce or augment the lips for cosmetic or functional reasons. Excessively prominent lips may

be aesthetically displeasing or interfere with oral functioning. In these cases, tissue from the lips may be removed to reduce the lips to the desired size. In contrast, when fuller, plumper lips are desired, the position of the lips may be changed to appear more prominent or may be enlarged with injected or implanted materials.

Prior to discussing techniques for altering the lip anatomy, this entry will first review the anatomy and functional and aesthetic properties of the lips. The lips are the dominant structure of the lower one third of the face. Externally they consist of both skin and mucosa. Skin from the subnasale to the vermillion border contains hair and glandular tissue. On the vermillion, hair is absent and glandular structures are essentially absent until the vermillion transitions from the wet to the dry portion. The dry portion consists of thin keratinized stratified squamous epithelium and transitions to the wet nonkeratinized stratified squamous epithelium oral mucosa. The lips are highly vascular structures that receive their blood supply from the superior and inferior labial arteries arising from the facial arteries and ultimately the external carotids. The labial arteries lie deep to the orbicularis oris muscle, the bulk of the lip. Lip musculature also includes the muscles of facial expression that insert into the lips laterally and superiorly. Sensory innervation is from the V2 and V3 branches of the trigeminal nerve.

Functional properties of the lips include oral competence, tactile sensation, and emotional expression. The orbicularis musculature acts as a sphincter and performs a vital role in mastication. Mimetic muscles surrounding the lips allow for expression, communication, and social interaction. The lips' shape and thickness express character and mood and can even be a sexual symbol where more swollen red lips may be associated with sexual excitation (Lassus 1992). Disruption of the function of the lips, which occurs with denervation or weakness of the muscles, may lead to serious deficits such as one dysarthria with air escape with speech, ptyalism, and difficulty with mastication (Flint et al. 2010). Other disorders that may disrupt lip function include macrochelia, lymphatic/vascular malformations, Melkersson-Rosenthal syndrome, cheilitis granulomatosa, Ascher syndrome, and neurologic disorders causing lower lip ptosis.

Aesthetic properties of the lips are fluid in definition; however, common landmarks and features of "an
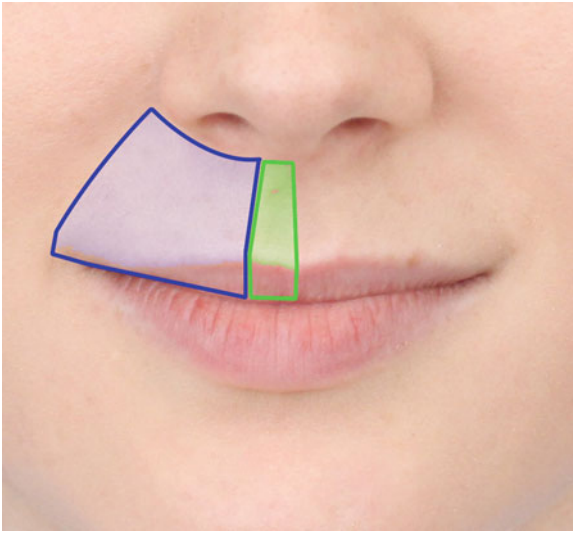
Cheiloplasty, Fig. 1 Aesthetic subunits of the upper lip. Berget and Menick describe aesthetic subunits of the upper lip that include bilateral, lateral (*blue*), and medial (*green*) subunits

ideal lip" exist. The lips should fit harmoniously with the neighboring structures of the face. Unbalanced characteristics and excessive deviation from anatomic normalcy can give an unnatural or unattractive appearance. Burget and Menick (1986) describe aesthetic subunits of the lips. The upper lip is divided into subunits consisting of the central philtrum and two lateral subunits (Fig. 1). The philtrum is divided into two medial subunits and are bordered by the philtral columns, which divide the medial and lateral subunits. The lower lip is viewed a single subunit. The cutaneous portion of the upper lip is separated from the vermillion by the white roll. The ratio between the cutaneous portion of the lip to the vermillion should be 2:1. The upper lip should have a cupid's bow shape. The upper lip generally projects slightly more than the lower lip.

The lips must also be carefully analyzed in aesthetic relation to the nose and chin. The ratio of the distance between the subnasal and the margin of the upper lip to the margin of the lower lip and the mentum should be 1:2. The degree of the nasolabial angle and the amount of incisor show are two important relationships that may influence the perception of the lips and are important to consider when selecting the appropriate augmentation technique. For example if a patient has inadequate incisor show while smiling, augmentation of lip volume alone may prove inadequate (Niechajev 2000). One should also consider other relationships

such as the position of the lips in relation to the vertical height of the maxilla and occlusion status. Some patients who desire lip alteration may actually benefit from orthognathic surgery instead of chelioplasty.

Many patients desire chelioplasty to correct the changes that occur with aging of the perioral complex. Some effects of aging on the perioral complex include radial perioral rhytids, extended melolabial folds, loss of fullness and projection, and disappearance or flattening of cupids bow. The cutaneous portion of the upper lip appears to elongate in relation to the vermillion creating a ratio closer to 3:1. The vermillion portion of the lip becomes much less prominent and the white roll thins and becomes less distinct. Patients who seek to create a more youthful appearing lip will often be interested in procedures to enhance the lips and reduce the visibility of perioral lines and wrinkles.

Surgical Techniques

Lip Augmentation
Youthful, voluptuous lips have long been thought of as a powerful and dynamic aspect of facial aesthetics. As describe above, the lips thin out with age and become less distinct. Patients may desire procedures to augment the lips to try and regain the perceived loss of their youthful, full lips. While considering the various techniques available for lip augmentation, it is important to recognize that the preference for lip appearance is very personal. Lips vary in appearance due to one's gender, age' and ethnicity and all of these must be accounted for when considering lip enhancement procedures. The various procedures and surgeries available to augment or rejuvenate the upper and lower lips should be thoroughly discussed with the patient. The aesthetic goal for most patients is to provide a full, youthful look while avoiding excess augmentation.

Tissue Rearrangement
Tissue rearrangement techniques may be used to manipulate existing tissue to provide augmentation. One such procedure that may be performed is the V-Y plasty. A horizontally oriented flap is created and advanced, allowing one to obtain central pouting and forward bulging with eversion of the upper lip. No additional bulk is obtained, rather tissue in areas of excess is redistributed to deficient areas (Fig. 2). A subnasal lip lift is another type of tissue
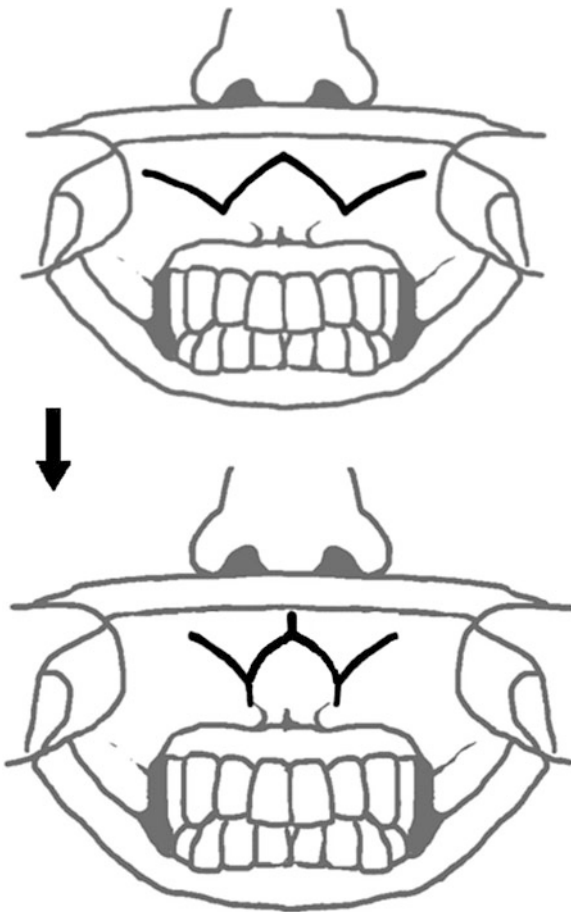
Cheiloplasty, Fig. 2 V-Y plasty lip augmentation. V to Y tissue advancement may be performed to advance and evert the deficient vermillion. The "V" flaps are incised, elevated, and advanced. The resultant closure resembles a "Y" after advancement

Cheiloplasty, Fig. 3 Subnasale lip lift. An excision of skin (*blue area*) is created on the upper lip directly below the nasal base. The wound edges are closed which results in reduction of the cutaneous portion of the lip and superior advancement of the vermillion, correcting the elongation of the cutaneous lip that may occur with aging

rearrangement procedure (Fig. 3). This technique, which has also been described as a buffalo horn, involves excision of subnasal skin with closure of the wound edges. By removing a portion of the cutaneous lip, the vermillion is advanced superiorly with the closure of the cutaneous defect under the nose and the vermillion becomes more visible. This helps to improve the ratio between the cutaneous portion and vermillion recreating a ratio closer to 2:1. Additionally, the excised skin and subcutaneous tissue may be used as a graft to augment the central portion of the lip. The incision is placed at the junction of the nose and lip, which allows for camouflage of the scar. This nasal base incision is particularly useful in young patients and those with an acute nasolabial angle; in older patients with perioral rhytids the incision may be made at the vermillion border (Niechajev 2000) or at the nasal base.

Injectable/Implantable Fillers

There are a number of injectable fillers and implants that are available in permanent and temporary forms to augment the lips. Augmentation may be achieved from a variety of xenograft, allograft, autograft, and synthetic sources. Patients should be educated about all of their options, including risks and benefits of each when deciding on which technique suits their desires best. Some patients may not mind repeat procedures, but do not want the downtime due to the temporary swelling that can be associated with implanting materials in the lip. Others may want a more permanent procedure and do not mind a week or two of healing time.

Temporary fillers may be injected into the lip in the clinic with minimal chances of swelling or bruising. These patients may proceed with their regular routine that some day. Bovine or human collagen has been a popular option to improve the contour of the lip. Collagen creates a brief augmentation effect lasting only 3–4 months and may generate an allergic reaction. Patients should undergo placement of a test dose to test

for sensitivity prior to full injection with collagen. Hyaluronic acid (HA) fillers are available as a synthetic injectable gel that is indicated for correction of the melolabial folds. HA's have been used to augment the lips as well, with longer lasting results than collagen, providing augmentation for 9–12 months. Another advantage of HA is the fact that the augmentation is correctable if the patient is displeased with the resultant augmentation or if there is asymmetry or palpable bumps. These cases may be corrected with thorough massaging to try and even out the gel, but hyaluronidase may be injected in order to dissolve unwanted areas of injection as well.

Autologous fat transfer has been used for soft tissue augmentation for over a century and remains to be an option for injectable lip augmentation. Success in fat grafting has been variable and seems to be dependent upon technique and location of the injection. In general, areas of less mobility have better success of achieving more permanent augmentation. Resorption of the graft is common in areas that are highly mobile such as the lips; however, many patients will achieve at least temporary augmentation of the lips with fat injections. Some percentage of the graft may survive and become permanent. Oftentimes, patients will require repeat injections to achieve longer lasting results.

There are longer lasting and even permanent synthetic fillers that are available, such as injectable silicone and polymethylmethacrylate. These injections may be associated with inflammatory reactions, permanent excessive augmentation, visible or palpable nodules, and visibility of the injectable material with movement (Smith 2008). For these reasons, it is generally not recommended to use permanent synthetic fillers for lip augmentation although some authors have described success with permanent synthetic injectable fillers (Moscona and Fodor 2010).

Temporalis fascia graft or superficial musculoaponeurotic system (SMAS) grafts may be implanted in the lips for augmentation. This technique is often performed in conjunction with a facelift or rhytidectomy. The fascia graft is shaped in an elliptical fashion and placed to augment the central lip alone or in a quadrangular form to build up the entire lip. Incisions are made through the vermillion laterally and a pocket is tunneled with blunt dissection before graft placement. The graft is then pulled through the tunnel with tendon forceps or similar instrument

Cheiloplasty, Fig. 4 SMAS lip augmentation. A strip of SMAS is excised during rhytidectomy and is passed through a tunnel that is dissected across the lip allowing for permanent lip augmentation (From Byrne and Hilger (2004), Fig. 10, p. 36)

(Lassus 1992; Leaf and Firouz 2002) (Fig. 4). One must consider the level of placement of the graft and bulk of the graft as irregularities may sometimes appear in grafts that are placed too superficial or are too bulky. A major benefit of autologous tissue is soft, full natural feel, which is of particular importance for the mobility and sensitivity of the lip.

Acellular allograft dermal matrix may be used in implantation lip augmentation with results that last on the order of a year. Donor site morbidity is avoided, which may offer an advantage over autograft implantation in certain situations. Permanent solid implantable products are available in a variety of materials including silicone and polytetrafluoroethylene (PTFE), also known as Gortex. Concern for the risk of extrusion, movement, infection, and local reaction or swelling complications is increased in synthetic implants (Byrne and Hilger 2004).

Lip Reduction

Patients with unusually large lips may desire reduction of their lips. It is important to remember that one's view of lip size and aesthetics may be very personal. Certain ethnic groups normally have larger lips and this may be considered to very attractive. Some patients within these ethnic groups may consider their lips to be bigger than normal, even for their ethnicity, and desire lip reduction. Other patients may seek lip reduction after the development of enlarged lips due to disorders such as vascular malformations or

Melkersson-Rosenthal syndrome. Melkersson-Rosenthal is a rare condition that consists of progressive and recurrent orofacial edema, intermittent facial palsy, and plication of the tongue. Lip swelling is the most common feature and may result in lips that have enlarged to three times their normal size resulting in both aesthetic and functional concerns.

Reduction cheiloplasty is generally a straightforward and predictable procedure with limited morbidity. Various techniques have been described to perform reduction cheiloplasty, but most include removing a fusiform-shaped section of tissue and closing the defect to change the posture of the lip (Niamtu 2010). Appropriate preoperative measurements are crucial. The anterior incision is planned so the resultant scar lines are kept posterior to the wet dry line so they are not as readily visible. The posterior scar placement must be balanced with being anterior enough to roll back the amount of visible vermillion. The mucosa is removed in a similar fashion to a skin only, upper lid blepharoplasty. With larger reductions it may be necessary to remove some deeper tissue including the submucosa and minor salivary tissue. In general, the orbicularis muscle is carefully avoided and not resected. Reduction may be further supplemented with a midline sagittal wedge resection of the lower lip and or excision of two sagittal triangular wedges at the lateral eminences of the philtrum.

Conclusion

The lips are the dominant structure of the lower third of the face. Lips contribute significantly to define one's facial appearance, provide for speech and display of emotions, and also are the focus of intimate touch on the face. Cheiloplasty or modification of the lips may be performed to reconstruct defects or to change the appearance of the lips. Patients may desire augmentation or reduction of the lips to attain aesthetic balance or to recapture a more youthful appearance of their lips. Preference for the appearance of the lips is very personal; therefore cheiloplasty remains a highly individualized process where the perfect implant, injectable procedure is still elusive. Patients should be intimately involved in deciding upon the correct technique to meet their desires for change in the appearance of their lips.

Cross-References

▶ Abbe Flap
▶ Cleft Lip
▶ Commissuroplasty
▶ Estlander Flap
▶ Lip Reconstruction

References

Burget GC, Menick FJ (1986) Aesthetic restoration of one-half the upper lip. Plast Reconstr Surg 78(5):583–593
Byrne PJ, Hilger PA (2004) Lip augmentation. Facial Plast Surg 20(1):31–38
Flint PW et al (2010) Cummings otolaryngology: head and neck surgery, 5th edn. Mosby, Philadelphia, 3-vol set
Lassus C (1992) Surgical vermillion augmentation: different possibilities. Aesthetic Plast Surg 16(2):123–127
Leaf N, Firouz JS (2002) Lip augmentation with superficial musculoaponeurotic system grafts: report of 103 cases. Plast Reconstr Surg 109(1):319–326 Discussion 327–328
Moscona RA, Fodor L (2010) A retrospective study on liquid injectable silicone for lip augmentation: long-term results and patient satisfaction. J Plast Reconstr Aesthetic Surg 63(10):1694–1698
Niamtu J 3rd (2010) Lip reduction surgery (reduction cheiloplasty). Facial Plast Surg Clin North Am 18(1):79–97
Niechajev I (2000) Lip enhancement: surgical alternatives and histologic aspects. Plast Reconstr Surg 105(3):1173–1183 Discussion 1184–1187
Smith KC (2008) Reversible vs. nonreversible fillers in facial aesthetics: concerns and considerations. Dermatol Online J 14(8):3

Chemodectoma

▶ Imaging for Parapharyngeal Space Tumors, Poststyloid Parapharyngeal Space Paraganglioma
▶ Magnetic Resonance Imaging, Paraganglioma of the Skull Base
▶ Osteoradionecrosis of Skull Base (Benign Neoplasia-Paragangliomas)
▶ Primary Neck Neoplasms

Chemodectomas

▶ Benign Neoplasia, Paragangliomas-Glomus Tympanicum

Chiari Malformations

Chris Sanders Taylor
Department of Neurological Surgery, University of Cincinnati, Cincinnati, OH, USA

Definition

Four categories of hindbrain abnormalities with the two most common types being characterized by varying degrees of neural herniation into the craniocervical junction.

Cross-References

▶ Craniocervical Junction, Abnormalities

Childhood Eating Disorder

▶ Feeding Disorders

Childhood Migraine Variant

▶ Benign Vertigo of Childhood

Childhood Paroxysmal Vertigo

▶ Benign Vertigo of Childhood

Chocolate Cyst

▶ Magnetic Resonance Imaging, Cholesterol Granuloma

Cholesteatoma (Congenital)

Eric A. Gantwerker[1] and Ellis M. Arjmand[2]
[1]Department of Otolaryngology-Head and Neck Surgery, University of Cincinnati, Cincinnati, OH, USA
[2]Department of Otolaryngology, University of Cincinnati, Cincinnati Children's Hospital Medical Center, Ear and Hearing Center Cincinnati, Cincinnati, OH, USA

Definition

Congenital ▶ cholesteatoma: Nonneoplastic, epithelial, keratinizing lesion that forms in the middle ear and temporal bone behind an intact tympanic membrane (TM) without prior history of otorrhea, surgical intervention, or previous perforation (Richter and Lee 2009).

Epidemiology

Incidence of congenital ▶ cholesteatoma (CC) has been estimated as 0.12 per 100,000. They account for 4–24% of all pediatric cholesteatomas, but the incidence is largely underestimated given the difficulty in diagnosis in advanced disease and the large proportion of asymptomatic patients (80%). CC accounts for approximately 2–4% of all cholesteatomas presenting to pediatric otologists. There is no male–female preponderance (Potsic et al. 2002a; Kazahaya and Potsic 2004; Persaud et al. 2007; Richter and Lee 2009).

History

Cholesteatoma was first described by Cruveilhier in 1829 and named by Muller in 1858. Derlacki and Clemis described criteria for CC in 1965.

Clinical Features

Cholesteatomas are nonneoplastic, epithelial, keratinizing lesions that form in the middle ear and

temporal bone. Acquired cholesteatomas (AC) are the more common type, characterized by destructive lesions within the middle ear (ME) and mastoid as a result of middle ear disease and/or eustachian tube dysfunction (ETD) (Olszewska et al. 2004). Pediatric or congenital cholesteatomas (CC) are a distinct subset of lesions that occur behind an intact tympanic membrane (TM), without preexisting ME disease (Potsic et al. 2002a; Kazahaya and Potsic 2004; Persaud et al. 2007; Richter and Lee 2009). Much controversy exists as to the origin of CC and several theories have been proposed. Histologically these lesions are indistinct from the acquired type and in advanced disease act similarly, necessitating similar management (Albino et al. 1998).

Cholesteatoma was first described by Cruveilhier in 1829 and named by Muller in 1858. Derlacki and Clemis described criteria for CC in 1965. Their criteria distinguished congenital cholesteatoma as a lesion behind an intact TM without prior history of otorrhea, surgical intervention, or previous perforation (Richter and Lee 2009). CC is usually diagnosed between the ages of 2 years to early teenage years with an average age of diagnosis of 4.5 years (Richter and Lee 2009). In contrast, a study of 991 children with AC showed an average age of 9.7 years (Koltai et al. 2002).

The idiomatic finding is that of a white pearl forming behind an intact, healthy appearing TM within the anterosuperior quadrant, but CC can be found in any quadrant. This typical picture accounts for approximately 80% of early lesions (Nelson et al. 2002; Richter and Lee 2009). CC are asymptomatic in 82% of individuals and are usually found incidentally by routine physical examination, by radiographic imaging, or during myringotomy procedures (Nelson et al. 2002; Richter and Lee 2009). Those that are symptomatic often present with otitis media due to eustachian tube (ET) blockade from expanding cholesteatoma. Rarely, in advanced disease TM rupture and otorrhea can present, but this is controversial given the diagnostic criteria for CC (Nelson et al. 2002; Richter and Lee 2009). CC can be as destructive as AC, and may result in conductive hearing loss (CHL) and bony destruction, and with mastoid obliteration and complications similar to AC.

Etiology/Origin

Four current theories exist as to the origin of congenital cholesteatoma. These include implantation, middle ear invagination, mucosal metaplasia, and epidermoid formation (Koltai et al. 2002; Kazahaya and Potsic 2004; Persaud et al. 2007; Richter and Lee 2009).

Implantation
Northrop et al. in 1986 described a theory of amniotic fluid implantation after examining 63 neonatal temporal bones. Given the high incidence of CC in the anterosuperior quadrant, Northrop et al. hypothesized that viable squamous epithelial cells migrated via the ET to the ME where they implanted in this quadrant (Koltai et al. 2002; Persaud et al. 2007). This theory has not received much support in subsequent years given the lack of evidence of the ability of the cells to implant in other tissues. This is further discounted by the fact that the remainder of the aerodigestive tract is bathed in similar cells without development of epidermoid lesions, and the potential volume or mass of migrated epithelial cells to the middle ear being significantly small. Hajioff et al. also point out that biological inhibition disallows one epithelial type cell to "invade" a different type (Persaud et al. 2007; Richter and Lee 2009).

Invagination
Ruedi et al. in 1959 described in utero and neonatal tympanic inflammation (otitis) leading to invagination of squamous epithelial cells into the ME (Koltai et al. 2002). Subsequently, Aimi in 1983 described the role of the tympanic ring as a barrier for migrating epithelial cells after examining four neonatal temporal bones. He postulated that a deficiency of this ring in certain locations provides a route for migration of squamous epithelial cells into the ME space. His theory is supported by findings on a 16.5-week human temporal bone. This can explain some cases that show CC in the posterior inferior quadrant but not the typical anterosuperior quadrant, and further research has not supported this theory (Koltai et al. 2002; Persaud et al. 2007).

Metaplasia
Sade et al. in 1983 described a theory that in utero and neonatal inflammation, similar to the theory of Ruedi

et al., caused squamous metaplasia. This was based on the finding of keratinizing and non-keratinizing metaplasia due to otitis media. The inconsistent location of metaplasia and the need for neonatal inflammation without definitive otitis fails to fully explain the typical nature of these lesions (Koltai et al. 2002).

Epidermoid Rests

Michaels in 1986 described a fourth and most plausible theory of epidermoid rest cells within the ME space. His theory was based on the finding of epidermoid rests (squamous epithelial cells) in embryonic specimens aged 10–33 weeks gestation, most often in the anterosuperior quadrant. These epidermoid rest cells generally involute and disappear by 33 weeks of gestation. The persistence of these cells in the ME was found by Karmody et al. and later Potsic et al. in several children aged 3½–7½ months (Karmody et al. 1998; Koltai et al. 2002; Kazahaya and Potsic 2004; Persaud et al. 2007; Richter and Lee 2009). Most recently, Liang et al. identified CK 14 positive cells consistent with squamous epithelia in the other three quadrants of the ME in 22 temporal bones aged 16 weeks GA to 8 months of age, further providing credence to this theory (Liang et al. 2003; Persaud et al. 2007).

Natural History

Most otologists have ascribed to the presence of epithelial rests retained in the middle ear (ME) space as the most likely theory and the natural progression of these lesions is quite predictable (Persaud et al. 2006, 2007; Richter and Lee 2009). Lesions that start in the anterosuperior quadrant (80% of the time) typically grow anteriorly, where they can block the ▶ eustachian tube and lead to ▶ otitis media with effusion (OME) (Koltai et al. 2002; Nelson et al. 2002; Richter and Lee 2009). The lesion then begins to grow inferiorly into the hypotympanum and stays as a well-encapsulated pearl. The lesions may then begin to grow posteriorly and superiorly passing inferiorly to the handle of the malleus toward the IS joint and into the anterior epitympanum. The lesion continues to grow posteriorly and superiorly usually sparing the footplate and it expands into the sinus tympani and fills the facial recess. Once the ME space is filled, growth advances toward the antrum and into the mastoid as is typical

for all cholesteatomas. As is the case for acquired lesions, expansion into other portions of the ME and mastoid leads to CHL and ossicular destruction (Koltai et al. 2002).

TM rupture as a consequence of CC is controversial. Theoretically these lesions can expand enough to cause rupture of the TM. This usually represents a late stage complication of disease when the mastoid and ME are completely filled with disease. In contrast, these events occur early in the disease process of acquired cholesteatoma, before the disease reaches the mastoid. Congenital cholesteatomas cause perforations in places other than the pars flaccida (typical location for acquired disease) (Koltai et al. 2002).

Classification/Staging

Disease severity largely depends on location of disease, age at the time of diagnosis, ossicular integrity, and number of sites involved. These factors have been borne out to have predictive value in probability of recidivism and recurrence, and they have been the basis of staging systems. These factors also can be used for predicting the need for imaging and for surgical planning (Potsic et al. 2002b; Richter and Lee 2009).

Roger et al., Grundfast et al., and Potsic et al. have all proposed staging systems that have variably been adopted. Potsic et al. in 2002 described a useful classification system based on 156 patients at a tertiary care facility.

- *Stage I disease is in a single quadrant without ossicular or mastoid involvement.*
- *Stage II disease is in multiple quadrants without ossicular or mastoid involvement.*
- *Stage III disease has ossicular involvement/erosion, regardless of quadrant, and without mastoid invasion.*
- *Stage IV disease is that which involves the mastoid cavity, regardless of ossicular integrity or quadrant of disease (Potsic et al. 2002b).*

The largest proportion of patients were categorized as stage I disease (39%) and stage IV (approximately 25%). The remainder of the patients were stage II (15%) and stage III (approximately 21%) (Potsic et al. 2002b).

Potsic et al. reported that the presence of residual disease varied from 13% for stage I disease to 67% of

stage IV disease following surgery (Potsic et al. 2002b). These findings of stage I disease are at the high end of the range for the predicted recurrence rate for early disease as reported in the literature (0–14%) (Koltai et al. 2002; Richter and Lee 2009). This appears to be due to the rate of posterior inferior and posterior superior disease within stage I, which typically portends slightly more difficult disease to treat than the typical anterior superior pearl. Koltai et al. classification system is similar and can predict the surgical approach needed for removal of disease, but again predicts more extensive involvement for lesions located in less favorable quadrants (Koltai et al. 2002).
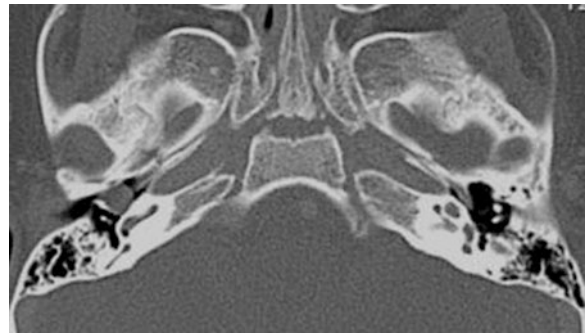
Cholesteatoma (Congenital), Fig. 1 Axial CT showing an early congenital cholesteatoma in the anterior mesotympanum (Courtesy of Dr. Koch, Cincinnati Children's Hospital)

Evaluation

A thorough ear examination and hearing evaluation are paramount to establishing the diagnosis. The history often alerts an examiner to secondary complications or presence of AC, including otorrhea, pain, hearing loss, etc. Often ▸ tympanometry is within normal range (A or As) owing to the lack of ME disease (Richter and Lee 2009). Hearing findings are variable, based on the disease location and severity. Nelson et al. described an average 12.5 dB air-bone gap (ABG) in patients with disease limited to the ME without posterior superior quadrant or attic involvement. An average 35.9 dB ABG was found in patients with posterior superior and/or attic involvement and a 47.7 dB ABG in patients with mastoid involvement (Nelson et al. 2002).

Age can be related to disease severity. In older patients (>6 years of age) ossicular erosion (incus and/or stapes) can be seen in up to 60%. Patients with ossicular erosion and mastoid invasion present at 5.6 years on average as opposed to those without who present at a much younger age (3.9 years) (Koltai et al. 2002).

Imaging

Stage I disease limited to the anterior superior quadrant whose full extent is seen by otoscopy typically does not require any further workup. Imaging is generally indicated if advanced disease (Stage III–IV) is present, if the full extent of disease cannot be seen by otoscopy,

or if complications (facial paresis, otorrhea, or other cranial nerve deficits) are present. Disease of the posterior quadrants, multiple quadrant involvement, and disease in older patients (>6 years of age) is more likely to result in mastoid invasion and ossicular erosion, and in these instances, imaging is more likely to be of benefit. A CT without contrast of the temporal bone is the test of choice, although MRI has had some applications in recurrent disease or complicated cases (Koltai et al. 2002; Nelson et al. 2002; Potsic et al. 2002b; Richter and Lee 2009) (Fig. 1).

Surgery

Regardless of stage, treatment involves surgical excision. The approach varies with location and severity of disease. As for any cholesteatoma surgery, the priorities are preventing complications, early and complete removal of the lesion, providing a safe and dry ear, preventing recurrence, and preserving/restoring hearing.

The major approaches are transcanal, canal wall up (CWU) ▸ mastoidectomy, or canal wall down (CWD) ▸ mastoidectomy. Other variations include extended tympanotomies with superiorly or inferiorly based flaps (Park et al.), atticotomies, sleeve tympanotomies, and transcanal antrotomies (Holt et al.). These more limited approaches are reserved for disease that can be fully accessed, with high probability of complete removal and without concern for mastoid involvement. The use of straight and angled endoscopes can largely improve visualization through these limited

approaches especially when disease extends into the attic (Koltai et al. 2002; Potsic et al. 2002a; Richter and Lee 2009).

The predictable progression of congenital cholesteatoma, as described previously, provides a virtual surgical road map for the surgeon. A standard transcanal approach can be utilized with uncomplicated, early disease that is restricted to a single quadrant, but this only account for 20–30% of congenital cases. Endaural approaches and post-auricular approaches to the canal can aid in visualization but these also are limited to disease restricted to the ME. The sleeve tympanotomy involves a complete tympanomeatal flap that remains attached to the umbo. This aids in access to the majority of the mesotympanum. Holt et al. describes the transcanal antrotomy for disease extending into the antrum without invasion of the mastoid cavity. This technically more challenging approach provides a minimally invasive approach to the attic without necessitating a mastoidectomy (Koltai et al. 2002; Potsic et al. 2002a; Richter and Lee 2009).

Stage I disease (no ossicular involvement) can often be treated with transcanal and extended tympanotomy approaches. Surgery for Stage II disease can often be treated similarly, but the presence of disease in the posterior quadrants is notoriously more difficult to treat. Transcanal antrotomy can be used to approach disease in posterior superior quadrant and antrum without mastoid invasion. Caution needs to be exercised with extension of disease into the sinus tympani and epitympanum, as transcanal approaches have limited access into these areas (Koltai et al. 2002; Potsic et al. 2002a; Richter and Lee 2009).

According to Nelson et al. and Potsic et al. transcanal and extended tympanotomy approaches for stage I–II disease (no ossicular involvement) resulted in a 0–14% recurrence rate. Stage III disease (ossicular without mastoid involvement) treated with extended tympanotomy plus possible scutum reduction or atticotomy showed a recurrence rate of 34–41% (Koltai et al. 2002; Nelson et al. 2002; Richter and Lee 2009). Stage IV disease (mastoid involvement) treated with tympanomastoidectomy (mostly CWU) showed a recurrence rate of 56–67% (Nelson et al. 2002; Potsic et al. 2002a; Richter and Lee 2009).

Canal wall up mastoidectomy (CWU) procedures are recommended for stage III–IV disease due to the high recurrence rate in these advanced diseased states. Ossicular erosion and mastoid involvement are correlated with a higher risk of recurrence (up to 67%). Mastoidectomy is recommended if there is involvement of greater than three subsites, presence of ossicular involvement, or extension into the antrum/mastoid (Koltai et al. 2002; Potsic et al. 2002a; Richter and Lee 2009).

CWD procedures are rarely needed unless markedly advanced disease is present or previous surgery has failed. Shirazi et al. published their surgical experience in 20 patients with congenital cholesteatoma. Average age of CWU was 4.5 years and for CWD procedures was 7 years of age, further illustrating the trend for more advanced disease in older patients. Only five of their patients required CWD procedures and these were limited to patients with failure of CWU, severe canal wall defects initially, labyrinthine fistula, poor health/compliance, sclerotic mastoid, and only hearing ear (Koltai et al. 2002; Shirazi et al. 2006; Richter and Lee 2009).

Second look procedures are rarely needed when early disease has been removed and when there is minimal or no ossicular involvement. Since these lesions are not due to chronic ear disease, and early eradication is feasible, in-office surveillance is often sufficient. Imaging or middle ear endoscopy may be useful when an increased risk of recurrence is suspected. Stage III–IV disease, due to the higher rate of recidivism, necessitates a second look procedure with possible ossicular reconstruction (OCR). Often once advanced disease is detected, a silastic sheet in the middle ear can facilitate reconstruction and aid in second look procedures. Surveillance for stage II disease is dependent on the extension of disease and on whether complete removal was achieved (Koltai et al. 2002; Shirazi et al. 2006; Richter and Lee 2009).

Conclusion

Congenital cholesteatomas are a rare entity accounting for only 4–24% of all pediatric cholesteatomas. They are of clinical importance as early detection and treatment can lead to excellent outcomes. The age of onset often predicts severity of disease, with children over the age of 6 years often portending more advanced disease. Although most lesions (80%) appear in the anterior superior quadrant, they can occur in any of

the three other quadrants. Posterior quadrant disease often predicts a more difficult entity to treat. Imaging is indicated if advanced disease (Stage III–IV) is present, if the full extent of disease cannot be seen by otoscopy, or if complications (facial paresis, otorrhea, or other cranial nerve deficits) are present. Imaging can be of benefit with posterior quadrant or multiple quadrant involvement and disease in older patients (>6 years of age). Surgery is the only intervention and is tailored to the extent and location of disease. Early single quadrant disease can often be treated with simple transcanal procedures. Extended tympanotomy procedures can preclude mastoidectomy if the full extent of disease can be accessed and removed. Canal wall up (CWU) mastoidectomy should be performed if greater than three subsites are involved, presence of ossicular involvement, or extension into the antrum/mastoid. Canal wall down (CWD) procedures are rarely needed and only indicated in failure of CWU procedures, severe canal wall defects initially, labyrinthine fistula, poor health/compliance, sclerotic mastoid, or only hearing ear. Outcomes are quite good in early disease but recurrence can approach 67% in advanced disease states (stage IV), often necessitating second look procedures.

References

Albino AP, Reed JA et al (1998) Increased numbers of mast cells in human middle ear cholesteatomas: implications for treatment. Am J Otol 19(3):266–272

Karmody CS, Byahatti SV et al (1998) The origin of congenital cholesteatoma. Am J Otol 19(3):292–297

Kazahaya K, Potsic WP (2004) Congenital cholesteatoma. Curr Opin Otolaryngol Head Neck Surg 12(5):398–403

Koltai PJ, Nelson M et al (2002) The natural history of congenital cholesteatoma. Arch Otolaryngol Head Neck Surg 128(7):804–809

Liang J, Michaels L et al (2003) Immunohistochemical characterization of the epidermoid formation in the middle ear. Laryngoscope 113(6):1007–1014

Nelson M, Roger G et al (2002) Congenital cholesteatoma: classification, management, and outcome. Arch Otolaryngol Head Neck Surg 128(7):810–814

Olszewska E, Wagner M et al (2004) Etiopathogenesis of cholesteatoma. Eur Arch Otorhinolaryngol 261(1):6–24

Persaud R, Liang J et al (2006) Epidermoid formation: the potential precursor of congenital cholesteatomas. Am J Otolaryngol 27(1):71–72, author reply 72

Persaud R, Hajioff D et al (2007) Evidence-based review of aetiopathogenic theories of congenital and acquired cholesteatoma. J Laryngol Otol 121(11):1013–1019

Potsic WP, Korman SB et al (2002a) Congenital cholesteatoma: 20 years' experience at The Children's Hospital of Philadelphia. Otolaryngol Head Neck Surg 126(4):409–414

Potsic WP, Samadi DS et al (2002b) A staging system for congenital cholesteatoma. Arch Otolaryngol Head Neck Surg 128(9):1009–1012

Richter GT, Lee KH (2009) Contemporary assessment and management of congenital cholesteatoma. Curr Opin Otolaryngol Head Neck Surg 17(5):339–345

Shirazi MA, Muzaffar K et al (2006) Surgical treatment of pediatric cholesteatomas. Laryngoscope 116(9):1603–1607

Cholesteatoma (Primary)

▶ Lateral Skull Base Epidermoids

Cholesteatoma of Childhood

C. Y. Joseph Chang
Texas Ear Center and Department of Otorhinolaryngology, University of Texas – Houston Medical School, Houston, TX, USA

Synonyms

Epidermoid

Definition

Cholesteatoma is defined as the presence of squamous epithelial tissue in the middle ear and/or mastoid associated with chronic inflammation. The most common type of cholesteatoma arises from the tympanic membrane and is called an acquired cholesteatoma. The congenital type is very rare.

The acquired form is classified as follows:

1. Primary acquired – The cholesteatoma results from a retraction of the tympanic membrane.
2. Secondary acquired – The cholesteatoma results from implantation of epithelial tissue into the middle ear or mastoid as a result of surgery or from migration of epithelial tissue from a tympanic membrane perforation.

The congenital type is defined as a middle ear cholesteatoma that occurs in a patient with no previous history of tympanic membrane perforation, ventilation tube placement, or other ear surgeries.

Etiology

The exact etiology of the primary acquired cholesteatoma is not fully understood, but there are various factors that may contribute to its formation:

1. Eustachian tube dysfunction
2. Recurrent or chronic otitis media

Primary acquired cholesteatoma can arise from the pars tensa or pars flaccida portions of the tympanic membrane. The pars tensa type may initially form as a result of eustachian tube dysfunction, starting as a retraction of the tympanic membrane. It is not clear why most of these retractions remain stable while a few develop into cholesteatoma. It is known that middle ear ventilation with placement of a ventilation tube will stabilize or reverse pars tensa retractions (Chang 2008). However, pars flaccida retractions do not appear to respond similarly to middle ear ventilation, indicating that factors other than middle ear pressure abnormalities are at play in the formation of these types of cholesteatoma. It is also clear that presence of chronic or recurrent otitis media predisposes patients to cholesteatoma formation, although it is not known why only a very few of the patients with this history eventually develop cholesteatoma. Following the formation of a tympanic membrane retraction of any type, the normal skin migratory pattern that moves debris out of the ear canal is disrupted, resulting in retention of squamous epithelial debris within the cholesteatoma. The debris typically becomes infected resulting in chronic inflammation which in turn induces changes in the surrounding bone to increase osteoclastic activity with subsequent bone resorption. The bacteria that are usually found in these cases are the same ones found in otitis externa and chronic suppurative otitis media and are often due to multiple organisms:

1. Pseudomonas aeruginosa
2. Streptococci
3. Staphylococci
4. Proteus
5. Enterobacter
6. Anaerobes
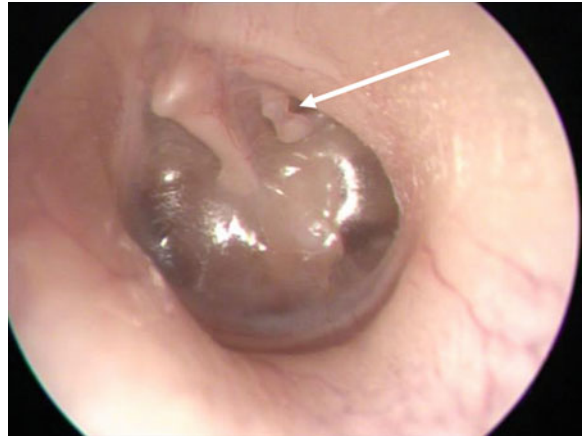
Cholesteatoma of Childhood, Fig. 1 Left tympanic membrane with pars tensa retraction with incus erosion (*white arrow*)

The congenital cholesteatoma has traditionally been thought to arise from a congenital rest of epithelial cells on the anterior promontory called the epithelioid formation which typically involutes but in rare cases remains and forms a congenital cholesteatoma (Meyer et al. 2006). A more recent theory promotes the idea of micro-retractions of the tympanic membrane that form the middle ear cholesteatoma and heal spontaneously, leaving an intact tympanic membrane (Tos 2000).

Clinical Presentation

The acquired form of the cholesteatoma initially causes a retraction of the tympanic membrane which may remain asymptomatic. As the disease progresses, there may be chronic infection and bone erosion which can lead to symptoms of otorrhea and hearing loss. Bone resorption typically affects the ossicles, ear canal, and mastoid bone (Fig. 1) (Chang 2009). Labyrinthine erosion is not as common possibly due to the intrinsic hardness of otic capsule bone. In rare advanced cases, it is possible for cholesteatoma to result in facial nerve injury or severe infectious complications such as epidural, subdural, or intraparenchymal brain abscess, meningitis, or sigmoid sinus thrombosis.

The patients with the acquired form of cholesteatoma may have a history of recurrent childhood otitis media. The primary acquired cholesteatoma typically presents with hearing loss and otorrhea,

Cholesteatoma of Childhood, Fig. 2 (**a**) Left tympanic membrane with primary acquired cholesteatoma of the pars flaccida (*white arrow*). (**b**) Right tympanic membrane with pars tensa perforation and secondary acquired cholesteatoma (*white arrow*). (**c**) Left tympanic membrane with congenital cholesteatoma (*white arrow*)
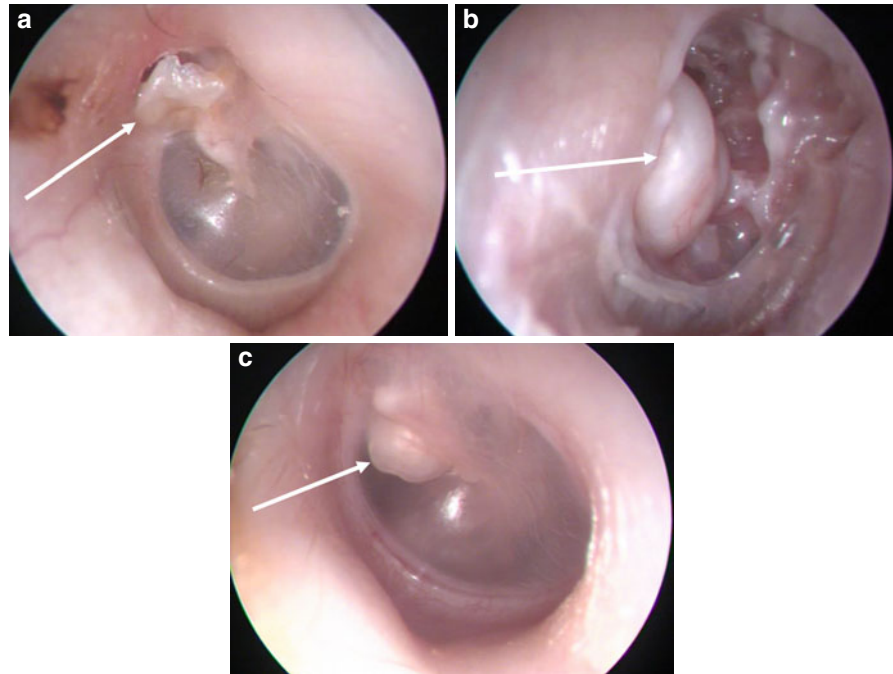
although a few patients are asymptomatic and the cholesteatoma is discovered on ear examination. Tinnitus is also common and is related to the hearing loss. Otalgia is unusual in this condition unless the patient has developed a secondary cervical myalgia or temporomandibular joint inflammation. It is typical for the otorrhea to subside with medical treatment only to continue to recur over time, although in some cases, the otorrhea may not subside with medical treatment alone. Dizziness can occur in a small number of cases and is thought to be related to a reactive inner ear inflammation due to the middle ear inflammation. In rare cases, a labyrinthine fistula, most commonly at the horizontal semicircular canal, may occur and cause dizziness.

The secondary acquired cholesteatoma may present with a tympanic membrane perforation with implantation cholesteatoma pearl or debris in the middle ear that is easily visible. In other cases, the tympanic membrane may be intact and the cholesteatoma may be more difficult to visualize. If the tympanic membrane is intact, otorrhea resulting from cholesteatoma will not occur and the patient may remain asymptomatic until the lesion causes disruption of the ossicular function with resultant hearing loss. The congenital cholesteatoma will have a similar presentation, remaining asymptomatic until a hearing loss occurs.
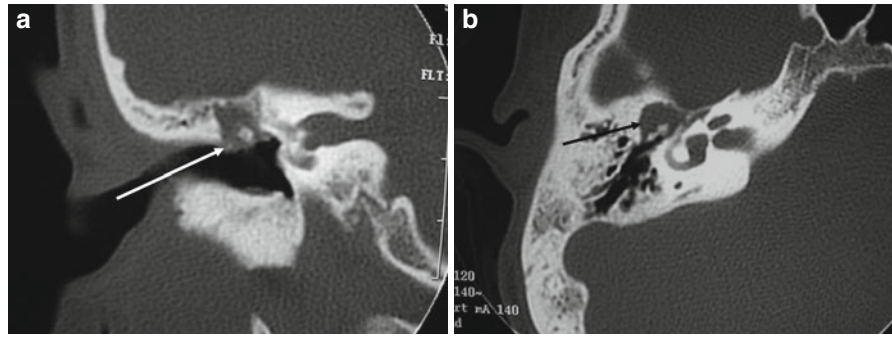
Diagnosis

The diagnosis of cholesteatoma is made based on microscopic evaluation of the ear canal and tympanic membrane. Most cases of acquired cholesteatoma can be diagnosed in this manner (Fig. 2a). The congenital and secondary acquired cholesteatoma with intact tympanic membrane may be more difficult to diagnose with visual inspection unless the tympanic membrane is adequately translucent (Fig. 2b, c). In some cases, there will be an unexplained conductive hearing loss that will require an imaging study for workup. Most patients undergo an audiogram to determine their hearing function. Younger or less cooperative patients may require auditory brainstem response (ABR) to obtain hearing thresholds.

The most useful imaging study for evaluation is computed tomography (CT) of the temporal bone, typically obtained in bone window with imaging thickness of 1–1.5 mm (Fig. 3a, b). The CT is very good at determining the anatomy of the temporal bone; presence of any bone erosion including ossicles, ear canal, mastoid, and tegmen; and presence of soft tissue abnormalities. The main limitation of the CT is that it cannot differentiate between cholesteatoma and noncholesteatoma tissues such as mucus or pus. It can be used to augment diagnosis with supportive findings,

Cholesteatoma of Childhood, Fig. 3 (**a**) Coronal CT scan of the temporal bone showing attic cholesteatoma with scutum erosion (*white arrow*). (**b**) Axial CT scan of the temporal bone showing attic cholesteatoma (*black arrow*)

but CT cannot be used alone to arrive at a definitive diagnosis. The CT may also be useful in surgical planning as it can show the mastoid and tegmen anatomy, and alert the surgeon to the presence of labyrinthine fistula or petrous apex disease (Chang 2008).

In general, magnetic resonance imaging (MRI) has not been as helpful as CT for cholesteatoma diagnosis. MRI does not show the bony anatomy well. It is superior to CT in differentiating between tissue types, but MRI's usefulness in cholesteatoma cases relates to the small dimensions of the ear and the similar signal characteristics of cholesteatoma and fluid. The MRI is very useful if a neoplasm of the ear is suspected. There are studies being done currently to see if diffusion-weighted MRI techniques may be more successful in detecting cholesteatoma (Ganaha et al. 2011).

Differential Diagnosis

For cases of chronic otorrhea, the diagnostic considerations include:
1. Otitis externa
2. Chronic suppurative otitis media
3. Chronic myringitis
4. Malignant otitis externa (skull base osteomyelitis)
5. Neoplasm of the ear
6. Cerebrospinal fluid otorrhea
   For cases of conductive hearing loss with intact tympanic membrane:
1. Ossicular chain dysfunction due to tympanosclerosis, erosion, or trauma
2. Otosclerosis
3. Superior semicircular canal dehiscence syndrome

Prophylaxis

The risk of secondary acquired cholesteatoma formation can be minimized by surgical technique. The surgeon should take care not to leave any squamous epithelial tissues in the middle ear or mastoid during ear surgery.

The risk of primary acquired cholesteatoma formation may be reduced by aggressively treating childhood otitis. This inference is made based on the significant decrease in incidence of cholesteatoma after the development of antibiotics in the developed world, and the much higher incidence of cholesteatoma currently in the developing world. Pars tensa atelectasis can be stabilized or reversed prior to cholesteatoma formation with ventilation tube placement (Chole et al. 2006). Pars flaccida retractions cannot be reversed with middle ear ventilation.

Once a cholesteatoma has formed, efforts to stabilize it include medical treatment to reduce the infection and inflammation as well as debridement of the cholesteatoma debris in the office setting.

Therapy

The treatment options consist of medical and surgical interventions. Medical treatment includes efforts to reduce the inflammatory and infectious components of the disease:
1. Keep water out of the ear with earplugs during water exposure.
2. Remove the collected debris in the middle ear and ear canal regularly.

3. Apply ototopical drops – quinolones, aminoglycosides. (Aminoglycosides cause no ototoxicity if there is no perforation of the tympanic membrane. Ototoxicity is possible if there is a perforation.)

The medical treatment may help stabilize the disease process but in many cases cannot eliminate the slowly destructive process associated with cholesteatoma, and definitely cannot cure the disease. The most effective treatment is to remove the cholesteatoma surgically and reduce the chance of recurrent disease. The decision for proceeding with surgical treatment is based on severity of the disease and patient risk factors for anesthesia and other risk factors. The surgery can be performed in an outpatient setting in most cases. The basic surgery types include:

1. Tympanoplasty
2. Atticotomy
3. Mastoidectomy – canal wall-up or canal wall-down mastoidectomy

A combination of these approaches is typically needed for adequate treatment. The decision regarding choice of surgical approach is complex and is determined by the surgeon's experience and training, and also the extent of the disease. The anatomic extent of the disease often determines the exact approach based on the surgeon's judgment. In many cases, the tympanoplasty is combined with mastoidectomy for the chosen approach (Chole et al. 2006). All the cholesteatoma must either be removed or exteriorized, meaning that the retracted squamous epithelium is incorporated into the reconstructed tympanic membrane. The ossicular chain is often dysfunctional or parts of it may need to be removed due to cholesteatoma involvement, so an ossicular chain reconstruction may be needed (Luetje 2006).

The canal wall-up mastoidectomy preserves the bony ear canal and leads to a more normal-appearing ear canal after surgery. However, the surgical exposure is often obscured by the presence of the ear canal which could compromise the cholesteatoma surgery. Because of the limited exposure, there is a higher risk of leaving behind cholesteatoma, depending on the skills of the surgeon. This type of surgery is most feasible in patients with a well-developed and non-contracted mastoid.

In many cases of cholesteatoma, the mastoid has poor development with few air cells present, low tegmen, and anterior sigmoid sinus, which makes the mastoid exposure very limited and makes the canal wall-up procedure very difficult or impossible for adequate cholesteatoma resection. The canal wall-down procedure can provide much improved surgical access to the cholesteatoma. It may also reduce the risk of recurrent pars flaccida cholesteatoma as the surgical procedure exteriorizes the attic and antrum where these cholesteatomas typically extend. However, the canal wall-down procedure results in a mastoid cavity, which is larger than a typical ear canal and is more prone to debris collection, requiring regular mastoid cavity cleaning, and infection with recurrent otorrhea. There are also opinions that indicate that the hearing results may not be as good with the canal wall-down procedure but this remains controversial (Chang 2008).

The possible risks of surgery include cholesteatoma recurrence, tympanic membrane perforation, hearing loss, dizziness, taste dysfunction related to chorda tympani manipulation, facial nerve injury, and cerebrospinal fluid leak.

Prognosis

There are several issues related to prognosis:
1. Cholesteatoma recurrence
2. Hearing results
3. Recurrent otorrhea

Cholesteatoma recurrence continues to be a significant concern despite surgery performed by the most skilled surgeons. There are few long-term follow-up studies but the little data that exist and anecdotal experience of surgeons indicates that the 5–10-year recurrence rate may be 30–40% (Lau and Tos 1987). This overall recurrence figure includes both new formation of cholesteatoma (recurrent disease) and residual cholesteatoma resulting from incomplete removal (recidivistic disease). Cholesteatoma found after initial surgery typically requires revision surgery.

The recurrence rate appears to be higher with the canal wall-up technique, although this is likely highly dependent on individual surgeons. Many surgeons perform a planned second stage surgery at 6–12 months after the initial surgery to check for any residual cholesteatoma and to perform the ossicular chain

reconstruction if needed. Some surgeons do not perform a routine second stage surgery but instead may rely on imaging such as CT to check for residual cholesteatoma, although this technology is still somewhat limited for this purpose due to its inability to differentiate between cholesteatoma and noncholesteatoma tissues. If the diffusion-weighted MRI technique is validated in the future, it holds promise as another tool to diagnose recidivistic disease (Ganaha et al. 2011).

The hearing results are quite variable based on various issues that are not typically under the surgeon's control. Factors that can lead to poor prognosis include:

1. Lack of stapes superstructure
2. Severe middle ear mucosal disease
3. Chronic eustachian tube dysfunction

The hearing results do not appear to be affected significantly by the type of implants used at the present time (Gelfand and Chang 2011). Hearing results can be negatively affected by implant extrusion, but this risk can be decreased with the use of cartilage grafting over the prosthesis to protect the tympanic membrane.

Recurrent otorrhea can occur as a result of tympanic membrane perforation, recurrent cholesteatoma, and mastoid cavity issues. Mastoid cavity issues include the following:

1. Poor anatomy including high facial ridge, large mastoid cavity size, irregular bony ledges
2. Tissue abnormalities such as exposed mucosa or myringitis
3. Inadequate size of the meatoplasty
4. Inadequate frequency or extent of mastoid debridement in the office after surgery

Most cases of recurrent mastoid cavity otorrhea can be treated medically, but revision surgery is needed in some cases.

Epidemiology

The incidence of acquired cholesteatoma in the developed world is low, with an estimated annual incidence of 9.2 cases per 100,000 inhabitants based on a Finnish study (Kemppainen et al. 1999). However, in the developing world, the incidence may be higher based on the higher incidence of chronic suppurative otitis media (Verma et al. 1995). Patients with a previous history of recurrent childhood otitis media appear to be at risk of developing acquired cholesteatoma.

Cross-References

▶ Acute Otitis Media
▶ Canal Wall Down Mastoidectomy
▶ Canal Wall Up Mastoidectomy
▶ Cartilage Tympanoplasty
▶ Chronic Otitis Media
▶ Congenital Conductive Hearing Loss
▶ Facial Nerve Imaging, CT and MRI
▶ Facial Nerve
▶ Meningitis
▶ Ossicular Chain Reconstruction

References

Chang CYJ (2008) Cholesteatoma. In: Lalwani AK (ed) Current diagnosis & treatment in otolaryngology – head & neck surgery, 2nd edn. McGraw-Hill, New York, pp 666–672

Chang CYJ (2009) Chronic disorders of the middle ear. In: Mitchell R (ed) Pediatric otolaryngology for the clinician, 1st edn. The Humana Press, New York

Chole RA et al (2006) Surgery of the mastoid and petrosa. In: Bailey BJ (ed) Head and neck surgery – otolaryngology, 4th edn. Lippincott Williams & Wilkins, Philadelphia, pp 2093–2111

Ganaha A et al (2011) Efficacy of diffusion-weighted magnetic resonance imaging in the diagnosis of middle ear cholesteatoma. Auris Nasus Larynx 38:329

Gelfand YM, Chang CYJ (2011) Ossicular chain reconstruction utilizing titanium vs. hydroxyapatite implants. Otolaryngol Head Neck Surg 144:954

Kemppainen HO et al (1999) Epidemiology and aetiology of middle ear cholesteatoma. Acta Otolaryngol 119:568–572

Lau T, Tos M (1987) Cholesteatoma in children: recurrence related to observation period. Am J Otolaryngol 8:364–375

Luetje CM (2006) Reconstruction of the tympanic membrane and ossicular chain. In: Bailey BJ (ed) Head and neck surgery – otolaryngology, 4th edn. Lippincott Williams & Wilkins, Philadelphia, pp 2113–2123

Meyer TA et al (2006) Cholesteatoma. In: Bailey BJ (ed) Head and neck surgery – otolaryngology, 4th edn. Lippincott Williams & Wilkins, Philadelphia, pp 2081–2092

Tos M (2000) A new pathogenesis of mesotympanic (congenital) cholesteatoma. Laryngoscope 10:1890

Verma AK et al (1995) Epidemiology of chronic suppurative otitis media and deafness in a rural area and developing an intervention strategy. Indian J Pediatr 62:725–729

Cholesteatoma, Acquired

Matthew Sitton and David R. Friedland
Department of Otolaryngology and Communication
Sciences, Division of Otology and Neuro-otologic
Skull Base Surgery, Medical College of Wisconsin,
Milwaukee, WI, USA

Synonyms

Epidermoid; Epidermoid cyst; Keratoma

Definition

Aural Cholesteatoma: Keratinizing squamous epithelial growth of the middle ear or mastoid.

Introduction

"Cholesteatoma" is a misnomer, as these growths are not made up of cholesterin or fat (i.e., steat-) as originally thought when first named. Cholesteatoma is made up of well-differentiated hyperkeratinizing squamous epithelium surrounding a paucicellular matrix.

Growth of cholesteatoma and associated bone destruction can lead to hearing loss, facial paralysis, and dizziness. Cholesteatoma often becomes infected, typically with *Pseudomonas aeruginosa*, leading to chronic suppurative otitis media (CSOM). Infection may lead to complications such as acute and chronic mastoiditis, bacterial labyrinthitis, sigmoid sinus thrombophlebitis, meningitis, and brain abscess.

Cholesteatoma is broadly classified as congenital or acquired (See ▶ Cholesteatoma (Congenital)). Aquired cholesteatoma may be further classified as primary or secondary. Primary acquired cholesteatoma arise from a retraction pocket, typically in the pars flaccida or the posterior-superior aspect of the pars tensa. Secondary acquired cholesteatoma arises in the setting of a history of tympanic membrane (TM) perforation or pressure equalization tube placement. Cholesteatoma can also be classified by their location. Attic cholesteatoma begins at the pars flaccida and usually spreads to the aditus or mastoid. Sinus cholesteatoma arise from posterior superior retractions or perforation of the pars tensa. Tensa cholesteatoma arise from retraction of the entire pars tensa. For a detailed review of cholesteatoma pathogenesis (see Olszewska et al. 2004).

Epidemiology

Cholesteatoma has an annual incidence of 3–13 cases per 100,000 patients (Tos 1988; Kemppainen et al. 1999; Homoe 2001). Cholesteatoma is more common in males than females. Caucasians have the highest incidence and cholesteatoma is rarely seen in Asians. Despite Inuit populations having a high predilection for COM, there is a relatively low prevalence of cholesteatoma among that population (Homoe and Bretlau 1994). In susceptible populations, however, COM is frequently associated with cholesteatoma (Sade and Halevy 1976; da Costa et al. 1992).

Clinical Presentation

Cholesteatoma typically presents with a history of chronic otorrhea or progressive conductive hearing loss (CHL). Patients may also more rarely present with complaints of vertigo from erosion of the labyrinth or facial paralysis (Gersdorff et al. 2000; Magliulo 2007; Siddiq et al. 2007). The severity of the CHL is often reflective of the middle ear structures involved. A mild loss may be seen for a small tympanic membrane perforation while a maximal loss may be noted in ossicular discontinuity with a posterior TM perforation over the round window membrane. The clinician must be cautious, however, as a mild CHL may be seen after cholesteatoma has eroded through the ossicular chain but bridged the ossicles so that sound is transmitted through the cholesteatoma or granulation tissue.

On otoscopy or otomicroscopy, cholesteatoma typically appears as a pearly white mass. Granulation tissue or polyps may be seen from inflammation around the cholesteatoma and eroded bone. This reactive tissue may obscure a view of the cholesteatoma but suspicion must be high, especially if such tissue appears in the posterior-superior quadrant. Numerous schemes have been developed to classify acquired cholesteatoma (Olszewska et al. 2004). The primary type is commonly considered a limited retraction at the

pars flaccida while secondary acquired cholesteatoma represents a posterior-superior perforation or extension of disease into the antrum and attic. Alternative schemes have described attic, sinus, and tensa cholesteatoma. Occurrence and extension relative to the labyrinth has also been proposed. Saleh and Mills have proposed a staging system describing the start and progression of cholesteatoma (Saleh and Mills 1999). This scheme is helpful in identifying structures that may be involved as it uses categories of: attic and antrum, middle ear, mastoid, Eustachian tube, labyrinth, and middle fossa.

Etiology

The etiology of cholesteatoma is unclear. The manner in which squamous tissue enters the middle ear and leads to non-neoplastic squamous epithelial hyperproliferation is not completely understood.

Five theories have been proposed to explain the introduction of squamous epithelium into the middle ear: (1) tympanic membrane invagination/retraction, (2) basal hyperplasia, (3) migration through a tympanic membrane perforation, (4) squamous metaplasia, and (5) implantation of squamous tissue. For a review see Olszewska et al. 2004. These theories are all likely potential mechanisms of cholesteatoma formation. The basic tenets of these theories are:

1. Negative pressure and/or inflammation can result in invagination or retraction of the tympanic membrane. This retraction pocket typically forms in the pars flaccida because it contains less fibrous tissue and is less resistant to displacement. The negative pressure is created by Eustachian tube dysfunction, inflammation, tympanic membrane atrophy, and/or poor mastoid pneumatization. As the pocket deepens, desquamated debris is unable to migrate out and accumulates leading to the formation of a cholesteatoma. The resultant cholesteatoma progressively enlarges into the middle ear and mastoid spaces.

2. The basal hyperplasia theory has been proffered to explain the formation of cholesteatoma behind a seemingly intact tympanic membrane (Chole and Tinling 1985). Disruption of the basement membrane, either spontaneously or through infection or inflammation, allows epithelial cells from the lateral surface of the tympanic membrane to migrate through these gaps and enter the subepithelium. Once in the subepithelial layer, these cells continue to proliferate causing microcholesteatoma and inclusion cysts which may progress to middle ear cholesteatoma.

3. Over a century ago, some of the greats of otology (e.g., Politzer, Bezold) suggested that epithelial migration into the middle ear from the lateral surface of tympanic membrane perforations could lead to cholesteatoma. This theory has been supported by animal studies.

4. One of the earliest theories regarding cholesteatoma formation is that it arises directly from middle ear mucosa. The metaplasia theory holds that middle ear mucosa, which is simple squamous and cuboidal epithelium, transforms to keratinizing squamous epithelium due to chronic inflammation.

5. Implantation of squamous epithelium into the middle ear space may be caused either iatrogenically or traumatically. Iatrogenic causes include surgeries for otologic conditions other than cholesteatoma such as tympanoplasty or pressure equalization tube placement. Trauma would include pressure-induced ruptures and direct accidental perforations of the tympanic membrane. In these cases, there is likely influence of other theories of cholesteatoma formation such as migration. The prevalence of cholesteatoma following tympanostomy tube placement is less than 1% but can be as high as 5% in those requiring multiple tubes (Spilsbury et al. 2010).

The epithelial cells that make up cholesteatoma are hyperproliferative but not dysplastic or neoplastic. Cholesteatoma is not considered a neoplastic process as no DNA abnormalities have been identified. Increased proliferation of epithelial cells in cholesteatoma has been linked to internal changes and external stimuli.

- Involucrin is a precursor to the cornified envelope found in the upper layers of normal skin. In cholesteatoma, involucrin has been found in all suprabasal layers resulting in higher accumulation of keratin within a larger portion of the epidermis (Stammberger et al. 1995; Huisman et al. 2006).

- There are alterations in the expression of genes related to signal transduction, cell cycle, apoptosis, and immune responses in cholesteatoma as compared to normal skin (Kwon et al. 2006).

- Upregulation of hsa-mir-21, a microRNA, with downregulation of tumor suppressor proteins, PTEN and PDCD4, has been shown in cholesteatoma (Friedland et al. 2009). Such RNA-based regulators may play a role in keratinocyte proliferation, migration, and invasion.
- Presence of chronic inflammation with or without infection recruits fibroblasts, Langerhans cells, mast cells, activated lymphocytes, macrophages, and keratinocytes to produce proinflammatory cytokines. Such cytokines have been found to stimulate basal keratinocyte proliferation. Biofilms have been demonstrated with cholesteatoma and may play a role in producing chronic inflammation (Chole and Faddis 2002).

Diagnostic Testing

Cholesteatoma is a clinical diagnosis made by physical examination and direct observation of the tympanic membrane and middle ear. A visible middle ear or retraction pocket mass, typically with a pearly white covering, is characteristic of cholesteatoma. If it is extensive and fills the middle ear space it may appear as a uniformly opaque tympanic membrane. Pneumatic otoscopy may help to delineate the cholesteatoma mass. Infection can obscure visualization of the mass. Friable granulation tissue is highly suggestive of chronic infection and underlying cholesteatoma. A large aural polyp may also suggest cholesteatoma. Treatment of granulation tissue, polyps, and acute infection with follow-up direct examination is necessary.

Additional elements of physical examination would be palpation and observation of the mastoid region. Tenderness, erythema, or edema may indicate underlying disease. Tuning fork examination consisting of the Weber and Rinne tests can identify a conductive hearing loss associated with restricted tympanic membrane or ossicular vibration, or of ossicular erosion. As noted earlier, cholesteatoma may bridge a gap in the ossicular chain and provide better conductive hearing than the anatomy would otherwise allow. Similarly, a patient with a history of cholesteatoma resection and postoperative conductive hearing loss who presents with an improvement in hearing should be carefully assessed for recurrent cholesteatoma.

Examination for complications of chronic otitis media and cholesteatoma is important. Even if the examination is normal, it establishes a baseline for assessment of disease progression or surgical complication. A fistula test can determine the presence of a labyrinthine fistula. Facial nerve assessment can suggest involvement in any location along the facial nerve course. Sensorineural hearing loss may suggest otic capsule erosion. Additional cranial nerve deficits may suggest intracranial or petrous apex extension or the development of intracranial complications such as sigmoid sinus thrombophlebitis, meningitis, or abscess.

An audiogram should be performed in order to detect and quantify any conductive or sensorineural hearing loss. The level of hearing loss in the affected and contralateral ear may help direct surgical considerations regarding the extent of dissection and is critical to informed consent.

Computed tomography (CT) is commonly performed in cholesteatoma assessment but is secondary to the physical examination in determining the presence of cholesteatoma. On CT, cholesteatoma appears smooth and with sharp margins that do not enhance with IV contrast. If there is surrounding inflammation or fluid, the margins of the cholesteatoma will be obscured. CT is useful for surgical planning and, in revision cases, delineating altered anatomy and recurrent disease.

Magnetic resonance imaging (MRI) is not commonly used in the primary assessment of cholesteatoma. It can be helpful in cases in which intracranial complications are suspected. On MRI, cholesteatomas (epidermoids) have low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Recently, MRI diffusion-weighted imaging has been used for assessment of recurrence of cholesteatoma (Flook et al. 2011; Khemani et al. 2011).

Complications

Recurrent infections and direct growth of cholesteatoma lead to the otologic complications seen with this disorder. Cholesteatoma causes ossicular chain destruction, erosion of the otic capsule, exposure of the facial nerve, and infection of the mastoid and intracranial spaces.

Cholesteatoma causes bone destruction by mechanical pressure, enzymatic-mediated bone resorption,

and chronic infections. Bone is a dynamic organ with osteoblasts being responsible for formation of new bone and osteoclasts responsible for turnover of bone. Receptor activator of nuclear factor KB ligand (RANKL) is a cytokine that stimulates osteoclastic activity. Osteroprotegrin (OPG) is a competitive receptor that inhibits the production of RANKL. Cholesteatoma tissue has been shown to have an increased RANKL/OPG ratio, which may thus promote bone resorption (Jeong et al. 2006). Lipopolysaccharide (LPS) is an antigenic component in Gram-negative bacterial cell walls known to induce RANKL. LPS is found in increased concentrations in samples from patients with otorrhea and bone resorption secondary to cholesteatoma (Peek et al. 2003). Inflammatory cytokines, specifically interleukin (IL)-1, IL-6, tumor necrosis factor (TNF) α, and prostaglandins are upregulated in cholesteatoma. These inflammatory cytokines promote osteoclastogenesis by either direct or indirect action on osteoclasts. Infected cholesteatoma are known to act more aggressively and erode bone more quickly.

Bone erosion can result in hearing loss, which is typically conductive and a result of ossicular chain destruction. The incus is the ossicle most commonly affected. The degree of hearing loss with ossicular chain disruption can range from a maximal loss of 60–70 dB with complete ossicular chain disruption to as little as 20 dB if a natural myringostapediopexy has developed. Some surgeons perform a primary ossicular chain reconstruction (OCR) at the initial resection of cholesteatoma but most elect to place a prosthesis at the time of second look surgery 6–18 months after initial resection.

Bone erosion may also involve the otic capsule causing a labyrinthine fistula. Erosion of the otic capsule is most commonly seen at the lateral semicircular canal (SCC) but may occur into the cochlea. Labyrinthine fistulas may be found in over 10% of patients with long-standing cholesteatoma (Quaranta et al. 2009). Erosion of the otic capsule leads to vertigo or SNHL either through damage of hair cells or the effects of labyrinthitis. Options for repair of labyrinthine fistulas and management of the matrix of cholesteatoma overlying the fistula varies according to the size of the fistula, hearing status of the ipsilateral and contralateral ears, infection status, and the surgeon's preference. Leaving the matrix over the fistula

and performing a canal wall down mastoidectomy puts the least risk on hearing status of the ear at the time of surgery and allows the remnant of cholesteatoma to be monitored. Another option for a small fistula of the SCC with normal hearing on the contralateral ear would be to perform a canal wall intact mastoidectomy, remove the matrix, and repair the fistula with fascia. This allows complete removal of the cholesteatoma and repair of defect, but puts the hearing at some risk. Care should always be taken to avoid suctioning around the fistula site. If an iatrogenic fistula is created, it should be immediately covered with fascia. A fistula may make the patient sensitive to airflow leading to vertigo and dizziness. This is most apparent when using suction to clean a mastoid cavity but is reported by patients when going outside in the cold or on a windy day.

Facial nerve paralysis may occur acutely through infection or progressively by expansion and pressure from cholesteatoma. Acute facial paralysis in an ear with cholesteatoma should prompt urgent surgical management. Imaging with either CT or MRI can be useful to determine the location of compression or involvement. Horizontal and vertical segments of the facial nerve may be exposed through a mastoidectomy and facial recess approach while the petrous apex requires a middle cranial fossa approach. Cholesteatoma should be removed and the nerve decompressed. Postoperative IV antibiotics and high-dose steroids may be used to attempt to decrease inflammation and infection. Even in the absence of preoperative facial symptoms, a dehiscent facial nerve may be identified during cholesteatoma surgery in approximately 30% of cases (Wang et al. 2006). As such, facial nerve monitoring is commonly used in these cases. Postoperative assessment of facial nerve function should be performed in all cases and steroids and reexploration considered with unexpected facial paralysis or weakness.

Erosion of the tegmen tympani or tegmen mastoidea can lead to meningitis, CSF leak, or brain herniation. Dehiscence can also be seen following previous mastoid surgeries and may reflect iatrogenic injury, bone resorption, or progression of cholesteatoma and infection. Tegmen dehiscences can be seen in up to 16% of cholesteatoma cases (Wang et al. 2006). If the defect is small and the dura is intact no intervention is needed. If there is a dural

defect, the dura is elevated circumfentially around the defect to create a pocket between dura and tegmen to place a graft. Fascia, typically temporalis fascia, larger than the defect, is inserted into the defect to lie between the dura internally and tegmen externally. For larger defects that need more support, bone chips or conchal cartilage can be used to lie between the fascia graft and tegmen. In cases with encephaloceles, the encephalocele is removed or reduced with bipolar cautery and the defect is repaired similarly. In cases of large encephaloceles or dural exposures, a craniotomy may be required to repair the defect from the middle fossa.

Recurrent and chronic otitis media is common with cholesteatoma and can lead to serious infections, such as subperiosteal abscess, lateral sinus thrombophlebitis, meningitis, and intracranial abscess. Infectious complications of cholesteatoma are often caused by the obstruction of normal drainage pathways, typically at the antrum leading to trapped infection within the mastoid. Subperiosteal abscess presents as an inflamed, fluctuant postauricular mass. Lateral sinus thrombophlebitis classically presents with a history of high spiking fevers in a "picket fence" pattern. Mental status changes or neurologic deficits should prompt investigation into intracranial involvement such as brain abscess or meningitis. Surgical management is essential in cases of complicated otitis media and mastoiditis. Options include urgent widefield myringotomy, tympanostomy tube placement, and mastoidectomy. Removal of all cholesteatoma in the acutely inflamed ear may be difficult and a staged procedure may be necessary after drainage of the ear and antibiotics have been established.

Treatment

Cholesteatoma is a surgical disease. In some cases, given medical concerns, close observation may be warranted but, in general, cholesteatoma needs to be surgically excised. Many surgical options and approaches exist based upon the nature and extent of the disease. These range from simple tympanoplasty to radical mastoidectomy. Cholesteatoma limited to the attic and lateral to the head of the malleus and body of the incus may be dealt with through an atticotomy approach with reconstruction of the scutal defect.

Cholesteatoma extending into the antrum and mastoid and those extending medial to the head of the malleus may require a complete mastoidectomy with/without a facial recess approach so that the cholesteatoma can be removed in its entirety. The goal of all cholesteatoma surgery is complete excision and removal of disease. The surgeon may perform a "2nd look operation" 6–18 months following initial mastoidectomy to identify an early recurrence of cholesteatoma and to perform an ossicular chain reconstruction. As noted above, MRI scanning is becoming increasingly popular as an alternative to second-look procedures. Many patients with cholesteatoma will undergo multiple procedures, each subsequent procedure being more ablative and less concerned with hearing status as opposed to eradication of cholesteatoma. Informed consent of patients is critical in cholesteatoma surgery as to the possibility of canal wall down procedures and radical resection.

Cross-References

▶ Canal Wall Down Mastoidectomy
▶ Canal Wall Up Mastoidectomy
▶ Cholesteatoma (Congenital)
▶ Mastoidectomy
▶ Meningoencephalocele
▶ Ossicular Chain Reconstruction
▶ Ossiculoplasty
▶ Temporal Bone Encephaloceles, Meningoceles, and CSF Leak, Repair of

References

Chole RA, Faddis BT (2002) Evidence for microbial biofilms in cholesteatomas. Arch Otolaryngol Head Neck Surg 128(10):1129–1133

Chole RA, Tinling SP (1985) Basal lamina breaks in the histogenesis of cholesteatoma. Laryngoscope 95(3):270–275

da Costa SS, Paparella MM, Schachern PA, Yoon TH, Kimberley BP (1992) Temporal bone histopathology in chronically infected ears with intact and perforated tympanic membranes. Laryngoscope 102(11):1229–1236

Flook E, Izzat S, Ismail A (2011) Cholesteatoma imaging using modified echo-planar diffusion-weighted magnetic resonance imaging. J Laryngol Otol 125(1):10–12

Friedland DR, Eernisse R, Erbe C, Gupta N, Cioffi JA (2009) Cholesteatoma growth and proliferation:

posttranscriptional regulation by microRNA-21. Otol Neurotol 30(7):998–1005

Gersdorff MC, Nouwen J, Decat M, Degols JC, Bosch P (2000) Labyrinthine fistula after cholesteatomatous chronic otitis media. Am J Otol 21(1):32–35

Homoe P (2001) Otitis media in Greenland. Studies on historical, epidemiological, microbiological, and immunological aspects. Int J Circumpolar Health 60(Suppl 2):1–54

Homoe P, Bretlau P (1994) Cholesteatomas in Greenlandic Inuit. A retrospective study and follow-up of treated cases from 1976–91. Arctic Med Res 53(2):86–90

Huisman MA, De Heer E, Grote JJ (2006) Terminal differentiation and mitogen-activated protein kinase signaling in human cholesteatoma epithelium. Otol Neurotol 27(3):422–426

Jeong JH, Park CW, Tae K, Lee SH, Shin DH, Kim KR et al (2006) Expression of RANKL and OPG in middle ear cholesteatoma tissue. Laryngoscope 116(7):1180–1184

Kemppainen HO, Puhakka HJ, Laippala PJ, Sipila MM, Manninen MP, Karma PH (1999) Epidemiology and aetiology of middle ear cholesteatoma. Acta Otolaryngol 119(5):568–572

Khemani S, Lingam R, Kalan A, Singh A (2011) The value of non-echo planar (HASTE) diffusion-weighted MR imaging in the detection, localisation and prediction of extent of postoperative cholesteatoma. Clin Otolaryngol 36(4):306–12

Kwon KH, Kim SJ, Kim HJ, Jung HH (2006) Analysis of gene expression profiles in cholesteatoma using oligonucleotide microarray. Acta Otolaryngol 126(7):691–697

Magliulo G (2007) Petrous bone cholesteatoma: clinical longitudinal study. Eur Arch Otorhinolaryngol 264(2):115–120

Olszewska E, Wagner M, Bernal-Sprekelsen M, Ebmeyer J, Dazert S, Hildmann H et al (2004) Etiopathogenesis of cholesteatoma. Eur Arch Otorhinolaryngol 261(1):6–24

Peek FA, Huisman MA, Berckmans RJ, Sturk A, Van Loon J, Grote JJ (2003) Lipopolysaccharide concentration and bone resorption in cholesteatoma. Otol Neurotol 24(5):709–713

Quaranta N, Liuzzi C, Zizzi S, Dicorato A, Quaranta A (2009) Surgical treatment of labyrinthine fistula in cholesteatoma surgery. Otolaryngol Head Neck Surg 140(3):406–411

Sade J, Halevy A (1976) The natural history of chronic otitis media. J Laryngol Otol 90(8):743–751

Saleh HA, Mills RP (1999) Classification and staging of cholesteatoma. Clin Otolaryngol Allied Sci 24(4):355–359

Siddiq MA, Hanu-Cernat LM, Irving RM (2007) Facial palsy secondary to cholesteatoma: analysis of outcome following surgery. J Laryngol Otol 121(2):114–117

Spilsbury K, Miller I, Semmens JB, Lannigan FJ (2010) Factors associated with developing cholesteatoma: a study of 45,980 children with middle ear disease. Laryngoscope 120(3):625–630

Stammberger M, Bujia J, Kastenbauer E (1995) Alteration of epidermal differentiation in middle ear cholesteatoma. Am J Otol 16(4):527–531

Tos M (1988) Incidence, etiology and pathogenesis of cholesteatoma in children. Adv Otorhinolaryngol 40:110–117

Wang HM, Lin JC, Lee KW, Tai CF, Wang LF, Chang HM et al (2006) Analysis of mastoid findings at surgery to treat middle ear cholesteatoma. Arch Otolaryngol Head Neck Surg 132(12):1307–1310

Cholesterin Granuloma

▶ Cholesterol Granuloma

Cholesterol Cyst

▶ Cholesterol Granuloma
▶ Magnetic Resonance Imaging, Cholesterol Granuloma

Cholesterol Granuloma

Brandon Isaacson[1], Joe Walter Kutz Jr.[2] and Peter Sargent Roland[2]
[1]Otolaryngology-Head and Neck Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA
[2]Department of Otolaryngology-Head and Neck Surgery, UT - Southwestern Medical Center, University of Texas Southwestern, Dallas, TX, USA

Synonyms

Cholesterin granuloma; Cholesterol cyst

Definition

Cholesterol granuloma is an inflammatory lesion that typically forms in a pneumatized mucosal-lined space.

Introduction

Cholesterol granuloma is a non-neoplastic, inflammatory lesion that originates in an aerated mucosal-lined space. The temporal bone is the most common location for a cholesterol granuloma. The petrous apex is the most common location within the temporal bone where cholesterol granulomas are identified. Two pathophysiologic mechanisms have been postulated for the origin of temporal bone cholesterol granulomas. The classic theory for the pathogenesis of a cholesterol granuloma ascribes negative pressure within the aerated temporal bone results in hemorrhage into a mucosal-lined air

space. Blood in a mucosalized space results in an inflammatory response with subsequent formation of hemoglobin breakdown products.

Jackler and Cho described the marrow theory in which the hemorrhage originates from bone marrow exposed into a mucosal-lined air cell (Jackler and Cho 2003). Pfister demonstrated thin to absent bone between petrous apex air cells and clival bone marrow in the contralateral petrous apex of cholesterol granuloma patients lending additional support to the marrow theory (Pfister et al. 2007).

Clinical Features

Cholesterol granulomas can present with a variety of signs and symptoms including hearing loss, vertigo, imbalance, retro-orbital pain, headaches, facial anesthesia, facial pain, facial weakness, facial twitching, pulsatile tinnitus, and double vision. Not uncommonly these lesions are discovered incidentally on imaging studies during the workup for unrelated symptoms. Sensorineural hearing loss is the most common presenting symptom and is secondary to erosion into the internal auditory canal or the otic capsule. Cholesterol granulomas that extend into the middle ear can cause a conductive hearing loss. Diplopia is secondary to compression/irritation of the Abducens nerve from medial extension of a cholesterol granuloma into Dorello's canal or into the cavernous sinus. Facial anesthesia or pain from trigeminal nerve compression/irritation also occurs with medial extension into Meckel's cave, the porus trigeminus, or into the prepontine cistern. Facial nerve symptoms typically result from cholesterol granuloma extension into the internal auditory canal or into the region of the geniculate ganglion. Aural fullness, ipsilateral headaches, and retro-orbital pain are not uncommon in patients with a petrous apex cholesterol granuloma. Headaches are thought to occur secondary to local irritation of the dura surrounding the petrous apex (Isaacson et al. 2007).

Diagnostics

Audiometry
Pure tone audiometry typically reveals unilateral or asymmetric sensorineural hearing loss in the affected ear. Hearing loss severity can range from mild to
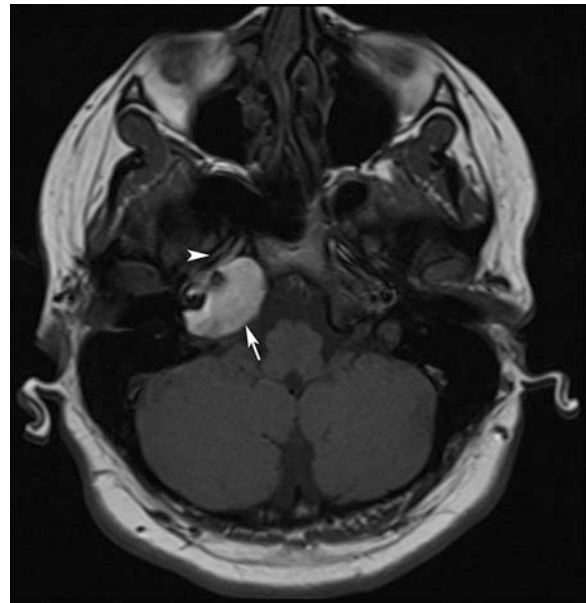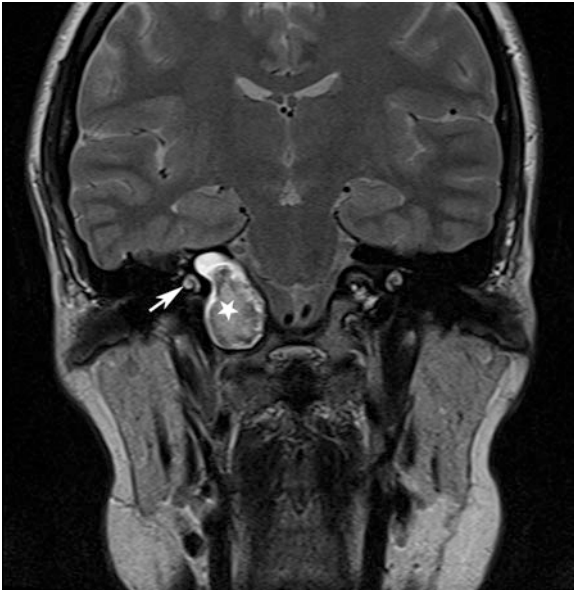

Cholesterol Granuloma, Fig. 1 Axial MRI T1 scan demonstrating right petrous apex T1 shortening (hyperintensity) (*arrow*). The petrous carotid artery is displaced anteriorly by the cholesterol granuloma (*arrow head*)

profound. Speech audiometry may have retrocochlear pattern with poor speech discrimination out of proportion to the pure tone audiometry in patients with lesions that extend into the internal auditory canal. Occasionally a mixed loss can occur from otic capsule invasion. Reflex decay may also be observed in lesions that affect the vestibulocochlear nerve. Absence of the ipsilateral acoustic reflex is sometimes present in lesions that affect the facial nerve.

Magnetic Resonance Imaging
High-resolution MRI of the temporal bone provides the most valuable information in the evaluation of petrous apex pathology. Petrous apex cholesterol granulomas have a unique appearance on MRI which includes a homo or heterogeneous hyperintensity on T1 (T1 shortening) and T2 images (Figs. 1 and 2). Blood and blood breakdown products are responsible for the hyperintense on the T1 shortening commonly seen with cholesterol signal granulomas. Heterogeneous hypointense signals on T1 and T2 images are often seen within the cholesterol granuloma which is secondary to bone fragments and solid material within the lesion. Gadolinium contrast does not reveal

Cholesterol Granuloma, Fig. 2 Coronal MRI T2 scan showing hyperintensity in the right petrous apex (*star*). The fluid-filled cochlea (*arrow*) is adjacent to the lateral wall of the cholesterol granuloma

significant enhancement since these lesions are typically hyperintense prior to contrast administration (Isaacson et al. 2007).

Petrous apex cephaloceles arising from Meckel's cave can often be confused with a cholesterol granuloma because of hyperintense signal seen in T2 images in both of these lesions. A distinguishing feature between a petrous apex cephalocele and a cholesterol granuloma is the former has an isointense signal to cerebrospinal fluid on T1 images whereas cholesterol granuloma shows T1 shortening. A petrous apex epidermoid may also be confused with a cholesterol granuloma given both lesions are hyperintense on T2 images. Epidermoids have an isointense signal to CSF on T1 images and also are hyperintense on diffusion-weighted (restricted diffusion) and sometimes FLAIR imaging. Petrous apex schwannomas arising from the trigeminal, abducens, vestibulocochlear, or facial nerve can also be mistaken for a cholesterol granuloma if the pre-contrast T1 images are not visualized. Schwannomas are hyperintense on T2 images and hypointense on T1 images without gadolinium. Administration of gadolinium results in significant enhancement in schwannomas which may have a similar appearance to T1 shortening seen in

cholesterol granulomas (Isaacson et al. 2007). Chordomas and chondrosarcomas also have a very hyperintense signal on T2 images but are isointense to brain on T1 images and show heterogeneous enhancement with gadolinium administration. Chordomas typically present in the central clivus and extend laterally to the petrous apex unlike cholesterol granulomas which are centered in the petrous apex. Chondrosarcomas are also centered in the petrous apex but like chordomas typically have an irregular margin unlike the smooth margin seen with cholesterol granulomas (Isaacson et al. 2007).

Asymmetric petrous apex pneumatization is commonly mistaken for a cholesterol granuloma. The petrous apex may be comprised of solid bone, bone marrow, or air cells. Not uncommonly the petrous apices are asymmetric with respect to the presence of pneumatization. On MRI asymmetric pneumatization can have a similar appearance to a petrous apex cholesterol granuloma since bone marrow appears hyperintense on T1 and T2 images without contrast. MRI is not as effective at differentiating between bone and air. A distinguishing feature of petrous apex bone marrow is the identical appearance of the adjacent marrow in the clivus. In addition, fat suppression of the T1 image will reduce the signal intensity of bone marrow, but not cholesterol granuloma. Temporal bone computed tomography CT can easily sort out asymmetric pneumatization from cholesterol granuloma (Roland et al. 1990).

Mucocele or trapped fluid is also one of the more common encountered incidental petrous apex findings. Trapped fluid is thought to arise from a similar mechanism as serous otitis media. This fluid has a hyperintense signal on T2 images and can also show slight hyperintensity on T1 images if protein is present within the fluid. Occasionally trapped fluid can show rim enhancement with contrast. The most important distinguishing feature of trapped fluid versus cholesterol granuloma is preservation of the air cell septations in the former. Cholesterol granulomas typically expand and erode through air cell septations unlike trapped fluid (Arriaga 2006).

Computed Tomography
Temporal bone CT provides valuable information in the evaluation of petrous apex pathology. Cholesterol granulomas produce smooth osseous expansion as opposed to irregular erosion (Figs. 3 and 4) typically
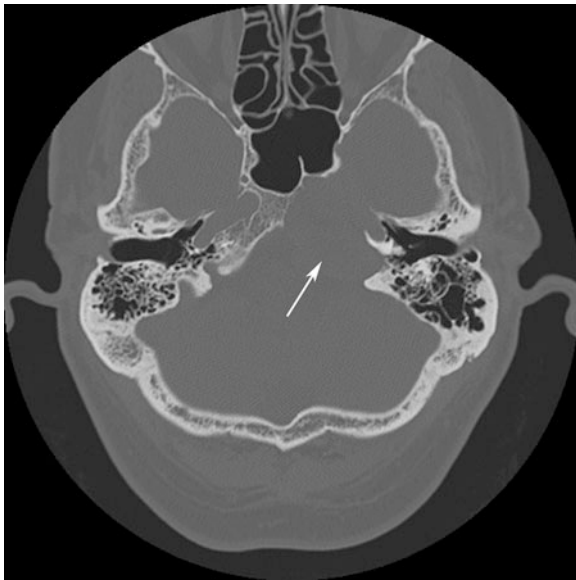
Cholesterol Granuloma, Fig. 3 Axial temporal bone CT scan demonstrates a smooth-walled left petrous apex lesion (*arrow*). The anterior aspect of the lesion abuts the posterior wall of the sphenoid sinus
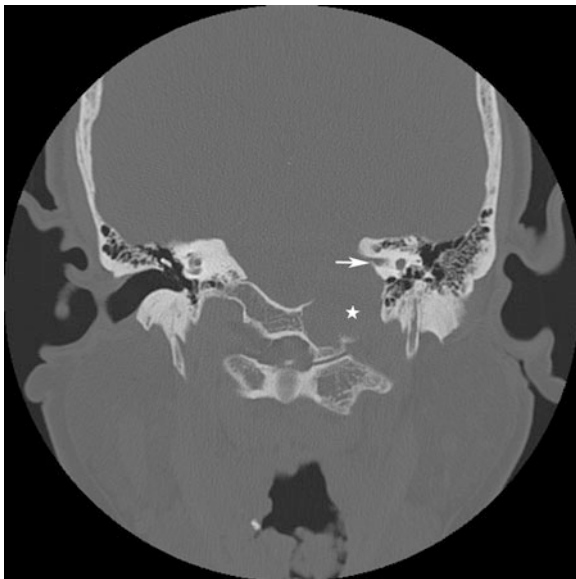
Cholesterol Granuloma, Fig. 4 Coronal temporal bone CT scan demonstrates a large smooth-walled left petrous apex lesion (*star*) which extends into the posterior inferior aspect of the internal auditory canal (*arrow*)

seen in paragangliomas, metastasis, chordomas, or chondrosarcomas. CT is also invaluable in differentiating petrous apex cholesterol granulomas from asymmetric pneumatization and trapped fluid/mucocele.

Temporal bone CT is imperative when operative intervention becomes necessary. CT provides information on potential surgical access to the petrous apex. The infracochlear and infralabyrinthine air cell tracts and their proximity to the petrous apex cholesterol granuloma can be easily visualized with a CT scan. A high-riding jugular bulb that obstructs the infralabyrinthine air cells tract is one indication for the infracochlear approach that can be identified on a CT. An aberrant petrous carotid artery can sometimes obscure the infracochlear tract making this approach unsuitable. CT also provides visualization of the cochlear aqueduct and its relationship to the petrous apex cholesterol granuloma and planned surgical corridor.

Occasionally a large cholesterol granuloma will erode the bone surrounding the jugular bulb and petrous carotid artery thus obscuring the boundaries between the cholesterol granuloma and the aforementioned structures. CT angiography/venography permits excellent visualization of the petrous carotid artery and jugular bulb in cases where their respective osseous walls have been compromised. CT angiography/venography in these cases provides critical information with respect to selecting a surgical approach (Isaacson et al. 2009).

Differential Diagnosis

Schwannoma, epidermoid/cholesteatoma, chordoma, chondrosarcoma, meningioma, petrous apex cephalocele, mucocele, effusion, hemangioma, metastasis, paraganglioma, skull base osteomyelitis, endolymphatic sac tumor, multiple myeloma (plasmocytoma), lymphoma, and asymmetric pneumatization (Isaacson et al. 2007).

Treatment

Observation
Petrous apex pathology is often discovered as an incidental finding for patients undergoing evaluation for headaches. Clinical examination and serial magnetic

resonance imaging is often the first-line management in patients with a petrous apex cholesterol granuloma. Incidentally discovered petrous apex cholesterol granulomas can be followed annually with serial MRI or CT scans. MRI scan is the preferred technique given the radiation exposure associated with a CT. A baseline study should serve as the comparison for all future scans when making a determination of cholesterol granuloma progression. Progressive symptoms such as double vision, facial anesthesia, facial pain, facial paresis, facial twitching, hearing loss, vestibular dysfunction, retro-orbital pressure or pain are all potential indications for microsurgical interventions. Impending complications of hearing loss or vertigo from a progressively enlarging petrous apex cholesterol granuloma eroding into the otic capsule is another potential indication for microsurgery. Microsurgery is also indicated in lesions that progressively enlarge on serial imaging (Isaacson et al. 2007).

Microsurgery

Microsurgery is the available treatment for a symptomatic or enlarging cholesterol granuloma. Mastoid and middle ear cholesterol granulomas are typically approached via a postauricular transmastoid approach with complete excision being the goal. The remainder of this section addresses the more challenging petrous apex cholesterol granuloma. A number of approaches have been described for removal and/or fenestration of a petrous apex cholesterol granuloma.

A subtemporal craniotomy or middle fossa approach can be used to completely excise, fenestrate, or marsupialize a petrous apex cholesterol granuloma. Complete excision reduces the chance of recurrence, but is associated with increased risk of complications secondary to injury of adjacent structures (i.e., trigeminal nerve, abducens nerve, facial nerve, vestibulocochlear nerve, dura, carotid artery, cavernous sinus, and the inner ear). Fenestration of the lesion often leads to temporary relief of symptoms as recurrence of the lesion is quite common if a drainage pathway is not established. Marsupialization into the osseous eustachian tube or mastoid provides a means of cholesterol granuloma content egress thus preventing enlargement. Placement of a small catheter from inside the lesion into the mastoid or osseous eustachian tube has been reported; however, occlusion of the catheter with subsequent recurrence is not uncommon (Isaacson et al. 2007).

The infralabyrinthine approach permits wide access for marsupialization of a petrous apex cholesterol granuloma. This approach involves a postauricular incision and a complete canal wall up mastoidectomy. The vertical facial nerve (anterior), jugular (bulb), posterior semicircular canal (superior), and presigmoid dura (posterior) are identified and serve as the boundaries for the infralabyrinthine approach. In some cases the jugular bulb may extend superiorly up to the level of the internal auditory canal effectively obstructing the infralabyrinthine air cell tract. A high jugular bulb can be identified with preoperative CT thus preventing the surgeon from selecting this approach inappropriately. Potential complications from this approach include facial paralysis, excessive bleeding from the jugular bulb, air embolism, sensorineural hearing loss (otic capsule fenestration), and a carotid artery injury with possible stroke. Cerebrospinal fluid (CSF) leakage can occur from injuring the presigmoid posterior fossa dura or the cochlear aqueduct. A CSF leak can also result in meningitis (Isaacson et al. 2007).

The infracochlear approach can be typically used to marsupialize most petrous apex cholesterol granulomas. The approach like the infralabyrinthine approach typically requires a postauricular incision. A superiorly based tympanomeatal flap is then elevated exposing the inferior annulus and tympanic bone. The tympanic bone and osseous inferior annulus is then removed using an otologic drill down to the level of the floor of the hypotympanum. A small diamond burr is then used to skeletonize the inferior basal turn of the cochlea (superior), the vertical petrous carotid artery (anterior inferior), and jugular bulb (posterior inferior). The infracochlear air cells are exenterated between the aforementioned skeletonized structures until the cholesterol granuloma is encountered. Care must be taken to direct the dissection anterior as bone is removed medially to reduce the risk of a presigmoid posterior fossa dura or cochlear aqueduct injury with resultant CSF leakage. Risks of this approach are identical to the infralabyrinthine approach.

The transotic or translabyrinthine approaches are appropriate in patients with non-serviceable hearing. The transotic approach provides wide access to the anterior petrous apex by removing the cochlea after elevating a tympanomeatal flap or removing the ear canal skin and oversewing the cartilaginous canal (Rambo closure) (Meyerhoff et al. 1988). Identification of the jugular bulb, petrous carotid artery, and

tympanic facial nerve are key steps of the transotic approach as they serve as the posterior-inferior, anterior, and the superior borders, respectively. Opening the modiolus will result in a cerebrospinal fluid leak, which requires gentle packing into the fundus of the internal auditory canals so as not to damage the facial nerve. The translabyrinthine approach provides access to the posterior petrous apex which is less frequently involved in petrous apex cholesterol granulomas (Isaacson et al. 2007).

Transnasal endoscopic marsupialization of a petrous apex cholesterol granuloma into the sphenoid sinus is another more recently introduced approach. This approach has the advantage of not requiring a skin incision and in some cases may provide a wide opening into the petrous apex cholesterol granuloma. As with the previously described approaches, careful patient selection is critical to a successful outcome. Petrous apex cholesterol granulomas that abut the posterior wall of the sphenoid sinus or the lateral recess of the sphenoid sinus are ideally suited for the transnasal endoscopic approach. Potential complications of this approach include cerebrospinal fluid leakage, orbital injury, optic nerve injury, carotid artery injury, pituitary injury, and mucocele formation (Isaacson et al. 2007).

Conclusion

Cholesterol granuloma is one of the most commonly identified lesions of the petrous apex. Petrous apex cholesterol granulomas are often identified incidentally and may present with a myriad of symptoms. These lesions have a unique and pathognomonic appearance on MRI. Many of these lesions can be followed if referable symptoms are absent. A number of surgical approaches are available with preference being for marsupialization instead of total excision. Long-term imaging follow-up with MRI is recommended as symptom recurrence or progressive enlargement after surgical treatment is occasionally encountered.

Cross-References

References

Arriaga MA (2006) Petrous apex effusion: a clinical disorder. Laryngoscope 116:1349–1356

Isaacson B, Kutz JW, Roland PS (2007) Lesions of the petrous apex: diagnosis and management. Otolaryngol Clin North Am 40:479–519

Isaacson B, Kutz JW Jr, Mendelsohn D, Roland PS (2009) CT venography: use in selecting a surgical approach for the treatment of petrous apex cholesterol granulomas. Otol Neurotol 30:386–391

Jackler RK, Cho M (2003) A new theory to explain the genesis of petrous apex cholesterol granuloma. Otol Neurotol 24:96–106

Meyerhoff WL, Stringer SP, Roland PS (1988) Rambo procedure: modification and application. Laryngoscope 98:795–796

Pfister MH, Jackler RK, Kunda L (2007) Aggressiveness in cholesterol granuloma of the temporal bone may be determined by the vigor of its blood source. Otol Neurotol 28:232–235

Roland PS, Meyerhoff WL, Judge LO, Mickey BE (1990) Asymmetric pneumatization of the petrous apex. Otolaryngol Head Neck Surg 103:80–88

Chondrodermatitis Nodularis Helicis Chronica

Simon Carr[1] and Chris Raine[2]
[1]Department of Otorhinolaryngology, Bradford Royal Infirmary, Bradford, UK
[2]ENT Department, Bradford Royal Infirmary, Bradford, West Yorkshire, UK

Definition

Chondrodermatitis nodularis helicis chronica (CNHC) is a common, benign, painful condition of the helix or antihelix. It was first described by Winkler in 1915 (Winkler 1915) and independently reported again by Foerster in 1918 (Foerster 1918). Winkler felt that the condition was due to degenerative changes in the cartilage which acted as an inflammatory stimulus on the skin. Degenerative changes similar to those in chondrodermatitis have been documented in a control population without chondrodermatitis. Newcomer et al. described it as the most common condition of the external ear seen in their clinic (Newcomer et al. 1953).

Etiology

There are many theories as to the cause of CNHC. In 1960, Barker et al. suggested that CNHC started as perichondritis and then involved the skin, whereas antihelical chondrodermatitis commenced in the skin following pressure or injury and then proceeded to involve the cartilage (Barker et al. 1960). Other causes such as pressure during sleep (Lawrence 1991), prominence of the antihelix (Burns and Calnan 1978), and frostbite (Ebenius 1941) have been proposed. Recently, the cause has been identified as specific perichondrial arteriolar changes (Upile et al. 2009).

Clinical Presentation

CNHC presents as a painful focal lesion or nodule on the helix or antihelix (Fig. 1), which usually rapidly expands to its maximum size and then remains stable.

It most commonly affects older men with fair skin who show signs of sun damage to skin in other areas but has been reported in women and also in some children (Grigoryants et al. 2007). Rex et al. reported a series of 74 patients with CNHC. Of these 72.9% of patients were men while 16.2% were women (Rex et al. 2006).

The nodules are firm, tender, well demarcated, and round to oval in shape with a raised, rolled edge and central ulcer or crust. Removal of the crust often reveals a small channel. Color is similar to that of the surrounding skin, although a thin rim of erythema may be noted. Size may range from 3 to 20 mm. The right ear is affected more commonly than the left; bilateral distribution has been reported. Lesions develop on the most prominent projection of the ear with the most common location being the helical apex. Distribution on the antihelix is more common in women (Oelzner and Elsner 2003).

The histological features of CNHC consist of epithelial hyperplasia, dermal inflammation, fibrosis, and collagen degeneration. Subdermally, the perichondrium is often disrupted with inflammation, hemorrhage, and necrosis (Zuber and Jackson 1999; Oelzner and Elsner 2003).

CNHC is mostly regarded as having no associated systemic symptoms. However, it can be associated with autoimmune or connective-tissue disorders, including lupus erythematosus, autoimmune thyroiditis, scleroderma, and dermatomyositis. Such cases may be more common in pediatric or young adult female patients. A 2009 report detailed CNHC in monozygotic twins, suggesting a possible hereditary factor (Chan et al. 2009).
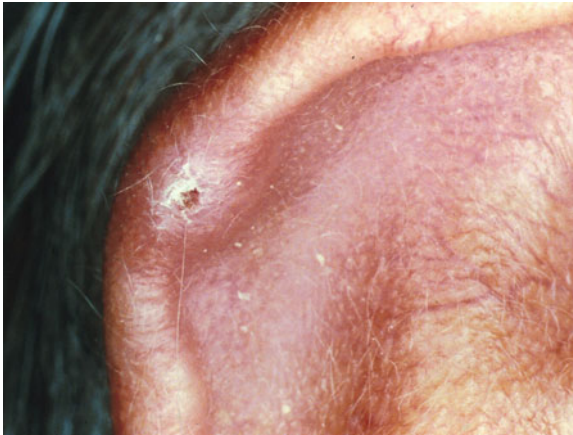
Chondrodermatitis Nodularis Helicis Chronica, Fig. 1 Chondrodermatitis nodularis helicis chronica

Differential Diagnosis

These include actinic keratosis, basal cell carcinoma, keratoacanthoma, and squamous cell carcinoma. A clinically distinctive feature of CNHC which helps to distinguish it from these other conditions is the associated pain. The other conditions tend to be painless, even the cutaneous malignancies. Cribier et al. found histological evidence of nerve hyperplasia or increased numbers of small nerves adjacent to the involved cartilage in chondrodermatitis nodularis chronica helicis patients (Cribier et al. 1991).

Therapy

Nonsurgical

Nonsurgical management of CNHC is often unsatisfactory. The primary goal should be to relieve or eliminate pressure at the site of the lesion. This is often difficult because of the patient's preference or necessity to sleep on the side with the lesion. CNHC also has a high recurrence rate.

Various nonsurgical methods have been tried. Singh et al. described two methods: the first being a custom-made foam pressure relieving prosthesis; the second being a modified pillow with an area removed to prevent pressure from the pillow on to the lesion (Singh et al. 2009). Cutting a hole in a bath sponge and holding it in place with a headband has also been described (Moncrieff and Sassoon 2004).

Topical antibiotics may relieve pain caused by secondary infections. Topical and intralesional steroids may also be effective in relieving discomfort. Collagen injections may bring relief by providing cushioning between the skin and cartilage. Cryotherapy also has been used as a treatment modality. If specific efforts to relieve pressure are unsuccessful, surgical approaches almost always are needed.

Surgical

The primary principle of surgical management is excision of the underlying cartilage, rounding of the cut edge, and preservation of the skin (Calnan and Rossatti 1959; Lawrence 1991).

Various procedures have been used in the treatment of chondrodermatitis nodularis chronica helicis. These procedures include wedge excision, curettage, electrocauterization, carbon dioxide laser ablation, and excision of the involved skin and cartilage (Kromann et al. 1983).

In general, the recurrence rate is high unless the underlying focus of damaged cartilage is removed and the pressure relieved. Treatment with cartilage removal alone, as described by Lawrence, provides excellent curative, functional, and cosmetic results (Lawrence 1991).

Various surgical methods have been described for different lesions. Affleck proposed two methods for surgical treatment of both helical and antihelical lesions. For lesions on the helix, an incision is made on either side of the nodule running along the rim of the helix. Bluntly dissect and reflect the skin from the perichondrium to reveal the helix cartilage. Trim the cartilage immediately under the ulcer with a flat shaving technique using a scalpel to a depth of approximately 3 mm. The remaining cartilage must be smooth to touch because rough cartilage may produce pressure points. The flap is then returned and sutured.

For antihelical lesions, a three-sided flap is raised that is approximately 25 mm wide and 15 mm long, with its attached margin directed toward the helix. Expose the perichondrium-covered cartilage, and excise cartilage with a scalpel until all edges are smooth to touch. Obtain hemostasis, and reapproximate and suture the flap. Conservation of the normal tissue is important for aesthetic outcome (Affleck 2008).

Rajan et al. reported a novel approach for small, localized lesions under local anesthetic. Using a punch

biopsy, the diameter of which is larger than that of the lesion, a deep punch of the skin and underlying cartilage is taken. This is then reconstructed with a full thickness skin graft (Rajan and Langtry 2007).

References

Affleck AG (2008) Surgical treatment of chondrodermatitis nodularis chronic helicis: conservation of normal tissue is important for optimal aesthetic outcome. J Oral Maxillofac Surg 66:2194

Barker LP, Young AW, Sachs W (1960) Chondrodermatitis of the ears: a differential study of nodules of the helix and antihelix. AMA Arch Derm 81:15–25

Burns DA, Calnan CD (1978) Chondrodermatitis nodularis antihelicis. Clin Exp Dermatol 3:207–208

Calnan J, Rossatti B (1959) Chondrodermatitis nodularis chronic helicis or glomus tumour of the helix? A report on twenty-one cases. Br J Plast Surg 12:55–68

Chan HP, Neuhaus IM, Maibach HI (2009) Chondrodermatitis nodularis chronica helicis in monozygotic twins. Clin Exp Dermatol 34:358–359

Cribier B, Scrivener Y, Peltre B (1991) Neural hyperplasia in chondrodermatitis nodularis chronic helicis. J Am Acad Dermatol 127:530

Ebenius B (1941) Chondrodermatitis chronic auriculae. Acta Radiol 22:563–572

Foerster OH (1918) A painful nodular growth of the ear. J Cutan Dis Incl Syph 36:154–156

Grigoryants V, Qureshi H, Patterson JW, Lin KY (2007) Paediatric chondrodermatitis nodularis helicis. J Craniofac Surg 18:228–231

Kromann N, Hoyer H, Reymann F (1983) Chondrodermatitis nodularis chronic helicis treated with curettage and electrocauterization: follow-up of 15-year material. Acta Derm Venereol 63:85–87

Lawrence CM (1991) The treatment of chondrodermatitis nodularis with cartilage removal alone. Arch Dermatol 127:530–535

Moncrieff M, Sassoon EM (2004) Effective treatment of chondrodermatitis nodularis chronic helicis using a conservative approach. Br J Dermatol 150:892–894

Newcomer VD, Steffen CG, Sternberg TH, Lichtenstein L (1953) Chondrodermatitis nodluaris chronic helicis: report of ninety-four cases and survey of literature, with emphasis upon pathogenesis and treatment. AMA Arch Derm Syphilol 68:241–255

Oelzner S, Elsner P (2003) Bilateral chondrodermatitis nodularis helicis on the free border of the helix in a woman. J Am Acad Dermatol 49:720–722

Rajan N, Langtry JA (2007) The punch and graft technique: a novel method of surgical treatment for chondrodermatitis nodularis helicis. Br J Dermatol 157:744–747

Rex J, Ribera M, Bielsa I, Mangas C, Xifra A, Ferrandiz C (2006) Narrow elliptical excision and cartilage shaving for treatment of chondrodermatitis nodularis. Dermatol Surg 32:400–404

Singh M, Wilson A, Parkinson S (2009) Two non-surgical treatments for chondrodermatitis nodularis helicis. Br J Oral Maxillofac Surg 47:327–328

Upile T, Patel NN, Jerjes W, Singh NU, Sandison A, Michaels L (2009) Advances in the understanding of chondrodermatitis nodularis chronic helicis: the perichondrial vasculitis theory. Clin Otolaryngol 34:147–150

Winkler M (1915) Knotchenformige Erkrankung am helix. Chondrodermatitis nodularis chronic helicis. (German) Arch Dermat u Syph 121:278–285

Zuber TJ, Jackson E (1999) Chondrodermatitis nodularis chronic helicis. Arch Fam Med 8:445–447

Chondroma

▶ Chondrosarcoma of Skull Base

Chondrosarcoma of Skull Base

Carrie M. Bush and Arturo Solares
Department of Otolaryngology, Medical College of Georgia, Augusta, GA, USA

Synonyms

Chondroma – A benign slow-growing cartilaginous tumor that harbors small potential for malignant degeneration

Definition

Chondrosarcoma – A malignant tumor of cartilaginous origin most often involving the axial skeleton, and rarely occurring in the skull base.

Etiology

Chondrosarcomas are locally aggressive malignancies of cartilaginous (mesenchymal) origin. Diverse in behavior, these tumors may be either slow growing and localized or highly aggressive with metastatic potential. Although most commonly arising in the axial skeleton at the pelvic bone, humerus, ribs, and

scapula, they rarely may present as skull base lesions. The most common age overall at presentation is 80–84 years, with a tendency for skull base lesions to present earlier (mean age 40). There is no race predilection, but a clear tendency for chondrosarcomas to occur more often in males than females (2:1) in all locations, including skull base lesions (Hide 2009; Gay et al. 1995).

Chondrosarcomas are classified as primary or secondary based on their origin. Primary lesions arise de novo (from normal cartilage or tissue), whereas secondary lesions arise from a preexisting tumor (chondroma or osteochondroma). There is increased risk of chondrosarcoma in multiple enchondromatosis syndromes (Maffucci's syndrome and Ollier's disease) and hereditary multiple exostoses (Paget's disease and fibrous dysplasia). There are three proposed theories regarding the development of chondrosarcoma. These include possible proliferation and transformation of congenital cartilaginous rests, abnormal ossification and malignant transformation of chondroid tissue, and secondary chondroplasia from chronic inflammation (Hong et al. 2009).

Approximately 10% of all chondrosarcomas arise in the head and neck, and skull base lesions account for 5–7% of all chondrosarcomas (Hong et al. 2009; Rapidis et al. 1997). ▶ Chordoma and chondrosarcoma comprise the majority of malignant skull base tumors, with chondrosarcoma being the less common of the two. Although chondrosarcoma is the second most common malignancy of bone (25%), it accounts for less than 0.15% of intracranial tumors (Hide 2009; Bloch et al. 2010). The skull base develops by endochondral ossification, in contrast to the skull vault, which undergoes intramembranous ossification. Most skull base chondrosarcomas arise from the cartilaginous remnants within synchondroses. There is some controversy as to whether chondrocytes in rests of endochondral bone or pluripotential mesenchymal cells serve as the primary precursors to malignancy.

Clinical Presentation

There are no pathopneumonic signs or symptoms for cranial base chondrosarcoma. Axial chondrosarcomas present with dull pain, and generally with 1–2 years of symptoms prior to diagnosis (Hide 2009). In contrast, cranial base chondrosarcomas present similar to other skull base malignancies, with diplopia (48%) as the most common complaint followed by headache (45%) (Oghalai et al. 2005). Signs and symptoms are determined by the location of the lesion. Within the skull base, most chondrosarcomas occur at fused junctions including the petroclival, petro-occipital, sphenooccipital, and sphenopetrosal synchondroses. Of these sites, the petroclival junction is the most commonly affected (Oghalai et al. 2005).

Given the anatomic density of the skull base, cranial neuropathies are frequent. The abducens nerve (CNVI) is most commonly involved secondary to the propensity for chondrosarcoma to impinge on Dorello's canal. The oculomotor nerve is also frequently affected, and as tumor infiltrates the skull base, palsies of CN's 2, 4, 5, 6, 7, and 8 may also develop. Pain and hypesthesia within the distribution of the trigeminal nerve is a concerning symptom at presentation. Visual loss is an unlikely presenting symptom, but may develop as the disease progresses. Temporal bone lesions may lead to early deafness and facial palsy. Rarely, chondrosarcomas may invade the posterior posterior fossa to involve the jugular foramen, at which time CN's 9, 10, 11, and 12 may also be affected. Onset of symptoms to time of diagnosis of cranial base chondrosarcoma varies from 18 to 60 months (Rapidis et al. 1997). Unfortunately, the combination of headache and vague neurologic symptoms may mislead the physician into suspecting psychosomatic complaints.

Although generally low grade in nature, most cranial base chondrosarcomas are greater than 2 cm in size at time of diagnosis. Smaller tumors tend to remain extradural, and are often located at the foramen lacerum (Oghalai et al. 2005). At late stages, lesions may grow to invade the sinuses and nasopharynx. Thus, chondrosarcoma may also cause symptoms of epistaxis, eustachian tube dysfunction, globus sensation, dysphagia, and dysarthria. Large chondrosarcomas may also extend intracranially, manifesting with symptoms of intracranial hypertension. Anterior brainstem compression is also a concern in patients with intradural extension. Although lesions may grow to be large in size, most are histologically grade 1 at time of presentation (Bloch et al. 2010). Metastases are uncommon, and rarely serve as a presenting sign of chondrosarcoma.

Of note, case reports of cranial base chondrosarcomas as a manifestation of hereditary

enchondromatosis syndromes are present in the literature. Ollier's disease consists of multiple enchondromatosis in the metaphysis and diaphysis of bones. Although risk of sarcomatous degeneration of enchondromas exist, Ollier's disease is only rarely associated with other malignancies. On the other hand, Maffucci Syndrome, which is characterized by the presence of multiple enchondromatosis and cutaneous hemangioma, is associated with a 23% change of developing multiple malignancies. Secondary chondrosarcoma arising in patients with these syndromes appears at an earlier stage than primary skull base chondrosarcoma. Also, unlike primary chondrosarcoma, prevalence is greater in females than males (Noël et al. 2004). These syndromes should be suspected in patients with chondrosarcoma and a history or enchondroma, especially if located in the hands or feet.

Diagnostics

As with all clinical encounters, a thorough history and physical examination should be performed. Often the presenting symptoms (headache and cranial neuropathy) will lead to the use of valuable imaging, including both CT and MRI. Plain film radiographs may permit identification of the lesion, but are of little clinical use. CT is a great asset in that it allows for assessment of the level of bony destruction and detects areas of matrix calcification better than MRI. With addition of contrast to CT, enhancement may be seen within soft tissue components of the lesion. MRI with fat suppression is ideal for establishing extent of brain and extracranial soft tissue involvement. A low intensity signal will be detected on T1 and a high intensity signal on T2. MRA may also be helpful to assess the proximity of the lesion to key vasculature, especially when intratemporal invasion is suspected (Rapidis et al. 1997).

Basic laboratory workup is unnecessary, although a chest radiograph is debatably warranted. PET scan as well as CT of the neck and thorax are not required unless clinical evidence of metastases exists. Diagnosis can only be confirmed by pathology, and tissue may be obtained by either FNA or open biopsy. Grossly, chondrosarcomas are mucosa-covered, smooth, gray-white lesions that may be pedunculated or friable.

There are several histologic subtypes of chondrosarcoma, with the conventional (hyaline-myxoid) being the most common type encountered at the skull base. It consists of large cells with single or multiple nuclei in a chondroid matrix composed of hyaline, myxoid, or a hyaline myxoid substrate. The World Health Organization (WHO) has subclassified conventional chondrosarcoma into Grades 1–3 based on mitotic rates, cellularity, and nuclear size. Grades 1, 2, and 3 correspond with well-differentiated, moderately differentiated, and poorly differentiated cells, respectively, with Grade 3 being the most aggressive subtype. The vast majority of skull base chondrosarcoma are Grade 1. In a retrospective review of 25 patients with skull base chondrosarcoma, 72% were Grade 1, 24% were Grade 2, and 4% were Grade 3 (Oghalai et al. 2005).

In addition to the conventional type of chondrosarcoma, mesenchymal, clear cell, and dedifferentiated subtypes have also been described. The mesenchymal type tends to present later and be more aggressive. It portends a worse prognosis than the conventional type of chondrosarcoma, and on cytology and immunohistochemical staining resembles Ewing sarcoma. The mesenchymal type consists of sheets of small, round or ovoid undifferentiated cells scattered among islands of well-differentiated cartilage. There will often be metaplastic bone formation and calcification present. The dedifferentiated type of chondrosarcoma is rare, and consists of anaplastic foci within a background of low-grade cartilaginous tumor. Clear cell chondrosarcomas may be seen as clusters of giant cells with clear cytoplasm. Interestingly, in a literature review of 560 patients, no clear cell or dedifferentiated skull base chondrosarcomas were identified (Bloch et al. 2010).

Differential Diagnosis

Chondromas are benign tumors of cartilaginous origin that are histologically similar to chondrosarcoma. Only subtle histologic findings may indicate the presence of a chondrosarcoma, and with inadequate specimen a benign diagnosis may be made erroneously. Should a chondroma be resected and recur, the surgeon should be highly suspicious of malignancy (Hide 2009).

Chordomas, like chondrosarcomas, are malignancies of the skull base and clivus. Differentiation

between the two tumors may be difficult, but has improved with technological advances. In the past, imaging was often not precise enough to detect the exact location of the lesion. The subtle difference in location (most commonly chordoma at midline clivus and chondrosarcoma at the petroclival junction) requires high resolution scanning to identify, and in itself is not pathopneumonic. Similar appearance of chordoma and chondrosarcoma may also be seen histologically. However, the presence of physaliphorous cell (cells with cytoplasm containing many small vacuoles) is indicative of chordoma. Immunohistochemistry may be a great asset in distinguishing the diagnosis. Chordomas are of both epithelial and mesenchymal origin, whereas chondrosarcomas of are of mesenchymal origin only. Thus, chordomas will stain for epithelial antigens, which will be absent in chondrosarcomas.

Other malignancies, including metastatic disease must be kept in the differential until definitive diagnosis is made. Rarely, a chondrosarcoma may lead to acute visual loss that can be mistaken for progressive optic neuritis (Hong et al. 2009). The combination of headache and vague neurologic symptoms can be attributed to psychosomatic disorders, which has potential to delay diagnosis. Headache with the presence of cranial nerve neuropathies is suggestive of skull base or intracranial pathology, and early imaging may assist in appropriate diagnosis.

Prophylaxis

Exposure to radiation, beryllium, and radioactive isotopes has been associated with chondrosarcoma. However, the rarity of the disease makes epidemiologic studies difficult. At present, there is no known prophylaxis for chondrosarcoma.

Therapy

Treatment may be separated into three different categories: Surgery, Radiation, and Chemotherapy.

Surgery

Surgery is the mainstay of treatment for chondrosarcoma, and until recent years was believed to be the only efficacious treatment. The location of skull base tumors, and the associated vital neurovascular structures, makes complete resection difficult. At present, the goal of surgery is to provide maximal tumor resection with minimal patient morbidity. Over the past 15 years, technological advances have greatly improved the ability of surgeons to approach the skull base. The additional use of image-guided surgery has improved surgical precision and permitted greater confidence in aggressive resection. Although gross total resection is ideal when feasible, partial resection can also be valuable. Removal of tumor is not only essential for establishing diagnosis, but has also been shown to improve patient symptoms and delay recurrence (Nguyen and Chang 2008).

Preoperative evaluation includes a basic assessment of the patient's overall health, as well as imaging with CT and MRI. MRA is recommended for evaluation of adjacent vascular structures, especially when intratemporal invasion is suspected. Angiography is at the discretion of the surgeon. In a study of 33 patients, 15 underwent angiography prior to surgery. In all patients the vascularity of the chondrosarcoma was noted to be low, and preoperative embolization was not required (Oghalai et al. 2005). Previous history of radiation should be documented, as these patients have an increased incidence of postoperative mortality. It has been speculated that this is due to subclinical brainstem injury and microangiopathy. Patients that have failed previous treatment are also more likely to have an aggressive malignancy (Gay et al. 1995).

Surgical approach is determined based on tumor location, presence of intradural versus extradural involvement, patient comorbidities, and surgeon preference (Oghalai et al. 2005). Traditional approaches (retrosigmoid, transsphenoidal, and frontotemporal) are still used in isolation or combination with newer approaches (subtemporal petrosectomy, transcochlear, transjugular, transpetrosal, and subtemporal). When choosing an approach, one should avoid an intradural approach for extradural disease. Transnasal endoscopic approaches are also continuing to gain wider acceptance for removal of skull base lesions. The endoscope allows for superior visualization leading to a more meticulous and complete resection. While no large series of endoscopic chondrosarcoma resections exists, extrapolation from the chordoma experience suggests that the endoscopic endonasal route has a promising future (Stippler et al. 2009). Resections

are often limited by tumor invasion of the cavernous sinus, and adherence of tumor to the internal carotid artery (Oghalai et al. 2005). In a study of 60 patients (with both chordoma and chondrosarcoma) that underwent surgical resection, gross total resection was achieved in 47%, near total resection (questionable remnants of tumor) in 20%, subtotal resection (>90% removal) and partial resection in 10% (Gay et al. 1995).

Mortality rates following surgical resection of skull base lesions are low (<5%) and often due to a secondary pathology, such as pulmonary embolus or myocardial infarction. Complications may be significant, and include postoperative infarction, hematoma, superficial wound infection, cerebrospinal fluid leaks, and meningitis. Cranial nerve dysfunction has also been reported, and includes hearing loss, facial nerve paralysis, diplopia, and visual decline. Studies have reported up to a 60% transient functional deterioration and 40% permanent functional deterioration in postsurgical patients. However, postoperative improvement of functional status has been noted in up to 20% of patients (Gay et al. 1995). When gross total resection of chondrosarcoma is achieved, recurrences are rare. Increased survival has been documented in patients that receive a total or near total resection.

Radiation Therapy

The efficacy of radiotherapy for chondrosarcoma has been controversial. The indolence of the disease and associated low mitotic rate leads to a prolonged response to radiation (Hong et al. 2009). In addition, molecular mechanisms of radioresistance, such as loss of tumor suppressor p16 and increased expression of antiapoptotic proteins, have been identified in chondrosarcoma (Onishi et al. 2011). Treatment is similar to other sarcomas, with doses of 40–70 Gy in 30–35 fractions. Most agree that radiotherapy is indicated when disease is surgically unresectable, high grade, metastatic, or recurrent. It also may replace surgery as the primary therapy in patients that refuse or are medically unfit for surgery (Hong et al. 2009).

Although surgery continues to be the mainstay of treatment, most small studies suggest that postoperative radiation therapy decreases recurrence rates and improves survival. There are some that advocate uniform use of radiation as an adjuvant therapy to surgery. Others prefer to follow postoperative patients with serial scans, and recommend radiation only with radiographic evidence of recurrence. In a meta-analysis evaluating skull base chondrosarcoma and recurrence, the authors found that a group of patients treated with surgery and postoperative radiation therapy fared better than a group treated with surgery alone. Recurrence rates were reported to be 9% and 44%, respectively. Interestingly, they also noted that patients receiving isolated radiation therapy (19% recurrence) did better than patients who underwent isolated surgical therapy (44% recurrence) (Bloch et al. 2010). Although this does not suggest that radiotherapy replaces the role of surgery in treatment, the value of radiotherapy has become increasingly more clear.

The use of proton beam therapy in treatment of skull base chondrosarcoma is promising. Proton radiotherapy, as opposed to conventional photon radiotherapy, allows for improved dose delivery. A sharp dose falloff outside of the target range permits higher dose delivery to the tumor, while sparing surrounding vital structures. At Loma Linda Medical Center, local control rates of 92% and 5-year survival rates of 100% were achieved in patients with chondrosarcoma undergoing proton beam therapy (Hug et al. 1999). The majority of these patients underwent proton radiotherapy as primary treatment, with no history of prior surgery. Similar results were found at Massachusetts General Hospital/Harvard Cyclotron Laboratory, where patients treated with combination conventional radiation and proton beam therapy were noted to have 10-year survival rates of 94% (Munzenrider and Liebsch 1999).

Although radiotherapy has the advantage of being less invasive than surgery, it is not without its own inherent risks and complications. Death from brainstem necrosis has been reported following irradiation of skull base tumors. In addition, endocrine disorders, loss of hearing, blindness, seizure, and secondary malignancy have all been reported. Studies are currently underway to look at the feasibility of radiosurgery in management of chondrosarcoma. The efficacy of radiosurgery would be advantageous, as it is vastly more available than proton beam therapy. Unfortunately, the rarity of skull base chondrosarcoma, in addition to selection bias, and

use of multimodality therapy, make clear differences in outcomes difficult to detect in the management of skull base chondrosarcoma.

Chemotherapy

Chondrosarcomas are characteristically resistant to chemotherapy. Although chemotherapeutic agents have been used in the past for high-grade lesions, they have shown no real benefit in treatment, including that of palliative care. Resistance mechanisms of chondrosarcoma are well documented and include the following: P-glycoprotein expression, telomerase activity, angiogenesis, COX-2 expression, melovanate synthesis, tumor suppressor p16 mutation, increased expression of antiapoptotic proteins, and hypoxia (Onishi et al. 2011). Knowledge of molecular resistance mechanisms has allowed for targeted therapeutic strategies that have shown efficacy in in vivo studies. The current interest in developing chemotherapeutic agents for chondrosarcoma is high, and yields great promise for future treatment.

Prognosis

The prognosis of chondrosarcoma is based on size, location, and grade of the tumor. Five-year survival rates for chondrosarcoma including all body sites are 90%, 81%, and 43% for Grade I, II, and III lesions, respectively (Bloch et al. 2010). Patients with skull base chondrosarcoma most often have Grade I histology, which is consistent with the reported 5-year survival rates ranging from 80% to 100% in multiple small studies. A study of 179 patients with chondrosarcoma of the head and neck, revealed a 5-year survival rate of 87.2% and 10-year survival rate of 70.6% (Hong et al. 2009). Exceptions occur in younger patients and patients with mesenchymal type tumors, who uniformly present with more aggressive disease.

Most skull base chondrosarcomas are slow growing and locally aggressive. Lesions tend to recur at the primary site, with rare metastases. In a review of 400 cases of head and neck chondrosarcoma 5.6% of patients developed regional metastases and 6.7% developed distant metastases (Koch et al. 2000). Although chondrosarcoma tends to travel to lymph nodes more often than other osseous malignancies, most metastases are to the lungs. The American Joint Committee on Cancer (AJCC) has developed a staging system that is rarely used. This is secondary to both complexity, and poor applicability to the head and neck, where location and adherence to vital structures are of additional relevance to the prognosis of chondrosarcoma.

A literature review focused specifically on skull base chondrosarcoma found recurrence rates of 22% following treatment (Bloch et al. 2010). Average disease-free survival was 32.5 months with a 16 month median. However, there are past reports of recurrence up to 20–30 years after treatment. As such, lifelong clinical and radiographic assessment is recommended. Recurrence has been noted to be rare with gross total resection. When looking at all sites in the head and neck, recurrence following gross total resection is approximately 7% (Hong et al. 2009). Should recurrence be detected, surgical salvage is encouraged. Although postoperative mortality is higher in previously irradiated patients, there is no association of previous surgery, radiation therapy, or pathology to postoperative disability (Gay et al. 1995). Overall, patients with chondrosarcoma may be expected to do well. However, the rarity of disease and diversity of presentation prove a challenge when attempting to provide patients with accurate prognosis.

References

Bloch OG, Jian BJ, Yang I, Han SJ, Aranda D, Ahn BJ, Parsa AT (2010) Cranial chondrosarcoma and recurrence. Skull Base 20(3):149–156

Gay E, Sekhar LN, Rubinstein E, Wright DC, Sen C, Janecka IP, Snyderman CH (1995) Chordomas and chondrosarcomas of the cranial base: results and follow-up of 60 patients. Neurosurgery 36(5):887–896

Hide G (2009) Chondrosarcoma imaging. In: Chew FS (ed) Emedicine. www.emedicine.medscape.com

Hong P, Taylor SM, Trites JR, Bullock M, Nasser JG, Hart RD (2009) Chondrosarcoma of the head and neck: report of 11 cases and literature review. J Otolaryngol Head Neck Surg 38(2):279–285

Hug EB, Loredo LN, Slater JD, DeVries A, Grove RI, Schaefer RA, Rosenberg AE, Slater JM (1999) Proton radiation therapy for chordomas and chondrosarcomas of the skull base. J Neurosurg 91(3):432–439

Koch BB, Karnell LH, Hoffman HT, Apostolakis LW, Robinson RA, Zhen W, Menck HR (2000) National cancer database report on chondrosarcoma of the head and neck. Head Neck 22(4):408–425

Munzenrider JE, Liebsch NJ (1999) Proton therapy for tumors of the skull base. Strahlenther Onkol 175(Suppl 2):57–63

Nguyen QN, Chang EL (2008) Emerging role of proton beam radiation therapy for chordoma and chondrosarcoma of the skull base. Curr Oncol Rep 10(4):338–343

Noël G, Feuvret L, Calugaru V, Hadadi K, Baillet F, Mazeron JJ, Habrand JL (2004) Chondrosarcomas of the base of the skull in Ollier's disease or Maffucci's syndrome–three case reports and review of the literature. Acta Oncol 43(8):705–710

Oghalai JS, Buxbaum JL, Jackler RK, McDermott MW (2005) Skull base chondrosarcoma originating from the petroclival junction. Otol Neurotol 26(5):1052–1060

Onishi AC, Hincker AM, Lee FY (2011) Surmounting chemotherapy and radioresistance in chondrosarcoma: molecular mechanisms and therapeutic targets. Sarcoma 38:1564–1572

Rapidis AD, Archondakis G, Anteriotis D, Skouteris CA (1997) Chondrosarcomas of the skull base: review of the literature and report of two cases. J Craniomaxillofac Surg 25(6):322–327

Stippler M, Gardner PA, Snyderman CH, Carrau RL, Prevedello DM, Kassam AB (2009) Endoscopic endonasal approach for clival chordomas. Neurosurgery 64(2):268–277

Chordoma

Carrie M. Bush and Arturo Solares
Department of Otolaryngology, Medical College
of Georgia, Augusta, GA, USA

Synonyms

Ecchordosis physaliphora – A non-neoplastic notochord remnant of the axial skeletal found in 2% of persons at autopsy.

Definition

Chordoma – A malignant tumor arising from notochord remnant in the axial skeleton.

Etiology

Chordomas are rare slow-growing malignant tumors derived from vestigial and ectopic notochord remnants. The notochord lies in the primitive axis of the embryo, and later forms the nucleus pulposis of the axial skeleton. Chordomas may arise at any point along the neuroaxis, but are most common at the cranial and caudal ends. Sacrococcygeal chordomas are most prevalent (60%) followed by skull base chordoma (25%) and vertebral chordoma (15%). Although originally described by Virchow in 1857, it was not until 1895 that the physaliphorous cells of chordomas were recognized as notochordal in origin, when rediscovered within the nucleus pulposis (Palmer 2010). Interestingly, non-neoplastic notochord rests (also known as ecchordosis physaliphora) are found at the dorsal aspect of the clivus in 2% of autopsies.

Like all malignancies, chordomas are thought to arise from an error in DNA coding. However, given the rarity of the tumor, the exact nature of this error is still largely unknown. On karyotype, 70% are normal. However, abnormalities on chromosomes 3, 4, 12, 13, and 14 are associated with increased recurrence of tumor and decreased patient survival (Almefty et al. 2009). It has also been speculated that loss of tumor suppressor loci on 1p is associated with the malignant behavior of chordoma (Riva et al. 2003; Sawyer et al. 2001). Cathepsin K, a protease involved in bone absorption, has been shown to be upregulated in chordoma and imparts the lytic properties of the lesion (Haeckel 2001). Multiple studies are currently underway to better understand the molecular characteristics of chordoma. Although generally sporadic in nature, a rare case of familial chordoma has been described and attributed to the locus 7q33 (Kelley et al. 2001).

The exact incidence of chordoma is hard to detect secondary to the rarity of the disease. According to the SEER (Survival, Epidemiology and End Results) database, 0.08 persons per 100,000 are affected with the disease (McMaster et al. 2001). The median age of onset is 58 years, but ranges vastly between 3 and 95 years of age. Chordomas are slightly more likely to occur in men than in women, and are even rarer in African and African-American populations. For unknown reasons, skull base and intracranial chordomas tend to occur in a younger population, and are more likely to be detected in adolescents. Some speculate that this may be due to earlier presentation of symptoms with skull base lesions rather than an actual difference in the nature of disease.

Almost all skull base chordomas involve the clivus, through which courses a rest of remnant notochord. The site from which the chordoma originates within the clivus determines its anatomical presentation. Origin at the most rostral aspect can present as

a sellar or parasellar lesion. Likewise, those arising from the lower clivus tend to involve the foramen magnum. Spheno-occipital and petrosal lesions originate in the body and dorsum of the clivus, and nasopharyngeal chordomas are ventral in origin (Lanzino et al. 2001). Thus, clival chordomas may manifest in a multitude of ways, and depending on such will harbor an eclectic array of symptoms and signs.

Clinical Presentation

Chordomas are slow-growing, expansive, lobulated masses that expand into adjacent tissue. The onset may be insidious, with symptoms dependent on the location of the lesion. Most skull base chordomas are 1–10 cm in size at the time of detection. The most common presenting symptom is diplopia, followed closely by headache. Initially, the diplopia may be intermittent due to CV VI (abducens nerve) palsy, which often proceeds to complete paralysis. Overall, cranial nerve deficits are present in greater than 50% of patients at presentation (Palmer 2010). In addition to involvement of the abducens nerve, both paralysis of the oculomotor nerve (CN III), as well as sensory deficits of the trigeminal nerve (CNV), are prevalent at the time of diagnosis.

Chordomas have a predictable course of local bony destruction, followed by dural infiltration and intracranial extension if untreated. As such, manifestations of disease are also local, as described above. On radiographic imaging, up to 75% of patients gave cavernous sinus extension at diagnosis (Lanzino et al. 2001). At late stages, dural invasion may lead to posterior fossa extension, brainstem compression, and invasion of vasculature. Lymphatic and hematogenous spread is uncommon, and as such metastases are exceedingly rare at time of presentation. However, as metastases are also slow growing, some patients may asymptomatically harbor distant disease.

Diagnostics

Initially, a complete history and physical exam should be performed. Imaging often leads to diagnosis, and often both a CT scan and MRI are obtained. The CT scan allows for delineation of bony anatomy and will often show decreased attenuation in the clivus. A lytic, expansive, and lobulated solitary lesion may be identified with the presence of matrix calcification in 70%. MRI reveals similar findings. Chordomas are hyperintense on T2, secondary to the high fluid content of vacuoles in physaliphorous cells. T1 images will reveal a hypointense lesion that may have scattered intensities if hemorrhage is present. Although rarely used in the modern era, plain films of chordoma reveal a destructive, well-demarcated lesion with bony erosion surrounded by sclerosis. Given the low rates of metastases, laboratory studies are not warranted unless suspicion arises during the history and physical examination. A simple chest radiograph (XR) may be obtained to observe for the presence of pulmonary metastases. CT of the chest and neck are only ordered if the chest XR causes concern or a palpable neck mass is present.

Diagnosis is confirmed by ▶ fine needle aspiration (FNA) or open biopsy. Depending on the site of the lesion, FNA may not be possible, and an open biopsy may be required. FNA tends to be preferred, as it has been associated with lower rates of local recurrence. Grossly, chordomas are soft, gelatinous, and may be smooth or lobulated. They are homogenous and gray-white in appearance, with occasional calcifications or hemorrhage. Chordomas may manifest as one of three types, which are determined on histology. The classic type is most common. Distinct physaliphorous cells, which have multiple vacuoles throughout the cytoplasm, are characteristic of chordoma. Smaller ovoid cells are seen surrounding the physaliphorous cells, and contain small ovoid or round eccentric nuclei. These cells may lie in sheets or clusters amongst a mucinous matrix. Mitoses may or may not be present. The chondroid type is similar in appearance to the classic type, but also contains hyaline chondroid or cartilaginous tissue. The dedifferentiated type is rare (2–8%) and resembles a high-grade sarcoma (Thompson 2011). This type most commonly occurs after radiation, and portends a poor prognosis.

Differential Diagnosis

Chordomas may be mistaken on histology for chondromas or chondrosarcomas. Special staining and immunohistochemistry may aid in correct diagnosis. Galactin-3, cell adhesion molecules, and MIB-1

are often present in chordoma and absent in chondrosarcoma (Mendenhall et al. 2005). Of note, chordoma is derived from both epithelial and mesenchymal components. This is in contrast to chondrosarcoma, which is solely of mesenchymal origin. Thus, epithelial membrane antigen and cytokeratin, which are present in chordoma, will be absent in chondrosarcoma. Cytokeratin currently stands as the single best diagnostic marker for distinguishing chordoma (Palmer 2010).

Rarely chordoma may be misdiagnosed as mucoepidermoid carcinoma. This is secondary to the presence of mucinous material that may be obtained on FNA. Providing key information to the pathologist in regard to site and imaging findings of the lesion may prevent this occurrence. In certain settings, chordoma may be mistaken for metastatic disease. On imaging of chordoma, generally a single lesion is present, rather than multiple lesions as often seen in metastatic disease. Histology can confirm the diagnosis. As mentioned above, ecchordosis physaliphora are non-neoplastic notochordal remnants adjacent to the clivus that are generally only discovered on autopsy.

Prophylaxis

There is no known prophylaxis for chordoma as the rarity of the disease prevents easy acquisition of epidemiological and medical data. Studies are ongoing and will continue to lead to better understanding of the disease.

Therapy

Treatment may be divided into three categories: surgery, radiation, and chemotherapy.

Surgery

Surgery is the mainstay of treatment for patients with chordoma. Harvey Cushing performed the first reported surgery for cranial base chordoma in 1909. He operated on a patient with a skull base lesion leading to transient improvement in symptoms of headache, diplopia, and visual loss. Unfortunately,

later progression of symptoms led to reoperation and perioperative mortality. Although a poorly known entity at the time, a retrospective review of the pathology confirms the lesion Dr. Cushing referred to was a chordoma. In his annals, Dr. Cushing wrote about the balance of surgical morbidity and mortality for such tumors, and concluded that perhaps the best method of treatment was conservative surgical intervention (Lanzino et al. 2001). This theory has held to this day, with the primary goal of surgery being optimal resection with minimal associated morbidity.

Selection of surgical candidates can be challenging. As surgical resection is the best chance of cure, surgeons tend to be aggressive within reason. There is some evidence to suggest that patients having undergone a subtotal resection followed by radiation therapy do no better than patients with FNA or biopsy followed by radiation therapy. As such, some will only attempt resection if they feel margins can be achieved. There is some controversy if surgery should be pursued in patients with cavernous sinus extension, which is present in 54–75% of patients at time of diagnosis. However, brainstem compression is an absolute indication for surgery as its presence not only decreases survival, but also limits the ability to administer radiation therapy. Mortality rates associated with surgery for skull base chordoma are low (<5%), but significant morbidity may occur. This includes neurological deficits (loss of visual fields, and CN III, V, VI, and VII injury), cerebrospinal fluid (CSF) leaks, meningitis, oronasal fistulas, ▶ epistaxis, and vascular infarction. In a study of 60 pts undergoing resection of chordoma and chondrosarcoma, 40% were noted to have permanent deterioration of neurologic function following surgery, in contrast to 20%, who had significant improvement (Gay et al. 1995). Actual success of surgery, which is gauged by incidence of local recurrence, is difficult to determine due to the multimodality of current therapy.

Even when a cure is not feasible, surgery has been shown to delay recurrence and decompress massive lesions. Vast technological improvements in the 1980s and 1990s led to an increased ability to surgically approach skull base lesions with limited morbidity. Additionally, the advent of image-guided surgery has allowed for improved navigation within the dense anatomical confines of the skull base. Surgical approach is based on a number of factors including surgeon preference, tumor location, patient health, as

well as history of previous surgery or radiation. If a tumor is extradural, every attempt is made to avoid intradural dissection in order to decrease the possibility of tumor seeding. Approaches are both anterior and lateral, or in some cases combined. Recently, endoscopic endonasal approaches have also been employed in chordoma resection. With all approaches, there are a number of vital structures at risk. It is recommended that bony margins be obtained if possible. Of note, while image-guided surgery is of great use when accessing the skull base, it may be misleading in resection of parenchymal tumors. This is secondary to the structural shift that may occur, which cannot be represented on imaging unless real-time systems are employed.

Despite advancements in skull base surgery, gross total resection is difficult to achieve, and in such cases patients may still harbor microscopic disease. The rarity of chordoma, its long natural history, and prevalence of prior treatments and multiple resections make data regarding surgical outcomes difficult to interpret. In a series of 25 patients with skull base chordoma, gross total resection was achieved in 43%, subtotal resection (>90%) in 48%, and partial resection (<90%) in 9% (Al-Mefty and Borba 1997). With the advent of endoscopic endonasal techniques, our ability to achieve a more thorough and complete resection may be improved. The endoscope provides superior visualization and the ability to look around the corners allowing for maneuverability around important structures (Solares et al. 2005, 2010). Gardner et al. published on 20 patients treated by an endoscopic endonasal approach. Eight chordomas (40%) were recurrent. Treatment of the 12 newly diagnosed chordomas included 8 total resections (66.7%), 2 near total resections (16.7%), and 2 subtotal resections (16.7%). Treatment of the 8 recurrent chordomas included 1 gross total resection (12.5%), 2 near total resections (25.0%), and 5 subtotal resections (62.5%) (Gardner et al. 2009). These data suggest that gross total resection is more likely when treating primary lesions. Based on the current endoscopic experience, one can conclude that it is at least as effective as open surgery, but results in less overall morbidity. While some advocate postoperative radiotherapy in all patients having undergone surgical resection, we prefer close observation in those patients in whom gross total resection was achieved.

Radiation

There has been an increased role of radiation therapy in current years following improvements in technology. The advent of ▶ Intensity Modulated Radiation Therapy and proton beam therapy has allowed for more targeted treatment, decreasing the incidence of injury to radiosensitive structures (such as the optic nerve and brainstem) which surround skull base chordomas. In the past, chordomas were believed to be radioresistant, with poor response to conventional radiation therapy at doses of 45–60 Gy. Since that time, with the use of IMRT and proton beam therapy, survival rates have been shown to improve with postoperative radiation.

There continues to be controversy as to which patients should receive adjuvant radiation therapy. It is well accepted that poor surgical candidates should undergo biopsy or FNA with radiotherapy as primary treatment. In good operative candidates, a greater conundrum exists. Most agree that radiation therapy should be used in patients that have postoperative radiological disease or a small area of recurrent tumor that can allow for focused therapy. In the case of patients with a complete gross resection, some advocate the use of postoperative radiation therapy while others observe the patient with serial imaging for evidence of recurrence.

Whether to use high-dose protons versus IMRT is a matter of opinion and availability. IMRT has been proven to provide better outcomes than conventional therapy, and targeted dose administration allows for a cumulative dose of 70 Gy (well above the 50–60 Gy provided by conventional radiation). IMRT also allows for the avoidance of metal prostheses through dynamic arcs, and is less expensive than proton beam therapy (∼1/10 the cost). Although only available in a few centers, proton beam therapy has shown an exceptional improvement in outcomes. It can be given alone or in combination with conventional photon beam radiation, and allows for an increased dose to the target while sparing surrounding structures. In a study at Harvard of 132 patients undergoing dual photon and proton radiotherapy, local control rate of 59% and 44% at 5 and 10 years, respectively, were reported. The same study also noted that men fared better than women overall (Terahara et al. 1999).

Unfortunately long-term studies are difficult to achieve secondary to the relatively new technology

(first available in 1970s) and the low incidence of chordoma. Overall, best results in treatment of chordoma have been obtained by surgical resection followed by proton beam therapy. Although low numbers of subjects lead to inherent study flaws, it is well recognized that most local recurrences following radiation occur at the brainstem, spinal cord, or optic apparatus. This is expected as these critical structures are often spared maximal doses of radiation. Of note, subtotal resection has not been shown to improve survival versus biopsy alone in patients that require radiotherapy.

Newer technologies continue to emerge that show promise in treatment of chordoma. Radiosurgery and interstitial brachytherapy have been shown to have efficacy in small trials. Anecdotal success is present for both techniques, but more meaningful data will be required to better assess these alternative treatment modalities.

Chemotherapy

In the past, chordoma has been considered insensitive to chemotherapy. Although rare case reports of success with anthracyclines and alkylating agents existed, there was essentially no role for chemotherapy in treatment. This paradigm has changed with the use of new molecular targeted agents. A promising phase II trial has shown Imantinib, a tyrosine kinase inhibitor, to be an efficacious medical treatment for chordoma. In a patient cohort, stabilization of tumor was achieved in 84% and tumor shrinkage in 16%. Imantinib is administered at 800 mg daily, and has a documented 1 year response rate in adult patients (Casali et al. 2007). Adverse outcomes may occur in patients with large bulky tumors, which undergo liquefaction and can lead to septic complications. There are also case series showing tumor response in patients treated with cetuximab and gefitinib (Casali et al. 2007). Results from these ongoing studies may later lead to routine use of chemotherapy in treatment of chordoma.

Prognosis

Chordomas are slow-growing locally destructive lesions with a long natural history. Recurrence may be detected decades after treatment, and even after

recurrence patients may survive for years. Recurrence is nearly always local (78%). The remainder of recurrence is attributed to distal metastases (21%), surgical pathway seeding (5%), and regional node metastases (3%) (Fagundes et al. 1995). After treatment, approximately 30% will recur, with only a small chance of salvage. At 3 years after recurrence survival is 43% and at 5 years declines to 7%. The overall survival rate for skull base chorodoma is 65% at 5 years and 47% at 10 years (McMaster et al. 2001). Local recurrence is the ultimate cause of death in 60% of patients.

Clinical and surgical staging systems exist for chordoma, and may be used as a rough assessment tool for predicting outcome. However, nearly all patients present with T1N0M0 tumor, making differentiation by these methods difficult. The staging system proposed by the American Joint Committee on Cancer (AJCC) also includes tumor grade in staging. This is valuable as histology may be predictive of outcome, with high levels of p53, evidence of mitoses, and dedifferentiated tumors portending a poorer prognosis. Young age, gross total resection, and use of radiotherapy are associated with a better prognosis. In the past, chondroid-type chordoma was thought to have a better prognosis. However, its increased prevalence in younger patients confounds this data, and many no longer consider chondroid histology as a favorable factor.

The average interval to recurrence depends on treatment type and resectability. With gross total resection, the average time to recurrence is 3.8 years. Subtotal resection, and subtotal resection with radiotherapy recur on average at 8 months and 2.1 years, respectively (Palmer 2010). It has been theorized that chordoma may exist as two different disease processes: aggressive and indolent. The aggressive type is associated with a high mortality rate within 3–5 years, and is supported by the presence of early recurrences in some patients despite gross total resection. The indolent type may progress for years, and is evident in patients that have had long-term survival with subtotal resection and no postoperative radiation.

Although primary disease is most predictive of prognosis, metastases may develop, traveling to lung, liver, and bone. Consistent with the course of local disease, metastases are slow growing and may fail to become symptomatic. Over the long course of the disease 10–20% of patients will develop clinical metastases. However, in those undergoing autopsy,

greater than 40% are found to have metastatic disease (Lanzino et al. 2001). Rarely, chordoma may further degenerate into fibrous histiocytoma, undifferentiated spindle cell tumor, and chondrosarcoma. These pathologies have been noted on histologic evaluation of primary tumor. Unfortunately, at this time it is difficult to provide each individual patient with an accurate prognosis. Continued research regarding the genetic and molecular aberrations of chordoma may assist in both individualized patient therapy as well as better determination of prognosis.

References

Al-Mefty O, Borba LA (1997) Skull base chordomas: a management challenge. J Neurosurg 86(2):182–189

Almefty KK, Pravdenkova S, Sawyer J, Al-Mefty O (2009) Impact of cytogenetic abnormalities on the management of skull base chordomas. J Neurosurg 110(4):715–724

Casali PG, Stacchiotti S, Sangalli C, Olmi P, Gronchi A (2007) Chordoma. Curr Opin Oncol 19(4):367–370

Fagundes MA, Hug EB, Liebsch NJ, Daly W, Efird J, Munzenrider JE (1995) Radiation therapy for chordomas of the base of skull and cervical spine: patterns of failure and outcome after relapse. Int J Radiat Oncol Biol Phys 33(3):579–584

Gay E, Sekhar LN, Rubinstein E, Wright DC, Sen C, Janecka IP, Snyderman CH (1995) Chordomas and chondrosarcomas of the cranial base: results and follow-up of 60 patients. Neurosurgery 36(5):887–896

Haeckel C, Krueger S, Kuester D, Ostertag H, Samii M, Buehling F, Broemme D, Czerniak B, Roessner A (2000) Expression of cathepsin K in chordoma. Hum Pathol 31(7):834–840

Kelley MJ, Korczak JF, Sheridan E, Yang X, Goldstein AM, Parry DM (2001) Familial chordoma, a tumor of notochordal remnants, is linked to chromosome 7q33. Am J Hum Genet 69(2):454–460

Lanzino G, Dumont AS, Lopes MB, Laws ER Jr (2001) Skull base chordomas: overview of disease, management options, and outcome. Neurosurg Focus 10(3):E12

McMaster ML, Goldstein AM, Bromley CM, Ishibe N, Parry DM (2001) Chordoma: incidence and survival patterns in the United States, 1973–1995. Cancer Causes Control 12(1):1–11

Mendenhall WM, Mendenhall CM, Lewis SB, Villaret DB, Mendenhall NP (2005) Skull base chordoma. In: Wax MK (ed) Clinical reviews: head & neck, vol 27, pp 159–165

Palmer CA (2010) Chordoma. In: Wyler AR (ed) Emedicine. www.emedicine.medscape.com

Riva P, Crosti F, Orzan F, Dalprà L, Mortini P, Parafioriti A, Pollo B, Fuhrman Conti AM, Miozzo M, Larizza L (2003) Mapping of candidate region for chordoma development to 1p36.13 by LOH analysis. Int J Cancer 107(3):493–497

Sawyer JR, Husain M, Al-Mefty O (2001) Identification of isochromosome 1q as a recurring chromosome aberration in skull base chordomas: a new marker for aggressive tumors? Neurosurg Focus 10(3):E6

Solares CA, Fakhri S, Batra PS, Lee J, Lanza DC (2005) Transnasal endoscopic resection of lesions of the clivus: a preliminary report. Laryngoscope 11:1917–1922

Solares CA, Grindler D, Luong A, Kanowitz SJ, Sade B, Citardi MJ, Batra PS (2010) Endoscopic management of sphenoclival neoplasms: anatomical correlates and patient outcomes. Otolaryngol Head Neck Surg 142(3):315–321

Stippler M, Gardner PA, Snyderman CH, Carrau RL, Prevedello DM, Kassam AB (2009) Endoscopic endonasal approach for clival chordomas. Neurosurgery 64(2):268–277

Terahara A, Niemierko A, Goitein M, Finkelstein D, Hug E, Liebsch N, O'Farrell D, Lyons S, Munzenrider J (1999) Analysis of the relationship between tumor dose inhomogeneity and local control in patients with skull base chordoma. Int J Radiat Oncol Biol Phys 45(2):351–358

Thompson LD (2011) Chordoma. Ear Nose Throat J 90(1):16–18

Chronic Cough in Children

Jonathan D. Finder
School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA

The definition of chronic cough varies by author, but is a term used to differentiate a cough associated with an acute illness from a long-term cough caused by a more chronic process. Cough associated with the common cold should resolve within 2–3 weeks, so some authors use greater than 3 weeks as a defining duration; 8 weeks is used by others, likely to exclude cough due to atypical bacterial pathogens that can last as long as 2 months.

Cough is one of two forms of airway clearance (along with mucociliary clearance) and is critical to the maintenance of health. The airway is lined with irritant receptors and other airway sensory nerves and is very sensitive to minor changes in pH, to a sensation of foreign body or secretions, and inflammation. Cough that persists beyond 3 weeks suggests an ongoing insult and therefore a chronic process. Approach to chronic cough is largely based on the age of the patient, the nature of the cough, triggering factors, and response to therapy.

History

It is important to include birth history when approaching cough in an infant. *Prematurity* and prolonged ventilatory support can lead to chronic lung disease (also called bronchopulmonary dysplasia) and respiratory insufficiency. In former premature infants, comorbidities commonly exist (asthma, tracheobronchomalacia, and gastroesophageal reflux). It is important in a cough history to identify triggers. The most common trigger of cough in patients of all ages is viral respiratory infections. When cough seems to occur whether or not the patient has a cold, the differential diagnosis shifts to the processes outlined below. Other critical aspects of the history include growth/failure to thrive, symptoms of malabsorption, and symptoms of *gastroesophageal reflux* disease (*GERD*). The symptoms of *GERD* can be subtle (back arching, a hoarse cry, irritability, recurrent croup, poorly controlled asthma, failure to thrive) or obvious (voluminous and effortless vomiting after feedings).

Cough in the young child or infant lasting for weeks is a worrisome sign and suggests one of several processes. As a rule of thumb, chronic infection is rare in infants and seen in congenital diseases of impaired mucociliary clearance (primary ciliary dyskinesia and cystic fibrosis). Contamination of the airways with gastric or upper gastrointestinal tract contents is a frequent cause of chronic cough in infants. Micro-aspiration in infants associated with gastroesophageal reflux can cause intense airway inflammation and chronic cough. Unrecognized anterograde aspiration can occur during feeding in infants with submucous cleft palate, tracheoesophageal fistula, and abnormal control of swallowing due to central factors.

The nature of the cough is an important part of the history. A wet-sounding cough is a red flag to the clinician and raises the possibility of a chronic bacterial infection. This finding tends to trigger an evaluation that is more invasive (bronchoscopy and/or CT scan). A chronic hacking, dry cough suggests an ongoing trigger such as reflux or allergic asthma.

Timing of cough is also important. A cough that occurs only with lying down (during naps and nighttime) suggests that the cough is related to GERD. A cough that is present equally in awake and asleep times suggests an ongoing inflammatory insult, such as asthma, but a foreign body can also cause a cough persisting during all hours of the day. Children with poor mucociliary clearance often "pool" secretions during sleep and will awaken with a wet-sounding cough in the morning. By comparison, the cough associated with GERD tends to occur early in the night, and is less present in the morning since the stomach has emptied by then. Disappearance of the cough during sleep suggests a behavioral component ("Habit Cough," see below).

Response to therapy is a critical part of one's assessment. A favorable response to antibiotic therapy suggests that bacterial infection is playing a critical role, while an absence of response may suggest that bacterial infection is not present. An exception to this rule is the chronic cough caused by *Bordetella pertussis*, which does not respond to any therapy aside from cough suppression; *Mycoplasma pneumoniae* can also result in a similar (but less severe) syndrome of prolonged coughing. A good response to inhaled or systemic corticosteroids strongly supports an asthma diagnosis, while an absence of response to asthma medications suggests that there is either a comorbidity or another diagnosis causing the cough.

Consideration of age is critical in assessing chronic cough. It is important to note that it is unusual for asthma to present in the first 6 months of life, and thus asthma should not be considered a cause of chronic cough in young infants without further investigation of other causes. Allergic causes for cough tend to occur after the third birthday. *Dysfunctional swallow* (either for anatomic or neurologic causes) tends to present very early and should be notable within the first month of life.

Chronic cough can commonly occur in those children attending daycare and may be due to recurrent viral respiratory infections. Children attending full-time day care have increased exposure to viral pathogens and will therefore have more frequent infections. In this setting it may be difficult to differentiate recurrent viral respiratory infections with cough (and bronchiolitis) from asthma. Persistence of symptoms beyond the acute phase of a viral illness suggests the possibility of asthma, or of complication of the original infection, such as acquired *ciliary dyskinesia* and/or localized *bronchiectasis*.

Physical Examination

The assessment of the pediatric patient always includes a careful physical examination. Many specialists routinely include the measurement of hemoglobin saturation by pulse oximetry with vital signs. Cough in the presence of significant hypoxemia suggests ventilation-perfusion mismatch, as seen in asthma (but also in aspiration syndromes). The upper airway should be assessed, including inspection of the mucosa of the nose to look for edema, a bluish discoloration (suggestive of allergic rhinitis), *rhinorrhea*, and *foreign body* (*an occasional finding in toddlers*). The posterior pharynx should be inspected for signs of *postnasal drip*, which can at times cause a cough. The examination of the chest in children can be achieved with patience and with the help of a parent. It is best to examine the infant and toddler in the parent's arms, since this is reassuring to the child and will result in less distress and crying during auscultation. Inspection is best achieved with the child's chest exposed to look for signs of retractions (intercostal, suprasternal, subcostal), decreased subcutaneous tissue (such as found in children with cystic fibrosis), and for midline placement of the trachea. Palpation is also useful in assessing chronic cough: palpable fremitus suggests either pooled secretions in the central airway or malacia of a central airway. Often in bronchomalacia the palpable fremitus is unilateral. The percussion note is also important: hyperresonance suggests air trapping and therefore peripheral airways obstruction. Percussion is also very useful for determination of air trapping. In children aged 5 and younger, the domes of the diaphragms will be located level with the tip of the scapulae in an upright child whose arm is at his or her side. Since this is a moving target, it is useful to percuss several times. The location of the dome of the diaphragm can be defined in fingerbreadths below the scapular tip. Conversely an elevated hemidiaphragm can be found with diaphragmatic eventration or paresis. Finally auscultation is important to assess for abnormal breath sounds. Wheezes are defined as monophonic (having a single pitch) or polyphonic. Wheezes can occur in either phase of breathing but are more common during expiration. Monophonic wheezes suggest involvement of a large airway (as seen in foreign body and bronchomalacia) while polyphonic wheezes are more typical of peripheral airways involvement (asthma, bronchiolitis, and post-aspiration events).

Specific Diagnoses Seen in Chronic Cough

Tracheobronchomalacia

Tracheomalacia and bronchomalacia present early in infancy (Boogaard et al. 2005). It is not uncommon for disorders of inadequate airway cartilage to present with chronic cough, although the term "congestion" is more often invoked by parents in describing symptoms. In children with tracheomalacia and bronchomalacia there is abnormal cough clearance, in which airway collapse leads to trapping of secretions and prolonged periods of coughing with colds. In this patient population there may be baseline congestion made worse with viral respiratory infections; comorbidities such as GERD should be considered when cough persists in sleep. Disorders of insufficient tracheal and bronchial cartilage generally resolve by the third birthday and are always present within the first year of life. When there is comorbid asthma in these children the disease can be quite severe and result in hospitalization from severe episodic airway obstruction.

Disorders of Impaired Mucociliary Clearance

Impaired mucociliary clearance will lead to stasis of secretions in the lower airways, secondary bacterial infection, airway inflammation with white cell infiltration of the airways, and a vicious circle of inflammation (a positive feedback loop) causing further inflammation and infection and airway damage. This is the case in cystic fibrosis (CF, see below), which is the most common cause of congenitally impaired mucociliary clearance. In all disorders in which mucociliary clearance is impaired (CF, primary ciliary dyskinesia, and acquired mucociliary dyskinesia), there is chronic cough that is productive in nature (Stafler and Carr 2010).

Primary ciliary dyskinesia is the term used to describe disorders of the ciliary apparatus. The original description, given the eponym Kartagener Syndrome, involves the triad of situs inversus (seen in 50% of PCD patients), chronic sinusitis, and bronchiectasis. The cause of PCD is an ultrastructural abnormality in

the cilia, most commonly a deficiency of the outer dynein arm, which prevents the "ratcheting" of the ciliary structure and thus prevents ciliary beating. The absence of coordinated mucociliary beating leads to impaired airway clearance, mucus stasis, chronic bacterial infection, airway damage, bronchiectasis, worsening airway obstruction, and ultimately respiratory insufficiency. Chronic bacterial rhinosinusitis is common, and recurrent/chronic otitis media despite placement of myringotomy tubes is generally present.

Therapy depends on the root cause but often involves a mechanical approach to improving mucociliary clearance such as manual chest physiotherapy, high frequency chest wall compression by an inflatable garment attached to a source of repetitive air pressure jets, and handheld airway oscillation devices. Antibiotics are used on an intermittent basis to treat acute exacerbations, but may be required on an ongoing basis for certain patients. Aerosolized recombinant human DNase is a standard therapy for patients with CF and has been used in other forms of ciliary dyskinesia. Routine use of bronchodilators is not the standard of care but is often used when there is a suggestion of reversibility to the airway obstruction. Lung transplant is an option in end-stage obstructive lung disease.

Cystic Fibrosis

Cystic fibrosis occurs at a rate of approximately 1:3,000 in Caucasian North American patients (Davis 2006; Farrell et al. 2008). CF is a primary disorder of impaired mucociliary clearance caused by a defect in the chloride channel, leading to desiccation of the periciliary fluid layer and impaired beating of cilia. The cough in CF is a productive one, and sputum will have increased white cells and bacteria. Airway bacterial flora in CF depends on the age of the patient: early on coliform bacteria are common, later replaced by *Hemophilus influenza* and *Staphylococcus aureus*. Eventually *Pseudomonas aeruginosa* will colonize the lower airways. Eradication of bacteria from the lower airways in CF is difficult, and persistent bacterial infection (purulent bronchiolitis) is the rule. When Pseudomonas becomes persistent, chronic suppression with inhaled antipseudomonal antibiotics has become the standard therapy, along with inhaled DNase to thin secretions and thrice-weekly azithromycin (felt to act as an anti-inflammatory or pathogen modulating therapy rather than as an antibiotic). Airway clearance therapies (manual chest physiotherapy, high frequency chest wall compression, and others) are the keystone of CF care.

Asthma

Asthma is the most common cause of chronic cough in pediatrics, affecting up to 20% of children (National Asthma education and Prevention Program 2007). As described above, younger patients tend to be symptomatic of asthma solely with respiratory viral infections. Early on it is difficult to distinguish asthma from recurrent bronchiolitis: Both are triggered by respiratory viral infections and result in wheezing and airway obstruction and hypoxemia. Response to inhaled bronchodilator tends to be minimal in bronchiolitis, while improvement with such medications is generally the rule in asthma. The gold standard for diagnosing asthma is pulmonary function testing (Weiner et al. 2003). Infant pulmonary function testing is helpful in differentiating fixed from reversible airway disease, but this modality of testing is available at relatively few academic centers. For children in the pre-school age group induction oscillometry can be used to evaluate bronchodilator responsiveness. For children aged 6 and older, spirometry (before and after administration of bronchodilator) is the chief means of diagnosing reversible airway obstruction. It is important to note that spirometry is more sensitive than a stethoscope examination for airway obstruction – a clear chest to auscultation can hide significant peripheral airways obstruction. Reversibility to inhaled bronchodilator is the hallmark of an asthma diagnosis, which can be quantified by spirometry. A 12% improvement in the volume exhaled in the first second (FEV1) is generally defined as a significant improvement; a 30% improvement in the FEF_{25-75} (also referred to as the mid-maximal expiratory flow rate) is also used for defining significant response to therapy.

As a rule of thumb, there need to be at least three discreet episodes of reversible airways obstruction (with or without frank wheezing) in order to establish a diagnosis of asthma. Asthma is often invoked as a cause of chronic cough in toddlers. In general, asthma in this age group leads to intermittent, rather than chronic symptoms (since the main trigger is respiratory viral illnesses rather than allergy). The major trigger for asthma in all ages is viral respiratory infections, and this is particularly the case in this age group.

Respiratory viral pathogens including influenza types A and B, parainfluenza virus, adenovirus, rhinovirus, metapneumonia virus, respiratory syncytial virus can all lead to symptoms of lower airway obstruction with cough, wheeze, and hypoxemia. As the viral infections resolve, so should the cough.

Once an asthma diagnosis has been established by history, physical examination, and pulmonary function testing, it is important to identify triggers of chronic cough. Allergic airway disease generally presents after the third birthday although can occur in younger children on occasion. Testing for IgE responses to aeroallergens (by skin-prick testing or by measurement of serum-specific IgE levels) is routinely performed in assessing for allergic asthma.

In order for an aero-allergen to penetrate to the lower airways and trigger an allergic airway response, the particle size must be less than 5 μM in size (Cohen-Cymberknoh et al. 2011). Particles of 10–15 μM diameter (pollens, e.g.) are removed by the nose (septum, turbinates, and nasal hair). Particles of 2–10 μM diameter can be carried into the peripheral airways and deposited there. Particles that can reach these smaller airways include animal danders, fungal spores, and mite feces. Particles of 0.5–1 μM in size can become deposited in the alveolar space, and particles of 0.1–0.5 μM will be exhaled. Thus it is helpful to know the particle size of the offending allergen. For example, ragweed pollen (particle size 15–25 μM) will cause a significant reaction in the nose and eyes of an allergic individual, while it cause little if any lower airway disease.

Tobacco Smoke Exposure

Among the most common reasons for chronic cough in children is environmental *tobacco smoke exposure*. The particle size of tobacco smoke is small enough to result in peripheral airway and alveolar deposition of the complex hydrocarbon particle. This particle is intensely irritating to the lower airways and leads to a number of changes, including transient impairment of mucociliary clearance, increased mucus production, and in susceptible individuals, bronchospasm (Chilmonczyk et al. 1993). Quite often, convincing parents to smoke outside the home is sufficient to stop a chronic cough without relying upon medication use. Without removing the offending irritant from the child's environment, no medication regimen will resolve a chronic cough triggered by tobacco smoke exposure. The key to success in convincing parents to smoke outside is to treat them with respect and suggest that smoking outside the home is the action of a loving, responsible parent, rather than using an approach focusing on guilt and harm. Once a relationship of trust has been built, the clinician can next focus on tobacco cessation in the parent.

Sinusitis

Sinusitis is often invoked as a cause of chronic cough and deserves mention in this context. The simplest approach to why sinusitis could cause chronic cough is that postnasal drip would lead to stimulation of laryngeal irritant receptors (Bourdin et al. 2009). The concept of the "unified airway hypothesis" is that allergic rhinitis and asthma exist as a continuum. The unified airway hypothesis has been proposed to link allergic rhinosinusitis to asthma. Clearly there are common causes of allergic rhinitis and asthma (IgE-mediated allergic inflammation with release of mediators of epithelial edema). Whether isolated nasal exposure to irritants can lead to lower airways inflammation or not remains unproven. From the standpoint of the physics of particle deposition, pollens are too large to enter the peripheral airways. Ragweed pollen exposure, for example, cannot directly lead to allergic lower airway inflammation. Any connection would have to be via neural or systemic pathways. Peaks of asthma incidence do not correspond to peaks in pollen levels. Since the release of these mediators leads to local effects in the majority of cases (rather than distant effects), this hypothesis remains unproven and controversial.

Habit Cough

Habit cough, also known as cough tic or psychogenic cough, is seen in children and adults. It is unusual in the first decade of life. Incidence peaks during adolescence. The cough starts as a pathological cough, most often with a viral respiratory infection. As the cold resolves the cough does not. It can last many months and often results in the patient missing a great deal of school. This behavioral disorder requires positive reinforcement. The reinforcement often is the attention that the cough garners from the parents. The cough in habit cough is often loud, bizarre, and with a honking, vibratory quality. This peculiar sound can result from high intrathoracic pressures causing the posterior wall of the trachea to hit the anterior trachea and vibrate.

Chronic Cough in Children, Table 1 Causes of chronic cough

Asthma
Gastroesophageal reflux
Dysfunctional swallow
Abnormal communication between airway and GI tract (clefts and fistulae)
Primary ciliary dyskinesia
Acquired (post-infectious) ciliary dyskinesia
Cystic fibrosis
Tracheomalacia and bronchomalacia
Environmental tobacco smoke exposure
Allergic rhinitis/chronic sinusitis
Habit cough

The single pathognomonic aspect of habit cough is that it disappears in sleep, regardless of how frequent the cough can be during awake time. Another critical aspect of habit cough is its failure to respond to any medical therapies (antibiotics, steroids, bronchodilators, cough suppressants). Basic evaluation includes a complete history and physical examination, pulmonary function testing, and a plain chest radiograph. These are invariably normal in habit cough. Treatment starts with reassurance that the patient is healthy. Removing the positive reinforcement is key, with the parents being instructed to ignore the cough. The "sips of water" technique involves instructing the patient to take a sip of water when he or she senses a "tickle" in the back of his or her throat. Discouraging coughing is critical, since the harsh coughing can result in edema and inflammation of the upper airway structures, making them more sensitive to minor irritation. In this sense habit cough is a positive feedback loop (vicious circle) of cough-induced coughing. Topical benzocaine lozenges, available over the counter, are also useful to remove the sense of irritation. A strong suggestion that the cough will stop if the patient wants it is also useful. Failure to respond to these therapies should prompt a referral to speech therapy. Occasionally a behavioral health consultation necessary in this disorder (Table 1).

References

Boogaard R, Huijsmans SH, Pijnenburg MW, Tiddens HA, de Jongste JC, Merkus PJ (2005) Tracheomalacia and bronchomalacia in children: incidence and patient characteristics. Chest 128:3391–3397

Bourdin A, Gras D, Vachier I, Chanez P (2009) Upper airway 1: allergic rhinitis and asthma: united disease through epithelial cells. Thorax 64:999–1004. doi:10.1136/thx.2008.112862

Chilmonczyk BA, Salmun LM, Megathlin KN et al (1993) Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. N Engl J Med 328(23):1665–1669

Cohen-Cymberknoh M, Shoseyov D, Kerem E (2011) Managing cystic fibrosis: strategies that increase life expectancy and improve quality of life. Am J Respir Crit Care Med 183:1463–1471

Davis PB (2006) Cystic fibrosis since 1938. Am J Respir Crit Care Med 173:475–482

Farrell PM, Rosenstein BJ, White TB et al (2008) Guidelines for diagnosis of cystic fibrosis in newborns through older adults: cystic fibrosis consensus report. J Pediatr 153(2)

National Asthma Education and Prevention Program (2007) Expert panel report 3 (EPR-3): guidelines for the diagnosis and management of asthma: summary report 2007. J Allergy Clin Immunol 120(Suppl):S94–S138

Stafler P, Carr S (2010) Non-cystic fibrosis bronchiectasis: its diagnosis and management. Arch Dis Child Educ Pract Ed 95:73–82. doi:10.1136/adc.2007.130054

Weiner DJ, Allen JL, Panitch HB (2003) Infant pulmonary function testing. Curr Opin Pediatr 15:316–322

Chronic External Otitis

Peter Sargent Roland[1], Joe Walter Kutz Jr. [2] and Brandon Isaacson[2]
[1]Department of Otolaryngology-Head and Neck Surgery, UT - Southwestern Medical Center, University of Texas Southwestern, Dallas, TX, USA
[2]Otolaryngology-Head and Neck Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA

Synonyms

Medial canal fibrosis

Definition

Chronic external otitis is a relatively uncommon inflammatory process involving one or both of the external auditory canals. It is often indolent and remits and relapses over months or years. Its relationship to acute external otitis is unclear but it does not usually evolve from untreated or undertreated acute otitis externa.

Etiology

The etiology of the disease remains unclear. It does not appear to be a primarily bacterial infection. Appropriately directed microbial therapy, while controlling infection and reducing inflammation acutely, is almost never sufficient to eradicate the pathologic process and prevent medial canal stenosis. Because the disease is bilateral in 50% of cases, a constitutional or genetic factor is suspected. Some clinicians have implicated environmental factors such as high temperature, high humidity, and mortar exposure, although exactly how these conditions contribute to the pathophysiology is unexplained. Some patients have a history of previous dermatitis or an allergic diathesis that is believed to be important in the pathophysiology of this disease.

The central pathophysiologic feature of chronic external otitis is low-grade inflammation of the external auditory canal that can persist long periods either treated or untreated. This inflammatory process may culminate in medial canal fibrosis and stenosis of the external auditory canal with conductive hearing loss (Hawke and Jahn 1987). The middle ear is not involved and radiographic imaging will demonstrate a normal middle ear and mastoid.

Cultures are commonly positive and pre-therapy isolates usually report the same bacteria as are encountered in acute bacterial external otitis, chronic suppurative otitis media, and chronic sinusitis. Gram-negative organisms, predominant with *Pseudomonas* species by far the most common, account for 30–50% of positive cultures. *Staphylococcus* species are recovered in 10–20% of cultures (Slattery and Saadat 1997; Selesnick et al. 1998).

Fungal organisms are not commonly recovered from cases of acute otitis externa. In a large clinical series, they represent less than 3–4% of primary infections. However, their role in chronic external otitis is less well understood. *Aspergillus* and *Candida* species are the most frequently recovered. It has been noted by some investigators that slow-growing fungi might be missed unless special detection techniques are utilized, such as immunofluorescent microscopy (Gurr et al. 1997). Because fungal organisms are more frequently recovered in chronic otitis externa than in acute, it is believed that fungal organisms may play a significant role in pathogenesis. The "id reaction" has been identified as the etiology of a few isolated cases of chronic external otitis. A focus of fungal infections found elsewhere in the body is believed to cause a secondary inflammatory process in the external auditory canal (Derebery and Berliner 1996; Busch 1998).

Hypersensitivity appears to be important in at least some patients. Early reports in the literature identified substances used in the manufacturing of matches to be pathophysiologically related to the onset of chronic external otitis among individuals who used matches to clean or scratch their ears. Phosphorus sesquisulfide, a component of "strike anywhere" matches, appears to be the principal allergen. Chrome and nickel are the material out of which ear molds are made or other common sensitizing agents that come in contact with the ear (Abdul Ghaffar and Todd 2009). Sensitivity to the components of antibiotic drops has also been implicated. Neomycin is especially likely to produce sensitization (Baer and Ludwig 1952). The incidence of sensitivity to neomycin appears to be rising. Skin testing in the 1970s, in patients with chronic external otitis, showed that neomycin sensitivity was present in approximately 8% of subjects (Rasmussen 1974). Studies conducted in the 1980s demonstrated that the rate had risen to 16% and in the 1990s the rate of neomycin sensitivity among subjects tested climbed yet again to 32–35% (Fraki et al. 1985; Van Ginkel et al. 1995). Neomycin itself may not be the culprit. Cross-sensitivity between neomycin and other aminoglycosides has been demonstrated. Sensitivity to a variety of excipients used in topical medications including topical anesthetics and topical antihistamines have also been demonstrated in patients with chronic external otitis (Van Ginkel et al. 1995).

Preexisting dermatologic disease is more common in individuals with chronic external otitis than in the population at large. Seborrheic dermatitis is the most common and affects the external auditory canal in a large number of persons; however, the majority never develop chronic external otitis. Psoriasis and neurodermatitis have also been identified as predisposing conditions.

Clinical Presentation

Clinically, the disease is characterized by pruritus (Slattery and Saadat 1997; Kesser 2011), scant otorrhea, and progressive narrowing of the lumen of the canal. Inflammation is often first seen in the anterior sulcus. Various types of chronic dermatitis may be

present for some time prior to the onset of infection in some cases. In the initial stage of infection, the external auditory canal is edematous. Histopathologically, fluid is found accumulating in the subepithelial layers of the canal skin and the edema is mild to moderate in intensity. Chronic inflammatory cells can always be demonstrated. Subdermal tissues are characterized by focal accumulations of inflammatory cells and mucopurulence that can take the form of microabscesses. Areas of calcification can develop within these focal areas. Over time, these areas of mild to moderate subepithelial inflammation develop in the areas of fibrosis (Hawke and Jahn 1987). This process may occur over only a few months but often takes years. This progressive subepithelial fibrosis is rarely a continuous process, it seems to remit and recur unpredictably. Over time, fibrous tissue concentrically obstructs the medial portions of the external auditory canal to produce canal stenosis and conductive hearing loss. The medial end of the auditory canal then terminates in a blind sac a few millimeters lateral to the tympanic membrane. Dense fibrous tissue fills the space between the end of the blind sac and the tympanic membrane. Once this process is complete, the inflammatory cycles seem to abate or cease. Cholesteatoma formation is uncommon, despite the fact that the epithelium of the lateral tympanic membrane has been trapped by the fibrotic tissues created by the inflammatory process (Hawke and Jahn 1987). In this aspect, the medial canal stenosis that arises as a consequence of chronic external otitis is quite different from traumatic canal stenosis, which often traps epithelium and results in the formation of cholesteatoma within the fibrotic segments of the external auditory canal.

While acute otitis externa features pain and tenderness as a characteristic symptom, chronic external otitis is distinguished by its painlessness (Slattery and Saadat 1997; Selesnick et al. 1998; Kesser 2011). Otalgia is rarely a complaint. Pruritus, however, is common and highly characteristic of this disorder. It is often intense and persistent. In the initial stages of the disease, pruritus is the most frequently reported symptom. Scant, watery, or milky otorrhea is often present, is generally odorless, and not very troublesome. Somewhat surprisingly, otorrhea is a less common initial complaint than hearing loss. Conductive hearing loss is a consequence of medial

canal fibrosis, which produces narrowing and obstruction of the external auditory canal and interferes with delivery of sound energy to the tympanic membrane. Hearing loss, however, is a relatively late sign (Slattery and Saadat 1997). Even a lumen as small as 2–3 mm is sufficient to permit normal or near-normal hearing. Because the last 2–3 mm may be closed relatively rapidly, hearing may appear to deteriorate over a period of weeks or months even though the disease has been present for months or years.

Diagnosis

The diagnosis depends on both history and physical examination. The history will reveal pruritis over weeks or months duration or pruritis that recurs frequently over similar periods of time. As noted above, there is often a scant, milky otorrhea. The canal itself may appear severely inflamed with granulation tissue along the medial margins and a "soft" subepithelial edema which allows canal tissues to be compressed with an instrument. In more advanced stages, areas of shiny skin with firm, underlying fibrotic tissue are noted. Patches of granulation tissue and erythema and hypervascularity of the skin may come and go over time. The medial canal is generally most severely affected and the lateral canal often appears normal (Hawke and Jahn 1987).

In the end stages of the disease, fibrosis concentrically occludes the medial canal. In its penultimate stages, just prior to complete stenosis, a narrow lumen usually occupies the center of the fibrotic tissue in the medial canal. In its final stages, the external auditory canal ends in a blind sac. The canal is almost always cerumen free but there is no longer any evidence of active infection or ongoing inflammation (Slattery and Saadat 1997; Selesnick et al. 1998; Becker and Tos 1998).

Differential Diagnosis

Carcinoma of the external auditory canal or temporal bone.

Eczematous dermatitis.

Prophylaxis

Aggressively treating acute otitis externa and dermatitis may prevent the progression to chronic otitis externa. However, medial canal fibrosis often progresses despite maximum medical therapy.

Therapy

In principle, the goal of medical treatment should be to arrest or eliminate the disease, eliminate progressive fibrosis, and prevent conductive hearing loss. Although the disease appears to respond well to initial management, clinicians are often frustrated by its frequent recurrence, and over long periods of time, relentless progression. The response of large groups of patients to medical management has not been studied and recommendations for medical treatment are made on a basis of anecdotal experience. It is widely conceded that steroids are the most critical component of successful medical management (Kesser 2011).

Jacobson et al. have published the results of a double-blind, placebo-controlled, crossover trial of budesonide. They found that the regular application of steroids decreased pruritus and otorrhea more effectively than no treatment at all. However, the study was short term and did not report the long-term outcome. It is unclear whether persistent use of budesonide would have prevented stenosis or conductive hearing loss (Jacobson et al. 1991).

Steroids have been delivered as drops and creams, and anecdotally, some otolaryngologists believe that steroid injections into the subepithelial tissues of the external auditory canal are more effective than topical applications. More potent steroids are generally preferred. Systemic steroids are not considered practical because of the long-term nature of the disease. Fluocinolone acetonide oil (Dermotic™) has demonstrated efficacy in clinical trials published (Kesser 2011).

Tacrolinus 0.1% is an immunosuppressant that has been used in the treatment of chronic dermatologic disease and has been shown to be effective for chronic otitis externa. A wick saturated with tracrolimus is placed in the ear canal and changed every 2–3 days for 9–12 days.

Antibiotics are generally included in treatment regimens since pathogenic bacteria are frequently recovered. However, given the role that hypersensitivity may play in the disease, they should be used cautiously and sparingly. The protracted nature of this disease seems prudent to limit the use of antibiotics to periods when the disease is particularly active and granulation tissue and/or significant otorrhea are prominent. Antibiotics can be delivered as drops, creams, and powders. Antibiotic powders can be mixed with dexamethasone. Because powders adhere to wet surfaces, they have a protracted dwell time and can produce more consistent levels of delivery than topical drops (Roland 2001).

Aural cleansing is considered to play an important role in the treatment of any infectious disease of the external auditory canal, and aural cleansing is usually performed by otolaryngologists at the time of office visits. However, even minor trauma to the involved tissues may hasten the progression of the disease. Consequently, cleansing the external auditory canal should be as atraumatic as possible and every attempt should be made to provide aural cleansing with a "no touch technique." Although it is tempting to use microwicks to prevent stenosis, the presence of a foreign body in contact with involved tissues may also be irritating and exacerbate or accelerate the progression of disease. Clinicians should remember that all recommended medical treatment is supported only by tradition and opinion and that no long-term outcomes are available (Roland 2001).

Once medial canal stenosis is complete and the patient experiences significant conductive hearing loss, surgical intervention is the only viable treatment option. The goal of surgical treatment is to completely resect the stenotic segment of the external auditory canal and to recreate a physiologically functioning tympanic membrane.

Surgery is relatively successful. In Slattery and Saadat's series of 24 patients, the mean preoperative air-bone gap was 25db. The air-bone gap was narrowed postoperatively to 15db at an average of 3.6 years follow-up (Slattery and Saadat 1997). In Becker and Tos's series of 53 ears (of 47 patients), 33 ears (62%) experienced a closure of air-bone gap to within 20db at late follow-up (greater than 2 years) (Becker and Tos 1998). Prerequisite to successful repair of medial canal stenosis is complete removal of all of the involved skin. This will leave the medial portion of the external

auditory canal without an epithelial lining. If the canal is not relined with epithelial tissue, restenosis will reliably occur in short order. Both local flaps and skin grafts have been used for this purpose. Pre-conchal and postauricular flaps have both been described. The advantage of flaps (as opposed to grafts) includes the potential for less scarring because of increased vascularity. The contractual forces developed during healing of a transposition flap favor pulling the ear canal open. However, it is often difficult to develop a local flap of sufficient length. Moreover, local flaps are bulky and may fill a significant portion of the external auditory canal (Slattery and Saadat 1997; Becker and Tos 1998).

Split thickness skin grafts are commonly used and are alleged to provide greater resistance to trauma. However, they often contain hair follicles that can make postoperative management more difficult. Skin grafts are easier to obtain but harder to place.

Selesnick has listed three requirements for successful repair of medial canal stenosis (Selesnick et al. 1998).
- Complete removal of the cicatrix
- Performance of a bony canalplasty
- Resurfacing of the bony canal with epithelium

Prognosis

As noted above, surgical repair is successful in the majority of cases. Slattery and Saadat reported 14 surgical procedures and only three patients experienced a recurrence (Slattery and Saadat 1997). However, one should note that the earliest of these recurrences took place more than 3 years following surgery. The long-term efficacy of surgical intervention will require longer periods of follow-up. Similarly, in Becker and Tos's series, 11 of 47 patients developed recurrence (23%) (Becker and Tos 1998). The authors noted that recurrence occurred relatively early in three of their cases (within 6 months) and believed that the earlier recurrences were attributable to incomplete removal of stenotic segment at the time of the primary procedure.

Epidemiology

The disease does not affect the sexes equally: women are more frequently affected than men by a ratio of 2:1.

The disease is bilateral in 50% of cases, which suggests that there is some systemic or constitutional component which predisposes individuals to this infection (Kesser 2011). In Slattery and Saadat's series of 24 patients, the mean age at the time of the first visit was 50.5 years and only a single patient was younger than 18 years of age (Slattery and Saadat 1997).

Cross-References

▶ Osteomyelitis of Temporal Bone
▶ Squamous Cell Carcinoma of Ear

References

Abdul Ghaffar S, Todd PM (2009) Chronic recurrent otitis externa secondary to allergic contact dermatitis to nickel and phosphorus sesquisulfide. Contact Dermatitis 61:124–125

Baer R, Ludwig J (1952) Allergic eczematous sensitization to neomycin. Ann Allergy 10:136–137

Becker BC, Tos M (1998) Postinflammatory acquired atresia of the external auditory canal. Treatment and results of surgery over 27 years. Laryngoscope 108:903–907

Busch RF (1998) Dermatophytid reaction and chronic otitis externa. Otolaryngol Head Neck Surg 118:420

Derebery J, Berliner KI (1996) Foot and ear disease – the dermatophytid reaction in otology. Laryngoscope 106:181–186

Fraki JE, Kalimo K, Tuohimaa P, Aantaa E (1985) Contact allergy to various components of topical preparations for treatment of external otitis. Acta Otolaryngol 100:414–418

Gurr PA, Evans K, Dewey FM, Gurr SJ (1997) Otomycosis: the detection of fungi in ears by immunofluorescence microscopy. Clin Otolaryngol 22:275–283

Hawke M, Jahn AF (1987) Diseases of the ear. Clinical and pathologic aspects. Lea and Febiger/Gower Medical Publishing, Philadelphia/New York

Jacobson S, Karlsson G, Rigner P et al (1991) Clinical efficacy of budesonide in the treatment of eczematous external otitis. Eur Arch Otorhinolaryngol 248:246–249

Kesser BW (2011) Assessment and management of chronic otitis externa. Curr Opin Otolaryngol Head Neck Surg 19:341–347

Rasmussen PA (1974) Otitis eternal and allergic contact dermatitis. Acta Otolaryngol 77:344–347

Roland P (2001) Chronic external otitis. Ear Nose Throat 80(6 Suppl):12–16

Selesnick S, Nguyen TP, Eisenman DJ (1998) Surgical treatment of acquired external auditory canal atresia. Am J Otol 19:123–130

Slattery WH III, Saadat P (1997) Postinflammatory medial canal fibrosis. Am J Otol 18:294–297

Van Ginkel CJ, Bruintjes TD, Huizing EH (1995) Allergy due to topical medications in chronic otitis externa and chronic otitis media. Clin Otolaryngol 20:326–328

Chronic Otitis Media

Katherine Green and Patricia J. Yoon
School of Medicine, Department of Otolaryngology, University of Colorado, Children's Hospital Colorado, Aurora, CO, USA

Synonyms

Chronic otitis media with effusion; Glue ear; Nonsuppurative otitis media; Persistent middle ear effusion; Secretory otitis media; Serous otitis media

Definition

Otitis media with effusion (OME) is defined as the presence of fluid in the middle ear, without signs or symptoms of acute ear infection or inflammation.

Etiology

The middle ear space is a closed space located behind the tympanic membrane. Its only communication with the outside world is through the Eustachian tube, which connects the middle ear space to the nasopharynx. The normal middle ear space is filled with air, and the system is lined by respiratory mucosa. The anatomy of the Eustachian tube in infants and young children differs from that of adults, contributing to the increased incidence of acute otitis media (AOM) and OME in this population. The ET reaches its adult length by the time a child is 7 years of age. The Eustachian tube equilibrates middle ear pressure and allows for drainage of middle ear. The ET is collapsed at rest, but intermittently opens through active movements of the jaw, such as yawning, or by actions such as swallowing, via contraction of the tensor veli palatini muscle. This allows for equilibration of pressure in the middle ear space with atmospheric pressure. If the ET is obstructed, pressure in the ear cannot be equalized and secretions cannot drain into the nasopharynx, leading to accumulation of fluid in the middle ear.

The Eustachian tube can become swollen and obstructed for a variety of reasons including upper respiratory infection, allergy, barotrauma, and environmental irritants such as second hand tobacco smoke. Most often, OME is residual fluid that remains in the middle ear following an episode of acute otitis media. Although the fluid in AOM is purulent, after treatment or resolution, fluid often persists within the middle ear space. The traditional teaching is that this fluid is sterile; however, studies suggest bacteria may exist and contribute to OME in the form of biofilms (Hall-Stoodley et al. 2006).

Clinical Presentation

By definition, the signs and symptoms of acute inflammation or infection are absent in patients with OME, although there may be history of a recent AOM which has since resolved. OME is frequently an incidental finding when a child's ears are examined. There are usually no obvious symptoms, but older children and adults may complain of decreased hearing or a feeling of fullness, or "popping" in the ears. Younger children may exhibit signs of hearing loss such as failure to respond to voices, speaking loudly, or turning the volume up on the television. In cases that have gone unrecognized for several months or more, children may present with speech or language delays, and even behavioral problems. Occasionally, OME can present with mild ear pain, vertigo, or imbalance. Approximately 90% of children will have OME at some time before school age (AAFP, AAO-HNS, AAP Subcommittee on OME 2004).

Diagnosis

Pneumatic otoscopy is the gold standard for the diagnosis of OME, and is the primary tool used to evaluate the tympanic membrane (TM) and the status of the middle ear. In order to perform a thorough otoscopy exam, it is important that obstructing cerumen be cleared from the canal under direct visualization. In OME, the tympanic membrane is usually in neutral position or retracted. It is usually gray, pale pink, or amber in color, and is typically not red or inflamed in appearance. Fluid in the middle ear space makes the TM appear cloudy or opaque, and an

air-fluid level or bubbles may be visible through the TM. Air-fluid levels will fluctuate with pneumatic otoscopy. Absent or decreased TM mobility is seen on pneumatic otoscopy.

Tympanometry and Audiometry

Tympanometry can be a helpful adjunct in assessing middle ear status and TM function, particularly when otoscopic evaluation is either inconclusive or difficult to perform. A small probe which emits a tone is placed in the ear canal with an airtight seal. The tympanometer measures the acoustic energy of the reflected tone, and graphically represents the relationship of air pressure in the ear canal to the impedance of the tympanic membrane. A "flat" tympanogram with a small volume is found in the presence of a middle ear effusion.

Fluid in the middle ear space can cause a mild to moderate conductive hearing loss, so abnormal audiometry is usually seen in patients with OME. Formal audiometric testing is recommended in children in whom OME has persisted for at least 3 months or in whom language delay, learning problems, or a significant hearing loss (≥ 21 dB) is suspected. There are several groups of children who are considered to be high risk for developmental problems as a result of hearing loss; in these children, earlier formal testing of hearing is warranted in the presence of an effusion. These groups include children with a known hearing loss independent of OME, suspected or diagnosed speech and language delay or disorder, autism spectrum disorders, craniofacial disorders, developmental delay, and uncorrectable visual impairment. In these children, even a very small amount of hearing loss can have a large impact on their speech and language development (AAFP, AAO-HNS, AAP Subcommittee on OME 2004).

Differential Diagnosis

It is important to distinguish acute otitis media (AOM) from otitis media with effusion (OME), as management of the two conditions differs. Myringosclerosis can be a sequela of AOM or OME, and is a condition that may mimic OME in presentation. In myringosclerosis, whitish plaques are seen in the TM.

When extensive, myringosclerosis may cause reduced TM mobility and a conductive hearing loss.

In children, OME is common, due to Eustachian tube immaturity. However if OME is found in an adult, the possibility of a nasopharyngeal mass causing anatomic obstruction of the ET must be considered. Although OME in adult is still most likely due to inflammation or infection, the following should be considered in a patient who presents with OME: benign nasopharyngeal masses, nasopharyngeal carcinoma, adenoid hypertrophy, congenital defects affecting the Eustachian tube and its egress, ciliary dyskinesia, immunoglobulin G (IgG) subclass deficiencies.

Therapy

Management of OME in children is dictated largely by audiometric results and degree of concern regarding the impact of the effusion on speech, language, and development (AAFP, AAO-HNS, AAP Subcommittee on OME 2004). Because of the self-limited nature of most OMEs, watchful waiting is recommended for healthy children at low risk for speech, language, or developmental problems, whose effusions have been present for 3 months or less. Patients should be reassessed at 3-month intervals until either the effusions have resolved or surgery becomes indicated. Audiometric testing is recommended when OME has been present for 3 or more months, if language delays, learning problems, or hearing loss are suspected, or if a child falls into a high-risk group for developmental delays as noted earlier.

If, at reassessment, OME is still present, but hearing is normal and there is no evidence of structural damage to the tympanic membrane, continued watchful waiting is recommended. If mild hearing loss (21–39 dB) is discovered, management may be dictated to some degree by caregiver preference, if the TM is structurally uncompromised. If watchful waiting is elected, measures should be taken to optimize the child's listening and learning. Examples of such measures include preferential seating in the classroom, and speaking clearly and in close proximity of the child.

Surgical treatment, with the placement of tympanostomy tubes, is recommended for children

with hearing loss $\geq$40 dB, if structural damage to the TM such as retraction pockets or TM atelectasis is seen, if speech, language, or developmental problems are noted, or if other symptoms of OME, such as pain or vertigo, are present. Tympanostomy tube insertion produces a significant reduction in time spent with effusion, according to numerous studies. Adenoidectomy in conjunction with tympanostomy tube placement has been shown to be a beneficial first-line surgery in children aged 4–8 years with chronic OME, or in younger children with persistent problems after extrusion of a first set of tubes, regardless of adenoid size. Tonsillectomy does not improve outcomes in OME (Rosenfeld and Bluestone 2003).

Antibiotics

The use of antibiotics has been studied in OME, and although there is some evidence that one short course of antibiotics may provide some short-term benefit, antimicrobial therapy does not produce a lasting response, and repeated or prolonged courses of antibiotics have not proven effective. There is no role for antibiotic prophylaxis in OME (Rosenfeld 2007).

Adjuvant Therapies

There is no data to support the use of antihistamines and decongestants in the treatment of OME. Intranasal steroids have also been studied, and may provide some short-term relief for OME. However, no long-term benefit has been proven (AAFP, AAO-HNS, AAP Subcommittee on OME 2004; Mandel 2007).

Adults with OME

When OME develops in an adult without a history of ear problems or without evident etiology, such as an upper respiratory infection, allergies, or history of barotrauma, flexible fiber-optic endoscopy should be performed to rule out a nasopharyngeal mass.

Prognosis

OME spontaneously resolves in most cases within 3 months of diagnosis, but approximately 30–40% of children have recurrent OME, and approximately 5–10% of episodes last 1 year or longer (AAFP, AAO-HNS, AAP Subcommittee on OME 2004).

Cross-References

▶ Acute Otitis Media
▶ Eustachian Tube, Anatomy and Physiology
▶ Middle Ear Physiology
▶ Otitis Media with Effusion
▶ Otitis Media, Complications

References

American Academy of Family Physicians, American Academy of Otolaryngology-Head and Neck Surgery, American Academy of Pediatrics Subcommittee on Otitis Media With Effusion (2004) Otitis media with effusion. Pediatrics 113(5):1412–1429

Hall-Stoodley L, Hu FZ, Gieseke A et al (2006) Direct detection of bacterial biofilms on the middle-ear mucosa of children with chronic otitis media. JAMA 296:202–211

Mandel EM (2007) Steroids for chronic otitis media with effusion in children. In: Alper CM, Bluestone CD et al (eds) Advanced therapy of otitis media. BC Decker, Ontario, pp 180–184

Rosenfeld RM (2007) Antibiotics for otitis media with effusion. In: Alper CM, Bluestone CD et al (eds) Advanced therapy of otitis media. BC Decker, Ontario, pp 175–179

Rosenfeld RM, Bluestone CD (2003) Clinical efficacy of surgical therapy. In: Rosenfeld RM, Bluestone CD (eds) Evidence based otitis media, 2nd edn. BC Decker, Ontario, pp 227–240

Chronic Otitis Media with Effusion

▶ Chronic Otitis Media

Chronic Rhinosinusitis

▶ Rhinosinusitis, Pathophysiology and Medical Management

Chronic Sinusitis

▶ Rhinosinusitis, Pathophysiology and Medical Management

Cinchonism

Erika Woodson
Head and Neck Institute, Cleveland Clinic Foundation, Cleveland, OH, USA

Definition

Quinine toxicity. May occur with therapeutic doses.

Cross-References

▶ Sensorineural Hearing Loss (Ototoxicity)

Cisplatin

Erika Woodson
Head and Neck Institute, Cleveland Clinic Foundation, Cleveland, OH, USA

Definition

Alkylating antineoplastic agent notable for ototoxicity. Frequently used in chemotherapy for head and neck cancer, carcinomas, sarcomas, and lymphomas.

Cross-References

▶ Sensorineural Hearing Loss (Ototoxicity)

Classification of Flaps

Gina D. Jefferson
Department of Otolaryngology and Communicative Sciences, University of Mississippi Medical Center, Jackson, MS, USA

Synonyms

Angiosome; Axial flaps; Composite flaps; Fasciocutaneous flaps; Free flaps; Muscle flaps; Osseocutaneous flaps; Osseous flaps; Random flaps; Regional flaps

Definition

A flap is a unit of tissue containing its own blood supply transferred from its native location, called the donor site, to another location in the body, either remote or distant, called the recipient site. The flap is sometimes transferred while leaving the blood supply intact, or sometimes the blood supply is interrupted temporarily to transplant the tissue to a distant location where the blood vessels require anastomosis to blood vessels near the recipient site.

Flaps are units of tissue used to reconstruct defects where primary closure is not possible, or is not desirable when severe dysfunction may result. The tissue unit maintains its own blood supply from the donor site in the transference of the tissue unit to the defect, or recipient site. For the ease and understanding among surgeons when communicating about "flaps," and when considering how to reconstruct an anticipated surgical defect, a variety of classification systems emerged. Initially, skin flaps were raised in a random fashion without regard to known blood tributaries into the region. These skin flaps were raised while maintaining the subdermal vascular plexus as the main source of nutrition and were simply classified by the *method of transference* of skin, that is, advancement or rotation, local or distant, or tubed or flat (Wei and Mardini 2009).

Classification by *composition* of the flap undergoing transfer is logical when considering the types of tissue missing from the planned defect and therefore the types of tissue necessary to accomplish reconstruction where restoration of form and function are the goals. There are stand-alone skin flaps, fascial flaps, muscle flaps, visceral flaps, and bone flaps with their own arteriovenous supplies. Composite flaps are composed of more than one type of tissue. Musculocutaneous flaps are those units of tissue based upon vessels traveling from muscle to the skin. The perforator travels through the septum or through the muscle to reach the skin. The fasciocutaneous flaps are based upon a confluence of subfascial, intrafascial, and suprafascial vascular plexuses contained within the dermis, subdermis, and superficial and deep adipofascial layers. The confluence of these vessels is a rich network of blood supply to the overlying flap skin. Septocutaneous vessel perforators supply the fascial, fasciocutaneous, and osteocutaneous flaps. For complex 3-dimensional reconstructions, composite

flaps are necessary where several tissue layers such as skin, muscle, and bone that rely upon a vascular pedicle are transferred into a defect (Ciresi and Mathes 1993).

The Mathes and Nahai classification system, originally used in reference to fasciocutaneous flaps, is also useful in the categorization of muscle-only flaps due to the systematic categorization of the flaps by origin of *blood supply*. The final common pathway of blood supply is via direct arterial input to the dermal plexuses, the primary blood supply to the skin itself. Axial pattern flaps rely upon a vascular pedicle containing an anatomically defined arteriovenous system that travels along the axis of the flap. Such axial pattern flaps were further subcategorized into Types I through V where Type I describes a flap with a single dominant pedicle such as the tensor fascia lata flap. Type II muscle flaps are those with a dominant pedicle and multiple minor pedicles such as the trapezius flap. Type III muscle flaps have dual dominant pedicles like the rectus abdominus flap. The rectus abdominus flap may survive with either the superior epigastric vascular pedicle or the inferior deep epigastric vascular pedicle, for example. Type IV flaps describes a unit of muscle that relies upon multiple segmental pedicles for survival. Each pedicle provides circulation to a portion of the muscle, and division of two or three of these pedicles will result in tissue necrosis. Type IV flaps are not ideal for free tissue transfer. An example of a Type IV muscle flap is the sartorius muscle or external oblique muscle. Type V flaps have one dominant pedicle and secondary segmental pedicles like the latissimus dorsi flap where the dominant pedicle is the thoracodorsal system and secondary segmental pedicles include a lateral row and medial row of segmental vessels off the posterior intercostal vessels. Of note, Types I, III, and V are the most suitable and reliable for free tissue transfer (Mathes and Nahai 1981).

Another concept that deserves mention is the concept of the angiosome. An angiosome is defined as a composite unit of tissue including, skin, muscle, fascia, tendon, nerve, and bone reliant upon source artery and linked together by anastomotic vessels that span between the skin and the bone. The anatomic territory supplied by a cutaneous perforator forms a basic angiosome where the perimeter of this territory is connected with its neighbor in all directions. The vascular connection zone between territories is most commonly via reduced caliber vessels referred to as "choke" vessels although occasionally the anastomosing vessels exhibit no decrement in vessel diameter. The concept of the angiosome is clinically relevant when planning a cutaneous flap, for example. Multiple authors note necrosis in the choke zone between the captured territory and the next territory beyond when incorporating multiple adjacent angiosomes in series. However, sometimes, inclusion of an additional territory in the series was found not to survive (Houseman et al. 1999; Taylor et al. 2011). Necrosis is avoided by carefully planning the orientation of the skin paddle realizing that the dominant cutaneous vessels perforate the deep fascia in anatomic regions where the skin is fixed or along the perimeter of muscles, such as the pectoralis major. Additionally, cutaneous branches are long where the skin is mobile as in the scalp. Finally, the vessel branches are long or form a chain-linked system without decrement in caliber between anastomosing vessels when they accompany cutaneous nerves. These cutaneous perforator vessel patterns are identified by the reconstructive surgeon using a Doppler device or even the SPY® machine. The SPY® machine allows fluorescent laser angiography dependent upon injection of indocyanine green dye intraoperatively. These techniques allow the flap design to include identified perforating vessels.

In conclusion, there are several classification schemes used to describe the type of tissue transfer employed in reconstruction. These schema allow the reconstructive surgeon to critically assess a patient's defect, devise a reconstructive method that will replace the missing tissue units, and restore form and function to the best of his or her ability. The classification methods also permit meaningful conversation among surgeons regarding patient care practices.

References

Ciresi KF, Mathes SJ (1993) The classification of flaps. Ortho Clin North Am 24(3):383–391

Houseman ND, Taylor GI, Pan WR (1999) The angiosomes of the head and neck: anatomic study and clinical applications. Plast Reconstr Surg 105:2287–2313

Mathes SJ, Nahai F (1981) Classification of the vascular anatomy of muscles: experimental and clinical correlation. Plast Reconstr Surg 67:177–187

Taylor GI, Corlett RJ, Dhar SC, Ashton MW (2011) The anatomical (angiosome) and clinical territories of cutaneous perforating arteries: development of the concept and designing safe flaps. Plast Reconstr Surg 127:1447–1459

Wei F, Mardini S (2009) Flaps and reconstructive surgery. Elsevier, Philadelphia

Cleft Lip

Eric J. Dobratz
Department of Otolaryngology, Eastern Virginia
Medical School, Norfolk, VA, USA

Synonyms

Cheilioschisis; Harelip (old term based on similarity of
the appearance of a cleft lip to that of a hare, generally
not used any longer)

Definition

Cleft lip – a disorder that occurs during the fusion of
the lateral lip elements with the central lip during
development. It may occur unilaterally or bilaterally.
A cleft lip may occur on its own or may be associated
with a cleft of the alveolar bone or palate.

Introduction

Orofacial clefting is the most common developmental
abnormality of the face and it has been studied exten-
sively. There are numerous books and volumes of
textbooks that have been published describing the
diagnosis and surgical treatment of facial clefts, espe-
cially cleft lip and palate. This entry will attempt to
provide an overview of the genetics/embryology,
clinical features, and surgical treatment of cleft lip
deformities. We encourage the reader to explore the
referenced texts for a more complete description of
cleft lip deformities and other types of facial cleft
abnormalities. Further details relating to cleft palate
deformities may be found in this text under the topic
Cleft Lip and Palate.

Epidemiology

Orofacial clefts are generally divided into two groups
when determining epidemiologic characteristics:
(1) cleft lip with or without palate and (2) isolated
cleft palate. The incidence of cleft lip with or without
cleft palate varies (Mooney 2009) with American

Indians and Asian populations having the highest
birth prevalence (15.0–36.0/10,000), followed
by European-derived populations (10.0/10,000).
African-Americans have the lowest incidence
(5.0/10,000). Isolated cleft lips are generally unilateral
(80%). Unilateral cleft lips occur with a left-sided
to right-sided ratio of 2:1. The majority of cleft lips
are associated with a cleft palate. Bilateral cleft lips
are associated with cleft palate 85% of the time
and unilateral cleft lips are with cleft palate 70% of
the time.

History

Facial development is a complex and coordinated
series of morphogenetic patterns that occur early in
embryogenesis. Abnormal facial development occurs
during the first 4–12 weeks of development and is
likely the result of genetic and environmental influ-
ences that interrupt the normal sequence of facial
development. Orofacial clefts may occur within or
outside of syndromes. A syndrome must include
a cognitive or structural abnormality that is distinct
from the cleft. Cleft lip with or without cleft palate is
related to a syndrome 14% of the time and cleft palate
alone is associated with a syndrome 55% of the time
(Sykes 2005).

Embryology and Pathogenesis

The orofacial region is identified at the 28th day of
embryogenesis with the formation of the prechordal
plate in the trilaminar germ disk. The germ disk contains
all three germ layers (ecto-, meso-, and endoderm) and
the prechordal plate lacks the intermediate mesoderm.
The ectoderm and endoderm fuse to form a temporary
oropharyngeal membrane, which is the location of the
future mouth. This membrane becomes the center of
development for five facial prominences that swell
during the fourth week of development. These five
facial prominences include the median frontonasal
prominence, the bilateral maxillary prominences, and
the bilateral mandibular prominences. The maxillary
and mandibular prominences are derived from the first
two pharyngeal arches (Fig. 1).

Bilateral nasal placodes develop on the inferolateral
corners of the frontonasal prominence. These placodes
sink to form nasal pits and result in the development of
an elevated horseshoe-shaped medial and lateral nasal
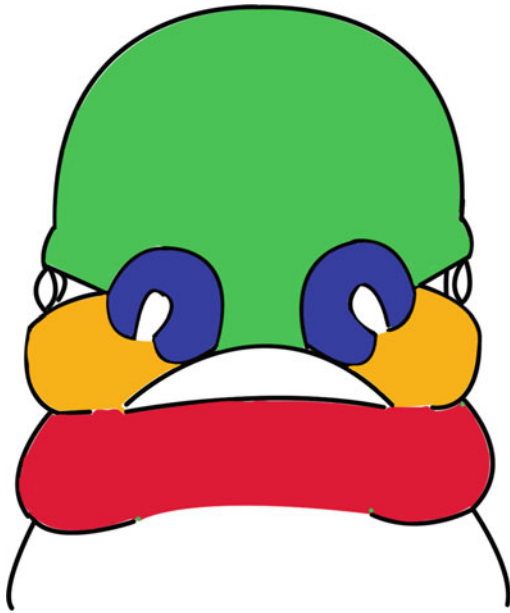
Cleft Lip, Fig. 1 Five facial prominences that lead to facial development. The frontonasal prominence (*green*) develops bilateral nasal placodes on the inferolateral corners (*blue*). The bilateral maxillary prominences (*orange*) and mandibular prominences (*red*) are derived from the first two pharyngeal arches

prominences. The lateral nasal prominence forms the alae of the nose and the medial prominence fuses to form the columella.

Development of the upper lip is initiated by the fusion between the lower edges of the medial and lateral nasal prominence. The bilateral maxillary prominences grow medially pushing the lateral nasal prominence medially as well, narrowing the space between the lateral and medial nasal prominence. The medial nasal prominence fuses with the bilateral maxillary prominence. At first there is an epithelial "nasal fin" separating the maxillary and medial nasal prominence. Normally this layer degenerates and allows for fusion of the tissues. Persistence of this epithelial nasal fin may contribute to clefting of the upper lip and anterior palate. All of these fusions involve apoptosis, programmed cell death, and development of new intervening tissues. Any disruption of the coordinated movements and fusions may lead to clefting of the upper lip (Sperber et al. 2009).

The paired medial nasal prominence fuses in the midline to form an intermaxillary segment, which develops into the tip of the nose, the columella, the philtrum, the labial tuberculum of the upper lip, the frenulum, and the premaxilla (primary palate, bone anterior to the incisive foramen). Clefting of the upper lip may occur between the lateral maxillary prominence and the fused medial nasal prominence on one side (unilateral) or both sides (bilateral). Rarely the medial nasal prominence will not fuse in the midline and a midline cleft will occur. Failure of fusion of the upper lip may impact the later-occurring fusion of the secondary palate, which can lead to combined cleft lip and palate defects. Cleft palate that occurs isolation of a cleft lip has a different pathogenesis.

Failure of fusion of the maxillary and mandibular prominences lateral can result in a lateral lip/facial cleft resulting in macrostomia. This rare deformity that occurs at the oral commissure is surgically corrected by a *commissuroplasty*.

Classification

Classification of orofacial clefts is important due to the heterogeneous, multifactorial etiology associated with the development of the clefts. Accurate classification assists the surgeon and others on the craniofacial team with surgical and clinical management, genetic counseling, and research. Multiple classification systems have been developed for orofacial clefts based on morphology or anatomy of the cleft, the pathogenesis of the cleft, or the etiology of the cleft. The heterogeneous nature of cleft deformities makes it difficult to develop an accurate yet simplistic classification system.

Fogh-Andersen (Mooney 2009) developed a classification system that divided oral clefts into three main groups based on affected anatomy:
1. Cleft lip (CL) group: clefts of the primary palate including lip, alveolus, and incisive foramen
2. Cleft lip and palate (CLP) group: Unilateral and bilateral clefts of the lip (complete or incomplete) that extend into the secondary palate
3. Cleft palate (CP) group: Midline clefts of the secondary palate, posterior to the incisive foramen

At their congress in 1967, the International Confederation for Plastic and Reconstructive Surgery developed a classification scheme based on the embryology and pathogenesis of the developing structure:
1. Clefts of the primary palate
   (a) Lip
   (b) Alveolus

Cleft Lip, Fig. 2 A patient with bilateral microform cleft lip. Note the disruption at the vermilion and the *white roll* (*arrow*)

Cleft Lip, Fig. 3 A patient with unilateral incomplete cleft lip on the *right side*. Note the moderate nasal deformity with a flattened alar rim and inferior-lateral displacement of the alar base

2. Clefts of the primary and secondary palate
   (a) Lip
   (b) Alveolus
   (c) Hard palate (secondary palate)
3. Clefts of the secondary palate
   (a) Hard palate
   (b) Soft palate

Cleft lip deformities may range from minor malformations to complete interruption of the lip, alveolus, and base/floor of the nose. A minor malformation includes the *microform cleft lip,* which is characterized by dehiscence of the orbicularis muscle with no overt clefting of the epidermis of the lip (Fig. 2). The cases may have disruption of the vermillion and white roll. An *incomplete cleft lip* (Fig. 3) is a cleft involving all layers of the lip (skin, muscle, and mucosa) that does not extend into the nose. A cleft that involves all layers of the lip and extends into the floor of the nose is a *complete cleft lip* (Fig. 4). Clefts may be unilateral or bilateral. Bilateral cleft lips may be complete or incomplete on both sides or may be complete on one side and incomplete on the other (Fig. 5).

Clinical Features

Care for children with orofacial clefts is often coordinated through a multidisciplinary craniofacial team. Members of this team will generally include a team coordinator, surgeon(s), otolaryngologist, pediatrician,


Cleft Lip, Fig. 4 A patient with unilateral complete cleft lip. Note the wider cleft involving the alveolar bone and floor of the nose. The nasal deformity is more significant as well

dentist, orthodontist, geneticist, speech therapist, and social worker. The treatments that may be provided to patients with cleft lip/palate deformities occur over a general timeline (Table 1) and are coordinated through follow-up appointments with the craniofacial team.

Prenatal

With improvements of ultrasonography and the prenatal diagnosis of orofacial clefts becoming more

Cleft Lip, Fig. 5 (**a**) A patient with a bilateral complete cleft lip and (**b**) a patient with a bilateral cleft lip that is complete on one right side and incomplete on the left side. Bilateral complete cleft lip deformities may lead to significant protuberance of the central segment (premaxilla) as it has no connection with the lateral palatal segments
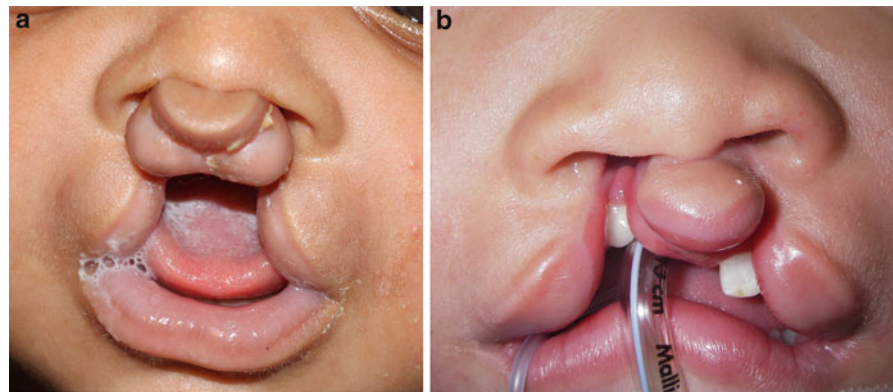
Cleft Lip, Table 1 Timeline of treatments for children with cleft lip and/or palate

Early infancy (0–6 months)	Presurgical orthopedics
	Cleft lip repair/primary rhinoplasty
Early toddler (9–15 months)	Palate repair
	Tympanostomy tubes
Preschool (2–5 years)	Manage VPI (pharyngoplasty)
Elementary (5–12 years)	Alveolar bone graft
	Columellar lengthening
	Orthodontics
Adolescents/early adult (12–18 years)	Orthodontics
	Orthognathic surgery
	Rhinoplasty

common, care for families of cleft children often begins during the prenatal time period. Expectant parents may meet with their pediatrician, surgeon, and social workers in preparation for caring for a child with a facial deformity. Parents may experience a wide range of emotions and may benefit from additional support services during this time. A thorough history should be obtained including the identification of family history of facial deformities or syndromes and any possible environmental or teratogenic exposures. This information will help to determine whether the parents should undergo genetic or prenatal counseling.

Newborn/Early Infancy

Neonates with clefts of the lip and palate should undergo a thorough examination to look for any other associated anomalies that may indicate a genetic syndrome. Parents should be instructed on the use of special bottles and nipples that are used to assist in feeding these infants. Their weight should be closely monitored to ensure proper feeding and growth. Infants that are not gaining weight appropriately should be referred to the cleft coordinator to arrange a visit with an infant-feeding specialist who has experience with cleft patients.

Some surgeons prefer to perform presurgical orthopedic interventions in children with wide complete clefts or a very protuberant premaxilla. These presurgical devices help to mold the lip/alveolus and nose in order to decrease the size of the cleft, lengthen the columella, and possibly improve the surgical outcomes. These orthopedic devices require a significant degree of cooperation by the caregiver and require frequent visits to adjust the device.

Plans will be made for repair of the cleft lip during this time. Some surgeons perform surgery on the lip during the perinatal period, within the first week of life. Other surgeons prefer to wait for the more traditional time period of when the infant reaches 8–10 weeks old. After surgery the patients should be monitored for appropriate growth and ensure that they are meeting normal developmental milestones.

Late Infancy/Early Toddler

Children with cleft lip and palate will generally undergo palate repair during this time (9–15 months). It is important to continue to monitor for appropriate feeding, growth, and development. Children who have an associated cleft palate will often have dysfunction of the eustachian tube and are at risk for conductive hearing loss due to fluid in the middle ear. These

children will benefit from placement of myringotomy tubes, often at the time of the cleft palate repair. These children should be monitored to ensure that they are meeting the appropriate developmental milestones. Developmental delays and/or learning disabilities may be more common in infants and toddlers with "isolated" orofacial clefting than in the general pediatric population (Heike and Cunningham 2009).

Toddler/Preschool

During this timeframe the children will likely not require surgical intervention. One of the most important things to monitor at this stage is for speech and language development. The speech therapist on the craniofacial team will evaluate the children to ensure that development is appropriate and will initiate treatment in patients who demonstrate impairment in speech and language development. Children with a history of a cleft palate repair may develop velopharyngeal insufficiency and may require surgery to correct this. Hearing should also be evaluated due to the increased incidence of eustachian tube dysfunction.

Elementary Years

Children aged 5–12 years will require less frequent craniofacial team assessments. The main focus during this time period is dental health. Patients with alveolar bone clefts will undergo bone grafting in preparation for eruption of permanent teeth. Patients may undergo orthodontic interventions during this time period. Children with bilateral cleft lip and a shortened columella may undergo a columellar lengthening procedure at age 5 or 6. There are various techniques that are used to release the tethered and shortened columella that allow for advancement and increased projection of the nasal tip.

Adolescence/Early Adulthood

Adolescents with a history of cleft lip become increasingly self-conscious and focused on their appearance during this time period. They will have increased social interactions and will be more interested in optimizing their facial appearance. Patients will continue or initiate orthodontic treatments during this time. They may undergo orthognathic procedures to correct occlusal abnormalities or to optimize the position of their maxilla. Patients will often undergo a secondary rhinoplasty during this time to optimize the appearance

and function of the nose. Some teenagers may also become interested in knowing the chances of children with an orofacial deformity. These patients may benefit from genetic counseling.

Tests

The diagnosis of cleft lip is a clinical one with the obvious orofacial deformity noted at birth. However, prenatal diagnosis of cleft defects is becoming much more common and different techniques have been proposed to prenatally detect and diagnose cleft lip including ultrasonography, fetoscopy, CT, MRI, and amniocentesis. Ultrasonography is noninvasive and used widely in prenatal evaluation and has become the technique of choice for prenatal diagnosis of orofacial clefting.

The recognition rate of cleft lip/palate deformities during prenatal ultrasound may vary from 18% to 70% (Rotten and Levaillant 2009). This variation is likely influenced by the protocol that the ultrasound technician follows. Protocols may vary from completely ignoring visualization of the face, to only selected views or comprehensive evaluation. Two-plane evaluation of the face leads to 20–30% recognition of facial anomalies. Three-plane (sagittal, coronal, and axial) evaluation leads to recognition rates as high as 90%. This three-plane evaluation is performed at many tertiary centers with high-risk patient populations and this may contribute to higher rates of prenatal recognition at these centers.

Etiology

The etiology of cleft lip formation is multifactorial and likely the result of genetic and environmental influences that interrupt the normal sequence of facial development.

Gene expression patterns have been analyzed in an attempt to establish an etiology for cleft lip formation and other facial cleft deformities. Of the estimated 25,000 protein-coding genes in the human genome, approximately 17,000 genes have been identified as contributing to craniofacial development (Sperber et al 2009). Thus far, two genes (MSX1 and TBX22) have been identified as being associated with the development of non-syndromic cleft lip/palate. More

genetic associations have been determined for clefts that are associated with various syndromes. However, there currently is no specific test available for genetic susceptibility to orofacial clefts.

Environmental factors have been shown to have an effect on the formation of clefting as well. Teratogens such as phenytoin, retinoic acid, and folic acid antagonists have all been shown to have a relation to the formation of clefts. Cigarette smoking and fetal alcohol exposures have been noted to be risk factors as well. Folic acid supplements are thought to reduce the incidence of nonsyndromic clefts.

Treatment

Unilateral Cleft Lip

Incomplete and complete unilateral cleft lip deformities involve the skin, muscle, and mucosa of the lip. The underlying alveolar bone and primary palate may be involved as well. The orbicularis muscle normally forms a sphincter encircling the oral aperature. In unilateral cleft lip deformities this sphincter is disrupted on the side of the cleft and the muscle becomes vertically oriented at the border of the cleft. The muscle on the medial side of the cleft becomes hypoplastic (Capone and Sykes 2009). The vertically oriented muscle segments attach superiorly to the base of the columella and nasal spine medially and to the alar base laterally. The pull of muscle then contributes to the resulting nasal deformity (Fig. 4). The collumella and caudal septum are pulled to the non-cleft side. The alar base is pulled inferiorly and laterally and the alar cartilage is flattened and deprojected.

The goals of surgical treatment of the cleft lip deformity are to close the defect while reconstituting the sphincter of the orbicularis muscle. Other goals may include closing the floor of the nose and primary rhinoplasty, if indicated. There are a number of closure techniques that have been developed and description of all of these is beyond the scope of this entry. The author will describe two techniques that they have used and have found to produce consistent and reliable results.

Millard Rotation-Advancement Flap

The rotation advancement flap technique is the most commonly used technique today (Ness and Sykes 1993). It allows for maximal flexibility during closure while discarding minimal amounts of tissue. Modifications may be made during the repair to allow for a "cut as you go" repair. The incisions are designed so the resultant scar is camouflaged in the new philtral column. However, there are disadvantages to this technique as well. Optimal results require experience and artistic design of the flap. Other techniques include geometric closures that produce reliable results through exact measurements and do not require artistic license. Rotation advancement closure may result in excess tension if used to close wide clefts. The surgeon must also be ware of tendency to create a small nostril. It is better to leave the nostril slightly larger as it is easier to correct this deformity than to repair nostril stenosis. The resultant vertical scar is an unbroken line that tends to develop vertical contracture. It is advisable to be sure that the height of the reconstructed lip is at least the length of the non-cleft side. The surgeon may want to make the lip 0.5–1.0 mm longer with anticipation of this contraction.

Although this technique allows for artistic license, there are key reference points that should be marked prior to designing the flaps (Fig. 6). The ultimate goal is to ensure that the length of the rotation flap on the medial lip $(3–5 + x)$ is equal to the advancement flap on the lateral lip $(8–9)$.

After designing the rotation (A), advancement flap (B), and minor skin flap (C), the incision is created. First the lip is released from the maxilla and pyriform through a buccal incision. Next a skin incision is created on the rotation flap. The incision starts at the x point, is carried through the 5 point, and on to the 3 point. An 11 blade is then used to make a full thickness incision through the muscle and mucosa, through the vermillion. The blade is placed such that it is beveled toward the cleft in order to preserve the muscle. The incision on the advancement flap is then created in a similar fashion. It is carried from the alar base (point 10) to point 9 and then through point 8. The vermillion is then excised from the C flap, which is preserved for possible future use to place into the nasal sill or the columella. The orbicularis muscle is then dissected and reapproximated while rotating and advancing the flaps. The skin and vermillion are then closed. If indicated, the surgeon may then perform a primary rhinoplasty to reshape the lower lateral cartilage and/or intranasal flaps to reconstruct the anterior floor of the nose.

Cleft Lip, Fig. 6 Millard rotation/advancement flap closure of cleft lip. Key reference points (**a**) are marked prior to infiltration of local anesthetic. Incision lines and flaps (**b**) are then drawn off of these reference points
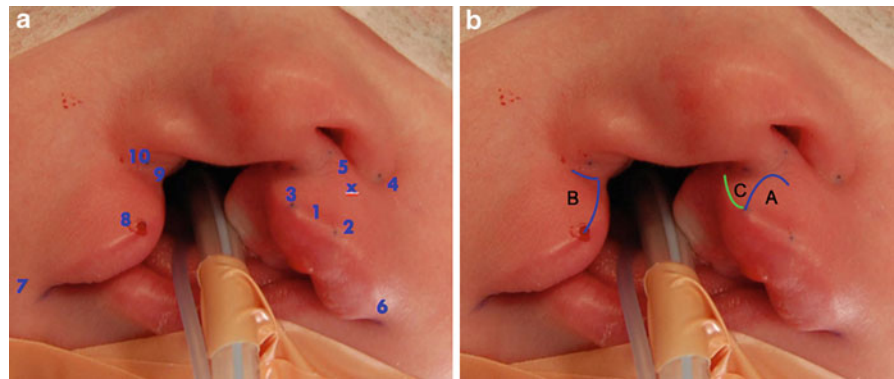
Cleft Lip, Fig. 7 Triangular flap closure of unilateral cleft lip. Key reference points (**a**) are marked prior to infiltration of local anesthetic. Incision lines and flaps (**b**) are then drawn off of these reference points. The triangular flap on the patients' right lip is placed into the defect created when the horizontal incision is created on the patients' left lip
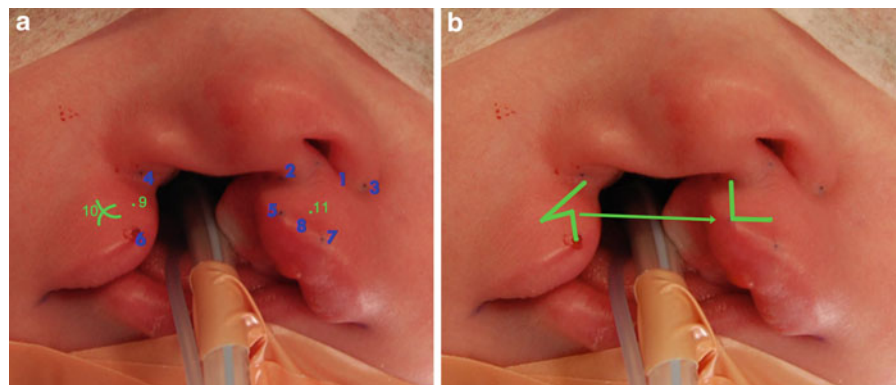
Triangular Flap

The trianglular flap is a geometric flap that was originally described by Tennison. There are several advantages to this type of closure for unilateral cleft lips (Sidman 1993). This technique may be used to close wide clefts with minimal tension. The flap is a mathematical design based on standard measurements and does not require the degree of artistic license and experience that the rotation/advancement closure requires. The main disadvantage of this and other geometric flaps is that the resultant scar crosses the philtral column. Due to the exact measurements, there is minimal flexibility for change during surgery. More tissue is discarded during these closures and the columella cannot be lengthened during this repair. The author reserves the use of this type of flap for patients with very wide unilateral clefts that are not able to undergo presurgical orthopedics.

Key points are marked for the triangular flap as well (Fig. 7). Once the points are marked, a caliper is used to measure the distance between points 2 and 5. This distance is then used to create two arcs from points 4 and 6. The intersection of these two arc points is marked as point 10. Next point 9 is created. This is the one point that is not reliant upon exact measurements and may be adjusted based on the amount of lip lengthening required. Point 9 is placed equal distance from points 6 and 10. Next point 11 is placed based on the distance between points 6 and 9 and points 10 and 9, which are equal. Point 11 is placed perpendicular to a line between points 2 and 5. An incision that is created between point 5 and 11 will create a defect that will fit the triangle created by points 6, 9, and 10.

At this point the incisions are started by releasing the lip from the maxilla and pyriform through a buccal incision. Next full-thickness incisions are created on

the lateral and medial lips extending through the vermillion. The orbicularis muscle is dissected and reapproximated while the flaps are advanced into place. The skin and vermillion are then closed. If indicated, the surgeon may then perform a primary rhinoplasty to reshape the lower lateral cartilage and/or intranasal flaps to reconstruct the anterior floor of the nose.

Bilateral Cleft Lip

Bilateral cleft deformities are due to complete or incomplete defects in the upper lip. A bilateral defect of the lip creates an isolated central lip segment, the prolabium. When the cleft lip is complete and it involves the underlying bone and the primary palate, or premaxilla, is left isolated from the lateral secondary palate segments. This may result in a significantly protuberant premaxilla with a substantial distance between it and the lateral lip segments. When one or both of the defects is incomplete there is some continuity of the primary palate with the lateral alveolar bone resulting in less protrusion of the premaxilla and prolabium.

The orbicularis oris sphincter is interrupted in bilateral cleft deformities as well. In fact, the central segment often does not have any muscle present. The muscle grows laterally to medial and the defect prohibits growth into the prolabium. In the case of an incomplete cleft lip, there may be a diminished amount of misdirected muscle fibers present in the prolabium. The lateral muscle segments are directed superiorly attaching to the alar base, resulting in lateral and inferior displacement of the ala (Fig. 5). The degree of columella shortening relates to the extent of protrusion of the premaxilla. Significant protrusion results in a very short columella. Presurgical orthopedics may be used to decrease the protrusion of the premaxilla and also stretch the columella to lengthen it prior to lip repair.

The goals of surgical treatment of the bilateral cleft lip deformity are to close the defect while reconstituting the sphincter of the orbicularis muscle. Other goals may include closing the floor of the nose and rhinoplasty if indicated. Repair of the bilateral defects may be performed in a single procedure or staged. Staged techniques include two unilateral lip repairs versus a lip adhesion procedure to create
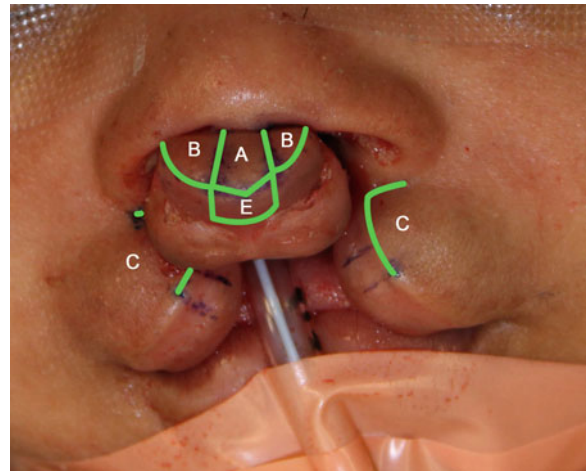
Cleft Lip, Fig. 8 Closure of bilateral cleft lip. Key reference points are marked prior to infiltration of local anesthetic. Incision lines and flaps are then drawn off of these reference points

a bilateral incomplete deformity and narrow the cleft gap followed by a formal repair. Lip adhesion and presurgical orthopedics may be used in cases of wide clefts and protruberant premaxilla to better align the cleft segments prior to repair. Presurgical orthopedics may be used to improve the nasal anatomy as well. Some surgeons alternatively advocate taping to decrease the protrusion of the premaxilla prior to surgery. Various techniques have been described for the cleft repair. The author prefers to perform a single-stage bilateral cleft lip repair as described by Millard (Dyleski and Seibert 2002).

Bilateral Cleft Lip Repair

The technique described allows for a single-stage reconstruction of the bilateral cleft deformity with resulting straight vertical scars that mimic the philtral columns. The orbicularis oris muscle from the lateral lip segments is sutured together across the prolabium, allowing for a dynamic central lip segment and reduced tension on the lateral lip incisions.

First the key points are marked (Fig. 8). The incisions are created to form the central prolabial skin flap (A) and the fork flaps (B). An "E" flap is created to add bulk to the central vermillion. The remainder of the central vermillion is rolled back to create the central gingivobuccal sulcus. Lateral lip flaps (C) are created with full thickness lateral lip incisions and 3 mm of

vermillion kept on either side beyond the lateral point of the incision to become the central vermillion segment. A suture is then placed to pull each alar base centrally. Sutures are then placed to approximate the lateral orbicularis muscle segments over the premaxilla. The skin and mucosal flaps are then sutured in place. The fork flaps may be placed in the nasal sill if needed or they may be discarded.

Conclusion

Cleft lip is a significant deformity with complex physical, social, and psychologic dynamics for patients and their families. These patients should be cared for within the context of a multidisciplinary craniofacial team. It is important to consider all aspects of the patients' care including feeding, development, and the possibility of other associated deformities. Surgical correction is technically demanding; however proper application of techniques may yield excellent results.

References

Capone RB, Sykes JM (2009) Evaluation and management of cleft lip and palate disorders. In: Papel IRA (ed) Facial plastic and reconstructive surgery. Thieme, New York, pp 1060–1069

Dyleski RA, Seibert RW (2002) Cleft lip and cleft palate repair. In: Bluestone CD, Rosenfeld RM (eds) Surgical atlas of pediatric otolaryngology. B.C. Decker, Hamilton, pp 763–790

Heike CL, Cunningham M (2009) Pediatric assessment and management of children with cleft lip and palate. In: Losee JE, Kirschner RE (eds) Comprehensive cleft care. McGraw-Hill, Singapore/China, pp 171–183

Mooney MP (2009) Classification of orofacial clefting. In: Losee JE, Kirschner RE (eds) Comprehensive cleft care. McGraw-Hill, Singapore/China, pp 21–26

Ness JA, Sykes JM (1993) Basics of Millard rotation-advancement technique for repair of the unilateral cleft lip deformity. Facial Plast Surg 9(3):167–176

Rotten D, Levaillant JM (2009) Prenatal diagnosis of facial clefts. In: Losee JE, Kirschner RE (eds) Comprehensive cleft care. McGraw-Hill, Singapore/China, pp 44–70

Sidman JD (1993) Triangular flap repair of the unilateral cleft lip. Facial Plast Surg 9(3):184–187

Sperber GH, Dent M, Sperber SM (2009) Embryology of orofacial clefting. In: Losee JE, Kirschner RE (eds) Comprehensive cleft care. McGraw-Hill, Singapore/China, pp 5–15

Sykes JM (2005) Syndromes and congenital anomalies. In: Park S (ed) Facial plastic surgery – the essential guide. Thieme, New York, pp 11–18

Cleft Lip and Palate

Jonathan M. Grischkan[1], Robert J. Tibesar[2] and James D. Sidman[3]
[1]Department of Otolaryngology, Nationwide Children's Hospital, The Ohio State University, Columbus, OH, USA
[2]Pediatric Otolaryngology-Facial Plastic Surgery, Pediatric ENT Associates, Children's Hospitals and Clinics of Minnesota and University of Minnesota, South Minneapolis, MN, USA
[3]Children's Hospitals and Clinics of Minnesota, University of Minnesota, Minneapolis, MN, USA

Definitions

Alveolus. The dental arch, where the teeth erupt. "The gum line."

Cleft palate. A cleft of any part of the hard or soft palate.

Complete cleft lip. The cleft lip extends into the floor of the nose. This includes clefts with a tiny bridge of skin at the floor of the nose known as a "Simonart's band."

Incomplete cleft lip. The cleft does not extend into the floor of the nose.

Micrognathia. Small mandible. Not the same as microgenia, or retrognathia.

Submucous cleft palate. The palatal mucosa is intact, but the underlying muscle of the soft palate is clefted. The cleft can extend into the hard palate also, still covered by mucosa, denoted by a palpable "notch" in the posterior edge of the hard palate. There is no overt "hole" in a submucous cleft palate as the defect is covered by normal mucosa.

Velopharyngeal insufficiency. Refers to a soft palate that does not adequately seal the nose during certain speech sounds resulting in excessive nasal air escape.

Basic Characteristics

Cleft lip with or without palate (CL ± P) is one of the most common birth defects in humans. Incidence varies among ethnic groups with the most common incidence in certain Asian groups as high as 1:300 births, to Caucasians at 1:1,000 births, to Africans at about 1:1,200 births. Most patients with CL ± P do not

have an identifiable syndrome or genetic error that can be identified by current testing; however, it is expected that most genetic markers for clefting will be elucidated in the next decades. Various teratogens, including some antiseizure medications and retinoic acid, are uncommon causes of clefting and are felt to account for a low percentage of the overall incidence. In most series, cause-effect relationships have not been definitively demonstrated. Folate supplementation during the first trimester of pregnancy may help prevent clefts; however, large-scale studies to prove this have not yet been completed. Environmental factors such as maternal alcohol consumption, tobacco and caffeine intake have either demonstrated weak association with increased risk (especially in high consumption) or no increased risk.

It is an unfortunate fact that in many cultures, clefts are felt to be secondary to events during pregnancy such as illness, poor diet, or even bad thoughts by the parents. Many communities shun children with clefts and in some cases they are allowed to die at birth because of the deformity. It is a common misconception that children with clefting have developmental delays or even gross mental retardation. In virtually every society, people with unrepaired clefts have significant social hurdles to overcome and many will never function to their fullest capacity in society because of appearance or impaired communication (i.e., speech) skills.

Recent advances in ultrasonography have allowed earlier diagnosis of clefting, and many expecting mothers are informed of the presence of the cleft during their routine prenatal ultrasounds. This early diagnosis may allow early referral to the cleft surgeon, and can assist in forming a prenatal relationship with the cleft surgeon. This early meeting may assist parents in understanding the implications of the cleft (Bentz et al. 2007).

Cleft Lip

Isolated cleft lip without cleft palate (CL) is generally not a functional issue, in that most children born with CL do not have problems with feeding. It is an obvious birth defect that is noted immediately. Cleft lip always involves a dehiscence of the oral muscular sphincter, which is composed of the orbicularis oris muscle; however, it should be noted that all components of the normal lip anatomy are present and simply must be rearranged (Fig. 1). Incomplete formation of this muscle therefore interferes with the normal smile, frown, pursing of the lips, and other oral functions.

Cleft Lip and Palate, Fig. 1 Normal lip anatomy demonstrating prominent philtral dimple, cupid's bow, and muscle bulk

Cleft Lip and Palate, Fig. 2 Unilateral microform cleft lip

Clefts of the lip can be unilateral or bilateral, complete or incomplete, and can involve a cleft of the alveolus and primary palate. In addition, microform clefts of the lip involve a subcutaneous dehiscence of the orbicularis oris muscle without an overt "gap" in the skin (Fig. 2). Clefts of the lip variably involve the nose, due to the altered muscular insertions of the orbicularis oris. This causes a characteristic nasal deformity consisting of relative elongation of the lateral crus of the ipsilateral lower lateral cartilage and relative shortening of the medial crus, displacing the nasal dome inferiorly and the nasal ala inferiorly, laterally, and posteriorly (Fig. 3).

Most experts recommend that all children with clefting undergo genetic evaluation at some point in their treatment course, though it will not likely change overall surgical treatment plans, and is often done in conjunction with the cleft team evaluation (see below).

Primary reasons to pursue genetic evaluation include predicting associated syndromic anomalies, directing further testing, and discussing recurrence risks for parents.

While the technical aspects of cleft lip repair are beyond the scope of this entry, several key concepts are of paramount importance in any lip repair, irrespective of specific repair techniques. First, re-approximation of the orbicularis oris muscle to reconstitute the oral muscular sphincter must be achieved. Second, reestablishment of the continuity of the vermillion-cutaneous junction requires meticulous attention to detail, as even discrepancies as small as 1–2 mm can cause a noticeable deformity. Furthermore, all unilateral cleft lip repair techniques involve some degree of rotation of the medial lip segment and

advancement of the lateral lip segment (Fig. 4). Finally, the lip is repaired such that forces of linear contracture do not re-create the deficient upper lip (i.e., ▶ z-plasty or broken line closure). Some cleft surgeons perform various degrees of cleft rhinoplasty at the time of initial lip repair (Fig. 5). (McCarthy 1990).

Cleft Palate

Cleft palate can occur in combination with cleft lip (CLP), or can exist as an isolated cleft palate (CPO). Isolated cleft palate is genetically and phenotypically different from CL ± P. Incidence of cleft lip with palate is about twice as common as isolated cleft palate. Interestingly, CPO is more commonly associated with other anomalies. It should be noted that the authors of this entry deliberately avoid referring to clefts of the palate as clefts of the "primary or secondary" palate, and instead use anatomical descriptions to more accurately describe the involved portion (Fig. 6).

Cleft palate with or without cleft lip CL ± P is a more complicated problem than isolated cleft lip, and represents more of a functional problem. The main neonatal issue confronted with a cleft palate is feeding and weight gain. Because of the defect in the palate, the infant is unable to generate an adequate, sustained suck and therefore cannot adequately feed from the breast. In the absence of practitioners experienced with cleft feeding and care, especially in underdeveloped nations, many of these children will become malnourished and can die without intervention. Special techniques and devices to assist with feeding and caloric intake are discussed below.

Cleft Lip and Palate, Fig. 3 Unilateral incomplete cleft lip and alveolus

Cleft Lip and Palate, Fig. 4 Pre- and post-op photographs of unilateral complete cleft lip repair

Cleft Lip and Palate, Fig. 5 Pre- and post-op photographs of asymmetric bilateral cleft lip repair (same patient at 6-month follow-up)
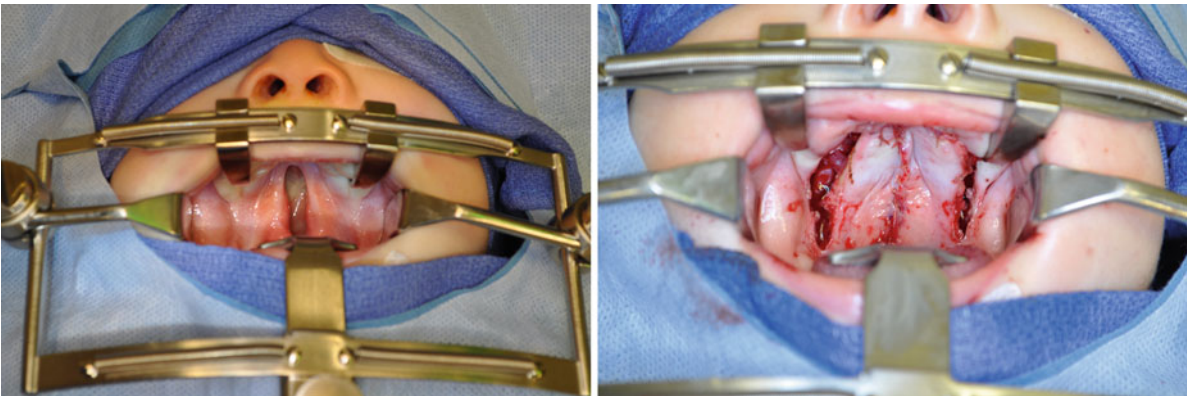
Cleft Lip and Palate, Fig. 6 Pre- and post-op cleft of soft and partial hard palate repair

The second issue faced by children with cleft palate is speech production. Because of the inability to seal off the nose during speech production, velopharyngeal insufficiency (▶ Velopharyngeal Dysfunction, Diagnosis and Management) ensues, causing excessive nasal air escape and interfering with overall intelligibility, irrespective of native language. This difficulty with speech production is the primary reason to intervene, as individuals with cleft palate will eventually adapt to eating and drinking even with an unrepaired cleft palate. Even after repair of the cleft palate, some children (or adults) continue to have nasal air escape, and benefit from additional attempts at decreasing the VPI. Speech therapy is often recommended in this situation, and can prove very beneficial; however, in some instances, the nasal air escape cannot be overcome with speech therapy alone. This can be accomplished nonsurgically with speech bulbs, palatal lifts, or obturators; but is most commonly treated with pharyngeal surgery. Combined with repair of the cleft palate and speech surgery, many children will benefit from speech therapy, particularly aimed at correction of compensatory speech patterns developed in response to the VPI.

Similar to cleft lip, cleft palate includes a spectrum of presentations, including unilateral or bilateral, complete or submucous clefts. Clefts can involve the soft palate only, the soft palate and a portion of the hard palate, or can be complete and include the soft and hard palate and the alveolus. Certain conditions present with a typical shaped cleft: Pierre Robin sequence (PRS) presents with a wide U-shaped cleft of the soft and partial hard palate.

While the technical details of cleft palate repair are beyond the scope of this entry, the overall aim is to separate the nasal and oral cavities. This is usually

accomplished with local tissue flaps involving the oral and nasal mucosa, and the soft palate musculature. The most common techniques involve advancing tissue from lateral to medial, approximating the nasal mucosal layer independently of the oral mucosal layer, and approximating the soft palate musculature (Fig. 6). It is worth emphasizing that two-layer closure is essential in repairing the cleft palate and avoiding oronasal fistula. Various modifications incorporating palatal lengthening techniques (z-plasty, palatal setback) have been developed in attempts to minimize the need for revision surgery, and these techniques are variably used among cleft surgeons in specific situations. All accepted techniques do utilize 2-layer closure, however (Salyer and Bardach 1999).

Team Approach

The authors of this entry are strong adherents to the team approach to cleft care. This means regularly scheduled, face-to-face meeting of key health professionals involved with the care of these patients. Key professionals include speech pathologist, audiologist, psychologist, social worker, nurse, pediatric dentist, orthodontist, geneticist, prosthodontist, oral surgeon, and cleft surgeon. The team meets to discuss treatment plans for the patient yearly. Depending on the team and the demographics of the patient population it serves, the team members may actually be the treating professionals, or may refer to other professionals, either closer geographically, or under contract by the health insurance carrier.

Adherents to the team approach believe that no single surgeon or primary care provider can know enough about all the key areas of cleft care to provide adequate, coordinated care and that the team approach allows for better long-term outcomes for these patients. Interestingly, this belief that team care is best has not yet been proven by any reasonably sized study, and remains to be verified. There are still many children in North America and most other countries where team care is not provided either because of lack of team coordination, or because the surgeon and primary care provider do not see the need.

Timing of Interventions

Although the cleft lip can be repaired in the newborn period from a technical standpoint, most authors prefer to wait until the infant is 6–10 weeks old. The rule of "10s," consisting of a weight of 10 lb, Hemoglobin of 10 g/dL, and age of 10 weeks is no longer a firm requirement in centers that have the capacity for the care of infants. There was a movement toward neonatal cleft lip repair in order to take advantage of the improved healing associated with fetal collagen, but this has been mostly abandoned as the results have not been shown to be superior.

The age of cleft palate repair remains somewhat controversial. Cleft palate repair is done to maximize speech acquisition. Repair of the palate offers little feeding advantage as children will have learned to eat normal foods and food textures well before palate repair. The controversy centers around the age at which palate repair yields the best long-term speech results. Current speech research suggests that the best age for palate repair is between 6 and 12 months. Cleft palate repair has far more potential morbidity than does cleft lip repair. Bleeding, anesthetic problems, airway compromise, and postoperative feeding issues all are potential complications. For these reasons, most surgeons feel that waiting until at least 9 months of age is safest. The benefits gained by early cleft palate repair must be balanced by the potential alteration in midfacial growth, which is thought to be due directly to the surgical repair (Fig. 7).

Alveolar bone grafting is best done when dental radiographs show early descent of the adult lateral incisors, prior to eruption. This usually occurs between 5 and 7 years old. By grafting solid bone stock in the alveolar cleft prior to descent, these teeth will erupt into stable bone, and will not be subject to loss due to inadequate root structural support. These teeth often will descend crooked, twisted, and out of position, but can be manipulated into proper position with orthodontia. It is worth noting that this too, is controversial, but good studies suggest that earlier bone grafting yields better long-term retention of teeth. However, recent papers suggest that many of these early grafted patients will need supplementary bone grafting prior to dental implant placement.

Other potential operations available to assist patients with cleft lip and palate include cleft lip revision procedures to optimize aesthetic lip appearance, septo-rhinoplasty to improve nasal appearance and to allow improved nasal breathing, and speech surgery to correct velopharyngeal insufficiency (▶ Velopharyngeal Dysfunction, Diagnosis and Management).
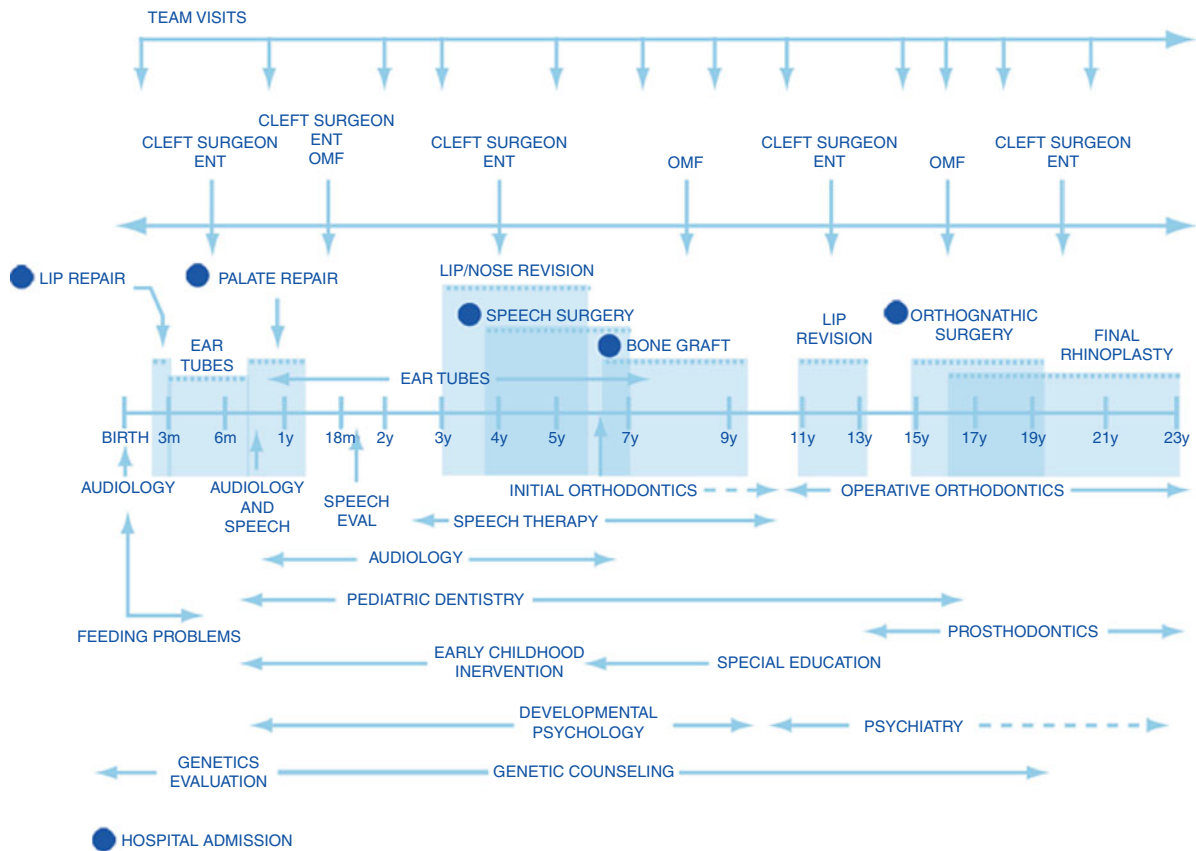
Cleft Lip and Palate, Fig. 7 Surgical timeline for typical patient with cleft lip and palate

Feeding Difficulties

Cleft lip alone generally has no implications for feeding and these babies feed from the breast or bottle just like any other infant. The lack of complete closure of the orbicularis oris muscle rarely interferes with the ability to feed.

Virtually all children born with cleft palate, with or without cleft lip, have feeding difficulties during infancy. The only exceptions are children born with tiny clefts of the distal soft palate, or those with submucous cleft palate. The cleft in the palate prevents generation of an adequate sustained suck with either the breast or bottle, so there is ineffective delivery of milk into the baby's oropharynx. The infant will tire of attempting to suck, and eventually will not be able to gain weight adequately and "fail to thrive." Various forms of cleft feeding bottles have been designed to overcome the infant's inability to suck effectively.

These all work by allowing the caregiver to squeeze the bottle and squirt milk into the infant's oropharynx, thereby bypassing the need to generate a strong suck. Once in the oropharynx, the infant can then swallow using normal swallowing mechanisms. Both the mother's pumped breast milk and formula can be used in these bottles. In countries where there is no access to these special bottles, elaborate systems of tubing, or frequent expressing of milk from the mother's breast can be quite effective.

Infants with cleft palate generally do swallow more air during feeding than do non-cleft children and require more "burping" and a longer time to feed. It has not been established whether these infants have more gastroesophageal reflux disease than non-cleft babies.

Introduction of textured foods for children with cleft palate can begin from age 4–6 months as would

be done with children without a cleft palate. There is certainly increased nasal regurgitation of liquids and solids in cleft palate children, but these children do eventually learn to cope with this. Adults with unrepaired cleft palates generally can eat a normal diet, without restrictions or excessive nasal regurgitation of food; however, there is a higher incidence of sinusitis in these patients possibly due to soiling of the nasal cavity with oral intake.

Airway difficulties

Except for infants with Pierre Robin sequence, cleft palate does not imply acute or chronic airway problems. Certain syndromes are associated with respiratory difficulties or central hypoventilation but these problems are not caused by the cleft palate.

Pierre Robin Sequence

Pierre Robin sequence (PRS) is a constellation of three findings in a newborn. The triad of characteristics are micrognathia, glossoptosis, and a wide "U-shaped" cleft palate. Most cleft surgeons agree that all three of these findings must be present in order to make the diagnosis of PRS. It is a common error to label all children with micrognathia and tongue base airway obstruction as PRS. Not all children with PRS have airway compromise, and the degree of airway compromise is frequently *not* related to the degree of observed micrognathia.

Pierre Robin sequence is a sequence and not a syndrome. As it relates to dysmorphology, a sequence is a pattern of multiple anomalies derived from a single prior anomaly or mechanical factor (Stedman 2005). The common underlying malformation in PRS is micrognathia, causing a retrodisplacement of the tongue, ultimately preventing the palatal shelves from rotating into a horizontal position, resulting in the wide cleft palate.

Pierre Robin sequence can be seen in many syndromes. Some of these syndromes that include this triad of characteristics are Treacher-Collins, Stickler's, Nager's, Velocardiofacial, and Trisomy 18. Isolated PRS is diagnosed when there are no other findings suggestive of a syndrome. Syndromic children are not thought to outgrow micrognathia, and generally grow up to be micrognathic teenagers and adults. The children with isolated PRS (without a syndrome) will sometimes outgrow micrognathia but recent longitudinal observations suggest that most

of these children remain micrognathic through adulthood (unpublished data).

Newborns with PRS commonly present with airway compromise, feeding difficulties, or both. The feeding problems in isolated PRS (i.e., children without any syndrome that includes neurological delays) are almost always secondary to airway problems. Treating the problem with nasogastric feeding or gastrostomy misses the primary etiology of airway obstruction. The severity of airway obstruction in these children is often overlooked. Diagnostic findings include poor air movement on chest *auscultation*, hypercapnia, respiratory acidosis, acute respiratory obstructive events, retractions with or without feeding, and findings of airway obstruction on polysomnography (sleep study).

There are a number of possible interventions for newborns with PRS, from simple maneuvers such as side or prone positioning to definitive airway management with tracheotomy. Prone positioning alone can improve the airway by allowing the tongue to fall forward simply by the help of gravity. This rarely works except in the mildest forms of airway obstruction. The next step in the approach to these infants is to insert a nasal airway (nasal trumpet) in either naris. This can be a trimmed endotracheal tube or a premade nasal airway tube. The tube must be long enough to extend past the base of tongue obstruction and into the hypopharynx. This is easily estimated by holding the tube up to the infant's palpated hyoid bone, and can be confirmed by flexible endoscopy if necessary. It is not clear whether the tube acts as an airway for the baby to breathe through, or whether the tube simply pushes the tongue base far enough forward to allow for an adequate airway. This latter theory would explain why the airway often seems improved with a nasal trumpet even if the nasal trumpet becomes obstructed with secretions or formula.

If the nasal airway is successful in alleviating respiratory compromise and allowing for adequate oral intake, then the baby can be discharged from the hospital with tube changes every 2–3 days at home, alternating nostrils to prevent excess inflammation. The tube is usually needed for at least 2–4 months, and can then be gradually weaned in most cases.

Infants in whom feeding is not adequate and airway obstruction persists despite prone positioning and nasal airway placement may benefit from surgical intervention. Various methods of tongue-lip adhesion (glossopexy) have been described to bring the tongue

forward and relieve airway obstruction. This operation essentially uses a suture technique through the tongue and tongue base in order to pull the tongue base forward. The authors and most pediatric otolaryngologists no longer employ this operation as it is felt to work only in mild cases of airway obstruction where a nasal airway would accomplish the same goal, without the need for surgery.

The surgical options for children with PRS in whom conservative management of airway obstruction and poor feeding fails are either distraction osteogenesis of the mandible, or tracheotomy. Mandibular distraction osteogenesis has been shown in numerous studies to relieve the airway obstruction in infants in whom the obstruction is totally caused by tongue base obstruction, and not neurological hypotonia (as seen, for example, in Trisomy 18).

Tracheotomy is still the "gold standard" treatment for severely affected Pierre Robin infants in many medical centers. The long-term prognosis for decannulation in these children is good, and most non-syndromic Pierre Robin children will be decannulated by 2–4 years of age. Many of the syndromic children cannot be decannulated and will eventually need orthognathic surgery or mandibular distraction to allow for adequate airway and decannulation. Morbidity of tracheotomy is the same in these children as in other children with tracheotomies and includes airway infections, bleeding, speech and language delay, difficulty with obtaining medically qualified caregivers, and problems with socialization.

Otologic and Hearing Problems

All babies born with facial clefting should have newborn hearing screening because of an increased rate of both conductive and sensorineural hearing loss (SNHL). The SNHL is more commonly seen in syndromic children, but these syndromes are often not recognized until later in childhood and it is important to recognize hearing loss and obtain rehabilitation as early as possible.

Middle ear problems are the predominant issue in patients with cleft palate. Cleft lip alone does not carry a higher than expected rate of middle ear effusions or cholesteatoma and does not require special care or surveillance.

Virtually all children with cleft palate (with or without cleft lip) have problems with chronic middle ear effusions during the first 2–4 years of life.

Placement of pressure-equalization tubes is recommended to drain the effusion and improve the hearing. Most children will eventually outgrow the propensity for middle ear effusions and replacement of the tubes past 2 years of age should depend on audiologic findings and clinical exam.

The cause of chronic otitis media with effusion (COME) is thought to be due to poor Eustachian tube function secondary to abnormal insertion of the tensor veli palatini muscles. Interestingly however, repairing the cleft palate does not seem to have a beneficial effect on Eustachian tube function and the COME will persist until age 2–4 years whether the cleft is repaired or not. It is possible that the newer technique of double reverse z-plasty repair of the soft palate will have a more favorable effect on the Eustachian tube and COME but this has not yet been shown in longitudinal studies.

It is true that many children with cleft palate will outgrow the COME without sequelae, but an estimated 10% of cleft palate children without placement of pressure equalization tubes (PETs) will develop either cholesteatoma and/or ossicular chain erosion and conductive hearing loss. Because of this high rate of significant middle ear disease in children with cleft palate, many authors advocate early placement of PETs in all children with cleft palate in order to prevent the complications of chronic hearing loss, ossicular erosion, and cholesteatoma. Although some cleft palate children will outgrow their early COME without any long-term complications, it is felt that the risk of developing these complications far outweighs the risk of pressure equalization tubes.

There is little consensus of opinion as to the correct age to place pressure equalization tubes in children with cleft palate. Some authors advocate placement at the time of lip repair (if cleft lip is also present), while other authors advocate waiting until 6 months of age, or even until 10–12 months of age when the palate repair takes place. The authors practice is to wait until 4–6 months of age, even if a cleft lip repair is to take place earlier. Their experience shows an unacceptable rate of chronic post-tympanostomy tube otorrhea if the PETs are placed too early. It is not uncommon to observe milk reflux through the PETs in young cleft palate children, probably from abnormally patent Eustachian tubes secondary to the cleft itself.

Ossicular erosion and cholesteatoma are not the only forms of conductive hearing loss seen in cleft

palate children. A number of syndromes such as Treacher-Collins, Moebius, and Marshall-Sticklers have associated problems of ossicular fixation, stapes footplate fixation, and other congenital abnormalities of the middle and external ear. The associated hearing loss should be identified during infancy and bone conduction hearing aids prescribed until the child is old enough for definitive surgical repair. In the cases where there is associated aural atresia or microtia, then great care should be taken to protect the facial nerve during surgery. The nerve is frequently found laterally (superficially) in these patients and can even be injured during postauricular tympanoplasty surgery.

Conclusions

The care of patients with cleft lip and palate is a challenge, encompassing many specialties, and requiring great care and patience. With dedication and effort, the lives of these patients can be significantly improved, allowing them to lead normal or nearly normal lives.

Cross-References

▶ Distraction Osteogenesis
▶ Velopharyngeal Dysfunction, Diagnosis and Management
▶ Z-Plasty

References

Bentz M, Bauer BS, Zuker RM, Michael L (2007) Principles and practice of pediatric plastic surgery [Har/DVD]. Quality Medical, St. Louis
McCarthy J (ed) (1990) Plastic surgery, 3rd edn. W.B. Saunders, Philadelphia
Salyer KE, Bardach J (1999) Salyer & Bardach's atlas of craniofacial & cleft surgery, 1st edn. Lippincott Williams & Wilkins, Philadelphia
Stedman TL (2005) Stedman's medical dictionary, 28th edn. Lippincott Williams & Wilkins, Philadelphia

CN 7

▶ Facial Nerve Imaging, CT and MRI

CN VII

▶ Facial Nerve Imaging, CT and MRI

Coagulopathy

Carrie M. Bush[1] and Melanie W. Seybt[2]
[1]Department of Otolaryngology, Medical College of Georgia, Augusta, GA, USA
[2]Department of Otolaryngology, Medical College of Georgia, Georgia Health Sciences University, Augusta, GA, USA

Definition

A disorder of the body's mechanism for coagulation of blood. May be represented by increased bleeding tendency (hypercoagulable) or increased risk for thrombosis (hypocoagulable).

Cross-References

▶ Tracheostomy, Complications

Cochlea

Gerald T. Kangelaris and Lawrence R. Lustig
Department of Otolaryngology-Head and Neck Surgery, University of California, San Francisco, San Francisco, CA, USA

Definition

The hearing organ of the inner ear housed within the temporal bone. It is responsible for transforming the mechanical energy of sound waves into the electrical energy of nerve impulses.

Cross-References

▶ Sensorineural Hearing Loss

Cochlea, Anatomy

Oliver F. Adunka
Division of Otology/Neurotology/Skull Base Surgery,
Department of Otolaryngology-Head and Neck
Surgery, University of North Carolina at Chapel Hill,
Chapel Hill, NC, USA

Synonyms

Morphology of cochlea

Definition

The labyrinth is a fluid-filled system containing the inner ear hearing (located anterior, cochlea) and balance (located posterior, vestibule and three semicircular canals) sensory organs. The labyrinth has a layered structure: The bony labyrinth surrounds the fluid-filled spaces within and is lined with an endosteal membrane. The membranous labyrinth is located within the bony labyrinth and filled with endolymph. The space between bony and membranous labyrinth is filled with perilymphatic fluid.

The cochlea (Greek for snail) is the auditory portion of the inner ear. In the human, the cochlea comprises of 2½ to 2¾ turns. The cochlea is subdivided into various fluid spaces demonstrating different ion concentrations. The critical portion facilitating the mechanoelectrical transduction of mechanical energy (sound pressure waves) into electrical signals (action potentials) is the organ of Corti, which is embedded within the basilar membrane. The action potentials are then sent via peripheral dendrites of the spiral ganglion cell bodies in the center of the cochlea, the modiolus. The central axons form the cochlear portion of the vestibulocochlear nerve.

Developmental Anatomy

Development of the ear begins with preliminary inductions of the surface ectoderm, first by the notochord (chordamesoderm) and then by the paraxial mesoderm. These inductions prepare the ectoderm for a third induction, in which the rhombencephalon induces the adjacent surface ectoderm to thicken and form the otic placode. Late in the fourth week, the otic placode invaginates and then separates from the surface ectoderm to form the otic vesicle, or otocyst (Rinkwitz et al. 2001) (Fig. 1).

The otic vesicle soon begins to elongate, forming a dorsal (utricle) vestibular and a ventral (saccule) cochlear region. At about 5-week gestational age, two ridges appear in the vestibular portion (Fig. 2). Ultimately, two of the three semicircular canals will develop from these two ridges. Altogether, these epithelial structures form the membranous labyrinth (Fig. 3). The sensory neurons that make up the eighth cranial nerve (statoacoustic ganglion) arise from cells that migrate from a portion of the medial wall of the otocyst. The cochlear portion (spiral ganglion) of the eighth cranial nerve fans out in association with the sensory cells of the organ of Corti. Neural crest cells invade the developing statoacoustic ganglion and ultimately form the supporting cells. The sensory cells of the organ of Corti are derived from the epithelium of the otocyst.

In the sixth week of development, the saccule forms a tubular elongation at its lower pole, which will eventually give rise to the cochlear duct. The cochlear duct penetrates the surrounding mesenchyme to form the human cochlea with its 2½ turns. The ductus reuniens remains as the residual connection of the cochlear duct with the saccule. Mesenchyme surrounding the cochlear duct soon differentiates into cartilage. This cartilaginous shell (with the cochlear duct in its center) undergoes vacuolation to form two perilymph spaces on both sides of the duct, the scala vestibuli and the scala tympani. The cochlear duct is partitioned from the scala vestibuli and the scala tympani by the vestibular (Reissner's) and basilar membranes, respectively. At the lateral, wide wall of the cochlear duct is the spiral ligament and at its medial, narrow part is the modiolus, the future axis of the bony cochlea. With further development, epithelial cells of the duct form two ridges: an inner ridge (spiral limbus) and an outer ridge. The outer ridge forms one row of inner and three to four rows of outer hair cells, which are sensory.

In summary, the embryological development of the cochlea is quite complex. Despite it's completion well before birth, knowledge on various stages seems relevant in order to understand the clinical appearance of various inner ear malformations (Buchman et al. 2004). Also, the lack of postnatal growth of the
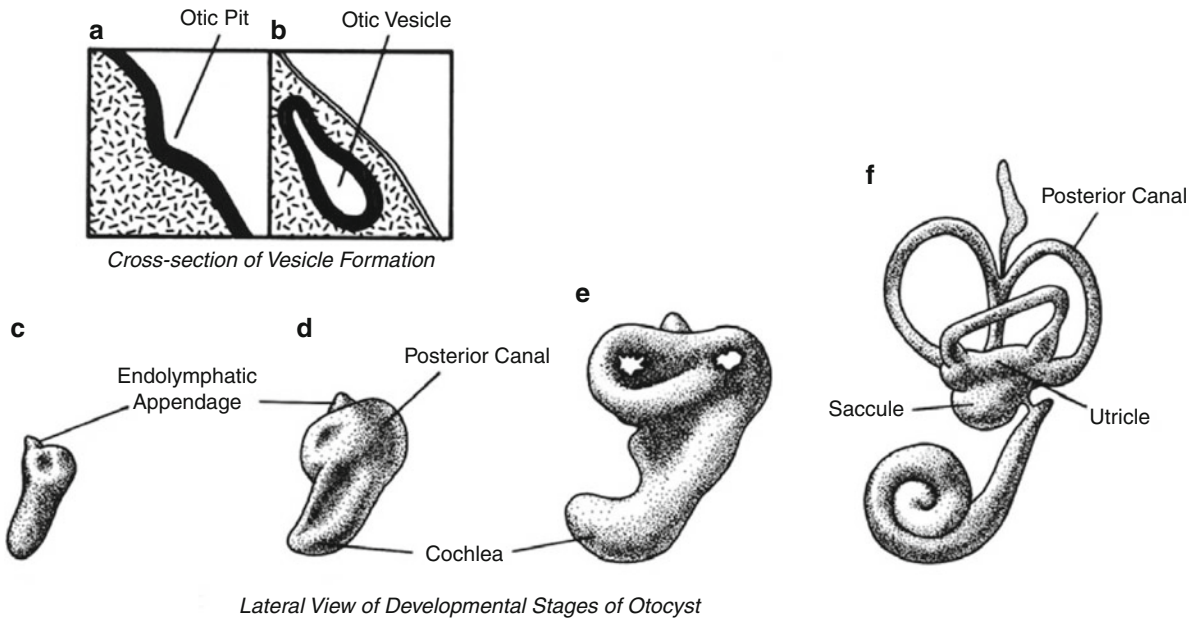
Cochlea, Anatomy, Fig. 1 Evolution of the membranous labyrinth: (**a**) 22 day, (**b**) 4 weeks, (**c**) 4½ weeks, (**d**) 5½ weeks, (**e**) 6 weeks, (**f**) from the eighth week forward (Reproduced with permission from Gulya AJ, Schuknecht HF. Anatomy of the temporal bone with surgical implications. 2nd edition. Pearl River (NY): Parthenon Publishing Group; 1995)
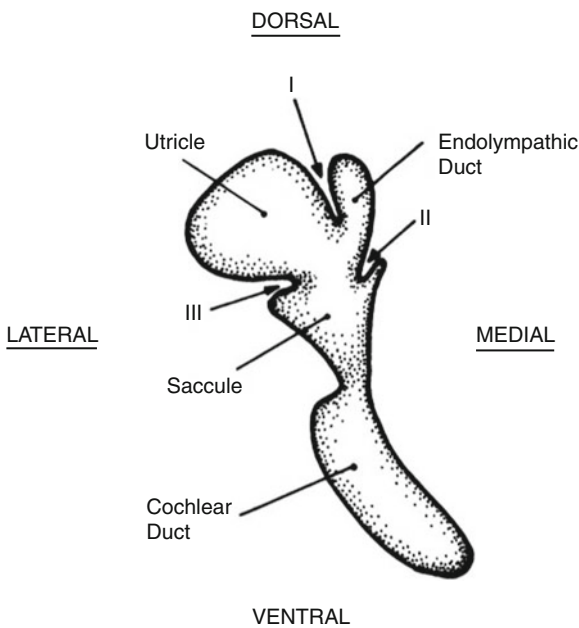
Cochlea, Anatomy, Fig. 2 The membranous labyrinth at about 6-week gestational age. Folds I, II, and III begin to indent into the otocyst (After Bast and Anson. Reproduced with permission from Gulya AJ, Schuknecht HF Anatomy of the temporal bone with surgical implications. 2nd edition. Pearl River (NY): Parthenon Publishing Group; 1995)

labyrinth has clinical implications mainly facilitating pediatric cochlear implantation.

Anatomical Overview of the Cochlea

The human cochlea features 2½ to 2¾ turns and spirals around the modiolus, its axis (Fig. 4). The spiral ganglion cell bodies are located in the modiolus and the dendrites project to the organ of Corti via the cribrose area of the basal cochlear turn and the osseous spiral lamina. The apex of the cochlea is located medial to the cochleariform process and the tensor tympani muscle. As detailed previously, the development of the cochlea has been completed long before birth. Thus, there is no postnatal growth, which is important for cochlear implantation. However, there are substantial interindividual differences in shape and size of the cochlea that deserve consideration and that have received recent attention.

The cochlea has three main fluid compartments: scala tympani and vestibuli, which contain sodium-rich perilymph and the scala media (also known as the cochlear duct), which contains endolymph and

Cochlea, Anatomy, Fig. 3 The mature membranous labyrinth, as viewed from medial (After Anson and Donaldson. Reproduced with permission from Gulya AJ, Schuknecht HF. Anatomy of the temporal bone with surgical implications. 2nd edition. Pearl River (NY): Parthenon Publishing Group; 1995)
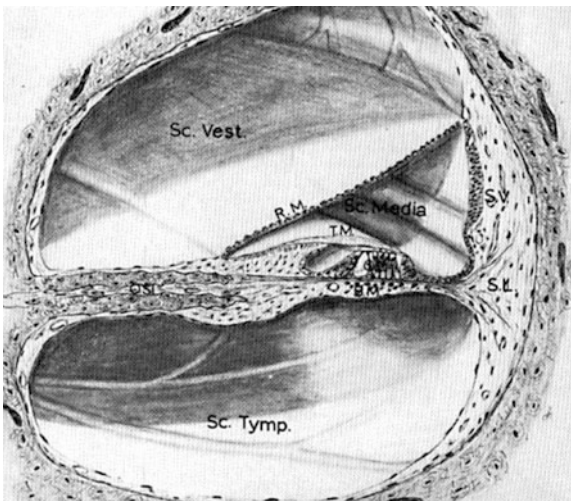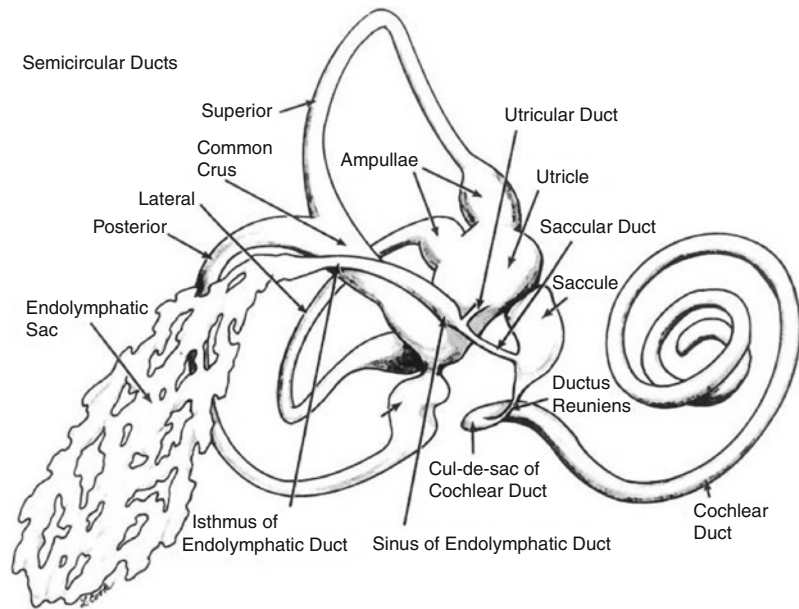
Cochlea, Anatomy, Fig. 4 Cross section through the fluid spaces of the cochlea. *Sc. Vest*. scala vestibuli, *Sc. Tymp*. Scala tympani, *Sc. Media* Scala media, *TM* tectorial membrane, *BM* basilar membrane, *RM* Reissner's membrane, *OSL* osseous spiral lamina, *SV* stria vascularis, *SL* spiral ligament (Adapted from Snow and Ballenger (2002))

houses the organ of Cori. The organ of Corti rests on the basilar membrane, which spans between the osseous spiral lamina and the spiral ligament on the outer wall. The spiral ligament also contains the stria vascularis in its upper portion, which contains a rich vascular network and produces potassium-rich endolymph. Reissner's (vestibular) membrane is a fragile two-cell-layered structure, which separates scala vestibuli and media. The more robust basilar membrane divides scala tympani and media. The organ of Corti contains the inner and outer auditory hair cells and thus carries the central sensory elements of hearing.

Organ of Corti

The organ of Corti rests on the basilar membrane within scala media of the cochlea (Fig. 5). It contains two types of cells: supporting cells and hair cells. Hair cells are the receptor cells transducing mechanical sound information into action potentials. As their name suggests, supporting cells take on a supporting role for hair cells. Each hair cell's top portion is formed by the reticular lamina, which isolates the hair cells' stereocilia from their cell bodies. It provides a solid surface so that the top portion of the hair cells penetrates into the endolymphatic space but the remainder of the hair cell body is embedded in perilymph (Anniko and Wroblewski 1986). One type of support cells, the Deiter's cells, fills the gaps between the top parts of the hair cells and thus helps form the reticular lamina.

Cochlea, Anatomy, Fig. 5 Detailed schematic of the organ of Corti: *RM* Reissner's membrane, *TM* tectorial membrane, *IS* inner sulcus, *BC* border cells, *IHC* inner hair cells, *TC* tunnel of Corti, *OHC* outer hair cells, *PHC* phalangeal cells, *CH* cells of Hensen, *CC* cells of Claudius, *BM* basilar membrane (Adapted from Snow and Ballenger (2002))
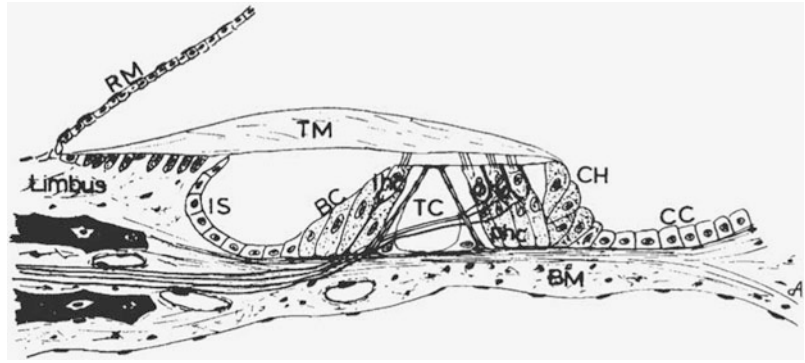
There are three to five rows of hair cells, one on the inner (modiolar) side of the tunnel of Corti formed by the pillar cells; these are the inner hair cells. Three rows are located on the outer side of the tunnel of Corti; thus, these are the outer hair cells. Overall, the organ of Corti contains about 15,000 hair cells; about 3,500 being inner hair cells and 12,000 being outer hair cells. Stereocilia on inner and outer hair cells are arranged in curved or v-shaped rows that face toward the tectorial membrane. Each row of stereocilia has its own height and each row is taller than the previous one. The tip of each stereocilium is linked to the side of the stereocilium in the previous row via a tip link.

The inner and outer hair cells differ morphologically in that the inner hair cells are more flash shaped and tightly surrounded by supporting cells. Their stereocilia are arranged in a linear fashion. The outer hair cells, on the other hand, are columnar in shape and are surrounded incompletely by phalangeal or supporting cells lying free in the perilymph of the organ of Corti. The stereocilia of outer hair cells are arranged in a special fashion and a basal body representing a rudimentary kinocilium is located on the spiral ligament side of the ciliary tuft. The inner hair cells are supported by interphalangeal cells, whereas the outer hair cells are supported by Deiter's cells inferiorly and laterally by Hensen's cells.

The tectorial membrane is a glycoprotein containing membrane that covers the organ of Corti. It is anchored at the limbus of the spiral lamina (spiral limbus) and the longest stereocilia of outer hair cells are embedded in its outer portion. Laterally, the tectorial membrane is attached to the Hensen's cells via a fibrous net. Although the tectorial membrane extends over the top of the inner hair cells, their stereocilia are free and not embedded in the membrane. The fulcrum of the tectorial membrane and the basilar membrane is separate. They are both displaced vertically by the travelling wave created by sound energy but due to their different attachments, they will slide horizontally, thus creating a shearing action which is then translated to a displacement of hair cell stereocilia. This initiates the action potential and subsequent auditory stimulation.

Spiral Ligament

The outer wall of the cochlea hosts the spiral ligament, a thickening of the cochlear periosteum (endosteum). In its upper portion, the spiral ligament features capillaries and small blood vessels as well as pigment-containing melanocytes and endothelial cells. This portion of the spiral ligament is termed the stria vascularis. It receives the majority of the blood supply to the cochlea and is responsible for producing endolymph (from perilymph) and maintaining its ion composition. Thus, the stria vascularis creates the endocochlear potential.

The ion transporters in the stria vascularis are the same as those found in the kidney and this seems to be the reason for the ototoxic nature of drugs impairing renal function (Anniko 1985; Walker et al. 1990; van Ruijven et al. 2005).

Spiral Ganglion

Hair cells are innervated by afferent and efferent neurons in a complex but orderly manner (Tylstedt et al. 1997).

The cell bodies of the first neuron in the auditory nerve are located in the spiral ganglion, which is hosted within the bony modiolus. In fact, the collection of cell bodies is termed the spiral ganglion. The spiral ganglion features clusters of ganglion cells spanning throughout the entire of the length of the cochlea. The dendrites project distally to the base of hair cells and the axon form the cochlear portion of the vestibulocochlear nerve. Like other craniospinal ganglia, most spiral ganglion cells are classified as pseudounipolar in structure (except for Type II cells which are unipolar, see below). A healthy human auditory system features about 35,000 spiral ganglion cells, a number that typically decreases with age (Adams and Schulte 1997).

Two main cell types can be differentiated within the ganglion: Type I and Type II cells (Nadol 1990). About 90% of the spiral ganglion is comprised of myelinated Type I cells, which innervate inner hair cells. Specifically, each inner hair cell is often innervated by many afferent Type I cells. Type II cells, on the other hand, are mostly non-myelinated and have a unipolar structure. Also, Type II cells innervate about 20 outer hair cells and they seem to carry both afferent and efferent fibers. Efferent synapses form large calyx-shaped contact on the outer hair cell body, whereas afferent synapses feature a small button-like contact.

The efferent information is mostly generated in the brainstem, more specifically in the superior olivary complex (Warr 1980). Fibers from both sides of the brain innervate both inner and outer hair cells but the fibers innervating the two types of HC originate in different places. One recent study suggests that the SOC receives input from auditory cortex – so fairly high level processing. The fiber tract containing the efferent fibers is known as the olivocochlear bundle. The tract from the same side of the brain is called the uncrossed olivocochlear bundle and the tract from the opposite side of the brain is called the crossed olivocochlear bundle.

Cochlear Aqueduct

The perilymphatic duct (cochlear aqueduct) is a small opening at the basal end of scala tympani. It traverses inferiorly and connects to the posterior fossa anterior to
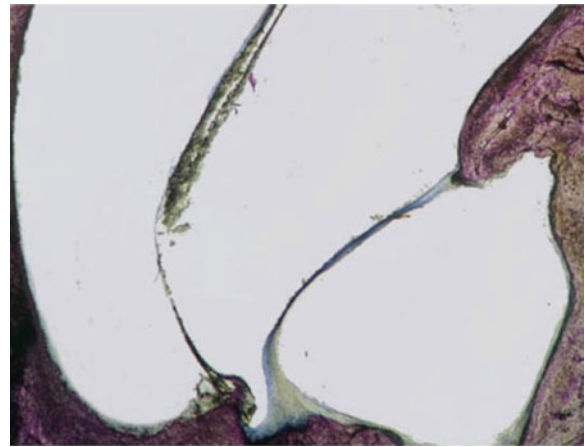

Cochlea, Anatomy, Fig. 6 Microscopic image of a cross section taken at the level of the round window. The conical shape of the round window with its bony attachment (annulus) can be seen as well as the very basal end of the basilar membrane and osseous spiral lamina. The close anatomic relationship of the posterior portion of the round window and the basal aspect of the basilar membrane can be appreciated

the jugular fossa. Its superior part is usually obliterated by connective tissue. The inferior part, however, is lined by dura and contains CSF (Aslan et al. 1998). The cochlear aqueduct can serve as a landmark for the pars nervosa of the jugular foramen during a translabyrinthine craniotomy (drilling inferior to the aqueduct might compromise the lower cranial nerves). Also, cerebrospinal fluid often gushes from the opening indicating the presence of the aqueduct. The cochlear aqueduct frequently hosts a cochlear vein (Rask-Andersen et al. 1977).

Round Window

The scala tympani terminates at the round window (Fig. 6). Similar to the tympanic membrane, the round window features a conical shape with its base projecting inward into scala tympani. It is subject to considerable size and position variations and has recently been rediscovered as a route for cochlear implant electrode insertion and cochlear opening. Despite the fact that the round window provides a direct opening into scala tympani, the resulting trajectory for cochlear implantation is often suboptimal
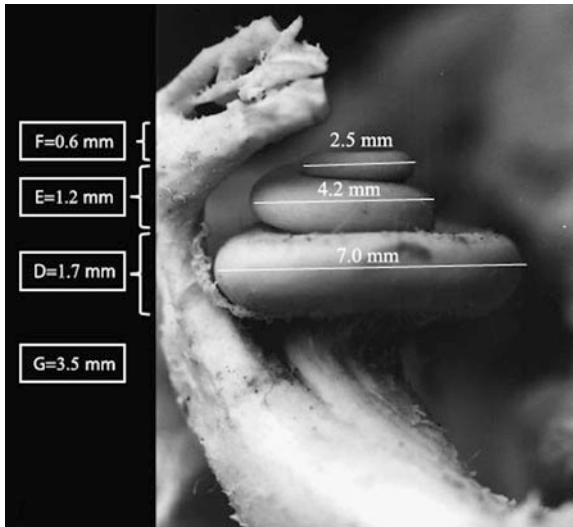
Cochlea, Anatomy, Fig. 7 Corrosion cast of the human cochlea demonstrating measurements and considerable interindividual size variations of the human cochlea (Taken from Erixon et al. (2009))

and a deflection of the electrode off the modiolus has been described. However, in contrast to a more blind cochleostomy, the round window provides a variable, yet reliable landmark for scala tympani.

Fissures of the Bony Labyrinth

Fissures are bony dehiscences of the osseous labyrinth. The fissula ante fenestram seems clinically relevant as otosclerotic bone remodeling might start in this area. As suggested by its name, it can be found directly anterior to the oval window. In the normal temporal bone, this fissula is usually filled with fibrous and cartilaginous tissue. The fissula post fenestram and Hyrtl's fissure are less constant features and are of unknown clinical significance.

Implications for Cochlear Implantation

Despite the fact that the cochlear size remains unchanged after birth, evidence suggests a change in position of the cochlea within the temporal bone over the first few years of life (Fig. 7). This can have a surgical effect on the insertion angle of cochlear implant electrodes. Specifically, in infants and

toddlers, the insertion trajectory of the basal scala tympani can assume a more superior angle compared to the adult situation (Meshik et al. 2010).

More importantly, however, the size of the cochlea and its shape are subject to interindividual variations. This has been demonstrated in various publications as early as the early 1980s (Zrunek et al. 1980). This has further been observed in clinical investigations of variable angular insertion depths with similar linear electrode insertion lengths of free fitting (lateral wall) electrodes. Clinical implications include considerations for different electrode lengths in a residual hearing setting when combined electric acoustic stimulation of the auditory system is intended (Adunka et al. 2005).

Cross-References

▶ Cochlear Implant
▶ Hearing Exam
▶ Physiology of Cochlea
▶ Sensorineural Hearing Loss

References

Adams JC, Schulte BA (1997) Histopathologic observations of the aging gerbil cochlea. Hear Res 104(1–2):101–111

Adunka O, Unkelbach MH et al (2005) Predicting basal cochlear length for electric-acoustic stimulation. Arch Otolaryngol Head Neck Surg 131(6):488–492

Anniko M (1985) Principles in cochlear toxicity. Arch Toxicol (Archiv fur Toxikologie) 8:221–239

Anniko M, Wroblewski R (1986) Ionic environment of cochlear hair cells. Hear Res 22:279–293

Aslan A, Falcioni M et al (1998) The cochlear aqueduct: an important landmark in lateral skull base surgery. Otolaryngol Head Neck Surg 118(4):532–536:official journal of American Academy of Otolaryngology – Head and Neck Surgery

Buchman CA, Copeland BJ et al (2004) Cochlear implantation in children with congenital inner ear malformations. Laryngoscope 114(2):309–316

Erixon E, Hogstorp H et al (2009) Variational anatomy of the human cochlea: implications for cochlear implantation. Otol Neurotol 30(1):14–22:official publication of the American Otological Society, American Neurotology Society (and) European Academy of Otology and Neurotology

Meshik X, Holden TA et al (2010) Optimal cochlear implant insertion vectors. Otol Neurotol 31(1):58–63:official publication of the American Otological Society, American Neurotology Society (and) European Academy of Otology and Neurotology

Nadol JB Jr (1990) Synaptic morphology of inner and outer hair cells of the human organ of Corti. J Electron Microsc Tech 15(2):187–196

Rask-Andersen H, Stahle J et al (1977) Human cochlear aqueduct and its accessory canals. Ann Otol Rhinol Laryngol 86(5 Pt 2 Suppl 42):1–16

Rinkwitz S, Bober E et al (2001) Development of the vertebrate inner ear. Ann N Y Acad Sci 942:1–14

Snow JB, Ballenger JJ (eds) (2002) Ballenger's otolaryngology, head and neck surgery. B.C Decker, Hamilton

Tylstedt S, Kinnefors A et al (1997) Neural interaction in the human spiral ganglion: a TEM study. Acta Otolaryngol 117(4):505–512

van Ruijven MW, de Groot JC et al (2005) The cochlear targets of cisplatin: an electrophysiological and morphological time-sequence study. Hear Res 205(1–2):241–248

Walker EM Jr, Fazekas-May MA et al (1990) Nephrotoxic and ototoxic agents. Clin Lab Med 10(2):323–354

Warr WB (1980) Efferent components of the auditory system. Ann Otol Rhinol Laryngol 89(Suppl (5 Pt 2)):114–120

Zrunek M, Lischka M et al (1980) Dimensions of the scala tympani in relation to the diameters of multichannel electrodes. Arch Otorhinolaryngol 229(3–4):159–165

Cochlear Echoes

▶ Otoacoustic Emissions

Cochlear Implant

Hinrich Staecker[1] and Jennifer Thompson[2]
[1]Department of Otolaryngology-Head and Neck Surgery, University of Kansas Medical Center, Kansas City, KS, USA
[2]University of Kansas Medical Center, Kansas City, KS, USA

Definition

Electronic device surgically introduced into the inner ear that is capable of bypassing damaged portions of the ear and directly stimulating the auditory nerve.

Cross-References

▶ Vestibular and Central Nervous System, Anatomy

Cochlear Implant Device Failure

Selena E. Heman-Ackah[1] and J. Thomas Roland Jr.[2]
[1]Department of Otolaryngology-Head and Neck Surgery, New York University, New York, NY, USA
[2]Department of Otolaryngology-Head and Neck Surgery, UT - Southwestern Medical Center, University of Texas Southwestern, Dallas, TX, USA

Definition

Error or malfunction with either the internal receiver/stimulator, leading to aberrant function of the cochlear implant device.

Cross-References

▶ Cochlear Implantation, Revision – Adult
▶ Surgical Devices (Cochlear Implantation, Revision – Pediatric)

Cochlear Implant Hard Failure

Thomas J. Balkany[1] and Daniel M. Zeitler[1,2]
[1]Department of Otolaryngology-Head and Neck Surgery, University of Miami Miller School of Medicine, University of Miami Ear Institute, Miami, FL, USA
[2]Denver Ear Associates, Denver, CO, USA

Definition

A cochlear implant device failure manifested by aversive stimuli (pain, shocking, screeching) or a deterioration in implant performance that can be objectively measured with existing in vivo integrity analysis testing, or after explantation with more accurate and thorough ex vivo bench tests. Hard failure can also on rare occasions be diagnosed by an inability to link the external processor with the internal receiver-stimulator device.

Cross-References

▶ Adult Bilateral Cochlear Implantation

Cochlear Implant Soft Failure

Thomas J. Balkany[1] and Daniel M. Zeitler[2]
[1]Department of Otolaryngology-Head and Neck Surgery, University of Miami Miller School of Medicine, University of Miami Ear Institute, Miami, FL, USA
[2]Denver Ear Associates, Denver, CO, USA

Definition

A cochlear implant failure in which a device malfunction is suspected but cannot be proven with in vivo or ex vivo integrity testing. It is a working diagnosis, based on aversive characteristic symptoms or unexplained progressive decrement in objective or expected performance.

Cross-References

▶ Adult Bilateral Cochlear Implantation

Cochlear Implantation, Revision – Adult

Selena E. Heman-Ackah[1] and J. Thomas Roland Jr.[2]
[1]Department of Otolaryngology-Head and Neck Surgery, New York University, New York, NY, USA
[2]Department of Otolaryngology, New York University School of Medicine, New York, NY, USA

Synonyms

Device failure; Explantation of cochlear implant

Definition

Explantation and reimplantation of cochlear implant device in an adult patient secondary device failure, procedural concerns or patient complications.

Basic Characteristics

Cochlear implantation is an increasingly common modality for auditory rehabilitation among patients with severe to profound sensorineural hearing loss. Within the adult population, cochlear implantation has successfully been performed for aural rehabilitation of individuals with hearing loss from a variety of etiologies including age-related hearing loss, noise-induced hearing loss, autoimmune inner ear disease, temporal bone trauma, ototoxic exposure, congenital progressive hearing loss, genetic hearing loss, inner ear malformations, and cochleo-vestibular anomalies. Although cochlear implantation has been successful in long-term aural rehabilitation, cochlear implant failure has been encountered in a small percentage of patients necessitating revision cochlear implantation. In a review of revision cochlear implantation at a large tertiary care cochlear implant program, Alexiades et al. reported a revision cochlear implant rate of 4.9% for all patients who had undergone cochlear implantation (Alexiades et al. 2001). Among the adult patients within this study, a revision rate of 4.7% was reported (Alexiades et al. 2001). In another review of 286 adult cochlear implant patients, a revision rate of 3.8% was noted (Sorrentino et al. 2009). In a similar study by Lassig et al., the overall revision rate for cochlear implantation in both the pediatric and adult population was reported as 5.1% (Lassig et al. 2005). Côté et al. noted an adult revision rate of 5.4% (Côté et al. 2007). In a review of 500 consecutive cochlear implant patients, a revision cochlear implantation rate of 7.2% was reported (Venail et al. 2008). In most reviews of revision implantation, the revision procedure commonly occurs within the first 4–6 years following the initial procedure; however, patients may require revision cochlear implantation at any time following the initial procedure (Alexiades et al. 2001; Lassig et al. 2005; Côté et al. 2007; Venail et al. 2008; Sorrentino et al. 2009). This entry describes the indications for cochlear implant revision, techniques for revision, and performance outcomes following cochlear implant revision among adult patients.

Indications for Cochlear Implant Revision

Various etiologies have been identified in association with revision cochlear implantation in the adult population including device failure, electrode malposition, electrode extrusion, receiver/stimulator migration, infection, soft tissue complications, technology upgrade, trauma, and cholesteatoma (Alexiades et al. 2001; Lassig et al. 2005; Venail et al. 2008). In the review by Lassig et al., the indications for adult and

pediatric revision cochlear implantation were stratified (Lassig et al. 2005). The most common indication for cochlear implant revision was device failure which was reported in 3.7% of all patients accounting for 46% of patient who underwent revision cochlear implant surgery (Lassig et al. 2005). Other reported indications for revision included scalp flap complications (17%), optimization of electrode placement (13%), unexplained deterioration of performance (12%), and technology upgrade (10%) (Lassig et al. 2005). Cholesteatoma was also cited as an etiologic factor in revision cochlear implantation (3%); however, cholesteatoma is more commonly encountered in the pediatric population (Lassig et al. 2005; Côté et al. 2007).

Device failure. The most common cause for revision cochlear implantation is device failure. In a review of 12,856 cochlear implant procedures, device failure was noted in 488 patients representing a 3.79% device failure rate (Battmer et al. 2007). Within a review of 500 consecutive cases of cochlear implantation, a revision cochlear implantation rate of 7.2% was reported (Venail et al. 2008). Device failure was found to be the etiological factor in the vast majority of revision cochlear implant cases (Venail et al. 2008). An overall device failure rate of 6% was noted with a rate of 4.5% among the adult subjects included within this study (Venail et al. 2008). Within this study, device failures were the etiologic factor in 83% of all revision cochlear implantation procedures (Venail et al. 2008). Similar results were reported by Alexiades et al. Within this review, device failure was cited as the etiologic factor for revision cochlear implantation among 85% of adult patients (Alexiades et al. 2001).

Cochlear implant device failures may be categorized as hard failures or soft failures. Hard failures describe malfunctions with the internal device (i.e., loss of function which can be confirmed by standard integrity testing) or loss of link (i.e., ability to communicate with the external processor). Patients may experience complete loss of cochlear implant function or progressive deactivation of the cochlear implant electrodes with associated decline in speech perception scores (Zeitler et al. 2009). Soft failures may be defined as a decline in performance, aversive symptoms, or intermittent function of cochlear implants which often cannot be confirmed by integrity testing. Symptoms associated with soft failures often

include decreased audiologic performance, pain with stimulation, hearing of aversive sounds at stimulation, vertigo, facial stimulation, and the need for frequent device adjustment (Sorrentino et al. 2009). In a review of 33 revision cochlear implant procedure secondary to device failure, 24% of the patients experienced a failure of the speech processor to lock with the internal device, 69% experienced aversive auditory symptoms, 63% experienced aversive nonauditory symptoms, and 48% experienced performance related issues (Buchman et al. 2004). Soft failures are less common than hard failures and may in fact precede hard failures (Sorrentino et al. 2009). In the review by Lassig et al., an overall device failure rate of 3.2% was reported among adult patients with hard failures identified in 2.4% of patients and soft failures identified in 0.7% of patients (Lassig et al. 2005). Within a retrospective review of 329 adult cochlear implant patients, 18 patients underwent revision cochlear implant procedures (Côté et al. 2007). A 3.3% overall adult device failure rate was noted (Côté et al. 2007). Among these patients, device failure represented the etiologic factor in 78% of patients with a 61% hard failure rate and 17% soft failure rate (Côté et al. 2007). In a review of 487 pediatric and adult patients following cochlear implantation, a low incidence of device failure was noted of 2.26% (Sorrentino et al. 2009). Among this cohort, 64% of patients experienced hard failures and 36% of patients experienced soft failures (Sorrentino et al. 2009). Deactivation of five or more electrodes coupled with decline in speech perception scores have been found to be significant risk factors for impending device failure (Zeitler et al. 2009).

Electrode Malposition. Electrode malposition has also been described as an etiologic factor in cochlear implant revision surgery. The malposition of the cochlear implant electrode may occur by one of two means: (1) malposition during cochlear implant insertion or (2) extrusion of the cochlear implant electrode at some point following conclusion of the cochlear implant procedure. In the review by Sorrentino et al., electrode malposition was noted in 0.4% of patients accounting for 10% of all patients who underwent revision cochlear implantation (Sorrentino et al. 2009). In all cases, electrodes were inserted within the vestibular system (Sorrentino et al. 2009). Although it may occur with normal anatomy, more commonly electrode malposition occurs as a function of cochlear malformations or ossification of the

cochlea. In the review by Lassig et al. eight patients (one adult) underwent revision surgery for optimization of electrode placement (Lassig et al. 2005). All of these patients had a history of meningitis with associated cochlear ossification present at the time of initial cochlear implantation (Lassig et al. 2005). Intraoperative fluoroscopy has been demonstrated to facilitate accurate cochlear implant electrode placement in patients with ossified and malformed cochleae. In the review by Côté et al., 0.6% of patients were noted to have implant malfunction secondary to extrusion of the electrode from the cochleostomy leading to electrode malposition (Côté et al. 2007). This accounted for 11% of all revision cochlear implant cases (Côté et al. 2007).

Infection and Soft Tissue Complications. Soft tissue complications and infections are associated etiology with revision cochlear implantation in a substantial proportion of patients. In the review of Sorrentino et al., 0.8% of cochlear implant patients underwent revision cochlear implantation for associated soft tissue infection (Sorrentino et al. 2009). This accounted for 20% of all patients who underwent revision cochlear implantation (Sorrentino et al. 2009). Of note all of these patients underwent endaural approach for the initial cochlear implant (Sorrentino et al. 2009). Of the patients within this series that underwent the curvilinear postauricular approach there were no incidences of soft tissue infection (Sorrentino et al. 2009). Within this review, an additional 0.2% of patients experienced chronic skin flap inflammation as the etiologic factor in revision cochlear implantation (Sorrentino et al. 2009). Venail et al. reported an infection rate of 0.6% leading to revision cochlear implantation (Venail et al. 2008). Côté et al. reported a 0.9% infection and soft tissue complication rate among adult cochlear implant patients (Côté et al. 2007). This represented 17% of all patients who underwent revision cochlear implantation (Côté et al. 2007). In the revision by Lassig et al., 28% of patients were cited as having infection or soft tissue complications as the etiologic factor in revision cochlear implantation (Lassig et al. 2005).

Biofilm formation has been noted in association with cochlear implant devices explanted secondary to infection. In a histopathologic review of implant devices following explantation, biofilms consisting of *Staphylococcus aureus* were identified from explant specimens (Antonelli et al. 2004). This finding was thought most likely to be secondary to contamination from skin associated with wound dehiscence (Antonelli et al. 2004). Chronic *Pseudomonas* infection has also been identified as an etiologic factor in cochlear implant infection (Germiller et al. 2005).

Device Upgrade. Device upgrade may be the inciting factor for revision cochlear implantation, particularly within the adult patients with implants performed more than a decade ago. Patients implanted in the remote past may have been implanted with single channel electrodes or with devices that are no longer serviceable by the manufacturer. This was reported by Lassig et al. regarding 4 patients who underwent revision cochlear implantation for upgrade from a single channel to a multichannel device (Lassig et al. 2005). One patient underwent upgrade from a Stortz UCSF implant which could no longer be serviced by the manufacturer (Lassig et al. 2005). Device upgrade, however, is a less common cause of revision cochlear implantation not cited in multiple other series (Côté et al. 2007; Venail et al. 2008; Sorrentino et al. 2009).

Techniques for Cochlear Implant Revision

Whenever possible reimplantation should be performed immediately; if not possible the shortest interval possible between explants and reimplantation should be employed. There are various surgical considerations in revision cochlear implantation including feasibility of electrode reinsertion, maintaining the patency of the cochleostomy, and maintaining insertion within the established fibrous tract.

In most cases, the traditional transmastoid facial recess approach may be utilized for revision cochlear implantation. The previous incision may be utilized for revision cochlear implantation. The device should be identified and the electrode lead (and ground if present) should be severed just distal to the receiver/stimulator upon its encounter. This allows for the device to be removed safely without concern for incidental removal of the electrode from the cochlea. The device should be returned to the implant distributor for interrogation and cause of failure analysis. The mastoidectomy and facial recess should be revised as needed to allow for adequate visualization of the cochleostomy. Depending upon the latency to revision cochlear implantation, osteoneogenesis may have occurred within the mastoid and facial recess. Care should be taken to ensure that the electrode is not accidentally

removed while drilling as well. This may be prevented by severing the electrode at the level of the facial recess sharply. The well and trough should also be revised. In certain instances, the shape and contour of the revision device may not be identical to the previous device. Revising the well and trough ensures proper seating of the revision device and minimizes the risk of soft tissue complications as well as unsightly contouring of scalp by the device. Once the mastoidectomy, facial recess, well and trough have been revised, the field should be copiously irrigated. The revision device should be introduced onto the field and secured within the well and trough. The electrode should then be removed and the new device electrode inserted within the previous cochleostomy site in the tract formed by the previous electrode. Intraoperative assessment of device impedance and neural response evaluation (known as NRT with Cochlear devices, NRI with the Advanced Bionics devices, and ART with the MED EL devices) are recommended to ensure the function of the device. Plain film x-ray is also recommended. An intraoperative plain film Stenver's view skull x-ray may be obtained to ensure full insertion and assess for tip rollover.

In the vast majority of cases, the technique described above may be employed with successful revision cochlear implantation. However, on occasion a more extensive approach may be necessary. This most often occurs as a function of cochlear ossification (i.e., secondary to meningitis). In such cases, circumodiolar drill-out may be necessary to accomplish revision implantation. In the review of revision cochlear implantation surgery by Lassig et al., 9% of patients required circumodiolar drill-out procedures to improve electrode position (Lassig et al. 2005).

With the revision cochlear implant procedure, intraoperative fluoroscopy may be of benefit in ensuring successful insertion. Intraoperative fluoroscopy facilitates the accuracy of electrode placement by allowing for visualization of the electrode position during the insertion process. Fluoroscopic images are obtained at the placement of the electrode at the cochleostomy and sequentially during insertion allowing for visualization of the course of the electrode during the revision procedure. This has been demonstrated to be safe and effective in ensuring accurate position of the electrode preventing untoward complications (i.e., tip rollover, vestibular insertion, or internal auditory canal insertion).

An alternative technique in revision cochlear implantation may be scala vestibuli insertion. The scala tympani is the target region of the cochlea for cochlear implantation as it allows for cochlear implant placement in closest proximity to cochlear nerve fibers. However, in certain patients, scala tympani insertion cannot be performed. As an alternative, scala vestibuli insertion may safely be performed in patients with partial or total obstruction of the scala tympani with improvement in postoperative phoneme and sentence scores in up to 88% of patients (Lin et al. 2006).

Outcomes in Revision Cochlear Implantation

Although performance has been demonstrated to improve in the vast majority of revision cases, revision does not guarantee improvement in outcomes. Patient may perform better, the same or worse following revision cochlear implantation. With revision cochlear implantation, insertional depth is often improved. In a review of 58 pediatric and adult patients who underwent revision cochlear implantation, electrode insertion of equal or increased depth was accomplished in 91% of patients (Lassig et al. 2005). Speech perception was reported to be decreased in 5.8% of adult patients following revision cochlear implantation with improvement experienced by 70.5% of adult patients and no change noted in 23.5% of adult patients (Lassig et al. 2005). In the review by Sorrentino et al., 90% of patients experiences speech perception performances (words and sentences in quiet and noise) stable or improved following revision cochlear implantation when compared to performance following initial implantation (Sorrentino et al. 2009). In most studies, greater than or equal to 90% of patients experience equal or improved implant performance following revision cochlear implantation (Buchman et al. 2004; Lassig et al. 2005). Thus, in patients were revision cochlear implantation is indicated, revision should be employed with an expectation of improvement in the vast majority of patients.

Cross-References

▶ Audiometry
▶ Auditory Brainstem Implant, Surgical Devices
▶ Congenital Cytomegalovirus and Sensorineural Hearing Loss

References

Alexiades G, Roland JT, Fishman AJ et al (2001) Cochlear reimplantation: surgical techniques and functional results. Laryngoscope 111(9):1608–1613

Antonelli P, Lee JC, Burne RA (2004) Bacterial biofilms may contribute to persistent cochlear implant infection. Otol Neurotol 25(6):953–957

Battmer RD, O'Donoghue GM, Lenarz T (2007) A multicenter study of device failure in European cochlear implant centers. Ear Hear 28(Suppl 2):95s–99s

Buchman CA, Higgins CA, Cullen R et al (2004) Revision cochlear implant surgery in adult patients with suspected device malfunction. Otol Neurotol 25(4):504–510

Côté M, Ferron P, Bergeron F et al (2007) Cochlear reimplantation: causes of failure, outcomes and audiologic performance. Laryngoscope 117(7):1225–1235

Germiller JA, El-Kashlan HK, Shah UK (2005) Chronic pseudomonas infections of cochlear implants. Otol Neurotol 26(2):196–201

Lassig AA, Zwolan TA, Telian SA (2005) Cochlear implant failures and revision. Otol Neurotol 26(4):624–634

Lin K, Marriana MS, Waltzman SB et al (2006) Multichannel cochlear implantation in the scala vestibule. Otol Neurotol 27(5):634–638

Sorrentino T, Côté M, Eter E et al (2009) Cochlear reimplantations: technical and surgical failures. Acta Otolaryngol 129(4):380–384

Venail F, Sicard M, Piron JP et al (2008) Reliability and complications of 500 consecutive cochlear implantations. Arch Otolaryngol Head Neck Surg 134(12):1276–1281

Zeitler D, Lalwani AK, Roland JT Jr et al (2009) The effects of cochlear implant electrode deactivation on speech perception and in predicting device failure. Otol Neurotol 30(1):7–13

Cochlear Implants (CIs)

▶ Implantable Hearing Devices

Cochlear Implants in Patients with Multiple Disabilities

Maura K. Cosetti[1] and Susan B. Waltzman[2]
[1]Department of Otolaryngology, New York University School of Medicine, New York, NY, USA
[2]New York University Cochlear Implant Center, New York University School of Medicine, New York, NY, USA

Synonyms

Cognitively impaired; Handicapped; Multiply handicapped

Definitions

Patients with multiple disabilities are a heterogeneous population that includes patients with hearing loss as well as diverse sensory, behavioral/emotional, cognitive, and motor handicaps.

Introduction

Since the advent of ▶ pediatric cochlear implantation (CI), candidacy criteria have slowly expanded as longitudinal experience with all aspects of CI has grown. Originally restricted to children over 2 years of age with profound deafness, CI technology is now being offered to increasing younger patients, including those less than 12 months of age, as well as those with multiple disabilities. A heterogeneous population with diverse sensory, cognitive and motor handicaps, children with multiple disabilities are an emerging candidacy group and an area of avid investigation. Between 30% and 40% of children with ▶ sensorineural hearing loss (SNHL) demonstrate additional disabilities, including cognitive impairment, motor disorders, visual impairment, and behavioral/

emotional spectrum disorders. In children with severe-profound SNHL, data suggests that up to 48% of children may exhibit one or more additional disabilities (Chilosi et al. 2010). These disabilities may be congenital or acquired, diagnosed prior to, concurrent with, or after the diagnosis of hearing loss and may range in severity across multiple dimensions. The significant heterogeneity of this population combined with unique challenges in diagnosis and outcomes assessment make generalized predictions of postimplant success difficult. Despite this, however, prior literature suggests that multiply handicapped children benefit from CI in multiple areas, including communication skills and quality of life. On more traditional assessments of postimplant success, multiply handicapped children generally score lower on tests of speech perception and language development than children without other disabilities. Although only a subset of multiply disabled children achieve open-set word recognition and oral language skills, the vast majority demonstrate significant improvement from preoperative measures. The following will highlight and discuss issues of CI in the multiply disabled child, from diagnosis, ▶ hearing assessment, therapeutic decision-making, device programming, postimplant outcomes, and rehabilitation.

Diagnosis and Assessment of Hearing Loss

Multidisciplinary evaluation is crucial for effective CI candidacy assessment of a child with multiple disabilities. Ideally, this team should be comprised of audiologists, otolaryngologists, developmental pediatricians, speech-language pathologists, special educators including teachers of the deaf, early intervention specialists, aural rehabilitation therapists, and any other expert deemed appropriate based on the severity and constellation of each child's disabilities. Additionally, parents or care-givers play an integral role in decision-making and treatment planning and are considered important members of the multidisciplinary team.

Although behavioral audiometry may be challenging in this population, attempts are made to obtain ear-specific air/bone thresholds or sound field behavioral thresholds, speech recognition and discrimination scores followed by aided thresholds and scores. Frequently, the extent of disabilities renders these methods inappropriate. If possible, visual response audiometry (VRA) and conditioned play audiometry are used to obtain behavioral data. Often, however, the child's age as well as the nature and extent of disabilities preclude extensive behavioral testing. Objective measures typically augment the behavioral evaluation and include ▶ otoacoustic emissions, ▶ tympanometry, acoustic reflexes, ▶ auditory brainstem response (ABR), and auditory steady-state response (ASSR).

Speech perception testing in this population is challenging as most tests are language based and are not necessarily appropriate for very young children or those with multiple disabilities and/or cognitive impairment. For these children, hearing impairment is not the only factor influencing response to sound. Neurologic deficits, visual impairments (including blindness), attention and hyperactivity disorders, ▶ central auditory processing disorders, retardation and developmental delay, fine and gross motor impairments, and learning disabilities prohibit the use of, or complicate the information gained from traditional assessments of speech and language development.

The Ling sounds, or Ling Developmental Scales, are a set of indices designed to capture auditory, speech, and linguistic developmental milestones in infants and toddlers with hearing loss and can be useful in the multiply disabled population. Similarly, the Preschool Language Scales (PLS) are designed to assess auditory comprehension and expressive communication in infants and toddlers. By targeting skills believed to be important precursors for language development, such as attention to speakers and object play, the PLS may be used to assess multiply handicapped, hearing impaired children (Zimmerman et al. 2002). Another multidimensional metric, the Rosetti Infant-Toddler Language Scale (RI-TLS) can be used to evaluate hearing impaired infants from birth to 36 months of age (Rossetti 1990). The RI-TLS combines professional observations, developmental hierarchies and behaviors to assess seven areas of communication: interaction-attachment, pragmatics, gesture, play, language comprehension, and language expression. Nontraditional measures such as joint attention and symbolic play have demonstrated utility in assessing linguistic development in children with additional disabilities (Johnson et al. 2008).

More sophisticated pediatric closed- and open-set speech perception tools, such as the Glendonald

Auditory Screening Procedure (GASP), Early Speech Perception (ESP) Test, Minimal pairs, TAC, Northwestern University-Children's Perception of Speech (NU-CHIPS) as well as the open-set lexical neighborhood test (LNT), multiple LNT, Phonetically Balanced Kindergarten (PBK), are typically inappropriate in multiply disabled patients, especially in the preimplant evaluation, although the age and degree of disability determine whether or not these tests can be reliably administered.

In all cases, use of standardized parental survey metrics, such as the Meaningful Auditory Integration Scale (MAIS) and its infant-toddler adaptation (IT-MAIS,) can provide useful information regarding early speech perception and linguistic development (Zimmerman-Philips et al. 1997). For children with significant disability, standardized parental surveys (such as the IT-MAIS) and objective electrophysiologic testing may be the only data available on which to base diagnostic and treatment decisions. Additionally, it is important to note that response to traditional amplification (i.e., ▶ Hearing Aid) may be similarly compromised by additional disabilities. While a trial of amplification is appropriate when response to auditory stimuli is difficult to determine, lack of progress with traditional amplification is not an indicator of postimplant benefit.

Developmental metrics, such as the Minnesota Child Development Inventory and the Gesell Developmental Schedule, are important adjunctive measures in this population (Ball 1977). The latter scale consists of five subcategories of skills: gross motor, fine motor, nonverbal cognitive performance, personal-social, and language. Recent studies on postimplant language performance in children with additional disabilities found the Nonverbal Cognitive Quotient (NVCQ, derived from the nonverbal cognitive performance domain in the Gesell Schedule) to be the strongest predictor of post-CI language development (Meinzen-Derr et al. 2010a, b). This will be discussed in greater detail an upcoming section on outcomes.

Expansion of pediatric CI criteria to include increasingly younger children has additional implications regarding predictions of postimplantation benefit as some disabilities may not be detectable in infancy. With implementation of universal newborn hearing screening and improved evaluation tools (such as those mentioned above,) an increasing number of deaf children are diagnosed with severe/profound SNHL in infancy, thus becoming CI candidates prior to 12 months of age. Despite comprehensive CI evaluation and best diagnostic efforts, it may not be possible for clinicians to diagnose or predict unseen disabilities that do not become evident until the child is older. Even multidisciplinary, developmental evaluations may be unable to predict future cognitive or developmental delay, such as autism. Preimplant parent and family counseling in both very young children and the multiply handicapped should be based on individual assessment data and expectations tailored to each child's specific set of disabilities.

Cochlear Implant Device Programming

As with preoperative assessment, postoperative device programming may be complicated in patients with additional disabilities. Psychosocial or behavioral responses may be inappropriate for multiply handicapped children, requiring increased reliance on objective measures. Historically, electrically evoked ABR (EABR) and acoustic reflex thresholds (EART) were used to estimate postoperative programming parameters; however, the need for correction factors and poor reliability rendered these obsolete. Currently in wide use, intraoperative measurements of the electrical compound action potential (ECAP) are a reliable clinical starting point in difficult to program populations. Each of the three commercially available cochlear implants is equipped with ECAP measurement capability. Termed neural response telemetry (NRT^{TM}) in the Nucleus $^{®}$ implant by Cochlear (Sydney, Austraila), neural response imaging (NRI^{TM}) in CIs by Advanced Bionics, LLC (SyLmlar, California) and auditory nerve response telemetry (ART TM) for MED-EL (Innsbruk, Austria), these objective measure are employed intraoperatively to assess the response of a patient's auditory system to electrical stimulation immediately following intra-cochlear insertion of the CI electrode. ECAPs are generated by applying a biphasic stimulus pulse or series of pulses to an electrode in the intra-cochlear array then measuring the voltage response on an adjacent or nearby electrode. Postoperatively, values obtained in the OR can assist with device programming by providing information for initial program creation, especially in difficult to program populations such as the multiply handicapped. Because ECAP

measurements are large, rapid, relatively uncontaminated by muscle artifact and do not require patient cooperation or sedation, telemetry can also be employed during postoperative programming sessions. Studies comparing ECAP-based fitting strategies (which utilize ECAP to predict T- and C- programming levels) with traditional, behaviorally obtained programs found that speech performance scores were higher with behaviorally obtained parameters (Seyle and Brown 2002). However, overall, programs based on ECAP threshold data were found to be of sufficient quality to support speech understanding and, while not optimal, may serve as a basis for initial T- and C- threshold values. In cases of severe disability where behavioral measures cannot be obtained or are unreliable or both, programming audiologists may rely on these objective, electrophysiologic measures when making decisions about strategy or threshold levels. While vigorous follow-up following initial stimulation is common in all children, schedules can be modified to meet the individual needs of each patient, with a baseline schedule of 2 weeks, 5 weeks, 9 weeks, then 3 months, 4.5 months, 6 months, 9 months then 1 year. Feedback from parents, therapists, and educators can be invaluable in programming adjustments, most especially in this difficult to assess population. While unscheduled program changes may be warranted by clinical symptoms, such as decrease in auditory responsiveness, speech changes or decreased environmental awareness, too frequent changes can be detrimental if the child is not given enough time to adjust to new program settings.

Outcomes of Speech Perception, Receptive and Expressive Language

Evaluation of postimplant outcomes, including speech perception, receptive and expressive language development, social interaction, environmental awareness, and quality of life suggest that CI in patients with multiple disabilities can lead to substantial benefit across many dimensions. With respect to auditory speech perception skills, early data suggest improved word and speech recognition following implantation in those patients able to complete perception testing (Hamzavi et al. 2000; Pyman et al. 2000; Waltzman et al. 2000). In each study, the multiply handicapped population included patients with a range of additional

disabilities, such cognitive and motor impairment, retardation, autism, and learning disorders. When compared to children without additional disabilities, overall speech perception scores were lower and rates of skill acquisition slower in the multiply handicapped group. Although some never received open-set speech recognition abilities, substantial benefit from implantation was demonstrated by increased social interaction and environmental awareness (Waltzman et al. 2000). More recently, Berrettini et al. (2008) reported on 23 pediatric CI recipients with additional diagnoses including cerebral palsy, mental retardation, autistic spectrum disorder, epilepsy, attention deficit and hyperactivity (ADHD) children, and learning disorders (Berrettini et al. 2008). For speech perception, four speech perception tests (3 closed and 1 open-set) were administered in Italian. Overall, 20/23 patients demonstrated improved speech perception abilities compared with preoperative values and 53% of patients attained open-set speech recognition skills. Results of a parental questionnaire documented significant perceived post-CI benefits: 100% of parents reported increased awareness of environmental sounds, 96% indicated improved interaction with peers and 74% noted improvement in "speaking skills." Additionally, the percentage of patients using oral language increased from 28% (preoperatively) to 67% postoperatively.

With respect to quality of life, Filipo et al. (2004) found improved quality of life and self-sufficiency in 18 CI recipients with additional disabilities (including visual impairment) (Filipo et al. 2004). Using a questionnaire specifically designed for parents of pediatric CI recipients with multiple disabilities, Wiley et al. (2005) found improved quality of life and access to services in all 16 study participants (Wiley et al. 2005). Parents reported progress in communication skills, improved awareness of environmental sounds, and overall increased attentiveness and interaction with their environment. The majority of children wore their device consistently and there were no parental regrets regarding the decision to undergo CI.

A few studies have focused on outcomes of CI in patients with specific additional disabilities, such as autism. Hamzavi et al. (2000) noted that among the 10 children in their study, those with severe learning disabilities and autism demonstrated minimal benefit. Donaldson et al. (2004) examined six CI recipients

with autism spectrum disorder diagnosed either prior to or following CI and found improved speech perception scores for patients able to complete objective testing (Donaldson et al. 2004). Only 1 of 6 study participants achieved expressive language. Using the MAIS, more than half of parents reported increased responsiveness to sound, improved eye contact, greater attempt at vocalizations, and increased environmental awareness. Donaldson et al. (2004) concluded that while CI afforded improved quality of life in patients with autistic spectrum disorder, specific gains in communication skills were small compared to non-autistic implanted peers. Similar results in autistic patients were demonstrated by Daneshi and Hassanzadeh (2007) who highlighted the need for intensive "disease-specific" rehabilitation to achieve minimal gains (Daneshi and Hassanzadeh 2007). Both studies emphasize the importance of appropriate preoperative parental counseling regarding expectations related to language acquisition in patients with autism spectrum disorder.

Studies on children with CHARGE syndrome support benefit of CI in this complex population. Characterized by coloboma of the eye (C), congenital heart defects (H), atresia or stenosis of the nasal choanae (A), retardation of growth or development and/or central nervous system anomalies (R), genital hypoplasia (G), and anomalies of the ear and/or deafness (E), these children manifest a range of auditory impairments, including deafness, as well as other disabilities. Cochlear implantation in this group is further complicated by frequent congenital malformations of cochleo-vestibular anatomy. Lanson et al. (2007) demonstrated varying, although limited, auditory benefit from cochlear implantation as evidenced by routine audiometry and the IT-MAIS in 10 patients with CHARGE syndrome (Lanson et al. 2007).

Fewer studies have focused on language development in children with CI and additional disabilities. Fukuda et al. (2003) reported improvement in language development at 2 years postimplant in a pediatric patient with moderate developmental retardation, although the language delay remained significant (Fukuda et al. 2003). Holt and Kirk (2005) found substantial linguistic gains in 69 children with cognitive delay, though these achievements were significantly lower compared to CI patients without

cognitive delays (Holt and Kirk 2005). More recently, two recent studies by Meinzen-Derr et al. (2010a, b) have shed light on preoperative predictors of language development following CI in multiply handicapped patients. In multiple regression analysis, NVCQ (described above) was found to be the strongest predictor of post-CI language in a group of 20 multiply handicapped children with CI (Meinzen-Derr et al. 2010b). Well-known predictors in the general pediatric CI population (i.e., patients without additional disabilities) such as age at hearing loss diagnosis, age at implantation, and implant duration were not found to be significant predictors of postimplant performance. Using the NVCQ, Meinzen-Derr et al. (2010a) matched 15 children with developmental disability and CI to hearing controls in an attempt to provide an appropriate comparison group for this complex population (Meinzen-Derr et al. 2010a). While prior studies have compared post-CI language development of multiply handicapped children with that of age and hearing matched controls, these authors attempted a novel control group based on assessments of cognitive function. Results with the PLS demonstrated the CI group to have significantly lower rates of receptive and expressive language when compared to age- and cognitively matched controls. Notably, they found their language delays to be disproportionate to their cognitive potential, meaning that children with CI did not reach language levels commensurate with their cognitive potential. This quantitative "linguistic-cognitive" discrepancy is a novel finding and may have implications for therapeutic strategy – specifically, children with CI and coexisting disabilities may need individualized augmentative and/or adaptive communication strategies to assist linguistic progress, such as speech generating devices or visual aids. As in prior studies, benefits of CI were recognized in many areas of quality of life and increased environmental awareness and social interaction.

Conclusion

Expectations of speech and language development in the multiply handicapped population do not mimic those of "traditional" CI candidates without coexisting disabilities and for many multiply disabled patients,

oral language development may not be an appropriate expectation. Nevertheless, access to auditory stimuli can provide a range of invaluable benefits to these patients, including improved quality of life, greater connectedness to their environment, and improved social interaction. While postimplant predictions remain difficult and dependent upon the nature and extent of the coexisting disabilities, data show that cochlear implantation in children with multiple disabilities is a crucial step in maximizing their ability to reach their full, individualized potential. Early diagnosis, rigorous multidisciplinary evaluation, familial counseling regarding appropriate postoperative expectations, and rigorous postimplantation intervention services are crucial components of CI success in the multiply handicapped population.

Cross-References

▶ Developmental Central Auditory Processing Disorders
▶ Hearing Aid
▶ Hearing Assessment in Infancy and Childhood
▶ Hearing Testing, Auditory Brainstem Response (ABR)
▶ Language Development and Disorders, Birth to 7 Years
▶ Sensorineural Hearing Loss
▶ Speech Development and Disorders
▶ Surgical Devices (Cochlear Implantation, Pediatric)
▶ Surgical Devices (Cochlear Implantation – Pediatric, Congenital Malformations)
▶ Tympanometry

References

Ball RS (1977) The gesell developmental schedules: Arnold Gesell (1880–1961). J Abnorm Child Psychol 5(3):233–239
Berrettini S, Forli F et al (2008) Cochlear implantation in deaf children with associated disabilities: challenges and outcomes. Int J Audiol 47(4):199–208
Chilosi AM, Comparini A et al (2010) Neurodevelopmental disorders in children with severe to profound sensorineural hearing loss: a clinical study. Dev Med Child Neurol 52(9):856–862
Daneshi A, Hassanzadeh S (2007) Cochlear implantation in prelingually deaf persons with additional disability. J Laryngol Otol 121(7):635–638
Donaldson AI, Heavner KS et al (2004) Measuring progress in children with autism spectrum disorder who have cochlear implants. Arch Otolaryngol Head Neck Surg 130(5):666–671
Filipo R, Bosco E et al (2004) Cochlear implants in special cases: deafness in the presence of disabilities and/or associated problems. Acta Otolaryngol Suppl 552:74–80
Fukuda S, Fukushima K et al (2003) Language development of a multiply handicapped child after cochlear implantation. Int J Pediatr Otorhinolaryngol 67(6):627–633
Hamzavi J, Baumgartner WD et al (2000) Follow up of cochlear implanted handicapped children. Int J Pediatr Otorhinolaryngol 56(3):169–174
Holt RF, Kirk KI (2005) Speech and language development in cognitively delayed children with cochlear implants. Ear Hear 26(2):132–148
Johnson KC, DesJardin JL et al (2008) Assessing joint attention and symbolic play in children with cochlear implants and multiple disabilities: two case studies. Otol Neurotol 29(2):246–250
Lanson BG, Green JE et al (2007) Cochlear implantation in children with CHARGE syndrome: therapeutic decisions and outcomes. Laryngoscope 117(7):1260–1266
Meinzen-Derr J, Wiley S et al (2010a) Children with cochlear implants and developmental disabilities: a language skills study with developmentally matched hearing peers. Res Dev Disabil 32(2):757–767
Meinzen-Derr J, Wiley S et al (2010b) Language performance in children with cochlear implants and additional disabilities. Laryngoscope 120(2):405–413
Pyman B, Blamey P et al (2000) The development of speech perception in children using cochlear implants: effects of etiologic factors and delayed milestones. Am J Otol 21(1):57–61
Rossetti L (1990) The Rossetti Infant -Toddler language scale. Linguisystems, East Moline
Seyle K, Brown CJ (2002) Speech perception using maps based on neural response telemetry measures. Ear Hear 23-(Suppl 1):72S–79S
Waltzman SB, Scalchunes V et al (2000) Performance of multiply handicapped children using cochlear implants. Am J Otol 21(3):329–335
Wiley S, Jahnke M et al (2005) Perceived qualitative benefits of cochlear implants in children with multi-handicaps. Int J Pediatr Otorhinolaryngol 69(6):791–798
Zimmerman I, Steiner VG, Pond RE (2002) Preschool language scale. Harcourt Assessment, San Antonia
Zimmerman-Philips S, Osberger MJ, Robbins AM (1997) Infant-Toddler meaningful auditory integration scale. Advanced Bionics Corporation, Symlar

Cochlear Nerve

▶ Central Auditory System, Anatomy

Cochlear Nerve, Anatomy

Max Pusz[1] and Philip Littlefield[2]
[1]Department of Otolaryngology-Head and Neck Surgery, Walter Reed National Military Medical Center, Bethesda, Bethesda, MD, USA
[2]Division of Otology/Neurotology, Walter Reed Military Medical Center Bethesda, Bethesda, MD, USA

Synonyms

Auditory nerve

Introduction

The cochlear nerve is one of the three divisions of the vestibulocochlear nerve and carries all auditory information from the cochlea's organ of Corti to the brain. The cochlear nerve originates at the cochlea, traverses the internal auditory canal (IAC), travels to the cerebellopontine angle, and synapses at the cochlear nucleus in the pons. The entire afferent auditory pathway is composed of four sequential synapses from the cochlea to the auditory cortex (Anson et al. 1981), and the auditory nerve is the first segment.

The nerve has approximately 31,400 myelinated axons in persons with normal or near normal hearing (Rasmussen 1940; Spoendlin et al. 1989). Each axon connects to an individual cell body in the spiral ganglion. The amount of fibers may differ between the right and left side of an individual by as many as 5,000. This number does not stay constant during normal aging. Schuknecht theorized that the neurons decrease by as many as 2,100 fibers/decade. Individual fibers are between 3 and 11 μm (Natout et al. 1987), with the average being 5–7 μm (Rasmussen 1940), making the thickness of the entire nerve 1.15–2.62 mm (Natout et al. 1987). In gross appearance, the cochlear nerve appears whiter than the vestibular nerve. This may be due to the higher count of nerve fibers in the cochlear nerve, as well as the presence of more myelin (Spoendlin et al. 1989).

The nerve is 90–95% thick myelinated fibers and 5–10% unmyelinated fibers. The myelinated fibers interface with type I (inner) hair cell bodies, and the unmyelinated fibers interface with type II (outer) hair cell bodies. Each inner hair cell sends information to the brain via multiple Type I neurons. A Type II neuron communicates with multiple outer hair cells (Spoendlin et al. 1989). The type I auditory neurons are large diameter, myelinated, bipolar neurons. The cell body of a bipolar neuron is located along the axon, not at its ending. Type II auditory neurons are unmyelinated, smaller in diameter, and pseudomonopolar, meaning that it has one axon with two separate branches.

Auditory neurons are arranged tonotopically. Fibers that originate from the apex of the cochlea (low-frequency hearing) are located in the center of the nerve, while fibers originating from the basal turn (high-frequency hearing) are at the periphery. Both the myelinated and unmyelinated fibers seem to be organized like this. The neurons keep a tonotopic organization throughout their course, but the arrangement changes to a superior-inferior orientation more medially. The low-frequency fibers enter the ventral portion of the cochlear nucleus, while the high-frequency fibers enter the dorsal cochlear nucleus (Ryugo 1992).

Embryology

The vestibulocochlear nerve starts to develop from the otic placode in the fourth week of embryonic development. The nerve separates into the three divisions during the fifth week: superior vestibular, inferior vestibular, and cochlear. Meanwhile, the ganglion forms near the 28th day, and this then divides into the pars inferior and superior. The pars inferior goes on to split into upper and lower segments. The upper segment becomes the saccular nerve, and the lower segment becomes the cochlear nerve (Lagercrantz 2002). The pars superior fibers innervate the utricular macula and the cristae of the superior and lateral semicircular canals. Cochlear nerve development continues through the eighth week of gestation at which time it is mature. The cochlear ganglion, also known as the spiral ganglion, is at the distal (lateral) portion of the cochlear nerve. The proximal (medial) portion of the nerve is enveloped by central nervous system glial cells, which travel distally to meet peripheral nervous system Schwann cells that migrate centrally (Gulya 2003). The junction occurs near the fundus of the internal auditory canal.

With advanced neuroimaging, such as high-resolution magnetic resonance imaging (MRI), it is possible to detect developmental anomalies of the cochlear nerve. The most widespread abnormalities are nerve aplasia or hypoplasia. Absence of the cochlear nerve is traditionally an absolute contraindication to cochlear implantation, but there are reports of patients with cochlear nerve aplasia found on MRI that have benefited from implantation. One explanation would be the failure of some cochlear nerve fibers to separate from the vestibular nerve, and thus they would not be seen separately on MRI (Roland 2010).

Origination

The cochlear nerve begins with unmyelinated dendrites passing through the habenular openings of the organ of Corti. These fibers synapse with the inner and outer hair cells. There are three rows of outer hair cells and one row of inner hair cells. The number of inner hair cells ranges between 2,800 and 4,400, and outer hair cells number between 11,200 and 16,000. Each inner hair cell is innervated by an average of 10–30 separate afferent nerve fibers (dendrites), each from separate neurons. These nerve fibers pass to the spiral ganglion and synapse at one of the 25,000–30,000 cell bodies in the spiral ganglion (Rasmussen 1940). The innervation density of the inner hair cells is not uniform throughout the cochlea. The inner hair cells at the lower second turn of the cochlea are innervated by around 15 fibers, and those at the base and apex are each innervated by three to four fibers. This results in an innervation density of 1,000–1,200 fibers/mm in the basal turn, and 2,000–2,800 fibers/mm in the middle turn (Spoendlin et al. 1989).

Course

The nerve course begins with its dendrites traveling from the cochlear hair cells to the spiral ganglion. Once the fibers pass through the habenular openings, the dendrites become myelinated and progress toward the auditory cell body, which is in the spiral ganglion of the cochlea. From here, the axon of the neuron progresses to the modiolus of the cochlea, then to the fundus, which is the lateral opening of the IAC. The cochlear and inferior vestibular nerves fuse 3–4 mm

from the lateral end of the IAC (Rubinstein et al. 1996), while the entire distance of the IAC is 8–10 mm. The cochlear nerve is in the anterior inferior position when it enters the lateral IAC. Here, it is separated from the facial nerve by the falciform (transverse) crest. The nerve then makes a 90° rotation that is mostly inside the IAC, so that it is caudal to the inferior vestibular nerve at the medial IAC (the porus acusticus). If one is looking from the brain laterally into the IAC of the left ear, the rotation is clockwise. It is counterclockwise if looking from the same position toward the right ear. The rotation continues to the cerebellopontine angle, and the result is that the cochlear portion is the inferior half of the vestibulocochlear nerve at the brainstem.

There often is a cleavage plane that can be taken advantage of during vestibular nerve sectioning. It is between the cochlear and vestibular nerves and is in the superior-inferior direction laterally. Because of the nerve rotation, the plane runs in the anterior-posterior direction at the cerebellopontine angle. It can be identified with tedious inspection in 75% of patients at the cerebellopontine angle (Silverstein et al.1986). The cochlear nerve appears whiter than the vestibular nerve, with a blood vessel that usually lies between them.

As the nerve exits the IAC, it travels 20–30 mm in the cerebellopontine angle of the posterior cranial fossa, and the flocculus of the cerebellum covers it for the final 5 mm. The cochlear nerve enters the brainstem caudal to the vestibular nerve and synapses at the second order neurons within the cochlear nucleus. The fibers either ascend or descend as they enter the cochlear nucleus. The ascending branch leads to the ventral cochlear nucleus. The descending branch leads to the posterior portion of the ventral nucleus, collects into a bundle, and enters the dorsal cochlear nucleus (Harrison et al. 1970).

The fibers leave the cochlear nucleus and follow either the direct or the indirect routes. In the direct route, the fibers cross to the lateral lemniscus of the contralateral side and continue to the medial geniculate body of the thalamus. The indirect route fibers travel to the trapezoid body. A portion of the fibers synapses at third order neurons here. Both synapsed and unsynapsed fibers travel to the superior olive and continue on to the lateral lemniscus, with some fibers synapsing here while others continue to the inferior colliculus. These fibers then continue on to their termination in the medial geniculate nucleus of the thalamus. The medial geniculate nucleus has a small

ventral and a large dorsal portion, and this is the location of the fourth order neurons (Anson et al. 1981). These axons travel to the auditory cortex, which is in the Sylvian fissure of the temporal lobe (Mills et al. 2006).

Efferent Innervation

The efferent nerve fibers run parallel to the afferent fibers. They are commonly termed the olivo-cochlear bundle due to their origination in the superior olivary complex. The efferent system is composed of 500–600 fibers. Seventy-five percent of the efferent fibers originate dorsomedial to the contralateral superior olivary nucleus, and are composed of large myelinated fibers. These fibers decussate beneath the floor of the fourth ventricle, where they join the remaining 25% of efferent fibers. These remaining fibers originate from ipsilateral cells dorsolateral to the superior olivary nucleus, and they are small and unmyelinated. The joined fibers exit the brainstem in the inferior division of the vestibular nerve and cross into the cochlear nerve via the vestibulocochlear anastomosis. The fibers enter through the habenula perforata and travel to the organ of Corti. Some of the fibers terminate on the afferent nerve fibers, but not on the inner hair cells themselves. The rest of the fibers travel to the outer hair cells and contact them directly (Schuknecht 1974; Lonsbury-Martin 2009). The exact function of the efferent system has been extensively studied, but is still unknown. It is thought to function to improve speech perception, extend the dynamic range of the cochlea, and to protect the cochlea against acoustic trauma.

Conclusion

Understanding of the cochlear nerve and its anatomy continues to evolve with research. Though the cochlear nerve has a short course from the cochlea to the cochlear nucleus, it is important to understand the anatomy in order to prevent injuries to it during surgery. Rarely does a surgeon actually operate on the cochlear nerve itself, but its relationships to the more frequently approached vestibular nerves and facial nerve are vital for the surgeon to comprehend.

Cross-References

▶ Adult Bilateral Cochlear Implantation
▶ Balance (Anatomy: Vestibular Nerve)
▶ Cochlea, Anatomy
▶ Facial Nerve Imaging, CT and MRI
▶ Surgical Approaches and Anatomy of the Lateral Skull Base
▶ Surgical Devices (Cochlear Implantation, Pediatric)
▶ Surgical Devices (Cochlear Implantation – Pediatric, Congenital Malformations)
▶ Surgical Devices (Cochlear Implantation, Pediatric)
▶ Temporal Bone Tumors
▶ Vestibular and Central Nervous System, Anatomy

References

Anson BJ et al (1981) Surgical anatomy of the temporal bone. WB Saunders, Philadelphia

Gulya AJ (2003) Developmental anatomy of the temporal bone and skull bone. In: Glasscock ME (ed) Glasscock-Shambaugh surgery of the ear, 5th edn. BC Decker, Hamilton

Harrison JM et al (1970) Anatomical aspects of the cochlear nucleus and superior olivary complex. Contrib Sens Physiol 4:95–142

Lagercrantz H (2002) The newborn brain: neuroscience and clinical applications. Cambridge University Press, Cambridge

Lonsbury-Martin BL (2009) Physiology of the auditory and vestibular systems. In: Snow J, Wackym P (eds) Ballenger's otorhinolaryngology: head and neck surgery. People's Medical Publishing House, Chelton

Mills et al (2006) Anatomy and physiology of hearing. In: Bailey BJ (ed) Otolaryngology head and neck surgery, 4th edn. Lippincott Williams and Wilkins, Philadelphia

Natout M et al. (1987) Topography of vestibulocochlear nerve fibers in the posterior cranial fossa. Laryngoscope 97:954–958.

Rasmussen AT (1940) Studies of the VIIIth cranial nerve in man. Laryngoscope 50(1):67–83

Roland PS (2010) Cochlear implants in adults and children. In: Gulya AJ (ed) Glasscock-Shambaugh surgery of the ear, 6th edn. People's Medical Publishing House, Shelton

Rubinstein D et al (1996) Anatomy of the facial and vestibulocochlear nerves in the internal auditory canal. Am J Neuroradiol 17:1099–1105

Ryugo DK (1992) The auditory nerve: peripheral innervation, cell body morphology, and central projections. In: Webster DB (ed) The mammalian auditory pathway: neuroanatomy. Springer, New York

Schuknecht HF (1974) Pathology of the ear. Harvard University Press, Cambridge

Silverstein H et al (1986) The unrecognized rotation of the vestibular and cochlear nerves from the labyrinth to the brain stem: its implications to surgery of the eighth cranial nerve. Otolaryngol Head Neck Surg 95(5):543–549

Spoendlin H et al (1989) Analysis of the human auditory nerve. Hear Res 43(1):25–38

Cochlear Neuroma

▶ Cochlear Schwannoma

Cochlear Nucleus

Hinrich Staecker[1] and Jennifer Thompson[2]
[1]Department of Otolaryngology-Head and Neck Surgery, University of Kansas Medical Center, Kansas City, KS, USA
[2]University of Kansas Medical Center, Kansas City, KS, USA

Definition

Two heterogeneous collections of neurons termed the ventral cochlear nuclei and the dorsal cochlear nuclei that receive aural input from the auditory nerve and send outputs to the higher-order auditory brainstem structures.

Cross-References

▶ Vestibular and Central Nervous System, Anatomy

Cochlear Schwannoma

Brandon Isaacson[1], Joe Walter Kutz Jr.[1] and Peter Sargent Roland[2]
[1]Otolaryngology-Head and Neck Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA
[2]Department of Otolaryngology-Head and Neck Surgery, UT - Southwestern Medical Center, University of Texas Southwestern, Dallas, TX, USA

Synonyms

Auditory nerve schwannoma; Cochlear neuroma; Eighth nerve schwannoma

Definition

Cochlear schwannoma is a benign neoplasm arising from schwann cells covering the cochlear division of the eighth cranial nerve.

Introduction

Cochlear schwannomas are rare benign neoplasms which arise in the cerebellopontine angle, internal auditory canal, or within the cochlea. These tumors are typically slow growing especially when they reside within the otic capsule. Hearing loss, aural fullness, and tinnitus are frequently experienced in patients with cochlear schwannomas. Magnetic resonance imaging (MRI) is the imaging modality of choice as schwannomas have a characteristic appearance. These tumors are quite common both clinically and subclinically in patients with neurofibromatosis II. Treatment options for a patient with a cochlear schwannoma include observation, radiation therapy, microsurgical excision, or combined microsurgery and radiation (Jiang et al. 2011; Kennedy et al. 2004).

Clinical Features

Hearing loss is the most common symptom in patients with a cochlear schwannoma. Patients with retrocochlear pathology typically present with progressive unilateral or asymmetric hearing loss with poor speech discrimination. In a recent study of 10 patients intracochlear schwannomas, 100% of the patients presented with subjective progressive hearing loss (Jiang et al. 2011).

Tinnitus is frequently experienced in patients with a cochlear schwannoma. Tinnitus is subjective, continuous, and can range from a low- to a high-frequency sound. The frequency and volume of the tinnitus may fluctuate and does not typically correspond to tumor growth.

Aural fullness is the sensation pressure in the ear which is frequently experienced in the setting of retrocochlear pathology. Patients with Meniere's disease, Eustachian tube dysfunction, petrous apex pathology, jugular foramen pathology, or middle ear pathology can also experience ear fullness.

Vestibular symptoms such as dizziness, vertigo, imbalance, and lightheadedness are frequently encountered in patients with retrocochlear pathology. Vertigo and imbalance associated with retrocochlear pathology can be secondary to poor central compensation, or involvement/irritation of the vestibular nerve or vestibular end organs (Jiang et al. 2011; Kennedy et al. 2004).

Diagnostics

Audiometry

Pure tone audiometry typically reveals unilateral or asymmetric sensorineural hearing loss in the affected ear. Hearing loss severity can range from mild to profound. Patients with intracochlear schwannomas often have a loss of hearing in the frequency range where the tumor is located within the cochlea (Jiang et al. 2011). Speech audiometry has a typical retrocochlear pattern with poor speech discrimination out of proportion to the pure tone audiometry in a patient with a cochlear schwannoma (Jackler 2005; Jiang et al. 2011).

Magnetic Resonance Imaging

High-resolution MRI of the temporal bone provides unparalleled visualization of the otic capsule and internal auditory canal. Fine-cut, high-resolution T2 (FIESTA, CISS, FSE) images allow direct visualization of the vestibular, cochlear, and facial nerves within the internal auditory canal and cerebellopontine angle. This T2 imaging technique provides excellent detail of the cochlea, vestibule, and semicircular canals. A mass within the otic capsule can readily be identified as a hypointense signal adjacent to the normally hyperintense signal within the cochlea (Fig. 1). Schwannomas demonstrate significant enhancement with the administration of gadolinium contrast both in the internal auditory canal and the otic capsule (Fig. 2). T1 MRI with gadolinium can identify schwannomas as small as 2 mm. MRI is also typically used to follow patients with schwannomas to evaluate for interval growth after treatment with microsurgery or radiation. Observation with serial MRI scans is frequently utilized as a management strategy in patients with a cranial nerve schwannoma (Jackler 2005).

Cochlear Schwannoma, Fig. 1 Coronal T1 MRI with gadolinium of a right intracochlear schwannoma which fills the ascending, middle and apical turns (*white arrow head*)
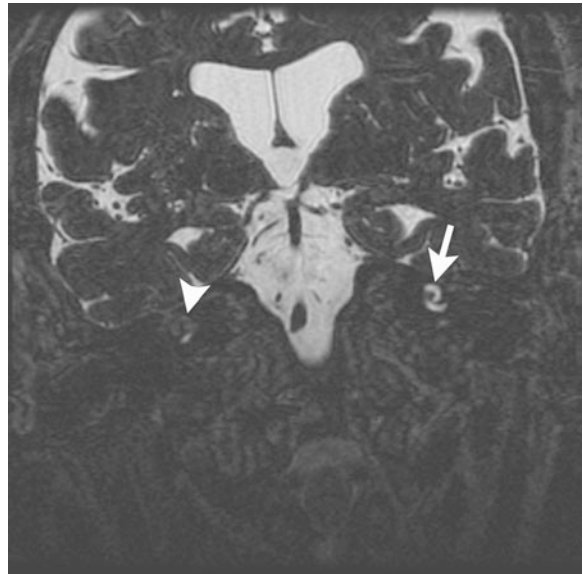
Cochlear Schwannoma, Fig. 2 Coronal T2 FIESTA MRI demonstrating a hypointense filling defect in the apical, middle and ascending basal turns of the right cochlea (*white arrow head*). The left cochlea shows a normal hyperintense signal (*white arrow*)

Differential diagnosis

Vestibular schwannoma, facial schwannoma, endolymphatic sac tumor, lipoma, meningioma, cholesteatoma, chordoma, chondrosarcoma, labyrinthitis ossificans (Jackler 2005).

Treatment

Observation

Clinical examination and serial magnetic resonance imaging is often the first line management in patients with a cochlear schwannoma. Interval scans are typically obtained annually with comparisons being made to the initial MRI which serves as the baseline study. The mean growth rate of a schwannoma is 1–2 mm/year. A number of observational studies examining the growth rates of schwannomas demonstrate no evidence of enlargement in some patients with up to 10 years of follow-up using MRI (Jackler 2005; Kennedy et al. 2004). Progression to active treatment with microsurgery or radiation therapy is indicated in tumors that demonstrate progressive enlargement, or patients with intractable life-altering symptoms such as vertigo, facial numbness, or facial weakness. A schwannoma with minimal growth or that enlarges within the confines of the otic capsule can still be managed with observation. Progressive hearing loss is not an indication for active treatment since both microsurgery and radiation therapy ultimately results in anacusis (Jiang et al. 2011).

Radiation Therapy

Stereotactic radiation therapy is a reasonable option in cochlear schwannomas which progressively enlarge or that are causing vertigo. The ultimate measure of treatment success with stereotactic radiation is cessation of growth. Radiation can be delivered as a single fraction (radiosurgery) or in multiple fractions (radiotherapy). Radiosurgery is delivered either by a fixed ionizing radiation source, or a mobile linear accelerator. Patient convenience and steep radiation gradients are significant advantages of stereotactic radiation over the classic opposed field radiotherapy treatments. Hypofractionated stereotactic radiation therapy utilizes a daily treatment delivered over 3–5 days which results in less toxicity to the adjacent structures.

Tumor control with stereotactic radiotherapy ranges from 92% to 98% with a minimum of 5 years of follow-up in most series. Some series considered need for further surgery as treatment failure; thus, patients with progressive tumor enlargement after radiation who had not undergone microsurgery were considered treatment successes. Long-term hearing preservation in patients with serviceable pretreatment hearing is approximately 50% in most series. Several studies have reported improved hearing preservation when treating vestibular schwannomas with hypofractionated treatments compared to single fraction radiosurgery. Complications from stereotactic radiation typically occur in a delayed fashion either several months to several years after treatment. Dizziness and imbalance can occur several days to months after treatment and is typically self-limited. The incidence of facial paralysis (2–5%) and trigeminal nerve dysfunction (2–5%) has significantly declined with reduction in single fraction doses. Facial paralysis typically occurs within the first year of treatment and in many cases returns to baseline function. New-onset facial weakness is typically managed with corticosteroids followed by facial nerve exercises once evidence of recovery is noted on physical exam. Trigeminal dysfunction including anesthesia or neuralgia is more common in patients with tumors that abut the trigeminal nerve or that have pretreatment trigeminal symptoms. Hydrocephalus occasionally occurs in patients following treatment with stereotactic radiation. Patients with hydrocephalus typically present with headaches, imbalance, nausea, decreased vision, and vomiting. Hydrocephalus can be managed conservatively with diuretics and corticosteroids, but often requires a ventricular peritoneal shunt (Jackler 2005).

Progressive tumor enlargement after radiation is not uncommon in the first 2 years after treatment which is thought to be secondary edema. Postradiation tumor edema is monitored with serial MRI which frequently demonstrates tumor regression on follow-up imaging. Tumor progression 2 years after radiation treatment while rare indicates treatment failure which eventually necessitates microsurgery. A number of reports indicate worse facial nerve outcomes in patients undergoing total tumor excision after failed radiation treatment when compared to primary microsurgery. Radiation-induced malignancies are rare following stereotactic radiotherapy, but these tumors are

typically fatal given their location in the posterior fossa. Radiation-induced neoplasia occurs in a delayed fashion (years) and by definition occurs in the field of radiation (Jackler 2005).

Serial MRI is typically performed yearly or every other year after stereotactic radiotherapy for the remainder of the patient's life to monitor for tumor progression. A significant advantage of stereotactic radiosurgery is that it is performed in an outpatient setting with minimal recovery time. Another advantage of stereotactic radiosurgery is it avoids the more serious immediate complications that can be encountered after microsurgery such as cerebrospinal fluid leak, stroke, meningitis, facial weakness, and immediate hearing loss (Jackler 2005).

Microsurgery

Advances in instrumentation, magnification, and intraoperative nerve monitoring have had a dramatic effect on microsurgery outcomes in patients with skull base pathology. Indications for microsurgery include progressive tumor enlargement, vertigo, and patient preference. The approach utilized depends solely on the location of the tumor and surgeon preference since hearing preservation is not possible. Tumors confined to the cochlea can be removed via the following approaches: transcanal, postauricular transcanal, or a postauricular transmastoid facial recess. The promontory is removed with an otologic drill with care being taken to not injure the genu of the petrous carotid artery or the tympanic facial nerve. A cerebrospinal fluid leak is typically encountered during tumor removal if the schwannoma extends into the modiolus. The modiolar defect can be readily packed off following tumor removal to prevent a postoperative cerebrospinal fluid leak. Transmodiolar tumors, which by definition extend into the cochlea and the internal auditory canal, typically require a transotic approach for complete tumor removal. In select cases, a transmodiolar tumor can be removed via a translabyrinthine approach using a medial cochleotomy. The transotic approach also allows for excision of tumors that extend into the cerebellopontine angle. Cochlear schwannomas confined to the internal auditory canal and/or cerebellopontine angle can also be removed using a translabyrinthine approach or a retrosigmoid approach. A retrosigmoid approach has a potential advantage of preservation of the vestibular portion of the eighth nerve and the vestibular labyrinth (Fisch and Chen 2010; Jackler 2005).

Total tumor excision, achievable in the vast majority of patients, is the goal for microsurgical management of a cochlear schwannoma. In rare cases, a small remnant of tumor is not removed if it is extremely adherent to critical structures such as the facial nerve, brainstem, trigeminal nerve, or posterior fossa vasculature (Fisch and Chen 2010; Jackler 2005).

Complications of microsurgery include facial paralysis which is more problematic in larger tumors, cerebrospinal fluid leak (10%), meningitis, cerebrovascular accident, death, acute vertigo, prolonged imbalance, and immediate hearing loss. Microsurgery also necessitates a 2–5 day hospital stay to monitor for complications and for recovery of balance function after sacrifice of the vestibular system. Recovery time after discharge can take weeks to months depending on a number of factors including but not limited to: underlying medical conditions, pretreatment physical conditioning, and preoperative vestibular function (Jackler 2005).

A follow-up MRI is typically obtained 6–12 months after surgery and serves as a baseline study to compare all follow-up imaging studies. If the initial scan shows no evidence of residual or recurrent tumor, a follow-up study is not performed for another 2–5 years. If a subtotal excision was performed, serial scans are obtained every 1–2 years for the patient's lifetime to monitor for recurrence. In the setting of recurrent or residual enlarging tumor, stereotactic radiosurgery is commonly employed to prevent additional growth (Jackler 2005).

Conclusion

Cochlear schwannomas are slow-growing benign tumors that most commonly present with progressive hearing loss. MRI has allowed for early identification and localization of these tumors. Treatment is recommended in patients who demonstrate progressive enlargement or who present with intractable symptoms such as vertigo, facial pain, numbness, or paresis. Management of a cochlear schwannoma depends on a number of variables including hearing

status, patient preference, vertigo, patient age, and medical comorbidities. Observation with spinal MRI scans microsurgery, and stereotactic radiation are all viable treatment options for patients with cochlear schwannomas.

Cross-References

- ▶ Audiometry
- ▶ Auditory System Exam
- ▶ Balance (Anatomy: Labyrinth and Otoliths)
- ▶ Balance (Anatomy: Vestibular Nerve)
- ▶ Benign Neoplasia-Schwannoma-Neurofibromatosis Type 2
- ▶ Bone-Anchored Hearing Aid in Single-Sided Deafness
- ▶ Canal Wall Up Mastoidectomy
- ▶ Cholesterol Granuloma
- ▶ Cochlea, Anatomy
- ▶ Cochlear Nerve, Anatomy
- ▶ ENG/VNG
- ▶ Facial Nerve Imaging, CT and MRI
- ▶ Hearing Testing, Auditory Brainstem Response (ABR)
- ▶ Implantable Hearing Devices
- ▶ Lateral Skull Base Surgical Approaches
- ▶ Mastoid Obliteration
- ▶ Mastoidectomy
- ▶ Middle Ear Adenoma
- ▶ Middle Ear Anatomy
- ▶ Nystagmus
- ▶ Osteoradionecrosis of Skull Base (Benign Neoplasia-Paragangliomas)
- ▶ Petrous Apicectomy
- ▶ Physiology of Cochlea
- ▶ Radiologic Evaluation of Central Skull Base
- ▶ Rotary Chair
- ▶ Sensorineural Hearing Loss
- ▶ Skull Base Neoplasms
- ▶ Stereotactic Radiation for Head and Neck Cancer
- ▶ Temporal Bone Tumors
- ▶ Testing, Posturography
- ▶ Translabyrinthine Approach
- ▶ Transotic Approach
- ▶ Vestibular and Central Nervous System, Anatomy

References

Fisch U, Chen JM (2010) Transotic approach. In: Brackmann DE, Shelton C, Arriaga MA (eds) Otologic surgery, 3rd edn. Saunders Elsevier, Phildephia, pp 621–630

Jackler RK (2005) Surgical neurotology: an overview. In: Jackler RK, Brackmann DE (eds) Neurotology, 2nd edn. Elsevier Mosby, Philadelphia, pp 702–704

Jiang Z, Isaacson B et al (2011) Cochlear schwannomas confined to the otic capsule. Otol Neurotol 32(7):1175–1179

Kennedy RJ, Shelton C, Salzman KL, Davidson HC, Harnsberger HR (2004) Intralabyrinthine schwannomas: diagnosis, management, and a new classification system. Otol Neurotol 25:160–167

Cochleotoxicity

- ▶ Sensorineural Hearing Loss (Ototoxicity)

Cognitively Impaired

- ▶ Cochlear Implants in Patients with Multiple Disabilities

Cold Sore

- ▶ Oral Mucosal Lesions

Coloboma

Michael M. Kim
Division of Facial Plastic & Reconstructive Surgery, Department of Otolaryngology-Head and Neck Surgery, Oregon Health & Science University, Portland, OR, USA

Definition

Colobomas are defects within a structure of the eye that may or may not affect vision. Defects can be found in iris, retina, choroid, or optic disc and are present
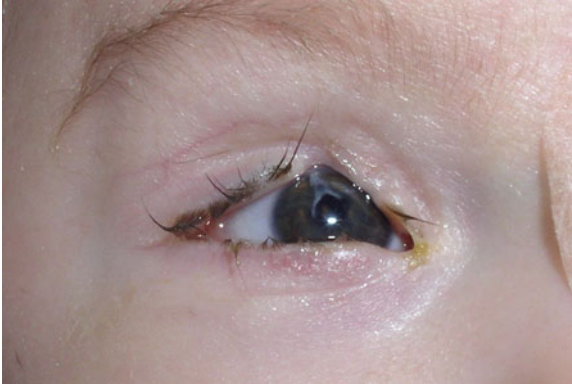
Coloboma, Fig. 1 Upper lid coloboma with iris involvement

from birth. They may be unilateral or bilateral, and can be associated with syndromes such as CHARGE syndrome.

Comfort Measures

▶ Palliative Care and Head and Neck Cancer

Commissuroplasty

Eric J. Dobratz
Department of Otolaryngology, Eastern Virginia
Medical School, Norfolk, VA, USA

Definition

A procedure performed to correct a deformity at the corner of the mouth or oral commissure. Commissuroplasty may be performed to correct macrostomia resulting from a lateral orofacial cleft. More often, commissuroplasty is performed to repair microstomia that develops as a result of trauma or reconstruction of defect of the lip involving the oral commissure.

Basic Characteristics

Commissuroplasty is a procedure that is performed to correct a deformity at the corner of the mouth or oral commissure. A commissuroplasty may be performed to correct macrostomia. More often commissuroplasty is performed to repair microstomia that develops as a result of scarring after trauma (including electrical and chemical burns) or after reconstruction of lip defects involving the oral commissure.

Macrostomia is an increased oral aperture that results from a rare facial malformation caused by failure of mesodermal migration merging to obliterate the embryonic grooves between the maxillary and mandibular processes during early gestation (Franco et al. 2007). This rare malformation occurs in 1:80,000 to 1:300,000 live births.

Microstomia is a term that is used to describe a congenital or more often an acquired reduction in the size of the oral aperture. This reduction in the oral aperture may result in compromise of cosmesis, function, nutrition, and quality of life for patients. In adults, microstomia generally results as an acquired disorder after reconstruction of a defect of the lip for malignancy. Microstomia may also result as a consequence from a connective tissue disorder such as systemic sclerosis (Kyomen et al. 2009). In children, microstomia occurs as a result of scarring from chemical and electrical burns or rarely as part of a genetic disorder.

Unilateral microstomia often results after reconstruction of lip defects using an ▶ Estlander flap. Estlander flaps are a one-staged cross-lip flap for reconstruction of lip defects involving the oral commissure. One of the major drawbacks of the Estlander flap is the resultant microstomia and rounding of the reconstructed oral commissure (Fig. 1). A secondary commissuroplasty is often performed after this type of reconstruction in an attempt to restore a more normal appearance and function of the distorted and medialized commissure.

Microstomia and deformities of the oral commissure may lead to significant functional and cosmetic concerns. Patients experience difficulty opening their mouth, which may lead to decreased function of speech and facial expression. They may also have difficulty maintaining adequate nutrition and dental hygiene. These defects may lead to stressful social interaction for those affected as well. Treatment options for correcting these deformities include both nonsurgical and surgical options. The ultimate treatment will depend on the cause and severity of the deformity and patient goals. The goals of
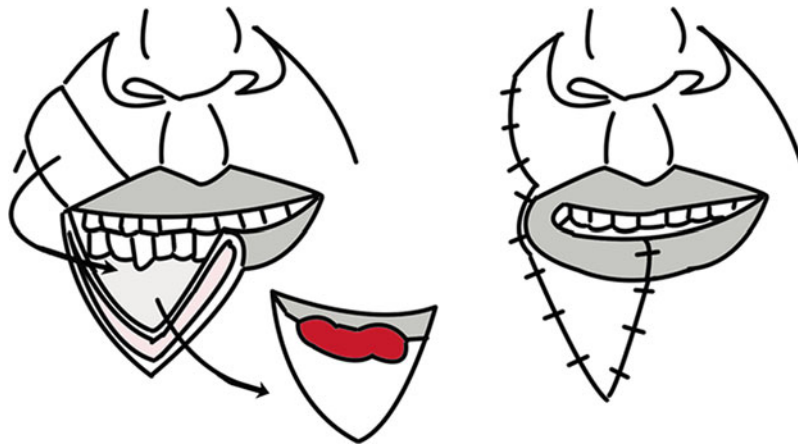
Commissuroplasty, Fig. 1 Estlander flap. Single-staged cross-lip flap where the rotation of the flap occurs at the medially located pedicle on the lip opposite from the defect. It is at this point of rotation that the newly created commissure is located, which results in medialization of the modiolus and the corresponding muscles that are lateral to the defect. The result is a rounded and medialized commissure that often requires a commissuroplasty to improve the microstomia

commissuroplasty, or surgical repair, include widening the oral aperture, reconstituting or maintaining the function of the orbicularis oris sphincter, and obtaining lip symmetry.

In 1954, Kazanjian and Roopenian (1954) described two methods for reconstructing the commissure. One method involved the use of mucosal advancement while the other used local vermilion flaps. There have been many modifications of these types of repairs to correct microstomia and deformities at the oral commissure, but it has proven to be difficult to produce an excellent result with a normal appearance and satisfactory function (Anderson and Kurtay 1971). The vermilion is a unique surface that is poorly simulated by grafts or pedicled flaps. The techniques that have been developed generally involve the creation of a new commmissure by creating a raw surface area lateral to the existing commissure that is then covered with mucosal advancement or vermilion flaps.

Macrostomia is a rare malformation that may occur unilaterally or bilaterally. It is characterized by a transverse facial cleft that extends out from the oral commissure in a horizontal and slightly upward diagonal line toward the tragus. The oral commissure is incompetent due a disconnected oral muscular sphincter. In most cases, the cleft ends at the medial border of the masseter muscle. Various methods have been described for commissuroplasty for macrostomia including double Z-plasty (Torkut and Coskunfirat 1997), mucosal flap with myoplasty (Taub et al.

2009), and myomucosal flaps (Franco et al. 2007). The goal of this surgery is to reconstitute the orbicularis sphincter to create adequate lip function and lip symmetry with well-positioned scars.

Techniques

The type of commissuroplasty performed will depend on the cause and degree of the deformity. In cases of microstomia that are caused by an Estlander cross-lip flap, there are two main methods that are generally used to correct the resultant rounding and medialization of the commissure that occurs after this type of reconstruction.

One method involves the excision of a triangle of skin and subcutaneous tissue located lateral to the commissure (Fig. 2). This triangle is designed to approximate the shape and location of the contralateral normal commissure (in unilateral cases). A full thickness transverse incision is created through the remaining muscle and oral mucosa to the apex of the triangle, which represents the location of the new commissure. A mucovermilion flap is then created from the buccal mucosa and advanced to cover the muscle and is sutured to the skin.

The second method involves the use of myomucosal vermilion flaps to recreate the commissure (Fig. 3). Again, a triangle of skin and subcutaneous tissues are excised lateral to the deformed

**Commissuroplasty,
Fig. 2** Commissuroplasty
with vermilion advancement.
A triangular-shaped area of
skin and subcutaneous tissue is
excised lateral to the blunted
commissure. A transverse full-
thickness incision is created
and the buccal mucosa is
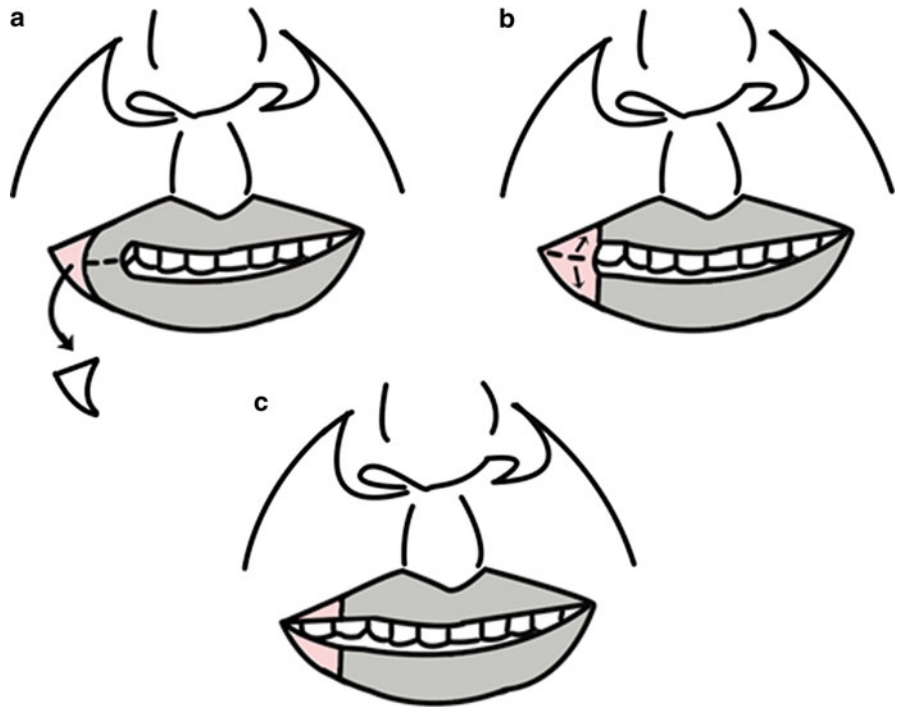elevated and advanced to
create a new vermilion

**Commissuroplasty,
Fig. 3** Commissuroplasty
with myomucosal vermilion
flap. A triangular-shaped area
of skin and subcutaneous
tissue is excised lateral to the
blunted commissure. The
donor flap from the inferior lip
is raised to include the mucosa
and orbicularis marginalis.
A transverse incision is then
created through the muscle to
the apex of the triangle. The
flap is sutured to create the
superior commissure.
A vermilion advancement flap
is created to cover the donor
defect of the lower lip
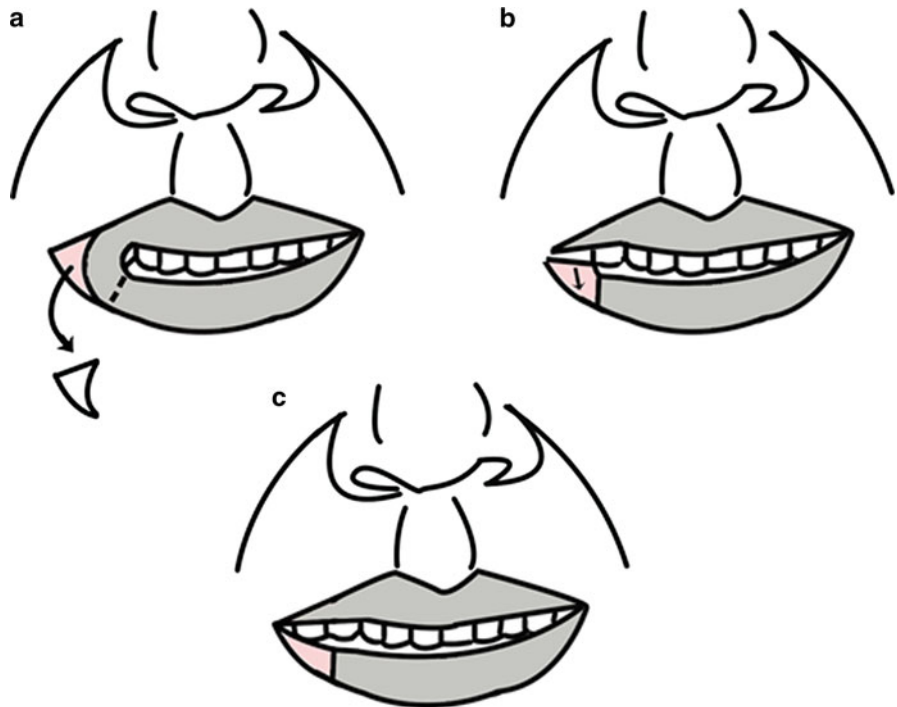
commissure. A myomucosal flap is created from the donor lip and is left pedicled on the opposite lip. The length of the donor flap is equal to the distance of the height of the triangle. A transverse incision is then created through the muscle lateral to the flap to the apex of the triangle and the distal end of the donor flap

is then sutured to the new commissure. A mucosal flap is then developed and advanced over the free border of the defect left at the donor lip, recreating the vermilion of the lip.

Conclusion

Commissuroplasty refers to a procedure that is performed to correct a deformity at the corner of the mouth or oral commissure. These procedures may be indicated for patients with microstomia resulting from trauma or the reconstruction of lip malignancies or from congenital causes. Other indications for commissuroplasty include patients who are born with a transverse facial cleft, or macrostomia. Whatever the cause, the goal of commissuroplasty is to restore or maintain function of the orbicularis oris sphincter at the oral commissure while creating lip symmetry.

Cross-References

► Estlander Flap
► Lip Reconstruction

References

Anderson R, Kurtay M (1971) Reconstruction of the corner of the mouth. Plast Reconstr Surg 47(5):463–464
Franco D, Franco T et al (2007) Commissuroplasty for macrostomia. J Craniofac Surg 18(3):691–694
Kazanjian VH, Roopenian A (1954) The treatment of lip deformities resulting from electric burns. Am J Surg 83:884
Kyomen R, Gulses A et al (2009) Treatment of microstomia with commissuroplasties and semidynamic acrylic splints. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 107:503–507
Taub PJ, Vecchione L, Losee JE (2009) Transverse facial clefts of macrostomia. In: Losee JE, Kirschner RE (eds) Comprehensive cleft care. McGraw Hill, Singapore, China
Torkut A, Coskunfirat O (1997) Double reversing Z-plasty for correction of transverse facial cleft. Plast Reconstr Surg 99:885–887

Communication Deficit

► Language Development and Disorders, Birth to 7 Years

Complications

► Sinus Surgery, Complications

Composite Face-Lift/Rhytidectomy

► Deep Plane Face-lift

Composite Flaps

► Classification of Flaps

Compound Muscle Action Potential (CMAP)

Amir Ahmadian, Angela E. Downes and A. Samy Youssef
Department of Neurosurgery, University of South Florida, Tampa, FL, USA

Definition

Compound muscle action potential is the synchronous activation of a group of motor neurons within a nerve bundle by brief electrical stimulation, producing a composite activity in the target muscles.

Cross-References

► Cranial Nerve Monitoring – *VIII, IX, X, XI*

Compound Z-Plasty

► Z-plasty

Computed or Computerized Tomography (CT)

Sébastien Schmerber[1,2,3], Arnaud Attye[1,2,4], Ihab Atallah[5], Cédric Mendoza[1,2,4] and Alexandre Karkas[1,2,6]

[1]Department of Otolaryngology-Head and Neck Surgery, Otology/Neurotology Unit, University Hospital of Grenoble, Grenoble, France
[2]Service ORL. Hôpital A. Michallon, Grenoble, France
[3]Otology, Neurotology and Auditory Implants Department, University Hospital of Grenoble CHU A. Michallon, Grenoble, France
[4]Department of Neuroradiology, University Hospital of Grenoble, Grenoble, France
[5]Department of Otolaryngology-Head and Neck Surgery, University Hospital of Grenoble, Grenoble, France
[6]Clinique Universitaire Oto–Rhino–Laryngologie, Centre Hospitalier Universitaire A. Michallon, Grenoble, France

Definition

An imaging method in which a cross-sectional image of the structures in a body plane is reconstructed by a computer program from the X-ray absorption of beams projected through the body in the image plane.

Computer Assistance in Sinus Surgery

Babak Sadoughi[1], Alla Solyar[3] and Marvin P. Fried[2]
[1]Laryngology/Neurolaryngology, New York Center for Voice and Swallowing Disorders, Head & Neck Surgical Group, St. Luke's-Roosevelt Hospital Center, Bronx, NY, USA
[2]Department of Otorhinolaryngology-Head and Neck Surgery, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA
[3]Coastal Ear, Nose and Throat, Neptune, NJ, USA

Synonyms

Frameless stereotactic surgery; Image-guided surgery; Surgical navigation

Introduction

Image-guided surgery (IGS) is a real-time correlation of the operative field to preoperative imaging, showing the precise location of a selected surgical instrument within the surrounding structures. The application of image guidance in endoscopic sinus surgery has revolutionized the field of rhinology by providing the surgeon with optimal anatomic localization, improving patient safety, minimizing invasiveness of difficult chronic sinus and extirpative procedures, and is at the forefront in the transition to minimally invasive sinus surgery for the management of chronic sinusitis, skull base lesions, repair of CSF leaks, and orbital surgery. Although instrumental in the evolution of the field of rhinology, IGS does not replace proper training and knowledge of anatomy. This entry reviews the history, technical considerations of IGS, clinical and educational applications of image guidance technology, as well as future directions and the development of new technologies.

History and Development
Modern image guidance systems for endoscopic sinus surgery provide the surgeon with precise localization and maintenance of target accuracy throughout the procedure. This technology has progressed significantly since its earliest description by Horsley and Clarke in 1908, who described the use of triplanar navigation to localize structures in the interior of the brain in animals just over a century ago. Their instrument consisted of a rigid quadrilateral rectangular frame fixed to the skull consisting of plates permitting sliding movement regulated by screws (Fig. 1). An excerpt from their work describes their design and purpose:

> To meet our immediate necessities, and at the same time to provide a plan of general application to the whole encephalon, a method of rectilinear topography and a stereotaxic instrument for applying it to direct an insulated needle to any desired point in the brain for excitation or electrolysis were devised by one of us (R.H.C.), and we have employed them for the last three years for the study of the structure and functions of the cerebrum and cerebellum in various animals.
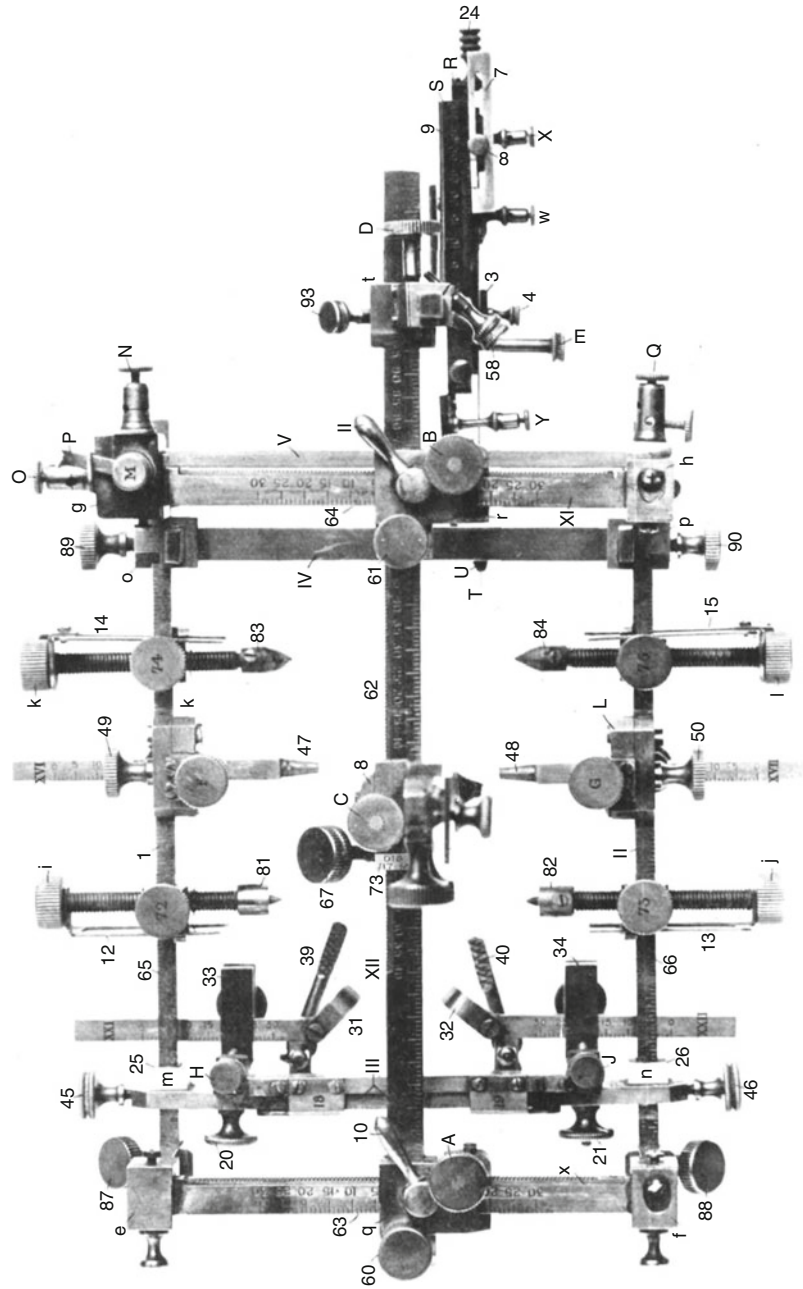
They also developed the following principles to guide their work:

1. Any irregular solid may be divided by three section planes in three dimensions into eight segments, in

Computer Assistance in Sinus Surgery,
Fig. 1 "Clarke's stereotactic apparatus for directing an insulated needle by graduated movement in three planes"

each of which the three internal surfaces are those of a cube.

2. In any solid body a constant point which can be measured from plane surfaces, representing the three dimensions of a cube, can be identified by three perpendiculars of correct length dependent from those surfaces, and it is the only point where those perpendiculars can meet.

3. A needle may be substituted for any of these perpendiculars, and in order that it may be directed mechanically to any required point in any of these rectilinear segments, an instrument is necessary which will introduce it in a direction perpendicular to one surface, and therefore, parallel to the other two, to any required distance from the first surface, any required distance from the others, i.e., the

needle must have a regulated movement in three dimensions.

This technology continued to evolve in the field of neurosurgery and in 1947, Spiegel et al. (1947) also used a fixed frame apparatus with the utilization of plain radiographs to determine the coordinates of lesion and identify the site of trepanation in human patients, resulting in a significant step toward minimally invasive surgery. This apparatus was used in psychosurgery to introduce lesions in the region of the medial nucleus of the thalamus, a procedure much less drastic than the traditional frontal lobotomy.

Introduction of computerized tomography (CT) technology allowed progression of stereotaxic navigation. In 1976, Bergstrom and Greitz (1976) devised a helmet-like plastic fixation device that used a metal ring to ensure stabilization throughout image acquisition procedure. Their use of CT scanning allowed for adequate anatomic detail; however, their apparatus did not provide for real-time instrument localization. While the work of Bergstrom and Greitz was limited to static orthogonal CT planes, Brown developed a system with a three-dimensional computer graphics display allowing for dynamic representations of key structures from many scans simultaneously. In 1980, Perry et al. (1980) described the development of a nearly artifact-free stereotactic frame, which spatially integrated with CT imaging. The surgical procedure was performed within the CT scanner itself allowing for repeat scans to be obtained during surgery to confirm the position of the probe tip. In 1986, Roberts et al. 1986 set out to overcome limitations of framed stereotactic computer systems, which included rigid frame impedance in the approach of the operative site and inability to ascertain the actual position of the instrument tip. They achieved this by reformatting and projecting CT data into the focal plane of the operating microscope by using a set of fiducial markers visible on the CT image and through the optics of the microscope. The position of the operating microscope was determined by means of an acoustic three-dimensional referencing system. Although elimination of stereotaxic frame showed to be less cumbersome, the new technology still had room for improvement with regards to accuracy of its localization algorithms.

Subsequent systems introduced new improvements such as an articulated arm and reformatting of CT images into 3D virtual images allowing better accuracy in determining probe tip position as well as allowing for precise preoperative planning. These developments prompted the widespread application of image guidance to neurosurgery in the late 1980s and early 1990s.

Some of the first applications of image guidance in otolaryngology came from the work of Schlondorff et al. and others at the University of Aachen, Germany in the mid-1980s. The term computer-aided surgery (CAS) describes a method that allows intraoperative navigation in the surgical field on the basis of digital image data and was originally chosen for the systems developed in Aachen, Germany. In 1986, the resulting CAS system was used in otorhinolaryngologic surgery for the first time. In 1991, the Aachen group further described their experiences with CAS in a report on 200 surgical procedures. Their indications included nasal, paranasal sinus and orbital tumors, skull base procedures, primary and revision paranasal sinus surgery, and acoustic neuromas. Risks of CAS were evaluated and included extra radiation from additional CT scanning, expense of equipment, and additional manpower. Benefits included dramatic increase in surgical information, leading to a more efficient surgery with a reduction in operative complications.

The first publication of computer-assisted endoscopic sinus surgery in the United States was reported in 1994 by Anon et al. The authors used a technology called the Viewing Wand System (ISG Technologies Inc., Mississauga, Ontario, Canada), which allowed correlation of the real-time surgical field and a previously obtained CT image with an accuracy of 1–2 mm (Anon et al. 1994). Subsequent advancement in the field of IGS was rapid with development of different types of localizers that will be reviewed later in this entry.

As experience has been gained and as the cost of technology has made it more widely accessible, IGS has become an integral part of surgery for many otolaryngologists performing endoscopic sinus surgery (ESS) in the United States. Today's image guidance systems are sophisticated machines that are able to provide data from CT and magnetic resonance (MR) devices. Image acquisition and transfer is straightforward and rapid, while the image resolution is excellent.

Current Technology

There are two basic systems that have been used for IGS: the optical (infrared) and the electromagnetic (radiofrequency) communication. The first electromagnetic-based tracking system introduced for sinus surgery was the InstaTrak system (Visualization Technology, Inc., Woburn, MA) and its application was first described by Fried et al. (1997). This and subsequent electromagnetic-based tracking systems use a radiofrequency transmitter and an electromagnetic receiver incorporated in a handpiece. The receiver may be attached to a variety of instruments including straight and curved suctions, as well as powered instruments. One of the drawbacks of the radiofrequency system is the chance for operational signal disruption with metallic objects in the field, including the metal operating table, instrument tables, anesthesia equipment, and other sizeable metallic devices. Proper positioning after anesthesia induction will alleviate these issues.

The optical systems utilize an infrared tracking system to monitor instrument and head position. Registration, calibration, and intraoperative navigation require direct line of sight communication between the receiver and the light-emitting diodes of the navigational systems (Anand and Schwartz 2007). As with electromagnetic systems, various instruments including powered tools may be used for navigation. Metson et al. described physician experience with the optical image guidance system using the LandmarX (Xomed, Inc., Jacksonville, FL). This study found that the use of image guidance has increased operative time by 15 to 30 minutes initially; however, this number decreased once experience with the equipment was acquired. Furthermore the researchers found that this image guidance tool provided sufficient accuracy and resulted in high level of physician satisfaction. Prospective comparison of the optical and electromagnetic systems by Metson et al. demonstrated similar accuracy in anatomic localization with no intraoperative complications and no significant difference in the blood loss. The duration of surgery was significantly higher in the electromagnetic group with the difference possibly being attributed to a longer learning curve with a system that was introduced first.

Despite variations between the image guidance systems, the basic set up is similar and includes a computer work station, monitor, keyboard, mouse, and a tracking device. Both radiographic and sometimes the endoscopic images are displayed on a computer monitor while integration of information between the surgical instruments and the computer is provided via a tracking device.

IGS begins with the acquisition of imaging data, with a standard 2-mm-thickness axial slice CT and reconstruction in the coronal and sagittal plane providing sufficient accuracy. MRI images may be obtained and incorporated as well. Some electromagnetic systems require the use of a specially designed headset during image acquisition. Different systems may have varying scanning protocols, with some requiring image acquisition in soft tissue windows and others in bone windows. Image data is then transferred onto the workstation, where the triplanar radiographic data is integrated to allow for intraoperative tracking. Prior to the procedure the data may be assessed to check for image quality and accuracy.

Registration provides a correlation between the position of the instrument in the surgical field with the corresponding computerized images. Registration methods vary between different technologies on the market and include external anatomical fiducials placed during the scan and anchored in place until surgery, immobile headsets with automatic registration, and fixed anatomic landmarks that are accessible externally and visible radiographically (Anand and Schwartz 2007). Upon completion of the registration, accuracy is confirmed by applying the instrument tip to known anatomic landmarks on the patient's face. Target registration error is the most clinically relevant descriptor of the accuracy of image guidance. It is defined as the difference between the anatomic location of a point and its position on the triplanar radiographic display with the accepted value in the 1.5–2 mm range.

Both CT and MR are important imaging modalities for the thorough assessment of skull base lesions, with CT imaging depicting accurate bony detail and MR best demonstrating soft tissue anatomy. The two systems complement one another and the development of fusion technology of these imaging modalities has found applications not only in neurosurgery, but also as an important tool for minimally invasive endoscopic sinus surgery in skull base procedures (Fig. 2).

Computer Assistance in Sinus Surgery, Fig. 2 Contemporary image guidance system

Applications

From Classic Sinonasal Indications to Advanced Cranial Base Surgery

Image-guided surgery was initially developed as a tool to help reduce the morbidity and mortality of ESS. As the use of navigation technology moved from selected use by tertiary referral centers for revision or unusual sinus cases and incorporated into clinical practice by surgeons outside these specialized practices, it quickly became an integral part of surgery for many otolaryngologists performing ESS in the United States. Furthermore the use of image guidance technology allowed surgeons to expand the use of endoscopic techniques in the sinonasal and skull base regions (Smith et al. 2007). In 2002, the American Academy of Otolaryngology – Head and Neck Surgery developed recommendations for the use of image-guided surgery:

1. Revision sinus surgery
2. Distorted sinus anatomy of development, postoperative, or traumatic origin
3. Extensive sinonasal polyposis

4. Pathology involving the frontal, posterior ethmoid, and sphenoid sinuses
5. Disease abutting the skull base, orbit, optic nerve, or carotid artery
6. CSF rhinorrhea or conditions where there is a skull base defect
7. Benign and malignant sinonasal neoplasms (AAOHNS 2002)

The advent of image-guided surgery along with the refinement of minimally invasive endoscopic techniques has greatly advanced the management of complex sinonasal and orbital pathology that previously required neurosurgical or craniofacial approaches. Endoscopic approaches have been successfully applied for the management of benign tumors such as inverted papilloma, juvenile nasopharyngeal angiofibroma, and pituitary adenomas. As the boundaries are pushed with respect to what is deemed acceptable in endoscopic treatment of sinonasal and intracranial lesions, IGS becomes more of a necessity for advanced applications such as the transsphenoidal approach. This route allows midline access and visibility to the suprasellar, retrosellar and parasellar space while eliminating the large risk of brain retraction, and makes possible to treat transsphenoidally a variety of midline cranial base and parasellar lesions traditionally approached transcranially. In the hands of experienced otolaryngologists and neurosurgeons, lesions involving the cavernous sinus and posterior fossa are accessible via the transphenoidal approach.

Neoplasms of the anterior skull base have also been successfully extirpated using endoscopic approaches. Concerns with this type of approach in regard to violation of the concept of en bloc resection and technical ability to obtain negative margins have been raised in literature. However, over the last several years multiple studies validated technical feasibility of minimally invasive endoscopic approaches and showed oncologic outcomes comparable to traditional craniofacial resection. Patients who underwent endoscopic resection had fewer complications and a better quality of life than patients who were managed with craniofacial resection. Endoscopic-assisted craniofacial resection may be utilized for large tumors with marked intracranial, dermal, or orbital extension necessitating gross intracranial tumor resection, skin excision, or orbital exenteration. IGS has proven to be of great value in the surgical approach to the orbit. White et al. described a transnasal approach with IGS for the drainage of

Computer Assistance in Sinus Surgery, Fig. 3 Optic nerve decompression in a patient with sinonasal malignancy. Optic nerve is the white structure above the suction
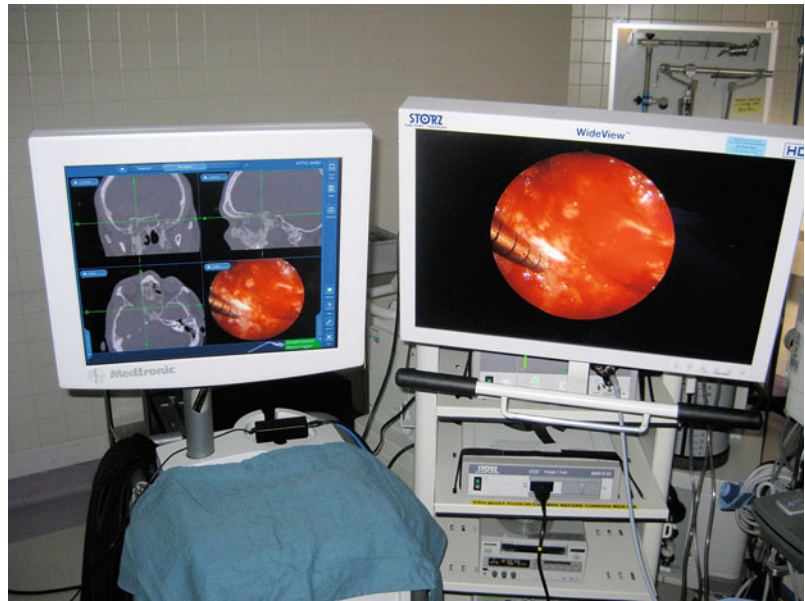
periorbital abscesses. Murchison et al. have recently described the transnasal removal of lesions within the orbital apex, which customarily require orbitotomy and craniotomy techniques. Batra and Lanza described an endoscopic power-assisted orbital exenteration for management of the orbit in patients with sinonasal malignancy or invasive fungal sinusitis. Endoscopic approach advantages included direct transnasal control of the ophthalmic artery as it emerged from the optic foramen and ability to preserve the uninvolved superior and lateral periorbita. The endoscopic approach has also been effective for the management of orbital pathology secondary to dysthyroid orbitopathy or optic neuropathy (Fig. 3). Management of encephaloceles and cerebrospinal fluid leaks has also seen an evolution over the last 20 years with minimally invasive endoscopic approach characterized by improved success rates and decreased morbidity being recommended as the technique of choice. Computer-assisted localization is useful in the management of chronic sinusitis aiding in the drillout approach to the frontal sinus in the setting of pathologies such as chronic frontal sinusitis or frontal sinus mucocele (Fig. 4).

The availability of image guidance technology allowed for the evolution of endoscopic nasal techniques from simpler procedures to ones involving more complex intranasal pathology. Image guidance aids in multiple aspects of the above procedures by including preoperative planning, resection, and reconstruction. In extirpative procedures, three-dimensional reconstruction of tumor and its relation to vital structures is possible. Furthermore approach to the skull base with dissection of surrounding paranasal structures and identification of landmarks facilitated by navigation systems allows for improved surgical confidence and avoidance of complications. Image guidance utilization is also useful in situations in which the nasal anatomy is altered by prior surgery, sinonasal disease, or unfavorable variations.

Pediatric Endoscopic Sinus Surgery

IGS is a valuable resource to help guide the pediatric surgeon dealing with sinonasal disease, as the embryological development of the sinuses leads to distinctive challenges for the otolaryngologist when dealing with pediatric sinonasal disease processes. With sinus development and maturation not completed until late into the second decade, the surgeon must be aware of the unique anatomy of the child.

Due to the relative scarcity of sinonasal surgery in the pediatric population compared to the adult population, there have been no specific studies looking at the safety or efficacy of IGS systems within the pediatric population (Lusk 2005); however, several authors reported on the use of IGS within the pediatric population, both for common sinonasal processes and for specific disease processes unique to the pediatric population. Postec et al. reviewed their experience with

Computer Assistance in Sinus Surgery, Fig. 4 Draf III approach to left lateral frontal sinus mucocele in a patient with a history of frontal sinus obliteration in the past

IGS in over 30 patients, and discussed its value in assisting with revision cases, polyp removal in children with cystic fibrosis, patients with re-stenosis of choanal atresia, patients with juvenile nasopharyngeal angiofibroma, and patients requiring tumor biopsy. Parikh et al. (2009) reviewed the largest series of pediatric patients to date, with 33 patients on whom image-guided sinus surgery was used. Image guidance was only used for advanced sinonasal procedures where there was an anatomic abnormality or disease that extended to the sphenoid sinus, frontal sinus, orbit, or skull base. The most common indications were chronic and acute rhinosinusitis, followed by juvenile nasopharyngeal angiofibroma and allergic fungal sinusitis, and they had no reported complications with IGS. There have been several other reports describing use of image guidance within the pediatric population for cases involving difficult anatomic locations such as the cranial base and petrous apex, or complicated disease processes including cholesterol granuloma, juvenile nasopharyngeal angiofibroma, and periorbital abscess.

Teaching

IGS has not only great clinical value intraoperatively, but it also is now a major aspect of the educational arsenal within teaching institutions, where the ability for the attending surgeon to monitor their resident's performance while pointing out specific anatomic features using the guidance system has greatly advanced the ability to teach sinus surgery in a safe and controlled environment. This was well illustrated by Casiano and Numa, who observed improved learning curves and safer technique implementation with novice otolaryngology residents practicing on cadavers with the aid of IGS.

Limitations

Surgeon Skills and Knowledge of Anatomy

Despite the recommendations, certain questions regarding the utility of IGS remained unanswered and in 2007, Smith et al. (2007) set out to investigate whether IGS reduced complication rates and improved clinical outcomes. They identified mostly level 4 (case series) and 5 (expert opinion) studies that focused mainly on complication rates and revision surgery rates with no studies examining patient-based outcomes such as quality of life. They concluded that because major complication rates of endoscopic sinus surgery are low, thousands of patients would need to be enrolled to detect a statistically significant difference in that parameter. Furthermore, they found insufficient evidence regarding improvement of clinical outcomes with IGS and acknowledged that performance of such a study may be unethical as it would entail randomization of patients away from technology that may benefit the patient.

Accuracy

During the perioperative equipment setup process, the registration step generates a correlation between the position of the instrument in the surgical field and the corresponding location on the imaging data set. The location is materialized by on-screen annotations, for instance, a set of crosshairs that move through the CT slices in concordance with the movement of the instrument. Once registration is complete and the instruments are calibrated by the system, accuracy is verified by testing various known landmarks on the patient's face and in the nasal passages. The coordinates are stored and used throughout the procedure to monitor any changes in the accuracy of the device. Normal navigation accuracy for modern systems is commonly between 1.5 and 2 mm. Anon et al. (1994) reported an accuracy of 1–2 mm in their seminal article. After the initial introduction of IGS for ESS in the United States, advancement within the field was rapid. Fried et al. (1997) introduced a system that allowed for an automated registration technique that eliminated the redundant computed tomography scan, compensated for head movement, and added the possibility of using interchangeable instruments. Moreover, thinner-cut CT scans and improved localization lead to greater accuracy, and advances in technology allowed for products that were less cumbersome and obstructive, permitting easier access to the surgical field with better visualization and precision.

Operative Time, Cost, and Complication Rate

Although the true measurement of any new technology within the medical domain is its ability to improve patient outcome, decrease complications, and increase postoperative satisfaction, a review of cost-effectiveness is also valuable before large-scale implementation. Several retrospective case series have reported lower rates of complication using image guidance systems (Fried et al. 2002; Kacker et al. 2005), though this reached statistical significance in only the study performed by Fried et al. (2002), who performed a retrospective study on 97 patients and found a significant decrease in complications in the IGS group.

A 2006 non-randomized prospective study by Javer and Genoway evaluated patient quality of life after sinus surgery over a 3-year enrollment period, comparing outcomes with and without IGS. The authors found significantly improved short-term quality of life when IGS was used. A study by Tabaee et al., where a retrospective chart review was performed and quality of life was assessed via a telephone survey, found no significant difference in major intraoperative and postoperative complications, revision procedures, and quality of life outcomes in patients who underwent image-guided versus non-image-guided endoscopic sinus surgery. A slightly increased risk of intraoperative CSF leak was suggested when IGS was not used; however, another review by Tabaee et al. did not find a significant improvement in the rates of successful closure of leaks with IGS. Though the studies showing actual risk reduction with IGS are lacking, expert opinion, published literature, and common sense support the current recommended indications for IGS (Smith et al. 2007).

Metson et al. prospectively compared an optical system and an electromagnetic system. Despite a significant decrease in operating time with the optical system, this difference was not readily explained. Furthermore, no significant difference was noted in other parameters (e.g., blood loss, complications). In addition, IGS was found to increase operative time by 15–30 min/surgery and cost on average $500 more per case, with the additional cost involving cases where disposable handpieces and headsets were utilized. IGS has also been associated with higher intraoperative bleeding and minor headset-related complications (Fried et al. 2002).

The decision regarding which IGS device to use is individual- and institution-dependent. Cost and surgeon preference are the major factors involved in deciding which system to use, and the systems on the market today are comparable with regard to efficacy, complication rate, and patient postoperative quality of life.

State of the Art and Future Horizons

Image guidance devices are subject to constant modernization, and as computerized devices, benefit from the rapid advances of informatics technology, generating less cumbersome devices with faster image processing capabilities and more user-friendly software interfaces. Those alterations are complemented by further instruments to enhance the surgical navigation experience.

Real-Time Image Guidance (Open-Magnet MR and Intraoperative CT)

Intraoperative image-guidance systems rely on a preoperative data set from either CT or MRI images,

which is a stagnant piece of information that is used by the surgeon to navigate the patient's anatomy throughout the procedure, although the anatomy is altered during the progress of the procedure. Naturally, the question has been raised of developing an intraoperative imaging system with fluid images and updated anatomical data being fed back to the surgeon throughout the procedure, thus allowing the surgeon to monitor progress in real time and identify any intraoperative risks that may arise from the changing anatomy. Work has been done to explore both MR-based and CT-based intraoperative systems.

MRI-Based Systems   Fried et al. (1998) were the first to explore this concept with an intraoperative MR-based system on a series of 12 patients undergoing uncomplicated procedures. The image plane was surgeon controlled, and the MRI updated images in as little as 14 s. The procedures were performed without any complications and provided optimum feedback to the surgeon during the performance. While the initial evaluation of the system was positive, extremely high costs and implementation constraints made routine use impossible. Another constraint to routine use of such a system was the need for system-specific instrumentation. This included metallic instruments and anesthesia devices that would function in a high magnetic environment. Suzuki et al. evaluated the effectiveness of MRI guidance using an optical tracking system. Fourteen patients, 11 of whom presented with mucoceles, were operated on using the real-time MR-based system. The prognosis was favorable, with no patients showing signs of recurrence of disease; however, they reported an additional 54 min of setup time for patients requiring general anesthesia and 17 min of additional setup time for patients requiring local anesthesia. Anand et al. used real-time MRI in endoscopic pituitary resection, finding that the image quality was sufficient to identify residual tumor in 3 of 10 cases while encountering no complications.

CT-Based Systems   CT-based intraoperative systems are easier to implement practically than MR-based systems and are more appealing to the otolaryngologist because they enable superior visualization of bony structures. However, unlike MR-based systems, CT-based systems come with the inherent increase in radiation exposure to the patient, which must be taken into account during development.

Rafferty et al. developed a cone-beam CT imaging system, and evaluated it on cadaver heads. The system generated intraoperative, volumetric CT images rapidly with an acceptably low radiation exposure to the patient and with image quality sufficient for most surgical tasks. They found that the system increased surgical confidence in accessing the frontal recess, resolved ambiguities with anatomical variations, and provided valuable teaching information to surgeons in training in both preoperative planning and correlation between triplanar CT scans and intraoperative endoscopic findings. Brown et al. (2007) demonstrated the feasibility of real-time image-guided surgery using fluoroscopic images, and Manarey et al. verified the safety of the same product by performing radiation dosimetry studies. However, the images produced by this product were deemed inadequate for routine use.

A study by Wise et al. looking at the use of CT-based intraoperative guidance systems have shown that inexperienced surgeons were far more comfortable identifying anatomic structures with IGS with intraoperative CT than they were with IGS with preoperative CT or endoscopy alone. Jackman et al. found that intraoperative acquisition of CT images led to an alteration of the surgical plan in 30% of cases. While these systems are not currently routinely used due to high costs and unperfected technology, these studies show that the idea of intraoperative real-time image guidance is an exciting perspective of the future in sinus surgery.

Robotic Surgery

Robot-assisted surgery is a rapidly growing sector in multiple fields of surgery, and entered the realm of otolaryngology through applications for transoral surgery of select upper aerodigestive tract malignancies. Sporadic efforts were also undertaken toward otologic surgery applications.

Endoscopic surgery of the paranasal sinuses and skull base seems to be the next focus of development for robotic surgery. The most remarkable reports originate from a number of state-funded German research collaborations, which have demonstrated the feasibility on cadaveric specimens of robotic manipulation of the endoscope with automated instrument tracking, alleviating the need for single-handed dissection (http://www.rob.cs.tu-bs.de/en/research/projects/endoscope), with the potential to develop fully automated transnasal approaches to the cranial base tailored

by image-guided robotic systems. These efforts are evidently at an early experimental stage but set the stage for potentially ground-breaking innovations to come.

Surgical Simulation and Preoperative Planning

Virtual reality simulation is the most promising means of safely training surgical trainees in a reproducible ex vivo environment, suppressing concerns of patient harm and liability. The integration of patient-specific imaging into simulation devices provides the trainee with an unprecedented medium for skill development. Conversely, future developments in surgical simulation will also contribute to broaden the applications of image-guided surgery for seasoned surgeons. Patient-specific preprocedural rehearsal systems would allow surgeons to add critical annotations and observations to the imaging data set preoperatively. These annotations would then be made available intraoperatively on the IGS system and allow the clinician to avert hazardous anatomic regions and anticipate the more arduous steps of a procedure. In addition to these surgical planning considerations, further applications could include simulated skills assessment for trainee selection or certification and credentialing of trained specialists.

Conclusion

Image guidance has become an extremely valuable resource for otolaryngologists and neurosurgeons. It allows surgeons to gain comfort with the surgical anatomy and extent of the disease processes that they are dealing with, and to explore further anatomic locations and be more aggressive in the treatment of complex pathology.

With the continued development of the technology involved in IGS, the boundaries of what can be explored continue to be pushed farther. As intraoperative real-time imaging becomes more practical, the confines of endoscopic interventions feasible by experienced sinonasal and skull base surgeons will continue to expand.

As we continue to see further advancement with the technology, it is imperative to retain the message echoed unanimously by those who have studied IGS, that the assistance provided by IGS will never replace knowledge of anatomy and proper surgical technique. While IGS should certainly continue to be used as part of the sinus surgeon's arsenal, it should only be used by proficient endonasal surgeons as an adjunct to surgical knowledge.

References

AAOHNS (2002) Policy on intraoperative use of computer-aided surgery. AAO-HNS Official Website, Policy Statements http://www.entnet.org/Practice/policyIntraOperativeSurgery.cfm. Accessed 19 Dec 2011

Anand VK, Schwartz TH (2007) Practical endoscopic skull base surgery. San Diego, Plural Pub

Anon JB, Lipman SP, Oppenheim D, Halt RA (1994) Computer-assisted endoscopic sinus surgery. Laryngoscope 104(7):901–905

Bergstrom M, Greitz T (1976) Stereotaxic computed tomography. AJR Am J Roentgenol 127(1):167–170

Brown SM, Sadoughi B, Cuellar H, von Jako R, Fried MP (2007) Feasibility of near real-time image-guided sinus surgery using intraoperative fluoroscopic computed axial tomography. Otolaryngol Head Neck Surg 136(2):268–273

Fried MP, Kleefield J, Gopal H, Reardon E, Ho BT, Kuhn FA (1997) Image-guided endoscopic surgery: results of accuracy and performance in a multicenter clinical study using an electromagnetic tracking system. Laryngoscope 107(5):594–601

Fried MP, Topulos G, Hsu L, Jalahej H, Gopal H, Lauretano A, Morrison PR, Jolesz FA (1998) Endoscopic sinus surgery with magnetic resonance imaging guidance: initial patient experience. Otolaryngol Head Neck Surg 119(4):374–380

Fried MP, Moharir VM, Shin J, Taylor-Becker M, Morrison P (2002) Comparison of endoscopic sinus surgery with and without image guidance. Am J Rhinol 16(4):193–197

Horsley V, Clarke RH (1908) The structure and functions of the cerebellum examined by a new method. Brain 31(1):45–124

Kacker A, Tabaee A, Anand V (2005) Computer-assisted surgical navigation in revision endoscopic sinus surgery. Otolaryngol Clin North Am 38(3):473–482, vi

Lusk R (2005) Computer-assisted functional endoscopic sinus surgery in children. Otolaryngol Clin North Am 38(3):505–513, vii

Parikh SR, Cuellar H, Sadoughi B, Aroniadis O, Fried MP (2009) Indications for image-guidance in pediatric sinonasal surgery. Int J Pediatr Otorhinolaryngol 73(3):351–356

Perry JH, Rosenbaum AE, Lunsford LD, Swink CA, Zorub DS (1980) Computed tomography/guided stereotactic surgery: conception and development of a new stereotactic methodology. Neurosurgery 7(4):376–381

Roberts DW, Strohbehn JW, Hatch JF, Murray W, Kettenberger H (1986) A frameless stereotaxic integration of computerized tomographic imaging and the operating microscope. J Neurosurg 65(4):545–549

Smith TL, Stewart MG, Orlandi RR, Setzen M, Lanza DC (2007) Indications for image-guided sinus surgery: the current evidence. Am J Rhinol 21(1):80–83

Spiegel EA, Wycis HT, Marks M, Lee AJ (1947) Stereotaxic apparatus for aperations on the human brain. Science 106(2754):349–350

Conchomeatoplasty and Canalplasty, Surgical Approaches

L. Frederick Lassen
Department of Otolaryngology, Lakeview Medical Center, Suffolk, VA, USA

Introduction

Surgically changing the shape of the bony ear canal is known as *canalplasty*, while altering the shape of the soft tissue and cartilage of the ear canal is called *conchomeatoplasty*. Depending on the anatomic problem, a canalplasty may be performed with or without a conchomeatoplasty.

Canalplasty is usually done to correct a tight bony ear canal narrowed due to exostoses/osteomas, ear canal cholesteatoma, traumatic or congenital narrowing, or, rarely, to help fit a hearing aid. Conchomeatoplasty is used to correct a tight ear meatus that can result in recurrent or chronic external ear canal infection due to accumulation of debris and moisture. This environment is, unfortunately, an ideal culture medium for bacteria and fungi resulting in external otitis.

Prevention

Over-the-counter preparations that dry the ear canal can help prevent external otitis. These are sold as brand names of Auro-Dri and Swim-Ear and consist of 95% isopropyl alcohol, with anhydrous glycerine.

In the early 1970s, the US Navy saturation divers found that chronic otitis externa could be prevented by using acetic acid/aluminum acetate solution (Otic Domeboro®). This is 2% acetic acid, water, aluminum acetate, sodium acetate, and boric acid (Edward Thalmann). It was felt that the "acid retards bacterial growth, while the aluminum and sodium acetate act as astringents, drawing excess water out of the cells lining the ear canal. (Edward Thalmann)" Divers put this solution in each ear canal twice a day for at least 5 min at a time. Such a regimen is also useful for sport diving when there are frequent dives.

Medical Office Management

Should problems persist, medical management of external otitis often requires topical ear drop solutions and suspensions. The simplest topical ear drops acidify the ear canal environment to retard bacterial growth (Vosol, Acetic Acid with or without Hydrocortisone 1%). Other ear drops may contain antibiotics and/or antifungal preparations with and without anti-inflammatory steroids to help reduce inflammation and itching. Some clinicians may prescribe oral antipseudomonal antibiotics especially if there is facial cellulitis.

For years, Cortisporin, a combination of two antibiotics (neomycin and polymyxin B) and a corticosteroid (hydrocortisone) was the mainstay of treating otitis externa; however, severe contact dermatitis from neomycin sensitivity was often a problem. This complication was addressed by the development of fluroquinolone otic drops and fluroquinolone-steroid combinations (Ciprodex®) (Alcon Web Site). Recently, DermOtic® Oil Ear Drops (Hill Dermaceuticals Inc Web Site) contain fluocinolone acetonide, a synthetic corticosteroid in a peanut-based oil formulation that, in the author's experience, eliminates the puritic symptoms of ear canal eczema in most patients with as little as twice a week use.

A somewhat novel solution to the problem of damp external ear canals is the Mack's Ear Dryer invented by Hamilton P. Collins II, MD, a practicing Otologist in California. The Ear Dryer is a rechargeable device that blows warm air into the external ear canal, evaporating water and moisture.

Most of the time, ear canal and ear conchomeatal problems can be managed in the office with interventions using long-established otology principles of microscopic debridement and topical treatments with frequent follow-up. Merocel wicks can be customized from nasal tampons and provide both a vehicle for getting the topical agent deep into the ear canal and expanding the narrowed and inflamed canal. Placing as much of the topical antibiotic solution into the ear canal first and then introducing a customized Merocel wick over the topical antibiotic solution has the benefit of causing much less pain than introducing a dry Merocel into an inflamed ear canal.

Surgical Management

The most difficult cases of chronic otitis externa occur when the ear canal is narrow because of chronic inflammation (especially in humid environments), or because of exostoses (Surfer's ear) or ear canal osteomas. It may not be possible to adequately treat these patients without enlarging the ear canal and meatus.

Conchomeatoplasty enlarges the lateral meatus by excising the sharp rim of cartilage at the junction of the conchal bowl and the posterior ear canal wall and thinning the skin. Various conchomeatoplasty techniques have been described but all techniques involve skin flaps, debulking soft tissue, and excising conchal cartilage (Selesnick et al. 1998; Becker and Tos 1998; Eisenman and Parisier 1999; Sharp et al. 2003; Kumar and Smelt 2007). In a retrospective study from Scotland, 64% of the patients had meatal stenosis from chronic otitis externa, and 80% achieved a satisfactory patent ear canal after surgery (Jacobsen and Mills 2006). The technique of Darrell H. Hunsaker, M.D., described in 1988 (Hunsaker 1988) avoids a postauricular incision and heals rapidly with excellent, consistent results, and is the technique I have used to correct meatal stenosis for the past 20 years with excellent results. After local anesthesia with epinephrine, a semilunar incision is made in the cavum conchum, and a medially based skin flap developed. Soft tissue and cartilage deep to the dermis is excised; this can be done with a needle-tip electrocautery. Bony canal stenosis or a large Spine of Henle can be corrected using a diamond ear drill. The skin flap is re-approximated; excess skin is trimmed and used as a free graft in the superior portion of the cavum conchum. A mastoid dressing is applied to hold the flap in place for 24 h.

References

Alcon Web site. http://www.alcon.com/en/alcon-products/ear-infection.aspx

Becker BC, Tos M (1998) Postinflammatory acquired atresia of the external auditory canal: treatment and results of surgery over 27 years. Laryngoscope 108(6):903–907

Eisenman DJ, Parisier SC (1999) Meatoplasty: the cartilage of the floor of the ear canal. Laryngoscope 109(5):840–842

Hill Dermaceuticals Inc, Web site. http://www.hillderm.com/prescribing-information/dermotic-oil.shtml

Hunsaker DH (1988) Conchomeatoplasty for chronic otitis externa. Arch Otolaryngol Head Neck Surg 114(4):395–398

Jacobsen N, Mills RJ (2006) Management of stenosis and acquired atresia of the external auditory meatus. Laryngol Otol 120(4):266–271

Kumar PJ, Smelt GJ (2007) A long term follow up of conchal flap meatoplasty in chronic otitis externa. J Laryngol Otol 121(1):1–4, Epub 2006 Oct 24

Mack's Web site. http://www.macksearplugs.com/products/eardryer

Selesnick S, Nguyen TP, Eisenman DJ (1998) Surgical treatment of acquired external auditory canal atresia. Am J Otol 19(2):123–130

Sharp HR, Oakley RJ, Padgham ND (2003) The Canterbury technique for canalplasty via an endaural approach in the surgical management of chronic refractory otitis externa. J Laryngol Otol 117(3):195–197

Thalmann E, Can you prevent otitis externa, or swimmers ear? The answer is in the Solution Divers Alert Network Web site. http://www.diversalertnetwork.org/medical/articles/article.asp?articleid=48

Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge®

Rudolf Hagen and Robert Mlynski
Department of Otorhinolaryngology, Plastic, Aesthetic and Reconstructive Head and Neck Surgery, University of Wuerzburg, Wuerzburg, Germany

Synonyms

Hearing restoration in conductive and mixed hearing losses (CHL, MHL) by means of an active middle ear implant (Vibrant Soundbridge®)

Definition

Active middle ear implants are used for enhancing sound conduction to the inner ear, either by amplification of the movements of an intact ossicular chain or by direct stimulation of the perilymph space via the oval or round window. Using a small electromagnetical stimulator, a disturbed sound transmission (CHL) and a reduced inner ear function (MHL) can be compensated through the use of this implant.

Purpose

The Vibrant Soundbridge® active middle ear implant was originally designed for patients with a moderate to profound sensorineural hearing loss who mainly due to adverse reactions in the external auditory canal could not be provided with a hearing aid (Ball and Maxfield 1996). Following the first implantation of the Vibrant Soundbridge® in 1996 by *Ugo Fisch*, the device was used successfully in a large number of patients (Snik et al. 2001) who fulfilled the indication criteria. In 2005 *Vittorio Colletti* first described the use of the Vibrant Soundbridge® in patients with mixed hearing losses using new positioning of the *F*loating *M*ass *T*ransducer (FMT), the active part of the implant, to the round window membrane (Coletti et al. 2006). This was the beginning of a subsequent extension of indications for the implantation of the Vibrant Soundbridge® to patients with a conductive or mixed hearing loss. Nevertheless implantation was still confined to patients who could not be fitted satisfactorily with a conventional hearing aid.

Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge®, Fig. 1 Classical application of the Vibrant Soundbridge® with fixation of the Floating Mass Transducer at the long process of the incus (schematic drawing of posterior tympanotomy approach)

Principle

The basic principle of the Vibrant Soundbridge® is the amplification of the vibrations of the intact ossicular chain by means of the FMT, which is coupled to the long process of the incus by a titanium clip (Fig. 1). These enhanced vibrations result in the amplification of perilymphatic excitation according to the individual needs of the patient.

In conductive and mixed hearing losses, the procedure has to be modified. Depending on the pathology of the middle ear (otosclerosis, chronic otitis media, malformation), the "coupling" of the FMT to the perilymph space is carried out via an intact ossicular chain or remnants of the chain, directly to the oval or round window, or to an artificial promontory window, if necessary.

Indications

1. *Otosclerosis* with additional moderate to severe sensorineural hearing loss

If stapedectomy with insertion of a standard stapes prosthesis in combination with a hearing aid is not sufficient for satisfactory speech perception, the implantation of the Vibrant Soundbridge® can lead to better amplification of the sound signal. As there is already a stapes prosthesis in place, the FMT has to be placed, similar to the classical application, at the long process of the incus, but in parallel to the axis of the prosthesis (Fig. 2).

2. *Chronic otitis media* resulting in conductive or mixed hearing loss

The placement of the FMT depends, in consideration of Eustachian tube function, on the individual anatomical characteristics of the middle ear.

2.1. *Aerated middle ear* with stable conditions for reconstruction of the tympanic membrane

   2.1.a. *Stapes intact* (including the head of the stapes or at least the arch):
   The FMT is fixed directly to the stapes by bending the titanium clip and crimping the branches of the clip directly around the arch of the stapes. The body of the FMT may be stabilized by direct contact to the reconstructed tympanic membrane (reinforcement by a piece of cartilage is recommended). In this case, middle ear reconstruction complies with a
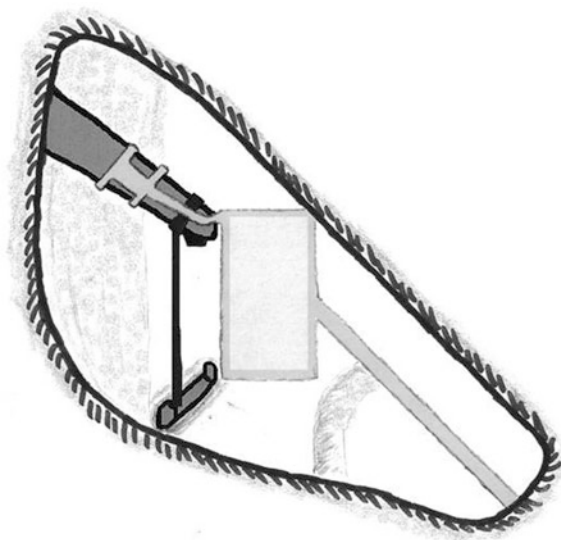
Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge®, Fig. 2 Application of the Vibrant Soundbridge® in otosclerosis with fixation of the Floating Mass Transducer at the long process of the incus in parallel to stapes prosthesis (schematic drawing of posterior tympanotomy approach)
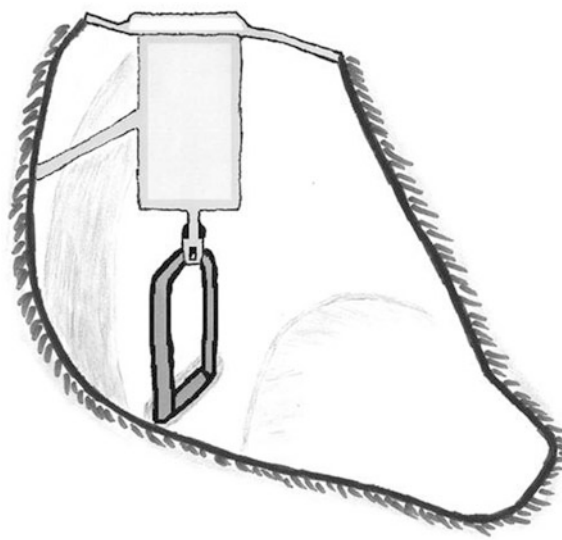
Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge®, Fig. 3 Application of the Vibrant Soundbridge® in chronic otitis media with fixation of the Floating Mass Transducer at the stapes, the titanium clip is bent, the body of the Floating Mass Transducer interposed between the stapes and the reconstructed ear drum (reinforced by a piece of cartilage) (schematic drawing of posterior tympanotomy approach)

tympanoplasty type IIIb (according to the *W*ullstein *Cl*assification, *WCL*), with the FMT connecting the stapes and the reconstructed ear drum (Fig. 3).

Alternative:

The FMT is used in combination with a special titanium prosthesis (*P*artial *O*ssicular *R*eplacement *P*rosthesis – PORP, "Bell"-Prosthesis, Kurz® Company, Dusslingen Germany) containing a small basket for the FMT or so-called Coupler (Bell-Coupler, CliP-Coupler, Kurz® Company, Dusslingen Germany, www.medel.com/int/show/index/id/361/title/Coupler-Vibroplasty) that allows fixation of the FMT in a titanium retainer and positioning between the head of the stapes and the ear drum (reinforcement by cartilage is recommended) (Fig. 4).

2.1.b. *Stapedial suprastructure missing, intact footplate*:

Depending on the anatomical findings and middle ear aeration, the FMT can be placed directly on the intact footplate using a bent titanium clip for fixation between the footplate and the reconstructed ear

drum (reinforcement by cartilage is recommended).

Alternative:

The FMT is used in combination with a special titanium prosthesis (*T*otal *O*ssicular *R*eplacement *P*rosthesis – TORP, "Aerial"-Prosthesis, Kurz® Company, Dusslingen Germany) containing a small basket for the FMT or so-called Coupler (Oval Window Coupler, Kurz® Company, Dusslingen Germany, www.medel.com/int/show/index/id/361/title/Coupler-Vibroplasty) which allows for fixation of the FMT in a titanium retainer and positioning between the footplate of the stapes and the ear drum (reinforcement by cartilage is recommended) (Fig. 5).

2.1.c. *Stapes missing, only fibrous tissue in oval window*:

The same procedure as described in 2.1.b may be chosen. In the case of direct placement of the FMT on a fibrous oval window coverage, a reinforcement of the oval window either by perichondrium, fascia, or a
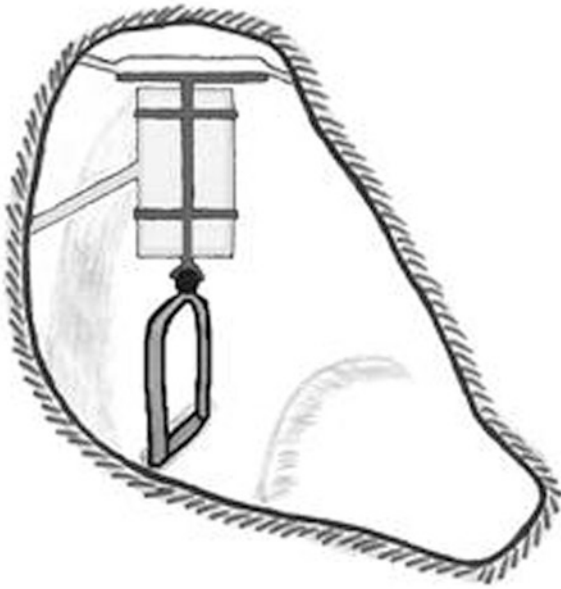
Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge®, Fig. 4 Application of the Vibrant Soundbridge® in chronic otitis media with placement of the Floating Mass Transducer by a titanium Partial Ossicular Replacement Prosthesis, the body of the Floating Mass Transducer interposed between the stapes and the reconstructed ear drum (reinforced by a piece of cartilage) (schematic drawing of posterior tympanotomy approach)
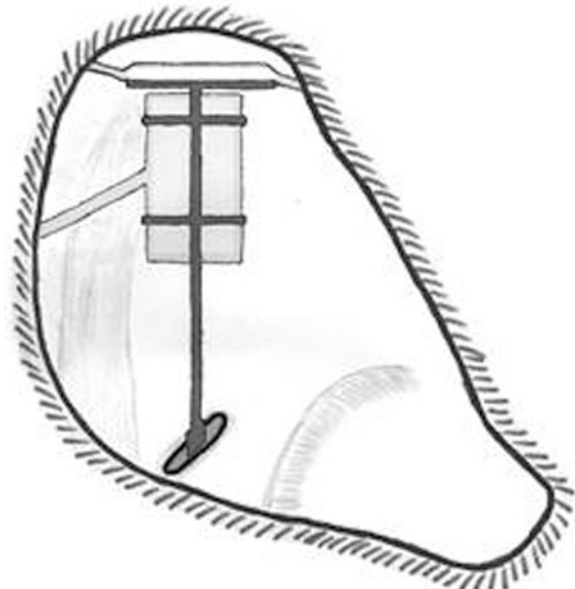
Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge®, Fig. 5 Application of the Vibrant Soundbridge® in chronic otitis media with placement of the Floating Mass Transducer by a titanium Total Ossicular Replacement Prosthesis, the body of the Floating Mass Transducer interposed between the footplate of the stapes and the reconstructed ear drum (reinforced by a piece of cartilage) (schematic drawing of posterior tympanotomy approach)

small piece of cartilage should be carried out. The use of a prosthesis or a coupler requires stable reconstruction of the footplate by cartilage. This approach should be used only in cases with sufficient aeration of the middle ear; otherwise, dislocation into the vestibulum could occur.

2.2. Chronic otitis media with missing aeration of the middle ear

    2.2.a. *Stapes intact* (including the head of the stapes or at least the arch):

        The fixation of the FMT to the stapes is carried out by bending the titanium clip and crimping the branches of the clip directly around the arch of the stapes. The placement of the body of the FMT depends on the method of reconstruction of the stable covering of the tympanic cavity. Bearing in mind, that there is no or poor aeration of the middle ear, the preferred technique may include a stable cartilage graft and the creation of a flat middle ear space, leaving little or no space for the FMT heading the stapes. In this situation, the round window approach (see below) may be a better alternative.

    2.2.b. *Stapedial suprastructures missing, intact footplate*:

        In cases with a normal footplate and with a good approach to the oval window, a direct placement of the FMT on the footplate is a reliable alternative. The titanium clip of the FMT can be removed or bent in such a way that it stabilizes the body of the FMT, in its position in the oval niche, by direct contact to the cartilage graft, covering the flattened tympanic cavity. If the footplate appears to be very thin, or if there is only fibrous tissue within the oval niche, a reinforcement by connective tissue, fascia, perichondrium, or cartilage might be necessary (Fig. 6).

Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge®, Fig. 6 Application of the Vibrant Soundbridge® in chronic otitis media with placement of the body of the Floating Mass Transducer in the oval window niche, directly to the footplate (schematic drawing of posterior tympanotomy approach)

2.2.c. *Oval window not suitable – round window approach*:

If the oval window cannot be used, the round window is an alternative for FMT placement. Due to the anatomy of the round window, a direct contact of the bottom plate of the FMT with the round window membrane is not possible in most cases. The safe exposition of the thin membrane is a delicate surgical measure. In particular, the removal of the bony lip bounding the round window must be performed carefully, in order to avoid any noise trauma to the inner ear (diamond burr, low engine speed, sufficient irrigation). The coupling between the membrane and the FMT should be improved through the positioning of a small piece of connective tissue, fascia, perichondrium, or – if necessary – a perichondrium-cartilage island (Fig. 7).
Alternative:
If the anatomical situation causes difficulty, coupling to the round window membrane can be facilitated through the use of a "round window coupler" (Round Window

Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge®, Fig. 7 Application of the Vibrant Soundbridge® in chronic otitis media with placement of the Floating Mass Transducer in the round window niche (RWN), parts of the bony lip of the RWN are removed, for better coupling the body of the Floating Mass Transducer is wrapped by perichondrium, fascia or something like that, fixation is performed either by bending the titanium clip in a proper way or by chips of cartilage (schematic drawing of posterior tympanotomy approach)

Coupler, Kurz® Company, Dusslingen Germany, www.medel.com/int/show/index/id/361/title/Coupler-Vibroplasty) which allows for fixation of the FMT in a titanium retainer and its positioning between the round window membrane and the hypotympanum.

2.2.d. *Oval and round window not possible: artificial promontory window*:

In rare cases of chronic otitis or cholesteatoma, the anatomical situation (following several surgeries) does not allow for coupling at the oval or round window (facial nerve hernia, tympanosclerotic plaques in both windows, etc.). The creation of an artificial window at the promontory may facilitate stimulation of the inner ear via the FMT. Drilling has to be carried out extremely carefully in order not to open the perilymph space. The stable placement of the FMT at this artificial window is also challenging. Depending on the size of this window, the

distances within the tympanic cavity, and the reconstruction of the tympanic covering, this could be achieved either by bending the titanium clip or through the insertion of small cartilage chips, wedging the FMT in a stable position. The use of a round window coupler (see above) might be another possibility to obtain a reliable connection to the perilymphatic space. As the creation of an artificial window has a high risk of postoperative deafness especially in chronically infected ears, this technique is reserved and used only under rare circumstances. Bone-anchored hearing aids (BAHA, Bonebridge®) probably offer a better solution under these conditions.

2.2.e. *Radical cavity*:

Vibrant Soundbridge® can also be used in a radical cavity. Fixation of the FMT is carried out as described above. Besides the stable fixation of the FMT, a reliable coverage of the rigid implant cable is necessary to avoid direct exposure of the lead within the cavity. For this purpose, reduction of the size of the cavity by means of cartilage or pedicled connective tissue flaps is performed.

2.2.f. *Subtotal petrosectomy*:

If chronic tympanic and mastoid disease cannot be eradicated by conventional tympanoplasty and mastoid cavity procedures, a subtotal petrosectomy with occlusion of the Eustachian tube and the outer ear canal and insertion of a free fat graft facilitate a long lasting sanation of the chronic focus of inflammation within the petrous bone. This makes meticulous drilling of all mucosa-bearing cells necessary. In these cases, implantation of the Vibrant Soundbridge® or the use of a bone conduction hearing implant (BAHA®, Bonebridge®) can be used for hearing restoration. The fixation of the FMT (oval or round window) depends on the individual anatomical characteristics and can be carried out as described above.

3. Ear malformation with CHL or MHL

Ear malformation is another indication for the use of the Vibrant Soundbridge®. The decision on the ideal hearing restoration technique depends, among other details, on the aeration of the middle ear cleft and the mastoid. Akin to classical reconstructive middle ear surgery for ear malformations, the *Jahrsdoerfer* grading system (Jahrsdoerfer et al. 1992) is helpful in preoperative assessment of reliable indications. Due to the diameters of FMT, the use of the Vibrant Soundbridge® especially requires a definite space for the placement either at the oval, the round, or an artificial window. In cases of doubt, the decision toward a bone-anchored hearing device (BAHA®, Bonebridge®) might be safer than the risk of a possible facial nerve injury or perioperative deafness due to surgical manipulations in a malformed middle ear.

4. Pediatric cases

In general there is no difference in indication and surgical techniques between children and adolescents. There is increasing experience in pediatric cases (Cremers et al. 2010), which demonstrates no general differences between these two groups. As accurate paedaudiological diagnostics are a prerequisite in establishing surgical indication for hearing restoration, Vibrant Soundbridge® implantation in CHL and MHL does not take place within the first 2–3 years of life. Furthermore, chronic otitis media is a disease that develops in higher ages and malformations are initially provided with head band bone conduction hearing aids limiting the indications for Vibrant Soundbridge® implantation in pediatric cases. On the other hand, the growing number of children with ear malformations successfully provided with a Vibrant Soundbridge® will lead to earlier indication in future.

Contraindications

Audiological Contraindications

In order to avoid an insufficient hearing gain, the maximum bone conduction threshold should not exceed 45 dB at 500 Hz, 50 dB at 1,000 Hz, and 65 dB at 2,000 Hz and 4,000 Hz. The audiological status should be stable, without progressive hearing loss within an interval of at least 1 year. A retrocochlear origin of hearing loss, as well as central auditory disorders should be ruled out preoperatively.

Anatomical Contraindications

Middle ear anatomy should allow a stable positioning of the FMT via the techniques described. If this is not the case, alternative methods for hearing restoration should be chosen (BAHA®, Bonebridge®).

Local Contraindications

A severe active infection in chronic otitis media is another contraindication for implantation and in addition skin conditions that do not allow the audio processor to be worn regularly. As chronic otitis – defined by its name – is a long lasting disease, minor infections or limited localized inflammatory foci are not a contraindication, as these are target of surgical sanitation. This is in contrast to malignant external otitis, which is a progressive bone-destructing process. Any malignant neoplasm within the operating field should be ruled out and in the case of prior treatment of a malignant tumor, the indication depends on the prognosis and former therapy modalities (e.g., radiotherapy).

General Conditions

Patients and parents of children being treated should be informed and fully understand the surgical procedure and necessary postoperative care. Hence, patients with psychological diseases like dementia or paranoia must be excluded, as severe complications post implantation may arise. Preoperative dialogue should identify patients with unrealistic expectations regarding the implant system and its potential for hearing gain.

Advantages/Disadvantages

Amplification of the normal excitation of the perilymph space results in a more natural hearing sensation. Thus, most patients report a clearly better sound quality in comparison to conventional hearing aids. The system allows intensive amplification in the mid- and high-frequency range, resulting in a significant improvement of speech understanding. Providing patients with CHL and MHL with conventional hearing aids is always a challenge, which often results in an unsatisfactory outcome. The possibilities of hearing restoration by means of classical middle ear reconstruction techniques alone are limited. For this reason, the expansion of the implantation criteria of the Vibrant Soundbridge® to patients with CHL and MHL has led to a considerable improvement in hearing restoration (Baumgartner et al. 2010; Cremers et al. 2010; Mlynski et al. 2010), a functional hearing gain of up to 50 dB has been reported.

However, in chronic otitis media – especially in chronic tubotympanic disease – there is a persistent pathologic process with further changes in the middle ear spaces and the mastoid cavity to be expected. For this reason, a considerable number of revision cases evolving on the basis of chronic disease may arise in the long term. A continuous underinflation in middle ear spaces, slowly developing scarring, and recurrent infections could lead to FMT dislocation. As close coupling of the Vibrant Soundbridge® to the perilymph space is the key point of the system, even minimal dislocations or loosening of the contact of the FMT will lead to progressive hearing deterioration, with the necessity of repeat surgery. On the other hand, these problems are well known in classical middle ear surgery, e.g., in cholesteatoma or tympanosclerosis cases, in which a revision rate of up to 20% has to be expected. However, long-term results, i.e., observation periods of 10 years and longer, are not yet existing for these new indications.

There is still a scientific discussion in progress as to whether bone conduction amplification is equal to natural perilymph stimulation by the oval or round window. Thus, there is a need for further scientific evaluation of the different methods used for active hearing implants.

Conclusions

The use of the Vibrant Soundbridge® in conductive and mixed hearing losses has widened the possibilities of successful surgical hearing restoration on a large scale. Present clinical results of Vibrant Soundbridge® use are extremely convincing and indicate that it is superior when compared to conventional hearing aids. However, extension of the implantation criteria to "difficult" ears may lead to a considerable number of revision surgeries, as is observed for conventional middle ear surgery.

References

Ball GR, Maxfield B (1996) Floating mass transducer for middle ear applications. In: Second international symposium on electronic implants in otology and conventional hearing aids, Göteborg 1996; Abstracts: 8

Baumgartner WD, Boeheim K, Hagen R, Mueller J, Lenarz T, Reiss S, Schlögel M, Mlynski R, Mojallal H, Coletti V, Opie J (2010) The vibrant Soundbridge for conductive and mixed hearing losses: European multicenter study results. Adv Otorhinolaryngol 69:38–50

Colletti V, Soli SD, Carner M, Colletti L (2006) Treatment of mixed hearing losses via im-plantation of a vibratory transducer on the round window. Int J Audio 45(10):600–608

Cremers CW, O'Connor AF, Helms J, Roberson J, Clarós P, Frenzel H, Profant M, Schmerber S, Streitberger C, Baumgartner WD, Orfila D, Pringle M, Cenjor C, Giarbini N, Jiang D, Snik AF (2010) International consensus on Vibrant Soundbridge® implantation in children and adolescents. Int J Pediatr Otorhinolaryngol 74(11):1267–1269

Jahrsdoerfer RA, Yeakley JW, Aguilar EA, Cole RR, Gray LC (1992) Grading system for the selection of patients with congenital aural atresia. Am J Otol 13(1):6–12

Mlynski R, Mueller J, Hagen R (2010) Surgical approaches to position the Vibrant Soundbridge in conductive and mixed hearing loss. In: Friedman M, McKinney B (eds) Operative techniques in otolaryngology – head and neck surgery, vol 21. Elsevier, Amsterdam, pp 272–277

Snik AF, Mylanus EA, Cremers CW, Dillier N, Fisch U, Gnadeberg D, Lenarz T, Mazolli M, Babighian G, Uziel AS, Cooper HR, O'Connor AF, Fraysse B, Charachon R, Shehata-Dieler WE (2001) Multicenter audiometric results with the Vibrant Soundbridge, a semi-implantable hearing device for sensorineural hearing impairment. Otolaryngol Clin North Am 34(2):373–388

Conductive and Sensorineural Hearing Loss

Conductive Hearing Loss-Otosclerosis, Genetics

Janez Rebol[1] and Maja Nahtigal[2]
[1]Department of Otorhinolaryngology, University Clinical Center Maribor, University Maribor, Maribor, Slovenia
[2]Department of ORL and MFS, University Clinical Center Maribor, Maribor, Slovenia

Definitions

Otosclerosis: A form of conductive hearing loss due to endochondral sclerosis of otic capsule. Involvement of stapedio-vestibular joint results in loss of stapes mobility.

Otic capsule: A bony capsule that encloses structures of inner ear, that is, labyrinth and cochlea. It is the densest bone of the body with a slow bone turnover.

Pedigree: A representation of ancestral relationship between individuals related genetically or by marriage.

Gene: Basic unit of a genome coding for a single peptide. It is a functional physical unit of heredity passed from parent to child.

Locus: Region of genome occupied by specific gene or other DNA sequence.

Introduction

Otosclerosis is a distinctive form of progressive conductive hearing loss abnormal bone remodeling in the *otic capsule*. Bone remodeling found in otosclerosis is confined to otic capsule. This process is not found in any other bone of the human body. The disease is unique to humans (Karosi and Sziklai 2010). Attempts have been made to identify genetic factors and the part they take in the pathogenesis of the disease. The idea of genetic role in otosclerosis first came to attention with reports of families with a higher incidence of the affected family members when compared to general population. It was Toynbee that in 1861 documented a form of familial conductive hearing loss, followed by other similar reports (Toynbee 1861). A compelling evidence for genetic etiology was provided by Fowler's study in 1966. He studied 40 pairs of identical twins, where concordance for otosclerosis was found in nearly all cases (Fowler 1966). The fact that prevalence of otosclerosis considerably varies among different ethnical groups suggests that genes play a role in the pathogenesis of the disorder (Emery et al. 2009), as well as the fact that in 80% of the patients the disease is bilateral.

Although the disease has distinctive features, not all investigators have the same criteria when it comes to *diagnosing otosclerosis*. The earliest studies that were dealing with otosclerosis simply included patients with a history of familial conductive hearing loss, or were based entirely on questionnaires. Therefore, inadequate otological diagnosis could have been criticized. Modern studies have refined diagnostic means and criteria for diagnosing the disease, although researches are not even when it comes to meeting these criteria. For clinicians, history of progressive hearing loss without episodes of inflammation and evidence of stapes fixation during stapes surgery along with audiometric results characteristic for otosclerosis prior to surgery are considered as diagnostic.

Some patients who are thought to have otosclerosis actually have stapes ankylosis due to joint fusion syndromes caused by mutations in the NOG gene (Emery et al. 2009). In these patients, hearing loss can be the only manifestation of a syndrome and is clinically indistinguishable from otosclerosis. Therefore, for the purposes of research, where the number of probands is small, together with the criteria used by clinicians, syndromic forms are to be ruled out.

For some investigators the definite diagnosis comes with histopathological examination of fixated stapes footplates which are removed during stapes surgery, since up to one third of stapes fixations are due to other etiology than otosclerosis (Karosi and Sziklai 2010). This criterion is hard to fulfill, as not all the patients with otosclerosis undergo stapes surgery and with some surgical techniques stapes footplate is not obtainable. Others consider the fact that a person underwent stapes microsurgery or high-resolution CT scan demonstrating the lesion in the oval window or otic capsule as diagnostic. Nonetheless, a negative CT scan does not exclude the disease, and the diagnosis is rather presumptive than absolute (Saeed et al. 2007). Another interesting issue is the age of otosclerosis onset. It is generally accepted that the disease starts between the third and the fifth decades, and some investigators believe that otosclerosis in children is not an existing entity (Karosi and Sziklai 2010). A study that recently identified a new locus for otosclerosis OTSC7 found that the hearing loss in that particular family arises at around age of 10 (Thys et al. 2007b).

Heredity and the Mode of Inheritance

The first studies dealing with heredity and the role of genetics in the pathogenesis of otosclerosis were focused on the mode of inheritance. Monogenic patterns of inheritance follow one of the Mendelian patterns of inheritance, namely, autosomal dominant, autosomal recessive, or X-linked. Regarding otosclerosis, all three forms have been proposed. Reviewing epidemiological studies, strongest support is gained by the autosomal dominant form of inheritance with reduced penetrance (Moumoulidis et al. 2007; Markou and Goudakos 2009). A closer look at epidemiological studies shows that the penetrance is only about 40% (Moumoulidis et al. 2007; Markou and Goudakos 2009). Autosomal dominant (AD) disorders become

phenotypically evident in heterozygous state, and males and females are equally affected. Important features of autosomal dominant disorders are reduced penetrance, variable expressivity, and delayed onset (Kumar et al. 2005). Reduced penetrance means that the AD trait is not necessarily transparent, and individuals can be phenotypically normal. Thus, in case of otosclerosis, there is 40% of a chance that a carrier of a mutant gene will suffer from the disease. Variable expressivity means that the degree of severity of a disorder, or the way it is expressed, varies among individuals. AD disorders have generally a delayed onset in life, that is, signs do not appear until adulthood. This mostly holds true for otosclerosis.

AD character of inheritance is insufficient to apply to majority of otosclerosis cases, as family history is often found to be negative in otosclerotic patients. Therefore, other variants were proposed for heredity. Autosomal recessive and X-linked mode of inheritance could not be completely ruled out in the past; however, these options did not gain much trust by the investigators (Moumoulidis et al. 2007; Markou and Goudakos 2009).

Due to a large number of patients with negative family history, further epidemiological studies started to focus more on the role of genes in sporadic cases. The percentage of sporadic cases highly varies in reports. Studies that were dealing with unraveling the mode of inheritance found positive family history in up to 80% (Larsson 1960), but later studies showed much lower percentage of positive family history. The autosomal dominant trait was present in only 13% of otosclerotic patients from North Tunisia (Ben Arab et al. 1993) and positive family history was found in 30% otosclerotic patients in a pedigree study by Saeed et al. (2007). The difference could be due to the nowadays-refined diagnostic tools that recognize the disease in individuals without positive family. Also the earliest studies tried to explain the role of heredity in terms of Mendelian patterns of inheritance. Even the first speculations about the role of genes for sporadic forms tried to deal with the problem in terms of a monogenic disease. It was thought that sporadic cases arise from new mutation, reduced penetrance, and even other modes of Mendelian inheritance (Morrison and Bundey 1970).

With numerous reports about different genes being involved in the pathogenesis of otosclerosis, polygenic or complex gene involvement was proposed. A trait in

polygenic inheritance is governed by the additive effect of two or more genes of small effect and conditioned by nongenetic factors. Certain trait becomes overt when the threshold is reached, that is, when a certain number of effector genes as well as necessary environmental factors are involved. Once the threshold is reached, the severity of the disease is directly proportional to the number and the degree of influence of the involved genes (Kumar et al. 2005). In a pedigree study on a group of patients that underwent stapes surgery, family history was positive only in 19%. In 7 out of 21 families with positive familial history, AD mode was observed. Out of these 7 families only 2 showed incomplete penetrance. Even an X-linked dominant trait was recognized in this study, and the remaining families were too small to ascribe inheritance pattern (Saeed et al. 2007).

In the modern understanding of role of genes in pathogenesis of otosclerosis, it is not an issue anymore whether it is one gene or more genes, one or the other type of inheritance, and whether environmental factors are important or not. It seems that many possible genetic variants coexist and that the impact of environmental factors also varies. Otosclerosis can be now considered as a multifactorial disorder that is a sum of many genes and environmental factors on one extreme and monogenic AD forms with full penetrance on the other extreme. In between lie variants of AD with reduced penetrance, and even X-linked and AR variants were recognized. In otosclerosis etiology, the role of environmental factors has been implicated as equally important, and many environmental factors have been described and studied (e.g., measles virus, fluorides), but are beyond the scope of this review.

Linkage Analysis Studies and OTSC Genes

Large families with many affected members are suitable for pedigree studies and linkage analysis. In such families, it is presumed that the disease has hereditary monogenic etiology. To prove statistically significant linkage, more than 10 affected members along with unaffected members are required (Thys and Van Camp 2009).

Linkage analysis is a statistical technique that helps to locate a given gene involved in a disease. This method evolved from the knowledge that the two genetic loci that lie in the proximity have the tendency to be inherited together. It is said that they are genetically linked. The farther apart two observed loci lie, the smaller the chance to be inherited together, due to a well-known phenomenon called "recombination." For the purposes of linkage analysis as well as for other genetic studies, genetic markers were designed. Genetic markers are segments of DNA with a known position in the genome. One can follow the transmission of genetic markers, as well as a presumably hereditary monogenic disease, from parents to progeny. If a disease and a certain genetic marker keep appearing together in many individuals, they are probably linked. Because genetic markers have known positions, we can assume that the gene we are looking for lies near the specific marker that keeps appearing in affected individuals. The likelihood of two loci to be inherited together can be calculated and expressed with LOD (logarithm [base 10] of odds). A LOD score that equals or is greater than 3 is by convention considered as evidence for linkage because it means there is 0.0001 chance that the linkage being observed occurred by chance (Evans 2008; Strachan and Read 1999).

To date, eight loci have been localized (OTSC 1-5, 7-8, 10) (data about OTSC6 remained unpublished). The area of a locus defined through linkage analysis is still vast, and is populated with many genes, and therefore, locus must be refined with additional markers.

The next step in this type of the study is to identify the culprit gene that occupies locus, which is often difficult. First, genetic databases are checked to see which genes reside in the linked region. Genes that might take part in the pathogenesis of otosclerosis are subjected to mutation analysis to identify the causal mutation (Thys and Van Camp 2009). Until recently, no responsible gene has been identified. The problem of these loci is that they are still huge and only 2% of the genes in these regions have been screened so far (Ealy and Smith 2010).

The first otosclerotic gene was localized in 1998 by Tomek et al. and was named OTSC1. The study was performed on a large multigenerational Indian family. The gene was localized to a chromosome 15q25-26 with a LOD score 3.4 (Moumoulidis et al. 2007). Thirty-three genes are found on this locus, and gene for aggrecan is a good candidate because it is a component of extracellular matrix, found in abundance in bone (Ealy and Smith 2010).

The next gene to be mapped was to OTSC2 locus by Van Den Bogaert et al. in 2001 in a large Belgian

family after excluding the linkage to OTSC1. It was located to 7q34-36 with a LOD score of 3.54 (Moumoulidis et al. 2007). This locus contains 152 genes, and several of them were considered as good candidates (Ealy and Smith 2010). A recent study pointed to human T-cell receptor beta locus (TRB locus) to be involved in the disease (Schrauwen and Van Camp 2010). TRB locus resides in OTSC2 region. Alterations in TRB locus seem to play a role in the development of otosclerosis in OTSC2 patients by causing disturbances in immune system that can influence bone homeostasis. The exact mechanism remains to be elucidated.

In 2002, OTSC3 was documented in a large Cypriot family. The locus was identified on chromosome 6p21.3-22.3 by Chen et al. (Moumoulidis et al. 2007). OTSC3 locus contains Human Leukocyte Antigen (HLA) region which was many times associated with otosclerosis (Ealy and Smith 2010).

OTSC4 was identified on chromosome 16q21-24 with a LOD score 3.97 in a large Israeli family in 2006 by Brownstein. Of the 74 known genes in this locus, good candidates for otosclerosis are genes involved in the immune system and bone homeostasis (Moumoulidis et al. 2007).

Van Den Bogaert et al. published a report about identifying locus OTSC5 in a Dutch family in 2004. Out of 59 known genes, two were cloned; however, mutations were not identified in either of them (Ealy and Smith 2010).

OTSC6 has been reported to Human Genome Organization (HUGO), but was never published in a scientific paper (Moumoulidis et al. 2007).

OTSC7 was mapped in a Greek family and later in a Dutch family to chromosome 6q13-16.1 in 2007 by Thys et al. (2007b). None of the genes residing in this region showed disease-causing mutation, and therefore, regulatory sequences are to be screened as well (Ealy and Smith 2010).

OTSC8 was mapped to 9p13.1-9q21.11 in a large Tunisian family by Bel Hadj Ali et al. in 2008. This region contains 24 known genes, and no mutation was found in candidate genes (Ealy and Smith 2010).

OTSC10 is the latest mapped locus by Schrauwen et al. It is mapped to chromosome 1q41-44 in a Dutch family where AD trait was recognized. The locus contains 306 genes; out of these, 37 are reported to be expressed in the inner ear and 62 in bone tissue (Schrauwen et al. 2011). The complete OTSC10 region

was screened but aberrations were not detected. Apart from that, two genes of this region, transforming growth factor beta 2 (TGF-beta2) and angiotensinogen (AGT), were selected for mutation analysis. TGF-beta2 and AGT were associated with otosclerosis before. In two individuals all exon-intron boundaries were sequenced in two otosclerotic patients, but no mutation was found (Schrauwen et al. 2011).

Families that are appropriate for linkage analysis studies are rare, and affected members represent only a minor part of otosclerotic patients. Another important characteristic of families, upon which linkage analysis studies were performed, is that the penetrance of otosclerosis is exceptionally high, about 90%. Therefore, even if the genes involved in familial forms of otosclerosis will be identified, they might not explain the etiology of the disease in sporadic cases. OTSC loci were found in families of different ethnic origins. Apart from two loci that are located on chromosome 6, the rest are found on different chromosomes. The number of the loci will surely grow in the future since many tested families do not show linkage to any of the known loci. Localization and identification of genes will get easier due to high-throughput sequencing analyses (next-generation sequencing era). All these data confirm that otosclerosis is a heterogenous disease with a rather uniform clinical manifestation.

Role of Genes in Non-familial Forms of Otosclerosis and Types of Research

It is generally accepted for patients without familial history of otosclerosis to have a complex form of the disease. In complex forms, a combination of genetic and environmental factors triggers the disease. Search for the culprit genes in the etiology in non-familial forms of otosclerosis demands different approach than that provided by linkage analysis. Association studies can be used instead to determine whether a genetic variant is associated with a disease (Thys and Van Camp 2009).

There are two types of association studies: candidate gene association (CGA) studies and genomic wide association (GWA) studies.

In CGA, a candidate gene is selected upon speculations of its involvement in the disease. For otosclerosis, some candidate genes were based on relatedness of otosclerosis with diseases such as *osteogenesis*

imperfecta and *osteoporosis*. Pathogenesis of osteoporosis is understood to some extent, while for osteogenesis imperfecta it is well understood. Genetic variants that underlie these diseases are speculated to play a role in otosclerosis as well. The candidate genes are the genes coding for collagens.

Candidate genes can be chosen also upon evidence of their involvement in pathogenesis from immunohistochemistry analyses of otosclerotic foci. The candidate genes from these studies are genes coding for proteins involved in chronic inflammation pathways and structural proteins.

A new way to derive candidate genes and to study pathogenesis of otosclerosis is gene expression analysis. This can be done by comparing gene expression between otic capsule and some other bone in a healthy individual. Stankovic et al. performed a study on mice. It showed distinctly different molecular profile of otic capsule when compared to tibia and parietal bone (Stankovic et al. 2010). The genes most characteristic of the otic capsule were genes that are very likely to have an inhibitory effect on bone remodeling. Dysregulation of these genes may contribute to otosclerosis (Stankovic et al. 2010).

Another possibility for gene expression analysis is to compare gene expression between stapes from healthy persons and stapes from otosclerotic patient. A study that was performed by Ealy et al. showed difference in the expression of 110 genes between normal and otosclerotic stapes. Of these, 92 were up-regulated and 18 were down-regulated. Many of them belong to interleukin signaling pathway and inflammation (Ealy et al. 2008).

Once a candidate gene is chosen, CGA study can be performed. In this type of study, genetic markers are used to cover the whole gene. Two groups are compared: one group is formed of healthy, that is, non-otosclerotic individuals and the other of otosclerotic sporadic, that is, non-related individuals. Genetic markers are then compared between the two groups. If the frequency of a certain genetic marker is significantly different between the two groups, that is, it is seen very often in the affected group, but only occasionally in non-affected group, association is found. Association studies point to a certain allele or haplotype that is associated with the disease.

Functional studies, where the function of the gene product of associated allele is studied, are needed to determine the significance of these findings.

GWA is a type of study without a candidate gene. Up to one million genetic markers are used to cover the entire genome. Again two populations are compared: non-affected and affected individuals. However, this time the whole genomes are compared, and genetic markers with significant difference in occurrence are sought. Once they are found, functional studies are to be performed in order to connect them with pathogenesis of otosclerosis.

Current Results of Candidate Gene Associaton Studies

CGA studies have shown associations with otosclerosis and COL1A1, TGFB1, BMP4, AGT, and ACE; associations with COL1A1, AGT, and ACE are controversial (Ealy and Smith 2011).

COL1A1 that encodes collagen type 1a was considered as a good candidate due to its well-established role in osteogenesis imperfecta. Osteogenesis imperfecta (OI) is a connective tissue disorder caused by mutations of collagen type I genes COL1A1 and COL1A2. Normally, collagen type I is a triple helix formed of two chains of col1a1 and one chain of col1a2. Mutations in either of the two genes lead to change of this ratio. Collagen type I in OI is formed of one chain of col1a1 and of one chain of col1a2. As such, it is much more susceptible to trauma. Several hundred mutations of COL1A1 and COL1A2 have been detected in OI. The disorder shows autosomal dominant inheritance with relatively high penetrance and is manifested by fragile bones, while hearing loss occurs in 30–50% of patients (Flint et al. 2010). Hearing loss is either sensorineural or conductive, the latter can be similar to that seen in otosclerosis; these patients can benefit from stapes surgery (Flint et al. 2010).

It is hypothesized that COL1A1 involvement in the otosclerosis is due to its up-regulation and consequent abnormal bone deposition (Ealy and Smith 2011). Several studies have been performed to associate COL1A1 to otosclerosis, but the conclusions are not equivocal. To clarify the role of COL1A1 gene in otosclerosis pathogenesis, other genetic studies performed on a suitable group of patients could be of value (Moumoulidis et al. 2007).

Transformation growth factor beta 1 (TGF-beta1) is important in embryonic development of the otic

capsule. It stimulates chondrogenesis and to promote growth, at a later stage it selectively inhibits chondrogenesis to allow perilymphatic space formation. In mature otic capsule, TGF-beta1 is a coupling factor between bone resorption and bone formation (Thys and Van Camp 2009). A CGA study by Thys et al. found a difference in the activity of different alleles coding for TGF-beta1; I263 allele is more active than T263 allele. This greater activity of I263 is protective against otosclerosis, presumably by inhibiting osteoclastic activity that would otherwise resorb the bone in the early stages of otosclerosis (Thys and Van Camp 2009). Gene expression analysis of otosclerotic stapes footplates showed different expression of genes that might decrease TGF-beta1 signaling which seems to have an inhibitory effect on bone resorption (Ealy et al. 2008).

Bone morphogenetic proteins 2 and 4 (BMP2 and BMP4) are members of TGF-beta superfamily. They have a known role in the development of otic capsule and presumably a role in otosclerosis. Genetic studies are unequivocal concerning their involvement in otosclerosis; further functional studies could determine the significance of these findings (Ealy and Smith 2010).

Association studies focused on renin-angiotensin-aldosterone system, that is, on genes coding for angiotensinogen (AGT) and angiotensin-converting enzyme (ACE) since they are up-regulated in pregnancy and possible progression of disease in that period. The results of studies on AGT and ACE are conflicting. Though association between AGT, ACE, and otosclerosis was found, results were not reproducible in another population (Ealy and Smith 2010).

A recent GWA study showed association to reelin (RELN), a gene with a known role in neuronal migration. Expression of RELN was confirmed in inner ear and stapes footplate specimens. The same study also provides evidence for RELN to play role in the pathogenesis of otosclerosis (Schrauwen et al. 2009).

Finding a connection between otosclerosis and HLA has been a matter of several studies. Identification of OTSC3 is suggestive for this connection because OTSC3 locus covers HLA region. The results of studies that associate HLA with otosclerosis are conflicting (Thys and Van Camp 2009). Studies upon this region are difficult because of its genetic complexity. However, with the advent of new technologies of

genetic research, we can expect further studies to be performed on elucidation of HLA region role in otosclerosis.

Conclusion

Advances in technologies of genetic research go hand in hand with advances in elucidating gene role in the pathogenesis of otosclerosis. Numerous data point to many genes, however, unequivocally. With the concept of a complex disease, this unequivocality does not necessarily mean that one or the other gene is not an existing entity in the pathogenesis of the disease. From today's standpoint, it can be expected that in the future we will be able to distinguish among different genotypes that predispose to otosclerosis, as well as to predict the impact of different environmental factors on the disease individually.

References

Ben Arab S, Bonaiti-Pellie C, Belkahia A (1993) A genetic study of otosclerosis in a population living in the north of Tunisia. Ann Genet 36(2):111–116

Ealy M, Smith RJH (2010) The genetics of otosclerosis. Hear Res 266:70–74

Ealy M, Smith RJH (2011) Otosclerosis. Adv Otorhinolaryngol 70:122–129

Ealy M, Chen W, Ryu GY, Yoon JG, Bradley Welling D, Hansen M, Madan A, Smith RHJ (2008) Gene expression analysis of human otosclerotic stapedial footplates. Hear Res 240:80–86

Emery SB, Meyer A, Miller L, Lesperance MM (2009) Otosclerosis or congenital stapes ankylosis? The diagnostic role of genetic analysis. Otol Neurotol 30:204–1208

Evans J (2008) Cell biology and genetics, 3rd edn. Mosby Elsevier, Philadelphia, pp 143–151

Flint PW, Haughey BH, Lund VJ, Niparko JK, Richardson MA, Robbins KT, Thomas JR (2010) Cummings otolaryngology-head and neck surgery, 5th edn. Mosby Elsevier, Philadelphia, pp 2110–2111

Fowler EP (1966) Otosclerosis in identical twins: a study of 40 pairs. Arch Otolaryngol 83:324–328

Karosi T, Sziklai I (2010) Etiopathogenesis of otosclerosis. Eur Arch Otorhinolaryngol 267:1337–1349

Kumar V, Abbas AK, Nelson F (2005) Robbins and Cotran pathologic basis of disease, 7th edn. Elsevier Saunders, Philadelphia, pp 150–152, 169–170, 1279–1282

Larsson A (1960) Otosclerosis. A genetic and clinical study. Acta Otolaryngol 154:1–86

Markou K, Goudakos J (2009) An overview of etiology of otosclerosis. Eur Arch Otorhinolaryngol 266:25–35

Morrison AW, Bundey SE (1970) The inheritance of otosclerosis. J Laryngol Otol 84(9):921–932

Moumoulidis I, Axon P, Baguely D, Reid E (2007) A review on genetics of otosclerosis. Clin Otolaryngol 32:239–247

Saeed SR, Briggs M, Lobo C, Al-Zoubi F, Ramsden RT, Read AP (2007) The genetics of otosclerosis: pedigree and linkage analysis. Adv Otorhinolaryngol 65:75–85

Schrauwen I, Van Camp G (2010) The etiology of otosclerosis: a combination of genes and environment. Laryngoscope 120:1195–1202

Schrauwen I, Ealy M, Huentelman MJ, Thys M, Homer N, Vanderstraeten K, Fransen E, Corneveaux JJ, Craig DW, Claustres M, Cremers CWRJ, Dhooge I, Van de Heyning P, Vincent R, Offeciers E, Smith RJH, Van Camp G (2009) A genome wide analysis identifies genetic variants in the RELN gene associated with otosclerosis. Am J Hum Genet 84:328–338

Schrauwen I, Venken K, Vanderstraeten K, Thys M, Hendricx JJ, Fransen E, Van Lear L, Govaerts PJ, Verstreken M, Schatteman I, Stinissen P, Hellings N, Van Camp G (2010) Involvement of T-cell receptor beta alteration in the development of otosclerosis linked to OTSC2. Genes Immun 3:246–253

Schrauwen I, Weegerink NJD, Fransen E, Claes C, Pennings RJE, Cremers CWRJ, Huygen PLM, Kunst HPM, Van Camp G (2011) A new locus for otosclerosis, OTSC10, maps to chromosome 1q41-44. Clin Genet 9:495–497

Stankovic KM, Adachi O, Tsuji K, Kristiansen AG, Adams JC, Rosen V, McKenna MJ (2010) Differences in gene expression between otic capsule and other bones. Hear Res 265:83–89

Strachan T, Read AP (1999), Human molecular genetics, 2nd edn. Wiley-Liss, New York S. http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hmg.section.1412. Accessed 23 April 2011

Thys M, Van Camp G (2009) Genetics of otosclerosis. Otol Neurotol 30:1021–1032

Thys M, Schrauwen I, Vanderstraeten K, Janssens K, Dieltjens N, Van Den Bogaert K, Fransen E, Chen W, Ealy M, Clausters M, Cremers CR, Dhooge I, Declau F, Claes J, De Heyning V, Vincent R, Somers T, Offeciers E, Smith RJ, Van Camp G (2007a) The coding polymorphism T263 in TGF-beta1 is associated with otosclerosis in two independent populations. Hum Mol Genet 16:2021–2030

Thys M, Van Den Bogaert K, Ilidaou V, Vanderstraeten K, Dieltjens N, Schrauwen I, Chen W, Elftheriades N, Grigoriadou M, Pauw RJ, Cremers CRWJ, Smith RJH, Petersen MB, Van Camp G (2007b) A seventh locus for otosclerosis, OTSC7, maps to chromosome 6q-16.1. Eur J Hum Genet 15:362–368

Toynbee J (1861) Pathological and surgical observations on the disease of the ear. Med Chir Trans 24:190–205

Congenital Airway Disorders

Congenital Aural Atresia

Tam Nguyen and Bradley W. Kesser
Department of Otolaryngology-Head and Neck Surgery, University of Virginia Health System, Charlottesville, VA, USA

Synonyms

Aural atresia; Congenital aural atresia; Ear atresia

Definition/Background

Congenital aural atresia (CAA) is the incomplete development of the external auditory canal (EAC) and middle ear structures.

Failure of embryologic development to progress can occur at any point during ontogeny, and severity of the malformation is related to the timing of the arrest. The most severely affected ears demonstrate no identifiable ear canal and underdevelopment of the middle ear space and middle ear structures. In milder cases, the EAC is merely narrowed, and there can be a rudimentary tympanic membrane with a functionally normal middle ear sound conducting system.

CAA is found in 1 out of 10–20,000 live births. It occurs seven times more often unilaterally, with the right ear affected more frequently than the left. The male to female ratio is about 2.5:1.

CAA is usually associated with some degree of microtia, the incomplete development of the auricle (Fig. 1). Despite their different embryologic origins, auricular development often mirrors the development of the ear canal, middle ear space, and ossicular chain (Kountakis et al. 1995). Because the inner ear develops from a completely separate anlage (otocyst) from the middle and outer ear (branchial system), inner ear malformations are not typically associated with CAA.

Etiology

The cause of the arrested development of first branchial arch derivatives with failure of canalization of the

Congenital Aural Atresia, Fig. 1 Grade III microtia in the setting of congenital aural atresia (Photo courtesy of Dr. Burt Brent)

EAC is unknown. Both position in the womb with pressure on the side of the head, and loss of arterial blood supply to first arch derivatives have been proposed, but no definitive etiology has been discovered. Loss of, failure of, or mutation in a specific transcription factor at a critical period during embryonic development may also underlie CAA, especially given its association with syndromes such as Goldenhar, hemifacial microsomia, and Treacher Collins. There is some evidence that a mutation in chromosome 18 may be associated with CAA (Dostal et al. 2006).

Embryology

The middle ear and EAC develop from the branchial apparatus. During the first 2 months of development, EAC formation begins with invagination of the first branchial groove located between the first (mandibular) and second (hyoid) branchial arches. This groove pushes in medially as an epithelial plate and meets the lateral advancement of the first pharyngeal pouch. The

pouch, of endodermal origin, will become the middle ear cleft and Eustachian tube lined by respiratory epithelium. The meeting of the branchial groove and pharyngeal pouch forms the meatal plate that later becomes the tympanic membrane.

Around 6 months of fetal development, the epithelial plate canalizes from medial to lateral and joins the primary meatus formed from invagination of the cavum conchae of the auricle. This primary meatus becomes surrounded by cartilage and develops into the fibrocartilaginous portion of the EAC. Failure of canalization of the epithelial plate leads to a stenotic or absent bony EAC.

Middle ear development from the first pharyngeal pouch parallels development of the EAC. The ossicles take origin from the first and second branchial arches and are initially enveloped in the mesenchyme of the first pharyngeal pouch. Arrest in the development of the branchial apparatus leads to a contracted middle ear space with deformed ossicles. The head of the malleus and body of the incus are derived from the first branchial arch, while the long process of the incus and stapes bone originate from the second arch. In CAA, the stapes and incus tend to be most developed, with the malleus displaying more, but varying degrees of, malformation. The umbo, manubrium, and neck of the malleus are commonly absent, with the head of the malleus fused to the body of the incus. Given the greater degree of malleus abnormality and the association of CAA with shortening of the mandible on the affected side, such as that seen in hemifacial microsomia, CAA is thought to be primarily a first branchial arch anomaly. Inner ear development, on the other hand, begins as early as the third week of gestation and is usually complete by the 20th week before canalization of the EAC. Thus, inner ear malformations are unusual with CAA.

Clinical Presentation

If microtia is present, CAA will be evident at birth. Very rarely, CAA is accompanied by a normal auricle; a careful otoscopic exam and newborn hearing screening should identify the absent EAC and hearing loss, and the baby should be referred for further evaluation.

On physical examination, associated anomalies of the mandible, oral cavity, cervical spine, and eyes may be apparent. Ear exam should include overlying skin, skin tags, pits, hairline, and position of the auricle as well as the severity of auricular deformity. Facial nerve function may show weakness, but this is not common. Other cranial nerves, cognitive, and balance function are generally not affected, especially in isolated unilateral CAA. Cardiac, renal, and pulmonary abnormalities have also been associated with CAA, although less often. CAA is associated with a named syndrome in 10–15% of patients.

Diagnosis

Audiometry

Hearing loss in patients with CAA is conductive, although a small minority of patients will also have a sensorineural component. The conductive loss is usually at the threshold of 40–60 dB depending on the ossicular deformity, ossicular mobility, and degree of pneumatization of the temporal bone. Complete audiological evaluation, including air and bone conduction auditory brainstem response (ABR) testing should be performed by 3 months of age. Even in patients with unilateral CAA, it is critical to document the hearing status of the normal ear to ensure it is hearing well. Older children can be tested behaviorally in the sound booth with techniques such as visual reinforced audiometry (ages 2–4) and conditioned play audiometry (ages 4–7). Sensorineural acuity level (SAL) is a technique to measure bone conduction thresholds for each individual ear in the patient with bilateral CAA.

In bilateral CAA, the level of deformity and degree of hearing loss may be different for each side. Early (by 3–6 months) hearing rehabilitation in these children is paramount for normal speech and language development. Such rehabilitation involves the use of special bone conducting hearing aids. For optimal bone conduction, a bone oscillator is tightly secured to the mastoid (or other area of the skull) by a strap or band worn around the head.

Benefits of amplification in the child with unilateral CAA are unclear, and the decision to place a bone conducting hearing aid on this group of patients is made after careful discussion among the family, otolaryngologist, and audiologist. Factors that must be considered include the possible benefits of stimulating the atretic ear, the possibility of a critical period for true binaural processing, psychosocial factors, and the lack of outcome data for children with unilateral aural atresia. For the normal hearing ear, hearing protection/conservation is crucial, and middle ear effusions should be closely monitored and treated aggressively.

Children with stenosis of the EAC are at risk for cholesteatoma from trapped skin within the narrow canal, especially if the canal is less than 2 mm (Cole and Jahrsdoerfer 1990). If the canal is of inadequate size to evaluate for cholesteatoma in clinic, a high resolution temporal bone computed tomography (CT) scan is warranted. Canal cholesteatoma would not generally be present before the age of 3 years; therefore obtaining a CT scan after this age is reasonable. CT scanning is not indicated in the newborn period – there is no reason to subject the newborn to the radiation delivered, although very small. No major clinical decisions (i.e., decision for surgery) will be made in the new born period or first year of life. If a CT is obtained in the newborn period, there will be need for a second CT prior to surgery or for suspected complications such as cholesteatoma.

Imaging

Thin section (1 mm minimum), high resolution CT has changed the ability to manage CAA by providing accurate anatomic detail of the middle and inner ear. This is important in determining eligibility for surgery and in surgical planning. If the family wishes to evaluate their child's candidacy for surgery, the CT scan is obtained when the child is old enough that sedation is not needed (around 4–5 years).

Radiographic Anatomy in CAA

Knowledge of the common radiographic findings in CAA is crucial in evaluation for surgery and the possibility of cholesteatoma. First the canal should be assessed for any patency or soft tissue; a large rounded density that has remodeled bone in the lateral temporal bone, often sparing the middle ear space, is concerning for cholesteatoma. The atretic plate is the bony region just lateral to the middle ear space (Fig. 2). The middle ear space and mastoid are evaluated for degree of pneumatization. Within the middle ear, each ossicle is assessed. The most commonly seen aberrations are a fused malleus-incus complex, shortened malleus (absent manubrium) and sometimes a hypoplastic

Congenital Aural Atresia, Fig. 2 High resolution coronal CT scan through the right temporal bone of a patient with congenital aural atresia. *Arrow* points to atretic plate. Fused malleus-incus complex seen just deep to the atretic plate

stapes suprastructure. Occasionally, the malleus-incus complex appears as a "boomerang." In this configuration, the incus is often not attached to the stapes bone and the middle ear space is constricted.

The facial nerve often has an aberrant course in CAA. The nerve may be located anterior and lateral in its proximal mastoid segment after the second genu which itself may have a more acute bend. With careful planning, facial nerve injury in atresia surgery is rare (Jahrsdoerfer and Lambert 1998). The round and oval windows are assessed for presence or absence. For surgical planning, the jaw joint and tegmen locations help determine the amount of room available for drilling the canal. Lastly, the inner ear structures are observed for malformations which may be present in as high as 20% of patients with CAA (Vrabec and Lin 2010).

Differential Diagnosis

The diagnosis of aural atresia is readily apparent due to the usual association of microtia. Rarely, aural atresia may be accompanied by a normal appearing auricle. The canal may be stenotic in these instances or completely atretic. The diagnosis is made by careful otoscopy.

Minor malformations, defined as those with a normal ear canal and tympanic membrane, include absent oval window, persistent stapedial artery, congenital stapes fixation (the most common), congenital

lateral chain (malleus or incus) fixation, single stapes crus, and congenitally shortened malleus. Hearing loss is identified from newborn hearing screening and further characterized as conductive on follow-up diagnostic (ABR) testing. Any child with an unexplained conductive hearing loss should undergo CT scanning to identify the malformation and to rule out middle ear mass such as congenital cholesteatoma. Decision for hearing rehabilitation – observation with monitoring of the hearing if unilateral, environmental modifications such as preferential seating in the classroom and/or FM system, conventional amplification, bone conducting hearing aid, or surgery – must be a shared, informed decision with the otolaryngologist, audiologist, family, and possible educational consultant. Surgical exploration of the middle ear is not generally undertaken until the child is cooperative and engaged in the process, around 7–8.

Prophylaxis

The etiology of aural atresia is unknown; as such, there are no known preventative measures for congenital aural atresia.

Therapy

Options for hearing rehabilitation for patients with aural atresia include observation with preferential seating in class and possible use of a frequency modulated (FM) system, a bone conducting hearing device, a bone anchored hearing device, and atresia surgery. Patients with bilateral aural atresia are highly recommended to wear a bone conducting hearing device from shortly after birth or risk poor speech and language development. The role of amplification (either bone conducting or bone anchored devices) is unclear in patients with unilateral aural atresia.

It is through both the audiometric and radiologic evaluation of the child with CAA that his/her candidacy for surgical repair is assessed. The patient must have normal bone conduction thresholds – normal inner ear function – on audiometry to be considered a candidate for atresia surgery. Exceptions can be made, but it is fruitless to open the canal of a child with a moderate or greater sensorineural hearing loss.

There are multiple scoring systems for CAA to assess a patient's anatomical surgical candidacy. Colman divided CAA into three categories: minor, moderate, and severe. Severe CAA is described as total canal atresia with a poorly developed middle ear and unfavorable anatomy for reconstruction. Moderate atresia has an aerated middle ear space, deformed ossicles, and an identifiable canal. In minor cases, the canal is present but narrow and the middle ear space is better developed.

Two more detailed classification systems have been developed, the De la Cruz classification and the Jahrsdoerfer grading system (Tables 1 and 2). The former classifies findings in CAA as minor or major, with minor findings being better surgical candidates. The latter is more commonly used today and incorporates a point system for the presence of certain structures to estimate successful hearing rehabilitation with atresia repair. Generally a score higher than 7 is considered a good surgical candidate anatomically (Jahrsdoerfer et al. 1992; Shonka et al. 2008).

Prognosis

Although uncommon, patients with bilateral congenital aural atresia require timely management to improve chances for good outcomes in hearing and language development. Preliminary data show that children with unilateral aural atresia should be monitored for language development and performance in school. These children may benefit from classroom interventions such as preferential seating, an FM system, or even amplification. Management of parental and patient expectations is also important. This requires knowledge of the pathophysiology, treatment options, and outcomes. In select patients, surgery to open the ear canal and restore the natural sound conducting mechanism of the canal, eardrum, and ossicles can bring hearing thresholds into the normal range with a clean, dry, well-epithelialized canal.

Epidemiology

Congenital aural atresia affects 1 in 10–20,000 live births. For unknown reasons, the right ear is more commonly affected than the left, and boys are more frequently affected than girls. The vast majority (70%)

Congenital Aural Atresia, Table 1 De la Cruz classification of congenital aural atresia (De la Cruz and Chandrasekhar 1994)

Minor malformations	Major malformations
Normal mastoid pneumatization	Poor pneumatization
Normal oval window/footplate	Abnormal or absent oval window/footplate
Reasonable facial nerve-footplate relationship	Abnormal course of facial nerve
Normal inner ear	Abnormalities of the inner ear

Congenital Aural Atresia, Table 2 Jahrsdoerfer grading system of candidacy for atresiaplasty (Jahrsdoerfer et al. 1992)

Parameter	Points
Stapes present	2
Oval window open	1
Middle ear space	1
Facial nerve normal	1
Malleus-incus complex present	1
Mastoid well-pneumatized	1
Incus-stapes connection	1
Round window normal	1
Appearance of external ear	1

Rating	Type of candidate
10	Excellent
9	Very good
8	Good
7	Fair
6	Marginal
≤5	Poor

of patients have unilateral atresia, and in 15% of patients with aural atresia, the condition is associated with other anomalies (e.g., Treacher Collins, Hemifacial microsomia).

Cross-References

▶ Atresiaplasty
▶ Congenital Aural Atresia

References

Bauer GP, Wiet RJ, Zappia JJ (1994) Congenital aural atresia. Laryngoscope 104:1219–1224

Cole RR, Jahrsdoerfer RA (1990) The risk of cholesteatoma in congenital aural stenosis. Laryngoscope 100(6):576–578

De la Cruz A, Chandrasekhar SS (1994) Congenital malformation of the temporal bone. In: Brackman DE (ed) Otologic surgery. W.B. Saunders, Philadelphia

De la Cruz A, Kesser BW (1999) Management of the unilateral atretic ear. In: Pensak M (ed) Controversies in otolaryngology-head and neck surgery. Thieme Medical Publishers, New York, pp 381–385

Dostal A, Nemeckova J, Gaillyova R, Vranova V, Zezulkova D, Lejska M (2006) Identification of 2.3-Mb gene locus for congenital aural atresia in 18q22.3 deletion: a case report analyzed by comparative genomic hybridization. Otol Neurotol 27(3):427–432

Jahrsdoerfer RA (1978) Congenital atresia of the ear. Laryngoscope 88(9 Pt 3 Suppl 13):1–48

Jahrsdoerfer RA, Lambert PR (1998) Facial nerve injury in congenital aural atresia surgery. Am J Otol 19(3):283–287

Jahrsdoerfer RA, Yeakley JW, Aguilar EA, Cole RR, Gray LC (1992) Grading system for the selection of patients with congenital aural atresia. Am J Otol 13:6–12

Kelley PE, Scholes MA (2007) Microtia and congenital aural atresia. Otolaryngol Clin North Am 40:61–80

Kesser BW, Ng M, Horlbeck DM, Megerian CA, Talavera F, Allen GC, Slack, CL, Meyers AD (2010) Aural atresia. http://emedicine.medscape.com. Accessed 27 Apr 2011

Kountakis SE, Helidonis E, Jahrsdoerfer RA (1995) Microtia grade as an indicator of middle ear development in aural atresia. Arch Otolaryngol Head Neck Surg 121(8):885–886

Shonka DC, Jahrsdoerfer RA, Kesser BW (2008) The Jahrsdoerfer grading scale in surgery for congenital aural atresia. Arch Otolaryngol Head Neck Surg 134:873–877

Trigg DJ, Applebaum EL (1998) Indications for the surgical repair of unilateral aural atresia in children. Am J Otol 19(5):679–684; discussion 684–686

Vrabec JT, Lin JW (2010) Inner ear anomalies in congenital aural atresia. Otol Neurotol 31(9):1421–1426

Congenital Conductive Hearing Loss

Sean M. Miller and Anthony A. Mikulec
Department of Otolaryngology, Saint Louis University School of Medicine, St. Louis, MO, USA

Synonyms

Middle ear hearing loss; Ossicular discontinuity; Stapes fixation

Definition

Congenital conductive hearing loss (CCHL) resulting from pathology of the middle ear represents a rare cause of hearing impairment. This entry discusses hearing loss caused by congenital middle ear abnormalities with an intact tympanic membrane. Other possible causes of congenital conductive hearing loss including external ear disorders, such as atresia, perforations of the tympanum, and congenital cholesteatoma, are discussed elsewhere. Enlarged vestibular aqueduct syndrome and dehiscence of the semicircular canals can cause a conductive component as part of what is often a mixed hearing loss. These entities are also discussed elsewhere. Eustachian tube dysfunction leading to middle ear effusion and associated conductive hearing loss is certainly the most common congenital type of hearing loss, but Eustachian tube dysfunction is generally considered as a distinct entity from congenital middle ear malformations.

Epidemiology

The incidence of congenital deformities of the middle ear is about 1 in 15,000 (Farrior 1987). Of these, only a small proportion are CCHL with an intact tympanic membrane. As a frame of reference, the senior author of this entry encounters less than one case of CCHL per year out of an annual pediatric new patient population of 3,300 clinic visits.

Despite the rarity of CCHL, the number of reported abnormalities is great, involving malformation or absence of nearly every middle ear component (Raz 2002). Congenital stapedial footplate fixation and the incudostapedial complex are the most commonly involved portions of the ossicular chain (Kuhn 2006; Cole 1980; House 1980; Teunissen 1993). In addition, case reports of congenital round window absence exist within the literature (Clifford 1990; Tringali 2002).

History

The natural history of the presentation of CCHL is similar to that of most children with hearing impairment. Infants who do not startle appropriately to stimuli, as well as children who have delayed language acquisition or learning disabilities, may be suspected of having a congenital conductive hearing loss. Patients with a unilateral loss may present at a later

age. In one series (Teunissen 1993), the average age at first surgery for patients with CCHL was 26. A more recent case series of 28 patients noted a mean age of 15.3 (Henricus 2010). Given the high prevalence of new born hearing screening in developed societies, hearing losses are generally identified within the first months of life, although differentiation between conductive and much more common sensorineural losses can be more challenging. Both CCHL and sensorineural hearing losses can initially be treated with hearing aids.

In order to further refine the differential diagnosis, House (1980) points out that children with congenital ossicular abnormalities will present with a nonprogressive hearing loss whereas the child with otosclerosis usually has a bilateral, progressive hearing loss and, perhaps more importantly, a family history. In a series by Paparella (1982), congenital stapes fixation was the second most common abnormality behind otosclerosis in patients with an intact, "normal" tympanic membrane. Fortunately for the clinician, a diagnostic battery exists which refines and focuses the investigation of hearing impairment etiology (see below for testing).

Clinical Features

The association of CCHL with a coexistent syndrome has been variably reported between 20% and 68% (Stewart 1993; Henricus 2010). Patients with known syndromes merit special diligence and clinical suspicion of possible hearing impairment, be it CCHL or otherwise. Fortunately, atretic canals are usually accompanied by microtia, hastening the recognition and diagnosis. Children with extremely small or stenotic ear canals and hearing impairment have an increased incidence of ossicular abnormalities, most commonly a fused malleus-incus complex (Carfrae 2010). Along the malformation spectrum, children with partial or complete stenosis of the EAC are most likely to have severe ossicular malformations. In these children, atresia repair often involves concomitant ossiculoplasty. Only 0.5% of patients in one series (Stewart 1993) had isolated middle ear anomalies in the absence of other abnormalities.

Various classification schemes of ear abnormalities have been proposed (Cole 1980; Teunissen 1993; Raz 2002). To date, none have been universally accepted.

The most common and most efficient classification scheme distinguishes between "minor deformities," which are those that demonstrate an intact EAC and tympanic membrane and only involve the middle ear, and "major deformities," which are those that involve agenesis or atresia of the EAC, with variable involvement of the pinna. Regardless of etiology, well over 50% of cases can be addressed with surgery.

A host of syndromes have been associated specifically with conductive hearing loss. Syndromic children may have comorbid pathology and anatomic malformations such as cleft lip and palate, which increase the likelihood of Eustachian tube dysfunction and chronic otitis media with effusion. This cause of conductive hearing loss must maintain a paramount position on a differential diagnosis for the practitioner, in both syndromic and nonsyndromic child. However, there are select syndromes which have specifically been identified with malformations leading to CCHL. The following list is representative but not exhaustive:

– Apert Syndrome – Congenital ossicular fixation and incus malformation (Phillips 1986)
– CHARGE Syndrome – A variety of ossicular malformations may be present
– Goldenhar's Syndrome (oculoauricular vertebral dysplasia) – Atretic canals and ossicular malformations
– Klippel-Feil Syndrome – One third of patients will have otologic defects, including atretic canals and ossicular chain abnormalities (Yildirim 2008)
– Nager acrofacial dysostosis – EAC stenosis and ossicular abnormalities (Hermann 2005)
– Noonan syndrome – Ossicular chain abnormalities
– Osteogeneis imperfecta – Secondary to a mutation in the COL1A1 gene, may present variably with mobile, atrophic stapes crura combined with a fixation of the stapes footplate, often there is a sensorineural contribution to hearing loss, as well (Swinnen 2009)
– Treacher-Collins Syndrome – Often bilateral, symmetric stenosis or atresia of the EAC coupled with a hypoplastic middle ear and malformed ossicles (Pron 1993)
– Wildervanck (Cervico-oculo-acoustic) – Congenital stapes fixation (Cremers 1984)
– Mucopolysaccharidoses – Patients are at an increased risk of chronic otitis media with effusion (Ruckenstein 1991)

Congenital Conductive Hearing Loss, Table 1 Evaluation of conductive hearing loss

	Otis media with effusion	Congenital cholesteatoma	Stapes fixation	Incus or malleus fixation	Semicircular canal dehiscence
Tympanogram	Flat	Variable	Normal	Normal	Normal
Stapedial reflexes	Usually absent	Variable	Absent	Normal	Normal
CT	Fluid in middle ear space	Middle ear mass	Normal	Abnormal	Abnormal

Tests

Evaluation of congenital conductive hearing loss requires an audiogram to evaluate the extent of the conductive component. As testing in children, particularly at a young age, can lead to inconsistent results, two or more audiograms are useful to confirm the extent and nature of the hearing loss before undertaking further evaluation. Tympanometry should be performed to exclude other common causes of conductive hearing loss such as Eustachian tube dysfunction or middle ear effusion. Stapedial reflexes should be performed to evaluate for stapedial fixation. They will be present in semicircular canal dehiscence but absent in congenital stapes fixation or otosclerosis (Table 1).

A computerized tomography (CT) scan is the next step, once a conductive hearing loss has been confirmed and can identify causes of CCHL such as semicircular canal dehiscence, high-riding jugular bulb, or other middle ear masses. Some CT scans, depending on power and slice thickness may be able to identify ossicular abnormalities such as malformed or missing ossicles. In most cases of CCHL, the CT scan will be normal. The CT scan can also help to identify situations where stapedectomy would not be advisable, such as a patent distal internal auditory canal which can lead to stapes gusher (the egress of CSF under pressure after the stapes footplate is opened) or an overhanging or malpositioned facial nerve.

Exploratory tympanotomy can be considered for diagnostic reasons when other routes of investigation fail to yield a diagnosis. In such cases, it is important, prior to surgery, to come to agreement with the parent and child as to which types of possible abnormalities will undergo attempted repair, and the risks involved.

Differential Diagnosis

1. Congenital cholesteatoma: Has a whitish mass visible behind the tympanic membrane and on CT scan

2. Eustachian tube dysfunction: Has a flat or negative pressure tympanogram
3. Otitis media with effusion: Has flat or negative tympanogram and fluid often visible behind tympanic membrane
4. Enlarged vestibular aqueduct: Usually causes a mixed hearing loss, but rarely can initially present as a conductive hearing loss)
5. Tympanosclerosis: Can cause ossicular (including stapes) fixation. Ossiculoplasty results tend to be much less favorable (Welling 2003)
6. Ossicular chain abnormalities: Will present as discussed in this entry case reports of congenital round window absence (Clifford 1990; Tringali 2002)

Etiology

CCHL is caused by a myriad of genetic abnormalities. A few familial strains have been mapped to certain genes (such as CHD7 in CHARGE syndrome) but the vast majority represent sporadic occurrence.

A brief review of the embryology of the ear aids is useful in examination of the probable insults which result in the observed malformations in CCHL. The malleus and incus originate mainly from the mesenchyme of the first branchial arch, also known as Meckel's cartilage, with a contribution from the second arch. The malleus and incus develop between the 6th and 8th week of gestation. The incus long process joins the stapes head during the 8th week. The IS joint ligament is formed by a condensation of mesenchyme that surrounds the lenticular process of the stapedial head. The development of this process is complex, which results in the high variability of the observed malformations (Suzuki 2008).

The stapes superstructure arises from the second arch, Reichert's cartilage. The stapes is the first of the ossicles to appear, arising during the 4–5th week of gestation. By the 7th week, the stapes has assumed

its annular configuration with the stapedial artery occupying its position between the two cruces. Hypoplasia of the superstructure is caused by disturbed development at this stage.

Similarly, aural atresia results from developmental abnormalities during week 6–10 of gestation (Carfrae 2010).

Treatment

All forms of conductive hearing loss can be successfully rehabilitated with a hearing aid, which simply amplifies incoming sound to a level that overcomes the hearing loss. There are two parts to hearing – being able to hear a sound or tone and being able to tell words apart, otherwise known as word discrimination. Unlike some types of sensorineural hearing loss, CHL features normal word discrimination, as the cochlea is normal. Hearing aids work well in such situations, as they can amplify sound readily, but rarely lead to significant improvement in compromised speech discrimination. Some patterns of hearing loss, such as a loss in the low frequencies but normal hearing in the high frequencies can be challenging to fit with a hearing aid. Such patients may perform better without amplification than with it. Western languages rely on consonants to distinguish between words, and bringing high frequency hearing to the normal range is useful in these linguistic groups. Tonal languages, such as Chinese, use lower frequency vowel sounds to differentiate among words, increasing the importance of maximizing low frequency hearing.

Preferential seating in the classroom should be employed for all children with hearing loss, irrespective of cause. This involves seating the child in the front of the classroom, with the *better* ear toward the teacher to maximize acoustic input. A note to the teacher should be provided explicitly stating which ear should be nearer the teacher, as these situations can become confused. Some school districts can also provide Frequency Modulation (FM) systems for children with hearing loss which allow the teacher to speak into a worn microphone and the sound to be wirelessly transmitted to the student. Rehabilitation through amplification can become problematic as children reach their teenage years and become aware of the social stigma attached to hearing aids. Conversely,

even very young children can be convinced to wear hearing aids with sufficient parental effort. For significant CHL, it is important to provide amplification even for unilateral cases as absence of input from one ear will lead to lack of creation of connections between the ear and brain and can negatively affect the results of later surgical repair. Patients with a long-standing unilateral CHL that is not repaired until adulthood often complain of confusion from the new sound input of their previously deaf ear, due to fewer central neural connections having formed during maturation of the auditory system.

Surgical management of a confirmed middle ear conductive hearing loss is a treatment option that requires careful consideration. Several authors have published excellent reviews of the approaches utilized in the surgical management of CCHL, particularly stapedotomy (Raz 2002; Welling 2003; DeLaCruz 1994; Syms 1996; Teunissen 1993). The choice between amplification and surgical intervention is a complex one, and depends on the suspected underlying cause of the hearing loss, parental and patient preference, and financial considerations, among other issues. Surgery for CCHL with an intact tympanic membrane can be broadly divided into two categories: repair of the malleus and incus or stapedotomy. It is possible to operate on abnormalities of the malleus and incus (ossiculoplasty) with a low risk of permanent sensorineural hearing loss while stapedotomy carries with it a risk of sensorineural hearing loss that must be accepted by the parent and child. As it is unwise to perform stapedotomy in an ear prone to otitis media due to the associated increased risk of sensorineural hearing loss from infection, it should not be attempted in children prone to recurrent otitis media. Some authors advocate waiting until the age of majority to perform stapedotomy for ethical reasons surrounding the risk of profound sensorineural hearing loss (Syms 1996; Welling 2003).

When exploring the middle ear of a patient with CCHL, the surgeon should be prepared for multiple contingencies, including a mastoidectomy approach. Having a speculum holder and laser available can be useful, particularly if surgery of the stapes may be performed. A variety of prosthesis and/or bone cement should be available. Such explorations should ideally be performed by a skilled and experienced ear surgeon familiar with stapedotomy and its variations.

Stapedectomy generally refers to removal of the entire stapes suprastructure and footplate while stapedotomy generally refers to removal of the entire stapes suprastructure and fenestration of the foot plate; however, the terms are often used interchangeably and there is incomplete agreement on their use.

Reparable causes of stapes fixation include juvenile otosclerosis and congenital stapes fixation, with some authors arguing that surgical repair of the latter lead to less favorable results (Bachor 2005). A progressive hearing loss, positive family history, and fixed anterior stapediovestibular joint make otosclerosis more likely (Bachor 2005). Congenital stapes fixation can be seen in isolation or as part of a syndrome and is the most common cause of CCHL (Raz 2002). Stapes fixation presents at a younger age, usually between 3 and 6 (Raz 2002; Welling 2003), than juvenile onset otosclerosis, which presents around age 10 (DeLa Cruz 1999). Postoperative hearing improvement after stapedotomy for juvenile otosclerosis approximates the results seen in adults, while postoperative results of stapedotomy for congenital stapes fixation are somewhat poorer due to increased incidence of associated abnormalities such as stapes gusher (DeLaCruz 1994).

Ossiculoplasty in the setting of CCHL differs from surgery for acquired ossicular abnormality in that in CCHL the surgeon is much more likely to encounter malformed ossicles, fused malleus/incus complex, or other type of ossicular fusion. Discontinuity of the ossicular chain can be seen, most commonly due to a deficiency of the long process of the incus (Teunissen 1993). The surgeon should be prepared to perform a mastoidectomy or trancanal drilling to access the entirety of the ossicles, if needed. Fixed ossicles can either be directly mobilized or bypassed with ossicular chain reconstruction.

Surgical repair of other less common abnormalities is tailored to the abnormality found, and may not be operable through standard middle ear techniques without undue risk to sensorineural hearing or facial nerve function. Mobilization of the facial nerve and vestibulotomy in the setting of an absent oval window and other similarly heroic middle ear procedures have been described. However, since the advent of modern digital amplification and osseointegrated implants, such interventions are rarely performed.

Fenestration of the lateral semicircular canal can be performed in rare situations when the oval window is absent. In one reported series, it was performed in 20 out of 1,200 middle ear explorations (Ashtiani 2010). This procedure is analogous to that used for treatment of otosclerosis by the early giants of otology, such as Julius Lempert, prior to the introduction of a successful stapedectomy approach by John Shea, Jr in 1956.

Osseointegrated implants can be used to treat CCHL associated with external ear abnormalities that preclude use of traditional amplification, such as a narrow ear canal. These implants bypass the external and middle ears and stimulate the cochlea directly. The use of implantable hearing aid systems to couple either with remnant ossicles or the round window membrane may in the future become a more common option for middle ear malformation, which is not readily reparable with ossiculoplasty or stapedotomy.

In summary, CCHL is a rare but complex entity, at times associated with other syndromes or abnormalities. It is sometimes treatable through direct surgical repair, most often stapedotomy. Almost all cases of CCHL can be rehabilitated with a hearing aid or osseointegrated implants.

References

Ashtiani MD et al. (2010)
Carfrae (2010)
Cole (1980)
Cremers (1984)
Hermann (2005)
House (1980)
Paparella (1982)
Phillips (1986)
Pron G, Galloway C, Armstrong D, Posnick J (1993) Ear malformation and hearing loss in patients with treacher Collins syndrome. Cleft Palate Craniofac J 30(1):97–103
Raz Y, Lustig L (2002)
Ruckenstein MF, Macdonald RE, Clarke JT, Forte V (1991) The management of otolaryngological problems in the mucopolysaccharidoses: a retrospective review. J Otolaryngol 20(3):177–183
Stewart JM, Down MP (1993) Congenital conductive hearing loss: the need for early identification and intervention. Pediatrics 91:355–359
Swinnen FK, De Leenheer EM, Coucke PJ, Cremer CW, Dhooge IJ (2009) Audiometric, surgical, and genetic findings in 15 ears of patients with osteogenesis imperfecta. Laryngoscope 119(6):1171–1179
Syms CA, De La Cruz A (1996)
Teunissen (1993)
Welling et al. (2003)
Yildirim (2008)

Congenital Craniofacial Malformations and Their Surgical Treatment

John F. Teichgraeber[1], Jaime Gateno[2,3] and James J. Xia[1,2,3]

[1]Department of Pediatric Surgery, The University of Texas Health Science Center at Houston, Houston, TX, USA

[2]Department of Oral and Maxillofacial Surgery, The Methodist Hospital, Houston, TX, USA

[3]Department of Surgery, Weill Medical College of Cornell University, New York, NY, USA

Synonyms

Acrocephalosyndactyly type II; Acrocephalosyndactyly type III; Acrocephalopolysyndactyly; Brachycephaly; Craniofacial microsomia; Craniofacial dysostosis; Fibrous osteoma; First and second brachial arch syndrome; Goldenhar syndrome; Mandibulofacial dysostosis; Maxillonasal dysplasia; Oculoauriculo-vertebral syndrome; Ossifying fibroma; Oxycephaly; Parry Romberg syndrome; Pierre Robin syndrome; Plagiocephaly; Progressive hemifacial atrophy; Scaphocephaly; Tessier 7 cleft; Treacher collins-franceschetti syndrome; Trigonocephaly; Turricephaly; von Recklinghausen disease

Embryology

A discussion of craniofacial anomalies starts with human embryology of the face and skull. The crucial period of organogenesis is the first 12 weeks of gestation. This is where most of the congenital craniofacial anomalies appear. In the fourth embryonic week, the migration of the neural crest cells begin as the face takes form from the migration of the frontonasal and the maxillary and mandibular processes. In the fifth embryonic week, the primary palate takes shape from the fusion of the intermaxillary segment of the medial nasal process and the maxillary processes. In addition, the external ear begins to form from the first branchial groove, and the first and second branchial arches. This is the time that the forebrain and midbrain divide. In the sixth week, the primary palate continues to form. The medial nasal process gives rise to the columella,

prolabium, and premaxilla, while the lateral nasal processes give rise to the nasal alae and the lacrimal duct. In the seventh week, the eyes and ears migrate medially as the auricular hillocks coalesce around the external auditory canal. The secondary palate begins to form as the lateral palatine processes change to a horizontal orientation in order to begin secondary palatal fusion. Finally, in the eighth week of embryogenesis, the face and ears become defined as the eyes continue to move medially and the nasal bridge begins to take shape. The oral commissure also becomes smaller at this stage.

Classification

The simplest classification for craniofacial anomalies was the one proposed by the American Cleft Palate Association (1981) (Whitaker et al. 1981). They enumerate five categories and deformities.

I. Clefts
II. Craniosynostoses (Isolated or Syndromic)
III. Atrophy/Hypoplasia
IV. Neoplasia/Hyperplasia
V. Unclassified

Clefts

The most common facial cleft is cleft lip and palate (1:750 live births). The next most common cleft anomaly is hemifacial microsomia. The pathogenesis of facial clefting is now believed to be caused by a failure of mesodermal penetration. The originators of the theory believe that the face is composed of a bilaminar ectodermal membrane with the facial processes composed of epithelial seams. The mesenchyme penetrates the ectodermal layers to form the facial processes. If the mesenchymal penetration fails, the overlying ectodermal layers dehisce and a cleft is formed.

Tessier (1976) system is commonly used to classify facial clefts, with the orbit as the focus of the system. The clefts are numbered from 0 to 14 circumferentially in planes, which extend from the lips to the cranium. The cranial clefts extend from the upper eyelid while the facial clefts pass through the lower eyelid. The clefts 0, 1, 2, and 3 are associated with cleft lip. Hemifacial microsomia is associated with the number 7 cleft, while Treacher Collins is associated with 6, 7, and 8 clefts. Hypertelorism, encephaloceles, and

Congenital Craniofacial Malformations and Their Surgical Treatment,
Fig. 1 Tessier's classification of craniofacial clefts (Downloaded from: http://upload.wikimedia.org/wikipedia/commons/1/12/Picture_Tessier_classification.jpg, license: GNU Free Documentation License)
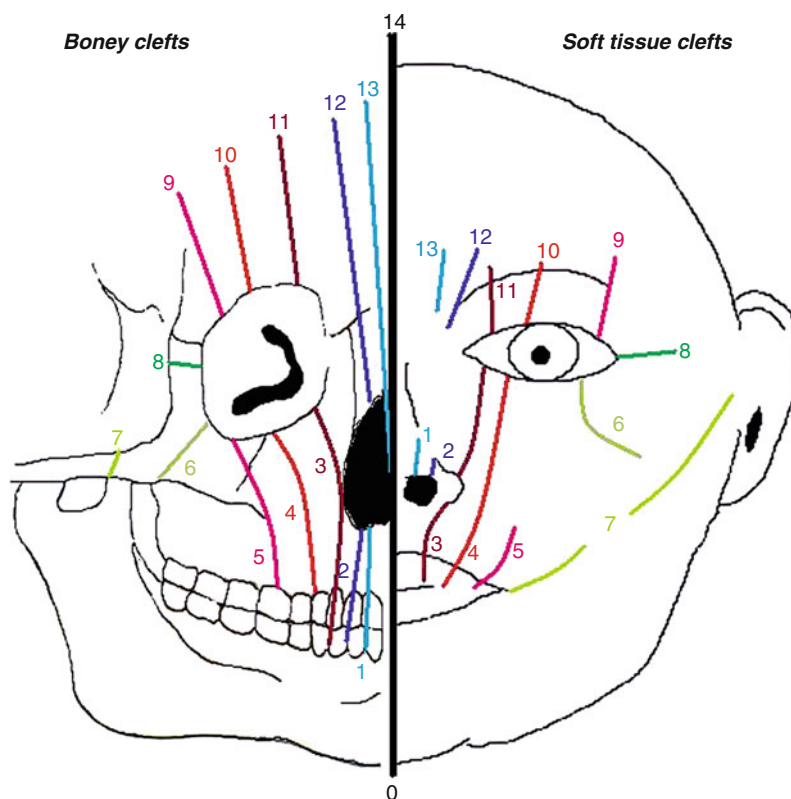
holoprosencephaly are associated with 12, 13, and 14 clefts (Fig. 1).

Hemifacial Microsomia

Definition Hypoplasia or aplasia of facial skeleton.

Epidemiology Hemifacial microsomia is the second most common craniofacial abnormality. The reported incidence is 1:5,600 live births. It is bilateral in 10–15% of patients (Poswillo 1973).

History The first recorded cases were by Canton in 1861 and von Arlt in 1881.

Clinical Features The deformity usually affects the external ear, mandible, and maxilla. However, it can also involve the orbit, zygoma, temporal bones, and frontal bones. Soft tissue deformities are found in the cheek, periorbital tissues, masticatory muscles, tongue, and soft palate. In addition, the patient may have macrostomia and facial nerve involvement. The spectrum of the disease varies from a simple

preauricular skin tag to craniofacial microsomia, affecting the bone and soft tissue of the face, the cranium, and the jaw. There is still controversy on whether the condition is progressive or nonprogressive (Fig. 2a–f).

There have been a number of classification systems developed to describe hemifacial microsomia. The most commonly used grading system was the one proposed by Pruzansky (Pruzansky 1969) and modified by Mulliken and Kaban (Mulliken and Kaban 1987). It is based on the extent of the mandibular deformity. In Type I, there is minimal mandibular hypoplasia. In type II, the ramus and condyle are small. Type IIA describes a patient with a normal glenoid fossa condyle relationship, while in Type IIB, the temporomandibular joint (TMJ) is nonfunctional. In Type III, there is only a small mandibular remnant with no TMJ.

Goldenhar's syndrome (oculoauriculovertebral syndrome) is a variant of hemifacial microsomia. It is bilateral and makes up 10% of the patient's with hemifacial microsomia. Besides mandibular

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 2 (continued)

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 2 A 16-year-old patient with hemifacial microsomia who underwent Le Fort I osteotomy, left side mandibular sagittal split osteotomy, and right side temporomandibular joint reconstruction using costochondral graft. (**a**) Preoperative frontal view; (**b**) Preoperative lateral view;

hypoplasia, these patients present with frontal bossing, low hairline, orbital epibulbar dermoids, and vertebral anomalies.

Tests Computed tomography

Differential Diagnosis
- Romberg' disease
- Treacher Collins syndrome
- Townes-Brocks syndrome

Etiology The etiology is thought to be linked to stapedial artery hemorrhage which results in damage to the first and second branchial arches. Tetragons, i.e., isotretinoin (Accutane) which is a vitamin A derivative, have been implicated in facial clefting and hemifacial microsomia. There is evidence that inheritance in these patients may be autosomal dominant with a low penetrance.

Treatment In patients with hemifacial microsomia, the macrostomia and preauricular tags are usually treated in the first year of life. In severe cases, orbitozygomatic grafts, rib grafts, and distraction osteogenesis of the mandible may be employed. This is usually begun at 5–6 years of age. This is done recognizing that with skeletal maturity, the patients will need additional orthognathic surgery and soft tissue reconstruction. Patients with mild hemifacial microsomia are usually treated with orthognathic surgery after they have completed facial growth (Fig. 2g–l).

Treacher Collins Syndrome
Definition Treacher Collins syndrome is a condition that affects the development of both the bones and soft tissues of the face. The characteristics features vary in severity. Most affected individuals have underdeveloped facial bones, particularly the cheekbones, and a very small jaw and chin. Some patients also

present with a cleft palate. In severe cases, the underdevelopment of the facial bones affects the infant's airway, causing potentially life-threatening respiratory problems.

Epidemiology Its incidence is 1:10,000–50,000 live births (Gorlin et al. 2000).

History The syndrome is named after Dr. Edward Treacher Collins (1862–1932), the English surgeon and ophthalmologist who described its essential traits in 1900. In 1949, Franceschetti and Klein described the same condition and first coined the term "mandibulofacial dysostosis."

Clinical Features The characteristic features of the syndrome include: sloping palpebral fissures, lower eyelid colobomas, malar and mandibular hypoplasia. The external ear deformities are also associated with hearing loss. Eyelashes are absent from the medial third of the lower eyelid. In addition, atypical hair growth is seen in a tongue-shaped extension of the hairline into the cheek. Most affected individuals have normal intelligence. The external and middle ear are malformed, although the inner ear is normal. A majority of patients (96%) have bilateral conductive hearing loss although neurosensory hearing loss has also been reported (Fig. 3).

Tests Genetic test for mutations of the *TCOF1* gene

Differential Diagnosis Nagger syndrome

Etiology This condition has an autosomal dominant pattern of inheritance, although 60% of cases resulted from new mutations. Mutations in the *TCOF1* (Treacher Collins-Franceschetti 1) gene cause Treacher Collins syndrome. This gene is located on chromosome 5 q31.3 to q33.3, and provides instructions for making a protein called treacle. This protein is

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 2 (continued) (**c**) Preoperative oblique view; (**d**) Preoperative frontal occlusion; (**e**) Preoperative frontal view of the three-dimensional model; (**f**) Preoperative lateral view of the three-dimensional model; (**g**) Postoperative frontal view; (**h**) Postoperative lateral view; (**i**) Postoperative oblique view; (**j**) Postoperative frontal occlusion; (**k**) Postoperative frontal view of the three-dimensional model; (**l**) Postoperative lateral view of the three-dimensional model

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 3 An 8-year-old patient with Treacher Collins syndrome. (**a**) Frontal view; (**b**) Lateral view

active during early embryonic development in structures that are precursors of the bones and soft tissues of the face. Studies suggest that treacle is involved in the production of ribosomal RNA (rRNA) within cells. rRNA helps assemble amino acids into functioning proteins. Treacle is active in the nucleolus which is the region inside the nucleus where rRNA is produced (Marsh et al. 1998).

Treatment Management of the airway is the first priority in Treacher Collins patients. In patients with a mild deformity, simple positioning with close monitoring is effective. In the neonatal period, tracheostomy and distraction of the mandible may also be needed. Lower eyelid colobomas are usually addressed early using the upper eyelid for reconstruction. The external ear reconstruction is begun at 5 years of age and utilizes autologous rib cartilage. The treatment of the facial skeleton is usually staged and delayed until 6–10 years of age. Bony reconstruction is similar to that in patients with hemifacial microsomia. Onlay bone grafting may be vascularized or nonvascularized. Orthognathic surgery, with or without distraction, is delayed until the adolescence. Soft tissue reconstruction may require fat grafts or free tissue transfer. Finally, nasal reconstruction is also completed at time of orthognathic surgery.

Binder Syndrome

Definition Patients with Binder syndrome usually present with a short and flat nasal bridge, short columella, and perialar flatness.

Epidemiology Unknown.

History The syndrome was first reported by von Binder in 1962.

Clinical Features The nose has a retracted columella lip angle, poor tip projection, lack of normal triangular base flare, crescent shaped nostrils without a sill. The lip has a shallow Cupids bow. There is a perpendicular alar-cheek junction and perialar flattening (Fig. 4).

Tests Computed tomography

Differential Diagnosis Binder syndrome must be differentiated from other syndromes with craniosynostosis. These include midline cleft Tessier I.

Etiology Sixteen percent of the patients have a hereditary basis. The inherence may be autosomal recessive with incomplete penetrance (Rival et al. 1974).

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 4 A 16-year-old patient with Binder syndrome. (**a**) Frontal view; (**b**) Lateral view
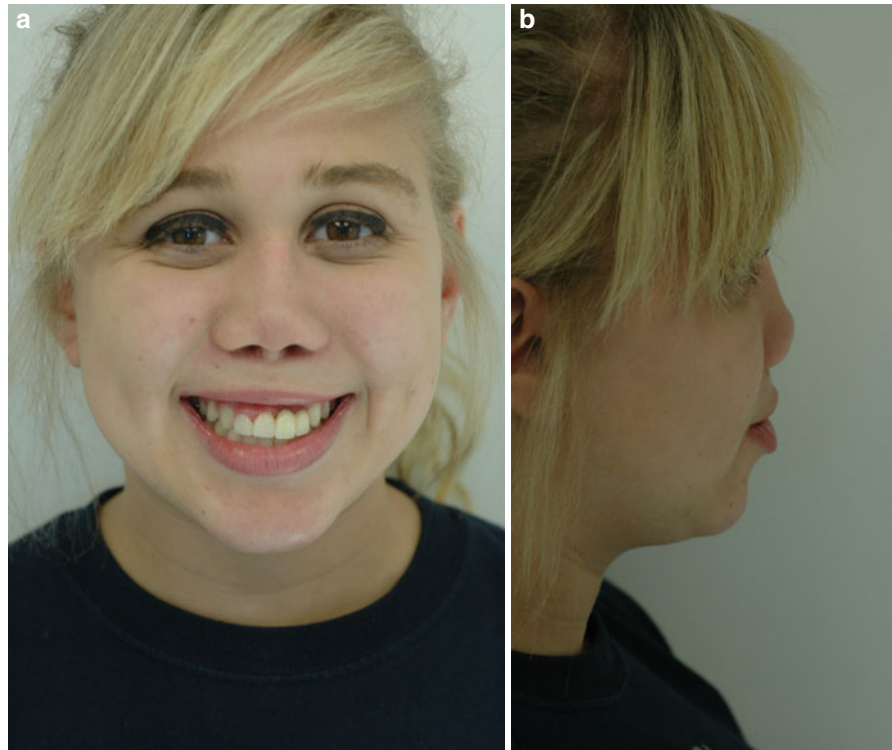
Treatment Nasal reconstruction is complex and involves autologous grafts. Ancillary procedures include nasofrontal osteotomies, Le Fort II or Le Fort I osteotomy.

Pierre Robin Sequence
Definition The features include: glossoptosis, micrognathia, and airway obstruction.

Epidemiology The reported incidence varies between 1: 5,000 and 1:50,000 live births (Fletcher et al. 1969).

History In 1923, Pierre Robin noted the characteristics which make up the sequence.

Clinical Features The classical triad is micrognathia, glossoptosis, and airway obstruction. Cleft palate is present in approximate 50% of the patients. The glossoptosis causes increased respiratory effort and energy expenditure. A combination of impaired feeding and respiratory compromise can produce cardiorespiratory failure. The sequence is associated with a number of other syndromes which include: Stickler syndrome, Fetal Alcohol syndrome, Treacher Collins syndrome, and bilateral hemifacial microsomia (Fig. 5).

Tests Nasal endoscopy, blood gas analysis, and polysomnography.

Differential Diagnosis
- Congenital temporomandibular joint ankylosis
- Bilateral hemifacial microsomia

Etiology Uterine constraint results in head flexion which impedes mandibular growth. The projection of the base of the tongue prevents normal palatal fusion.

Treatment Most infants can be managed by positioning. Surgical treatment is reserved for patients who fail to thrive and demonstrate obstructive apnea. The surgical treatment includes tongue-lip adhesion, mandibular distraction, and tracheostomy.

Congenital Craniofacial Malformations and Their Surgical Treatment,
Fig. 5 A 3-year-old patient with Pierre Robin sequence. (**a**) Frontal view; (**b**) Lateral view
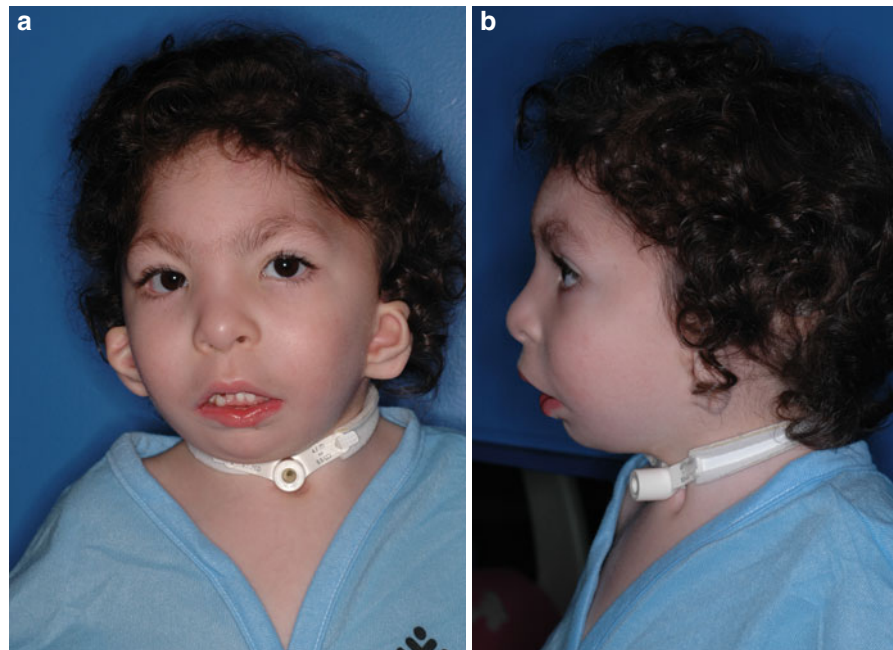
Isolated Craniosynostoses

Definition

Premature fusion of one or more cranial sutures.

Epidemiology

The incidence of isolated craniosynostosis is estimated at 1 to 2,000–2,900 live births. Eighty percent of patients with craniosynostosis present with isolated suture involvement and 20% are syndromic (Cohen 1979). The distribution of nonsyndromic patients based on frequency of presentation is: sagittal, unicoronal, metopic, bicoronal, lambdoidal, and multiple.

Sagittal craniosynostosis is the most common nonsyndromic craniosynostosis (50–60%). The incidence is 1:4,200 live births. The incidence of increased intracranial pressure (ICP) is 7–13% and the incidence of learning or behavior problems is reported to be as high as 50% (Gorlin et al. 2000; Cohen 1979; Renier and Marchac 1988).

Unicoronal craniosynostosis is the next most frequently occurring isolated craniosynostosis (20%). Its incidence is 1:5,000 to 1:10,000 live births. The incidence of increased ICP is 3–12.5%. The most frequent reported sequelae associated with unicoronal synostosis is strabismus (72%) (Gorlin et al. 2000; Cohen 1979; Renier and Marchac 1988).

Metopic craniosynostosis makes up 4–15% of the reported cases of nonsyndromic craniosynostosis. Its incidence is 1:5,000 to 1:10,000 live births. The incidence of increased ICP is 7.9%, and the incidence of learning and behavioral problems is 30–50% (Gorlin et al. 2000; Cohen 1979; Renier and Marchac 1988).

Bicoronal craniosynostosis makes up 5% of the reported cases of isolated craniosynostosis. It is most commonly associated with syndromal craniosynostosis. The incidence is 1:50,000 lives births, and the incidence of increased ICP is 30% (Gorlin et al. 2000; Cohen 1979; Renier and Marchac 1988).

Lambdoidal craniosynostosis is the least common of the nonsyndromic craniosynostoses (less than 1%). The incidence is usually less than 1:100,000 live births. It primarily presents unilaterally but can also present bilaterally. The incidence of increased ICP is 3% (Gorlin et al. 2000; Cohen 1979; Renier and Marchac 1988).

History

Virchow in 1851 noted that skull growth was promoted in the direction of the synostosed suture and restricted perpendicularly.

Clinical Features

Patients with sagittal craniosynostosis present with frontal bossing, an occipital shelf and bilateral

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 6 A 2-month-old patient with sagittal craniosynostosis. (**a**) Preoperative frontal view; (**b**) Preoperative lateral view; (**c**) Preoperative vertex view; (**d**) Postoperative frontal view (7 year-old); (**e**) Postoperative lateral view; (**f**) Postoperative vertex view

parieto-occipital narrowing. The skull is oblong with increased sagittal length and decreased coronal width (Fig. 6a–c).

Patients with unicoronal craniosynostosis present with ipsilateral flattening of the forehead and orbit, and elevation and recession of the supraorbital bar. This results in a harlequin eye. There is also contralateral bossing of the frontal forehead with deviation of the nasal root to the affected side (Fig. 7).

Patients with metopic craniosynostosis present with a midline frontal ridge, bifrontal temporal narrowing, and orbital hypotelorism (Fig. 8).

Patients with bicoronal craniosynostosis present with brachycephaly. The skull has an increased temporoparietal diameter and a decreased anterior posterior diameter. In addition, the vertical height of the skull is increased as is the forehead. The patients have hypoplastic orbital rims and protuberant frontal and temporal bones (Fig. 9).

Patients with lambdoidal craniosynostosis present with ipsilateral occipital temporal mastoid flattening. There is also ipsilateral posterior positioning of the ear, and a contralateral parietal and frontal bossing (Fig. 10).

Tests

Computed tomography and genetic test for mutations of the *TCOF1* gene
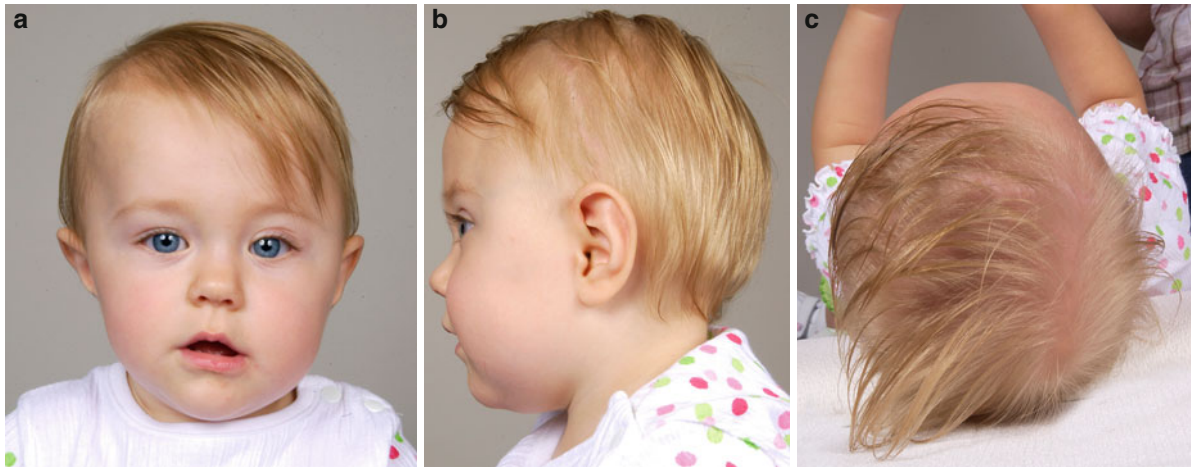
Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 7 A 2-month-old patient with unicoronal craniosynostosis (*left side* affected). (**a**) Frontal view; (**b**) Left view; (**c**) Vertex view
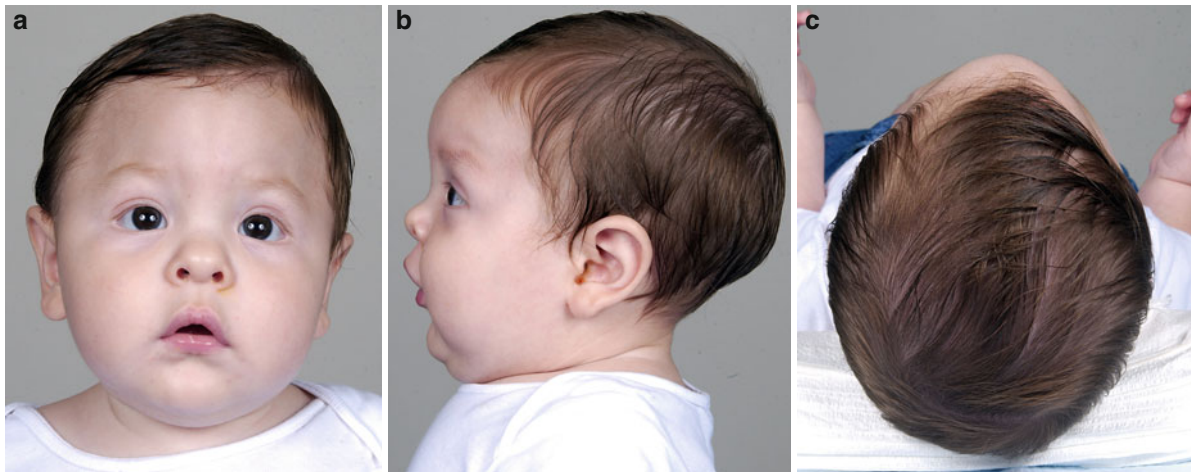
Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 8 A 6-month-old patient with metopic cranio-synostosis. (**a**) Frontal view; (**b**) Lateral view; (**c**) Vertex view

Differential Diagnosis
- Positional plagiocephaly
- Syndromic craniosynostosis

Etiology

The inheritance is sporadic with a random hereditary component seen in 2% of patients. The pathogenesis of craniosynostosis is still unclear but it is clearly multi-factorial. Craniosynostosis results from a combination of dura-related, genetic, molecular, and cellular causes (Cohen 1979). FGR3 has been implicated in isolated unicoronal synostosis (Gripp et al. 1998).

Treatment

The treatment goal of craniosynostosis is to normalize the skull, reduce the orbital and facial deformities, and to relieve the increased ICP. The surgical management of isolated sagittal synostosis varies from limited strip craniectomies to extensive reconstruction of the forehead and cranial vault. There are proponents of the open and the minimally invasive approach in these patients. The surgery is performed at less than 3 months of age with the minimally invasive approach, and after 6 months of age in the open approach (Fig. 6d–f).

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 9 A 3-month-old patient with bicoronal craniosynostosis. (**a**) Frontal view; (**b**) Lateral view
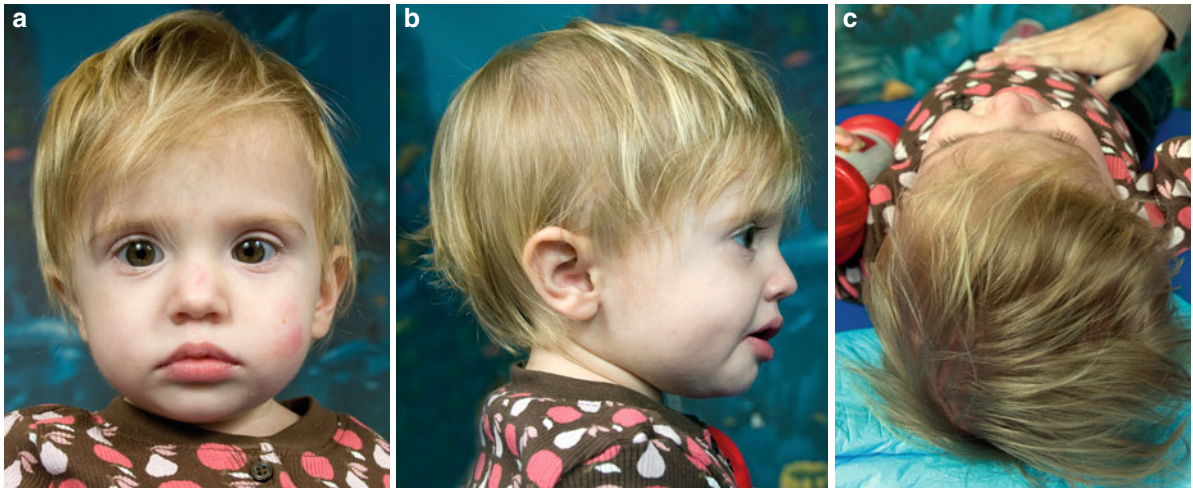
Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 10 A 6-month-old patient with lambdoidal craniosynostosis (*right* side affected). (**a**) Frontal view; (**b**) Lateral view; (**c**) Vertex view

The treatment of unicoronal and metopic craniosynostosis involves an open approach with bifrontal reconstruction and supraorbital bar reconstruction. There are some reports on the use of the minimally invasive approach in less severely affected patients (Baumgartner et al. 2005). Significant dimorphism can be seen in patients with unicoronal craniosynostosis, necessitating the orthognathic surgery in adolescence.

The treatment of bicoronal craniosynostosis also involves the open approach between 6 and 9 months of age, and entails a bifrontal craniotomy reconstruction and supraorbital bar reconstruction. In addition, there have been also reports on the minimally invasive approaches (Baumgartner et al. 2005; Barone and Jimenez 1999).

The treatment of lambdoidal craniosynostosis prior to 3 months of age may involve a minimally invasive approach with a lambdoidal strip craniectomy and helmet therapy. After 3 months of age, the open approach is used with biparietal-occipital craniotomy and reconstruction.

Syndromic Craniosynostosis

Crouzon Syndrome

Definition Patients with Crouzon syndrome present with exorbitism, proptosis, midface hypoplasia, and retrogenia. They also have bicoronal craniosynostosis.

Epidemiology The incidence of the Crouzon syndrome is 1:25,000 live births (Cohen 1979).

History Crouzon syndrome was first described by the French neurosurgeon Dr. Crouzon in 1912.

Clinical Features Patients with Crouzon syndrome present with normal intelligence. The cranial vault is brachycephalic with recess supraorbital rim and frontal bones. They have midface hypoplasia, retrogenia, exorbitism, and arched nose which resembles a parrots beak (Fig. 11a, b). They often have strabismus and increased ICP (30–60%).

Tests Genetic tests for FGFR2 (Britto et al. 2001a).

Differential Diagnosis
- Apert syndrome
- Pfeiffer syndrome
- Saethre-Chotzen syndrome
- Carpenter syndrome
- Bicoronal craniosynostosis
- Jackson-Weiss syndrome

Etiology The inheritance is autosomal dominant. Recently FGFR2 has been associated with Crouzon patients (Britto et al. 2001a).

Treatment Bifrontal craniotomy and supraorbital bar advancement and reconstruction are performed at 6 months of age. The midface deformity is managed at 6–8 years of age with a Le Fort III or monobloc, with or without distraction osteogenesis (Fig. 11c–f). At skeletal maturity, most patients require orthognathic surgery (Le Fort I osteotomy and mandibular split.

Apert Syndrome

Definition Patients with Apert syndrome present with exorbitism, proptosis, midface hypoplasia, and retrogenia. They also have bicoronal craniosynostosis. In addition, they present with syndactyly of the hands and feet. This usually involves the digits 2–4 with 1 in 5 being variably fused. In 30% of the patients, there is a cleft palate.

Epidemiology The incidence of the syndrome is 1:100,000 to 1:160,000 live births and the incidence of increasing ICP is 45% (Tessier 1985).

History Apert syndrome was originally described by Wheaton in 1894.

Clinical Features The median IQ for patients with Apert syndrome is lower (70%) than the standard population, but the patient's are not mentally retarded. The skull is brachiocephalic with a bregmatic bump and a hypertelorism. The face is flat with short zygomatic arches, maxillary hypoplasia, exorbitism, antimongoloid slant to the palpebral fissures (Fig. 12). Their limbs have syndactyly of the fingers, leaving the thumb free. In their adolescence, they develop significant facial acne.

Tests Genetic tests for FGFR2 (Britto et al. 2001b).

Differential Diagnosis
- Apert syndrome
- Pfeiffer syndrome
- Saethre-Chotzen syndrome
- Carpenter syndrome
- Bicoronal craniosynostosis
- Jackson-Weiss syndrome

Etiology The inheritance is autosomal dominant. Recently FGFR2 has been associated with Apert patients (Britto et al. 2001a).

Treatment Bifrontal craniotomy and supraorbital bar advancement and reconstruction are performed at 6 months of age. The midface deformity is managed at 6–8 years of age with a Le Fort III or monobloc, with or without distraction osteogenesis. At skeletal maturity, most patients require orthognathic surgery (Le Fort I osteotomy and mandibular split). Surgical correction of the syndactyly should begin at 6 months, and the digital separation should be completed by 3 years.

Pfeiffer Syndrome

Definition Patients with Pfeiffer syndrome usually present with turribrachycephaly, coronal

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 11 A 5-year-old patient with Crouzon syndrome. (**a**) Preoperative frontal view; (**b**) Preoperative lateral view; (**c**) Intraoperative view of the Le Fort III internal distractor; (**d**) Lateral view during midface distraction; (**e**) Postoperative frontal view; (**f**) Postoperative lateral view

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 12 A 2-year-old patient with Apert syndrome. (**a**) Frontal view; (**b**) Lateral view
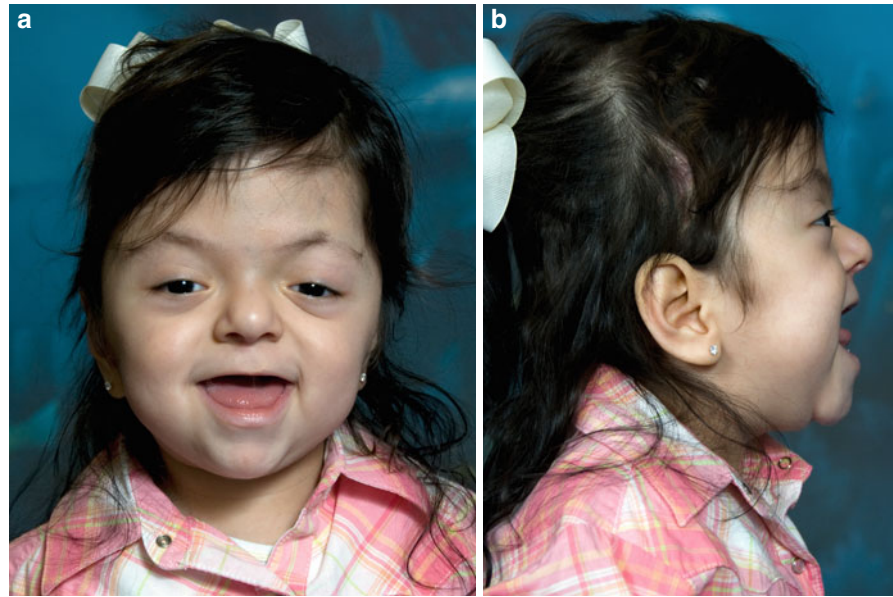
craniosynostosis, maxillary hypoplasia, and broad thumbs and toes.

Epidemiology The incidence of the syndrome is 1:100,000 of live births (Gorlin et al. 2000).

History The syndrome was first reported by Rudolf Pfeiffer in the 1963.

Clinical Features The patients are described as a low Apert syndrome. They present with broad thumbs and toes, severe midface hypoplasia, and bicoronal craniosynostosis. Their intelligence quotient is normal but varies according to subgroup. Cohen I is the classic Pfeiffer but with only bicoronal craniosynostosis. Cohen II has multi-suture craniosynostosis with hydrocephalus and increased intracranial pressure (Fig. 13). Cohen III has multi-suture craniosynostosis with hydrocephalus, severe ocular proptosis, and a short anterior cranial base. Neurologic and airway compromise are common in Cohen II and III patients. Moreover, there is a high infant mortality in both groups.

Tests Genetic tests for FGFR1 and FGFR2.

Differential Diagnosis Pfeiffer syndrome must be differentiated from other syndromes with craniosynostosis. These include Crouzon, Apert, Saethre-Chotzen, and Carpenter syndromes.

Etiology The inheritance is usually sporadic but autosomal dominant transmission with complete penetrance has also been frequently reported (Tolarova et al. 1997). Recently fibroblast growth factors (FGFR1 and FGFR2) have been found to be associated with Pfeiffer syndrome (Britto et al. 2001b).

Treatment Bifrontal craniotomy and supraorbital bar advancement and reconstruction are performed at 6 months of age. The midface deformity is managed at 6–8 years of age with a Le Fort III or monobloc, with or without distraction osteogenesis. At skeletal maturity, most patients require orthognathic surgery (Le Fort I osteotomy and mandibular split).

Saethre-Chotzen Syndrome

Definition Patients with Saethre-Chotzen syndrome usually present with simply syndactyly of the hands, bicoronal craniosynostosis, low hairline, and upper eyelid ptosis.

Epidemiology The incidence of the syndrome is 1:25,000–50,000 of live births (Gorlin et al. 2000).

History The syndrome was first reported by Saethre in the 1931 and by Chotzen by 1932.

Clinical Features The patients are described as an upper Apert. They present with bicoronal

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 13 A 7-year-old patient with Pfeiffer syndrome. (**a**) Frontal view; (**b**) Lateral view; (**c**) Intraoral view

craniosynostosis, a low hairline, and upper eyelid ptosis. Their hands have partial cutaneous syndactyly, usually involving the second and third fingers. They usually have normal intelligence.

Tests Genetic tests for FGFR2, FGFR3, and TWIST.

Differential Diagnosis Saethre-Chotzen syndrome must be differentiated from other syndromes with craniosynostosis. These include Crouzon, Apert, Pfeiffer, and Carpenter syndromes.

Etiology The inheritance is usually sporadic but autosomal dominant transmission with complete penetrance has also been frequently reported (Tolarova et al. 1997). Recently fibroblast growth factors

(FGFR2 and FGFR3) have been found associated with Saethre-Chotzen syndrome (Britto et al. 2001b).

Treatment Bifrontal craniotomy and supraorbital bar advancement and reconstruction are performed at 6 months of age. The midface deformity is managed at 6–8 years of age with a Le Fort III or monobloc, with or without distraction osteogenesis. At skeletal maturity, most patients require orthognathic surgery (Le Fort I osteotomy and mandibular split).

Carpenter Syndrome
Definition Patients with Carpenter syndrome usually present with craniosynostosis, brachydactyly, simple syndactyly, congenital heart disease, obesity, hypogenitalism, and umbilical hernia.

Epidemiology The incidence of the syndrome is 1:1,000,000 of live births (Gorlin et al. 2000).

History The syndrome was originally reported by Carpenter in 1901.

Clinical Features The patients present with variable craniosynostosis. The coronal, sagittal, and lambdoidal sutures can all be individually affected. Patients may also present with pansynostosis and Kleeblattschädel anomaly. In addition to syndactyly and brachydactyly of the hand, the feet may have various deformities and pre-axial polysyndactyly. Cardiac anomalies occur in a third of patients while 75% of the patients have intellectual impairment.

Tests Magnetic resonance angiogram (MRA) and magnetic resonance venogram (MRV) for vascular anomalies prior to surgery.

Differential Diagnosis Carpenter syndrome must be differentiated from other syndromes with craniosynostosis. These include Crouzon, Apert, Pfeiffer, and Saethre-Chotzen syndromes.

Etiology The inheritance is autosomal recessive (Gorlin et al. 2000).

Treatment If the patients present with pansynostosis, they must be treated with early craniotomy for their increased intracranial pressure. Otherwise, bifrontal craniotomy and supraorbital bar advancement and reconstruction are performed at 6 months of age. The midface deformity is managed at 6–8 years of age with a Le Fort III or monobloc, with or without distraction osteogenesis. At skeletal maturity, most patients require orthognathic surgery (Le Fort I osteotomy and mandibular split).

Atrophy/Hypoplasia
Romberg's Disease
Definition Romberg's disease is progressive hemifacial atrophy which involves skin, soft tissue, and bone.

Epidemiology Unknown

History Initially described Parry and later detailed by Romberg in 1846.

Clinical Features Romberg's disease usually presents in the first decade of life with progressive atrophy of the skin, soft tissue, and bone of the face. It is most commonly seen in females, and it is unilateral in 95% of the patients. The classic coup de saber is where there is soft tissue loss in the upper face. This is seen in 50% of the patients (Fig. 14).

Tests Clinical photographs

Differential Diagnosis
• Hemifacial microsomia

Etiology The etiology is unknown. A number of theories have been proposed which include: infection, trigeminal peripheral neuritis, scleroderma, and lymphocytic neurovasculitis. The tissue analysis of Romberg's patients reveals lymphocytic vasculitis with changes in the vascular endothelium and basement membrane (Pensler et al. 1990).

Treatment The treatment of Romberg's disease is usually delayed until the disease has been inactive for a year. The treatment involves both bone and soft tissue reconstructions. It utilizes free and/or pedicle flaps, autologous fat injection, and orthognathic surgery.

Neoplasia/Hyperplasia
Fibrous Dysplasia
Definition Fibrous dysplasia is a benign bone disease in which the medullary bone is replaced by fibrous tissue. The bone tumors of fibrous dysplasia are monostotic or polystotic.

Epidemiology Unknown

History Fibrous dysplasia was first described by von Recklinghausen in 1891 (Edgerton et al. 1985).

Clinical Features The disease may be present in a monostotic or a polystotic form. The monostotic form is commonly seen in ribs, femur, tibia, cranium, maxilla, and mandible. In the craniomaxillofacial skeleton, the most commonly affected bones are frontal, sphenoid, and maxilla. Albright syndrome is a rare form of fibrous dysplasia. In this syndrome, the polystotic form of fibrous dysplasia is seen with abnormal pigmentation, premature puberty, and hyperthyroidism (Fig. 15).

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 14 A 25-year-old patient with Romberg's disease. (**a**) Frontal view; (**b**) Lateral view

The presentation varies according to the location of the tumor. It may include cranial nerve palsies and ophthalmic symptoms. The incidence of malignant degeneration has been reported as 0.4% and is associated with radiation.

Tests Computed tomography

Differential Diagnosis
- Giant cell tumor
- Osteoma
- Osteogenic sarcoma

Etiology Unknown

Treatment The current treatment involves radical resection and primary reconstruction for midface and orbital involvement. Conservative resection is advocated for the cranium, skull base, and tooth-bearing bone. Fronto-orbital decompression is employed in patients with orbital involvement and decreasing visual acuity.

Neurofibromatosis
Definition Neurofibromatosis (NF) is a hereditary neuroectodermal disease which affects skin,

subcutaneous tissue, and bone. There are two types of neurofibromatosis: NF1 and NF2. NF1 is the most common type and is known as von Recklinghausen disease. NF2 is known as bilateral acoustic neurofibromatosis.

Epidemiology The reported incidence is 1 in 3,000 live births for NF1, and 1 in 45,000 live births for NF2 (Krastinova-Lolov and Hamza 1996).

History Neurofibromatosis was first described by Friedrich Daniel von Recklinghausen in 1882.

Clinical Features NF1 patients present with cutaneous neurofibromas and plexiform neurofibromas involving neural tissues. Additional dermatologic signs include: café au lait spots, and freckling of the groin or axilla. Skeletal abnormalities include sphenoid dysplasia and cortical thinning of the long bones. Ophthalmologic findings include optic nerve tumors and freckling of the iris (Lisch Nodules) (Fig. 16). Central nervous system findings include epilepsy and macrocephaly without hydrocephalus.

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 15 A 13-year-old patient with fibrous dysplasia. (**a**) Frontal view; (**b**) Intraoral view; (**c**) Frontal view of the three-dimensional model

NF2 patients present with bilateral acoustic neuro-fibromas. The characteristic sign of NF2 is hair loss around the age of 20. The tumors may also affect the vestibular system and facial nerve.

Tests Genetic test for chromosomal abnormalities of chromosome 17 (NF1) and 22 (NF2).

Differential Diagnosis
- Lipoma
- Hemangioma
- Lymphangioma

Etiology Genetic mutations on two different chromosomes are responsible for NF1 and NF2. The gene for NF1 is located on the long arm of chromosome 17, while the gene for NF2 is located on the long arm of chromosome 22 (Krastinova-Lolov and Hamza 1996).

Treatment Surgical treatment is conservative since the tumor growth is slow and irregular. Segmental debulking procedures are employed. Orbitotemporal neurofibromatosis is particularly problematic. Surgery is characterized by incomplete excision and high complication rates.

Congenital Craniofacial Malformations and Their Surgical Treatment, Fig. 16 A 22-year-old patient with Neurofibromatosis (*right* side affected). (**a**) Frontal view

Unclassified

There are a number of abnormalities that do not fit in the four listed categories of cranial anomalies. These include: macroglossia and epicanthal folds (Whitaker et al. 1981).

Cross-References

▶ Hemifacial Microsomia
▶ Lipoma
▶ Lymphangioma
▶ Romberg's disease

References

Barone CM, Jimenez DF (1999) Endoscopic craniectomy for early correction of craniosynostosis. Plast Reconstr Surg 104(7):1965–1973, discussion 74-5

Baumgartner JE, Teichgraeber JF, Waller AL, Grantcherova E, Gateno J, Xia JJ (2005) Microscopic approach to craniosynostosis. J Craniofac Surg 16(6):997–1005

Britto JA, Evans RD, Hayward RD, Jones BM (2001a) From genotype to phenotype: the differential expression of FGF, FGFR, and TGFbeta genes characterizes human cranioskeletal development and reflects clinical presentation in FGFR syndromes. Plast Reconstr Surg 108(7):2026–2039, discussion 40-6

Britto JA, Chan JC, Evans RD, Hayward RD, Jones BM (2001b) Differential expression of fibroblast growth factor receptors in human digital development suggests common pathogenesis in complex acrosyndactyly and craniosynostosis. Plast Reconstr Surg 107(6):1331–1338, discussion 9-45

Cohen MM Jr (1979) Craniosynostosis and syndromes with craniosynostosis: incidence, genetics, penetrance, variability, and new syndrome updating. Birth Defects Orig Artic Ser 15(5B):13–63

Edgerton MT, Persing JA, Jane JA (1985) The surgical treatment of fibrous dysplasia. With emphasis on recent contributions from cranio-maxillo-facial surgery. Ann Surg 202(4):459–479

Fletcher MM, Blum SL, Blanchard CL (1969) Pierre Robin syndrome pathophysiology of obstructive episodes. Laryngoscope 79(4):547–560

Gorlin RJ, Cohen MM, Hennekam RCM (2000) Syndromes of the head and neck. Oxford University Press, New York

Gripp KW, McDonald-McGinn DM, Gaudenz K, Whitaker LA, Bartlett SP, Glat PM et al (1998) Identification of a genetic cause for isolated unilateral coronal synostosis: a unique mutation in the fibroblast growth factor receptor 3. J Pediatr 132(4):714–716

Krastinova-Lolov D, Hamza F (1996) The surgical management of cranio-orbital neurofibromatosis. Ann Plast Surg 36(3):263–269

Marsh KL, Dixon J, Dixon MJ (1998) Mutations in the Treacher Collins syndrome gene lead to mislocalization of the nucleolar protein treacle. Hum Mol Genet 7(11):1795–1800

Mulliken JB, Kaban LB (1987) Analysis and treatment of hemifacial microsomia in childhood. Clin Plast Surg 14(1):91–100

Pensler JM, Murphy GF, Mulliken JB (1990) Clinical and ultrastructural studies of Romberg's hemifacial atrophy. Plast Reconstr Surg 85(5):669–674, discussion 75-6

Poswillo D (1973) The pathogenesis of the first and second branchial arch syndrome. Oral Surg Oral Med Oral Pathol 35(3):302–328

Pruzansky S (1969) Not all dwarfed mandibles are alike. Birth Defects 5:120

Renier D, Marchac D (1988) Craniofacial surgery for craniosynostosis: functional and morphological results. Ann Acad Med Singapore 17(3):415–426

Rival JM, Gherga-Negrea A, Mainard R, Delaire J (1974) Binder's maxillo-nasal dysostosis. Apropos of 10 cases. J Genet Hum 22(3):263–268

Tessier P (1985) Ch 27, Apert's syndrome: acrocephalosyndactyly type I. In: Caronni EP (ed) Craniofacial surgery. Little Brown, Boston, pp 280–303

Tolarova MM, Harris JA, Ordway DE, Vargervik K (1997) Birth prevalence, mutation rate, sex ratio, parents' age, and ethnicity in Apert syndrome. Am J Med Genet 72(4):394–398

Whitaker LA, Pashayan H, Reichman J (1981) A proposed new classification of craniofacial anomalies. Cleft Palate J 18(3):161–176

Congenital Cysts, Sinuses, and Fistulae

Aaron Wood[1] and Kevin D. Pereira[2]
[1]Department of Otorhinolaryngology-Head and Neck Surgery, University of Maryland School of Medicine, Baltimore, MD, USA
[2]Department of Otorhinolaryngology-HNS, University of Maryland School of Medicine, Baltimore, MD, USA

Introduction

The embryologic processes that create the uniquely complex anatomy of the head and neck may also produce regional anomalies later identified as congenital cysts, sinuses, or fistulae. These lesions are usually identified in childhood, but at times may not manifest until adulthood. They can be classified by location (midline versus lateral) or developmental precursor (branchial, glandular, germ cell layer, or vascular). Nearly all exhibit benign behavior and complete excision is generally curative, although recurrence or malignant degeneration is occasionally seen. Understanding the embryology of these anomalies is critical for differentiating them from similar acquired infectious, inflammatory, or neoplastic lesions.

Branchial Cleft Anomalies

Normal Branchial Embryology

The branchial apparatus refers to a series of mesodermal arches at the cranial portion of the developing embryo with intervening external ectoderm-lined clefts and internal endoderm-lined pouches. The entire apparatus extends from the developing oral cavity to the respiratory diverticulum. The four main arches are numbered in a craniocaudad direction; the fifth and sixth arches are rudimentary. Each arch is fed by a different arterial branch off the aorta and is served by a different cranial nerve (see Table 1). First identified in the fourth week of gestation, the branchial arches are ultimately obliterated by mesenchymal growth and fusion by the end of the seventh week. The first cleft persists, with the dorsal portion forming part of the external auditory canal. The corresponding pouch gives rise to the tubotympanic recess, which then forms the eustachian tube, tympanic cavity, and mastoid antrum. Externally, the first and second arches each develop three hillocks (of His) of tissue by the sixth week. These ultimately fuse to form both the auricle and cartilaginous portion of the external auditory canal (EAC). Around the fifth week, the ventral aspect of the second arch enlarges and grows over the lower third and fourth arches to form the cervical sinus (of His), an ectodermal depression which is obliterated during further development. This explains the observation that external openings of second, third, and fourth sinuses/fistulas are found in the same region of the neck. Internal openings correspond to the final destination of the corresponding branchial pouches: The second pouch forms part of the tonsillar fossa, the third produces the inferior parathyroid glands and thymus, and the fourth develops into the superior parathyroid gland and parafollicular cells of the thyroid (from the intermediate ultimobranchial body). Both third and fourth pouches are ultimately associated with formation of the pyriform sinuses (see Fig. 1).

Definition of Anomalies

First described by von Ascherson in 1832, branchial cleft anomalies account for 30% of all congenital head and neck lesions (Waldhausen 2006). Cysts, sinuses, and fistulae of branchiogenic origin are epithelium-lined structures derived from the embryonic precursors described above. Cysts refer to hollow structures lined with squamous and/or pseudostratified columnar epithelium that have no opening either externally or internally. This epithelium is frequently associated with follicular lymphoid tissue and occasionally sebaceous or salivary tissue. Sinuses are blind tracts with a single opening, although they may exhibit a complex arborized pattern within tissues. These tracts may extend either outward to skin or inward connecting to foregut structures. Fistulae extend from skin surface to foregut mucosa and follow convoluted courses determined by the embryologic development of structures adjacent to the branchial cleft/pouch in question. Specifically, these tracts pass deep to structures derived from the branchial arch above them and superficial to structures arising from the arch below. Both sinuses and fistulae usually display pseudostratified columnar epithelium and only occasional lymphoid tissue (Mandell 2000).

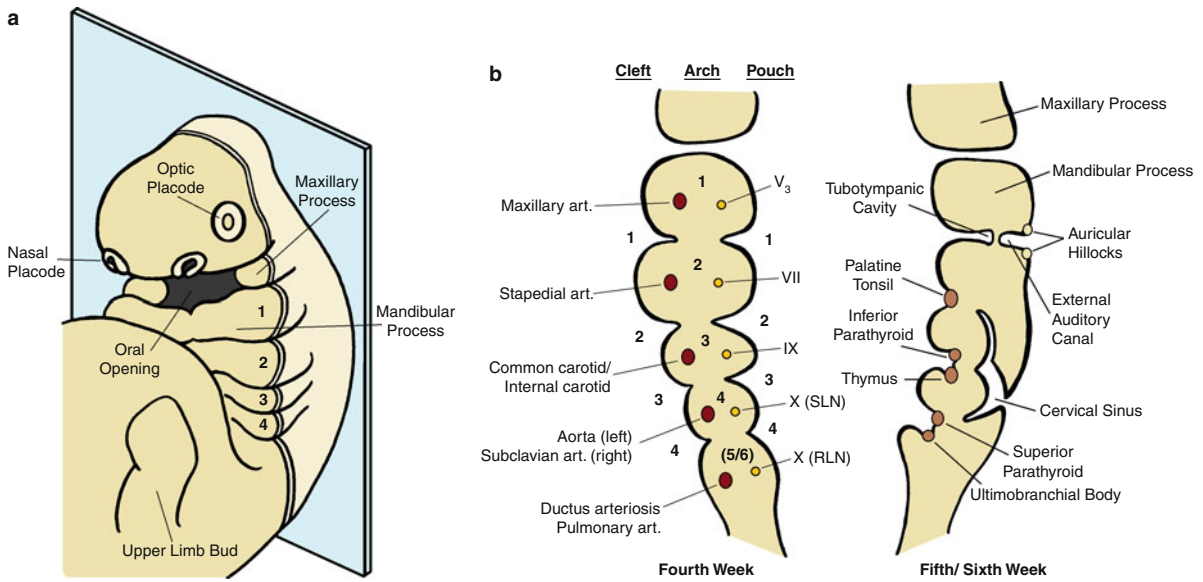**Congenital Cysts, Sinuses, and Fistulae, Table 1** Branchial arch derivatives

Arch	Artery	Nerve	Muscle	Cartilage/Bone
First	Portion of maxillary artery (degenerates)	V_3 branch of Trigeminal nerve (V)	Temporalis	Mandible
			Masseter	Sphenomandibular ligament
			Medial and lateral pterygoids	Maxilla
			Mylohyoid	Zygoma
			Anterior belly of digastric	Head/neck of malleus
			Tensor veli palatini	Anterior ligament of malleus
			Tensor tympani	Body/short process of incus
Second	Stapedial artery (degenerates)	Facial nerve (VII)	Muscles of facial expression	Styloid process
			Buccinator	Stylohyoid ligament
			Platysma	Superior portion of hyoid
			Posterior belly of digastric	Manubrium of malleus
			Stylohyoid	Long process of incus
			Stapedius	Stapes superstructure
Third	Common carotid artery, Internal carotid artery	Glossopharyngeal nerve (IX)	Stylopharyngeus	Inferior portion of hyoid
			Superior pharyngeal constrictor	Greater cornu of hyoid
			Middle pharyngeal constrictor	
Fourth	Aorta (left), Subclavian artery (right)	Superior laryngeal nerve (X)	Cricopharyngeus	Thyroid cartilage
			Inferior pharyngeal constrictor	Cuneiform cartilage
			Cricothyroid muscle	
Fifth/ Sixth	Ductus arteriosus, Pulmonary artery	Recurrent laryngeal nerve (X)	Intrinsic muscles of larynx	Cricoid cartilage
				Arytenoids cartilages
				Corniculate cartilages

Auricular Hillock Anomalies

Preauricular sinuses (pits), cysts, and skin tags are believed to arise from defects of auricular hillock development and are sometimes mistaken for first branchial cleft defects. These defects occur along the fusion line of the first and second branchial arches and may therefore be found anywhere between the external auditory canal and oral commissure. The majority of hillock abnormalities are unilateral, right-sided, and sporadic, with bilateral defects more frequently inherited and/or associated with genetic syndromes. They are usually identified incidentally just anterior to the helical root or tragus. Recurrent infection is the primary indication for surgical excision, although delaying surgery until the acute inflammatory process is resolved reduces recurrence. These lesions do not involve significant neurovascular structures but often follow a tortuous and branching course extending down to auricular perichondrium or temporal bone periosteum. The proximity of the upper branches of the facial nerve should be kept in mind during dissection. Recurrence has been reported to occur anywhere from 0% to 40%. To minimize the risk of recurrence, standard operative technique involves removing a cuff of tissue around the lesion, including its deep attachments, to ensure complete excision (Tan et al. 2005).

Preauricular pits are one of the most prominent components of branchio-oto-renal (BOR) syndrome. This autosomal dominant disorder also exhibits variable types of hearing loss due to middle or inner ear anomalies (95%), other branchial cleft anomalies (86%), and renal malformations (60%). Minor criteria include auricular or palate malformations, preauricular tags, lacrimal duct stenosis, facial asymmetry, and shoulder

Congenital Cysts, Sinuses, and Fistulae, Fig. 1 (**a**, **b**) Embryology of the branchial apparatus

defects. Significant phenotypic variability is seen in BOR syndrome, with recent genetic studies showing corresponding genetic heterogeneity between families. In addition to audiometric evaluation of hearing loss, all suspected cases should undergo abdominal imaging to avoid delay in diagnosis of occult renal abnormalities (Senel et al. 2009; Acierno and Waldhausen 2007).

First Branchial Cleft Anomalies

The most widely accepted definition of a first branchial cleft anomaly is one resulting from a defect in the fusion of the first and second branchial arches. Accordingly, they are intimately associated with the EAC, parotid gland, and facial nerve. First cleft anomalies are generally accepted to constitute 10% of all branchial anomalies. Cysts are twice as common as sinuses or fistulae, and most come to clinical attention following infection. Female and left-sided preponderance has been suggested by some groups, although others have noted equality of gender and sidedness (Mandell 2000). Cysts are generally seen in young adults, whereas sinuses and fistulae are more common in children.

Several classification systems have been developed to describe these lesions. The first system, proposed by Arnot in 1971, divided first cleft defects into two groups based on anatomy and histology. Type I defects travel between the mandible and stylohyoid ligament to become closely associated with the lower parotid and facial nerve branches. Type II defects pass from the EAC below the parotid to terminate anteroinferior to the angle of the mandible. Histologically, only type II anomalies contain adnexal structures. The following year, Work proposed a similar system (Work 1972), which has become the most widely accepted classification scheme. Work Type I defects constitute duplications of the membranous external auditory canal, run parallel to the EAC passing superior to the facial nerve, and contain only ectodermal components. In contrast, Work Type II defects are duplications of both membranous and cartilaginous portions of the external canal and therefore contain skin and cartilage. They are more intimately associated with the facial nerve and the parotid gland than Type I lesions. Unfortunately, these anatomic defects and their histologic contents do not always correlate with their proposed origin. Several reports have found anatomically defined Work Type I anomalies which contain mesodermal structures, while some Type II anomalies display only epidermal tissue. Of course, any classification that relies on histologic criteria is of limited value for preoperative planning. Olsen et al. suggested identifying a first cleft defect simply as a cyst, sinus, or fistula to determine a preferred operative approach (Triglia et al. 1998).

Cysts often mimic preauricular/parotid masses, while sinuses and fistulae classically present with

Congenital Cysts, Sinuses, and Fistulae, Fig. 2 Infected first branchial cleft fistula with a sinus opening located inferior to the tragus

Congenital Cysts, Sinuses, and Fistulae, Fig. 3 Excision of a first branchial cleft fistula via a modified parotidectomy incision
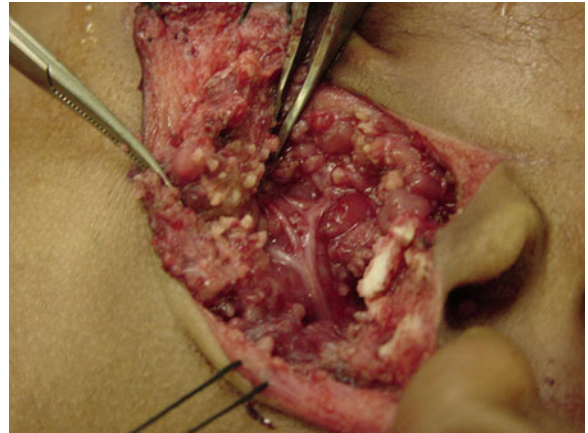
otorrhea in an ear with an intact tympanic membrane. In the latter, special attention should be paid to involvement of skin and cartilage of the EAC. Sinus tract openings may be found at any point along the length of the EAC, although most occur at the anteroinferior bony cartilaginous junction. A large case series noted that 10% of first cleft tracts exhibit a membranous attachment between the canal floor and tympanic membrane (Triglia et al. 1998). External tract openings are found superior to the hyoid bone within a roughly triangular area bounded by the EAC meatus, border of mandible, cervical midline, and hyoid bone (Triglia et al. 1998) (see Fig. 2). Imaging is of little value in defining the course of these tracts, which usually involve the parotid gland and may run medial, lateral, or through the facial nerve trunk (Mandell 2000). Because of this, a formal parotidectomy incision and facial nerve dissection should be part of all first branchial cleft excisions (see Figs. 3 and 4). Intraoperative dissection may be facilitated by injecting methylene or contrast dye into a tract or cannulating the defect with a lacrimal probe. Transient facial nerve weakness is relatively common following excision. Fortunately, permanent facial paralysis and recurrence is rare, as long as surgery is delayed until any acute infection has resolved.

Second Branchial Cleft Anomalies

The vast majority (60–90%) of branchial cysts, sinuses, or fistulae are derived from the second branchial apparatus. These defects occur along a tract

Congenital Cysts, Sinuses, and Fistulae, Fig. 4 Facial nerve visible after excision of a first branchial cleft fistula and superficial parotidectomy

that passes from the superior tonsillar fossa, between the internal and external carotid arteries, over the glossopharyngeal and hypoglossal nerves, and pierces the platysma along the anterior border of the SCM. Cystic lesions are identified three times more often than fistulas or sinuses. These may be classified as lateral to the carotid sheath (Type I), adjacent to the carotid bifurcation (Type II), passing between the internal and external carotid arteries (Type III), or adjacent to the pharynx (Type IV) (Waldhausen 2006). They are usually first noted as an enlarged and/or painful neck mass in the setting of upper

respiratory infections (see Fig. 5). Rarely, Type IV cysts present as an oropharyngeal mass with associated dysphagia and/or dyspnea. CT or MRI, along with needle biopsy, is frequently used to distinguish these cysts from cervical abscesses or neoplasms (see Fig. 6). Sinuses and fistulas are usually identified with chronic drainage from an opening anterior to the SCM (see Fig. 7). CT or MRI is less successful with noncystic lesion, although injection of radiopaque contrast into a cannulated opening may be used to define these tracts. In general, cysts are identified more often in adults, and sinuses/fistulae more often seen in children, with 6% having a family history of branchial lesions (Mandell 2000).

Although incision and drainage is best avoided to minimize scarring, many second branchial cleft cysts

Congenital Cysts, Sinuses, and Fistulae, Fig. 5 Right second branchial cleft fistula with an inflamed sinus opening in the lower neck

are identified only after multiple episodes of acute infection. Definitive treatment requires complete surgical excision once the acute infectious process has resolved. Cannulation of the tract or injection of methylene blue has been used to facilitate identification of the tract intraoperatively. Use of several small transverse "stairstep" incisions minimizes conspicuous scar while maintaining acceptable exposure (see Fig. 8a, b). Care is taken to excise the tract with an adequate cuff of normal tissue to minimize the risk of recurrence. Functional neck dissection may be required for heavily scarred tracts. In a classic retrospective series of over 200 patients treated for cervical branchial cleft cysts at the Mayo Clinic, the overall recurrence rate was 5.8%. Significantly, patients with a history of previous surgery had a recurrence rate of 21%, while those with no history of surgery or infection recurred only 2.7% of the time (Deane and Telander 1978).

Of special note is the controversial entity of branchiogenic carcinoma. There have been over 300 case reports of neck masses in adults believed to be branchial cleft cysts and found to contain squamous cell carcinoma. On the other hand, it is generally believed that regional lymph node metastases from occult head and neck primaries are much more common than branchial cleft cysts. Tonsillar cancer is especially known for developing cystic metastases. Utilizing strict criteria proposed by Martin et al. in 1950 and refined by Khafif et al. in 1989, the majority of reported cases cannot be confirmed as definitively branchiogenic. In fact, less than 20 cases have successfully been shown to both demonstrate anatomic/histologic characteristics of branchial anomalies as well as fail to demonstrate an alternative mucosal primary tumor (Girvigian et al. 2004). Ultimately, these cases are treated in the same manner
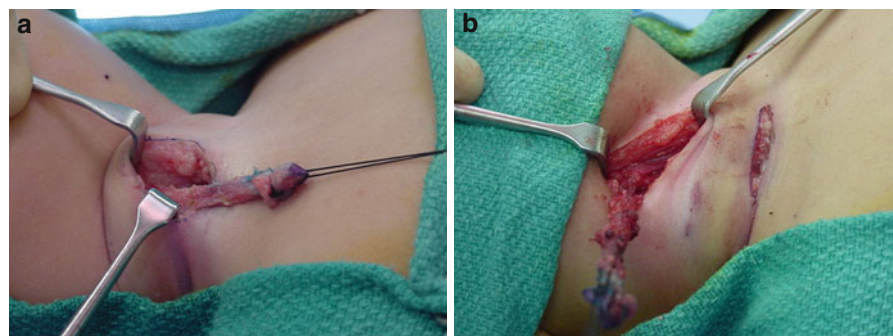
Congenital Cysts, Sinuses, and Fistulae, Fig. 6 (a, b) Excision of a second branchial cleft fistula via a stepladder incision

Congenital Cysts, Sinuses, and Fistulae, Fig. 7 Second branchial cleft cyst of the right neck
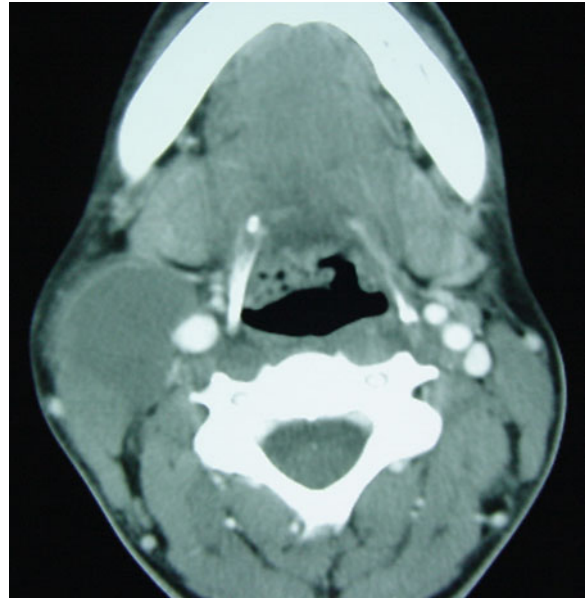
Congenital Cysts, Sinuses, and Fistulae, Fig. 8 CT with contrast showing a second branchial cleft cyst anterior to the SCM and lateral to the carotid sheath (Type II)

as isolated cervical squamous cell carcinoma, namely, a complete excision as part of a formal neck dissection usually followed by external beam radiotherapy.

Third and Fourth Branchial Cleft Anomalies

Much has been written about these rare anomalies due to controversy over identification, etiology, and management. They constitute 3–10% of all branchial anomalies and usually present as lateral neck abscesses or recurrent thyroiditis. In neonates, cystic lesions may be associated with obstructive airway symptoms (Pereira et al. 2004). Several series suggest a slight female preponderance and a significant left-sided predominance. The classic embryological course of a third cleft fistula would be expected to pass from the upper lateral pyriform wall, through the thyrohyoid membrane, behind the internal carotid artery, cranial to the superior laryngeal nerve, between glossopharyngeal and hypoglossal nerves, and down along the carotid sheath to pierce the platysma at the anterior border of the SCM. A fourth cleft fistula would pass from the pyriform to the cricothyroid joint, between superior and recurrent laryngeal nerves, and dive down into the mediastinum to loop around the aorta (on the left) or subclavian artery (on the

right). From there, it would ascend to pass above the hypoglossal nerve before piercing platysma and at the anterior SCM border. Ultimately, third and fourth branchial cleft anomalies can only be differentiated from one another at the time of surgery. Third cleft tracts should pass cranial to the superior laryngeal nerve (a fourth branchial arch derivative) while fourth cleft tracts are found beneath this nerve. Furthermore, histologic examination should show thymic tissue limited to third cleft defects and parafollicular C cells to fourth cleft defects. However, reports of accessory thymic tissue derived from fourth pouch precursors do complicate histologic identification of third and fourth tracts (Pahlavan et al. 2009).

In practice, it is often difficult to establish the identity of a third or fourth branchial cleft defect. To date, no definitive description of a complete tract following the theoretical path of a fourth cleft fistula has been reported. This has prompted several investigators to propose alternative etiologic explanations for these lesions. Due to association of these tracts with the

Congenital Cysts, Sinuses, and Fistulae, Fig. 9 (**a**) Sagittal T1-weighted MRI showing air present in a third branchial cleft cyst. (**b**) Coronal T2-weighted MRI showing air present in a third branchial cleft cyst
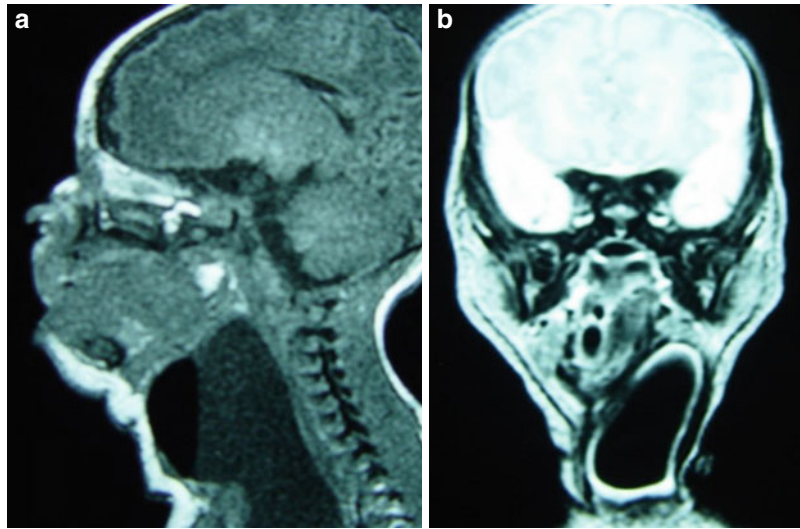

thyroid and thymus, it has been proposed that they actually represent remnants of a thymopharyngeal duct. This structure descends from each third branchial pouch into the anterosuperior mediastinum during the seventh and eighth week of gestation. The ducts pass through the area of the developing thyroid to form the two halves of the thymus gland. Previous identification of thymic rests within the thyroid gland as well as thyroid tissue within the thymus lends support to this theory (James et al. 2007).

The diagnostic evaluation of third and fourth cleft anomalies usually begins with recognition of a pattern of recurrent supportive neck infections (see Fig. 9). Asymptomatic neck masses or sinus openings are uncommon. Initial imaging usually involves ultrasound or CT, with air within a cyst or sinus tract considered pathognomonic for a branchial anomaly (see Figs.10a, b, and 11). Barium swallow has an 80% sensitivity for a pyriform sinus tract, but must be delayed until acute infection has resolved to avoid false-negative results due to edema of the pyriform opening (see Fig. 12) (Pahlavan et al. 2009). Aspiration of a cystic mass can provide material for microbiologic culture. Nonbranchial cervical cysts typically contain skin flora such as Staph and Strep, while those with a connection to the pyriform sinus have been shown to harbor oral flora and anaerobes (Pahlavan et al. 2009). Ultimately, definitive diagnosis requires direct visualization of a pyriform sinus tract opening by direct laryngoscopy.

Congenital Cysts, Sinuses, and Fistulae, Fig. 10 Recurrent supperative thyroiditis after previous incision and drainage of a fourth branchial cleft anomaly

Treatment has traditionally involved surgical excision of the entire tract including any pyriform sinus or cutaneous openings. As with first and second branchial cleft defects, cannulation of the tract may assist with identification of its course in the neck. Special care must be employed when dissecting near the cricothyroid joint to avoid injury to the recurrent laryngeal nerve. Oblique thyrotomy has been shown to provide good surgical exposure while avoiding joint
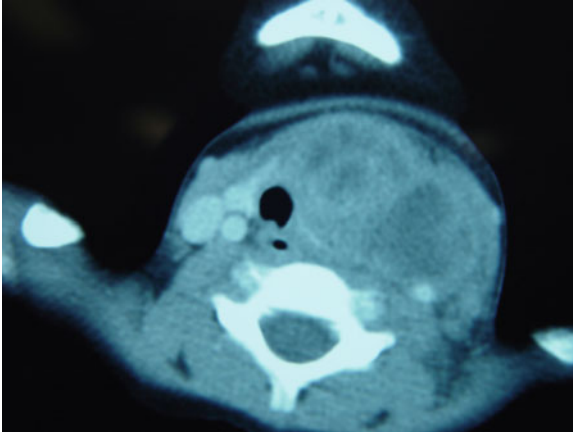
Congenital Cysts, Sinuses, and Fistulae, Fig. 11 Axial CT with contrast showing a left-sided fourth branchial cleft cyst with compression of the internal jugular vein
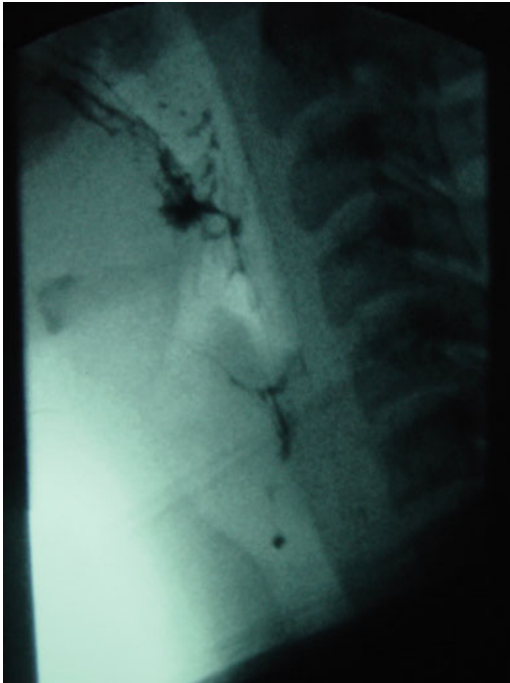
Congenital Cysts, Sinuses, and Fistulae, Fig. 12 Barium swallow showing a fistula tract from the left pyriform fossa

manipulation. Because of the close association of these anomalies with the thyroid gland, hemithyroidectomy is routinely performed by many surgeons to decrease recurrence. However, a review by Nicoucar et al. did suggest similar failure rates following excision with or without partial thyroidectomy for third cleft defects associated with recurrent thyroiditis (Nicoucar et al. 2010). More recently, minimally invasive surgical interventions have been contemplated. Cauterization with electrocautery, silver nitrate (Pereira and Davies 2006), or trichloroacetic acid (Nicoucar et al. 2010) may be used to close a mucosal pyriform sinus tract visualized on endoscopy. This simple procedure has recently emerged as a successful primary treatment modality in approximately 75% of patients. Formal surgical excision can then be reserved for those patients with recurrent disease.

Midline Cervical Clefts

Although branchial cleft anomalies are typically lateral structures, rare midline defects have been associated with abnormal branchial development. Less than 100 cases of midline cervical clefts have been reported to date. They present as asymptomatic, congenital, vertically oriented clefts in the midline cervical skin between the mandible and sternum. These clefts histologically lack skin appendages but may contain muscle or cartilage. The superior portion of the cleft usually exhibits a protruding "nipple" of thickened skin, while the inferior cleft is continuous with a short sinus tract (see Fig. 13). These clefts may be associated with other midline defects of the oral cavity, sternum, or cardiac structures. Theories of origin include development from bronchial primordia or a thyroglossal duct. However, the most widely accepted theory is that the cleft represents impaired fusion of the first and second branchial arches. Due to the obvious cosmetic deformity and contracture over time producing torticollis, this anomaly is treated with surgical excision followed by Z-plasty closure prior to the second year of life (Mlynarek et al. 2003).

Thyroglossal Duct Cysts

Normal Thyroid Embryology

The anatomic location of thyroglossal duct cysts (TGDCs) is a direct consequence of normal thyroid development. Beginning in week four of gestation, the median thyroid anlage develops between the anterior (first branchial arch derivative) and posterior (second and third branchial arch derivative) muscle groups of the tongue. As the embryo elongates, this anlage becomes a diverticulum which descends in the cervical
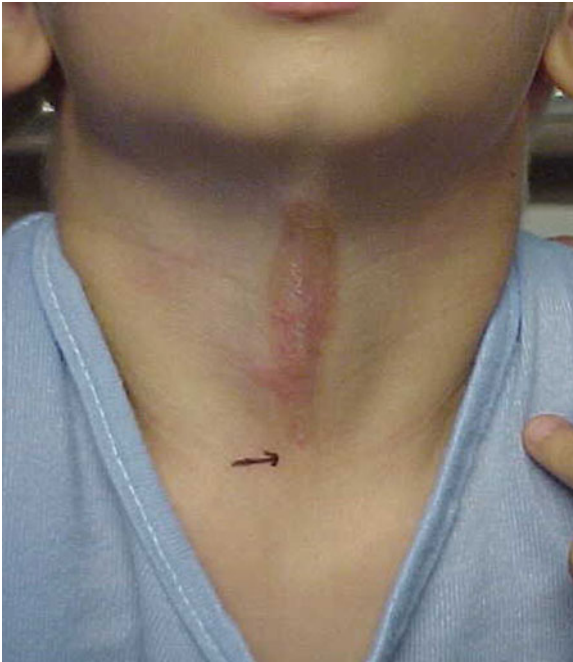
Congenital Cysts, Sinuses, and Fistulae, Fig. 13 Midline cervical cleft. *Arrow* denotes a punctum at the inferior aspect of the cleft

soft tissues anterior to the airway to rest in the midline lower neck. During descent, the fourth branchial pouch contributes the lateral thyroid anlage, which provides future parafollicular C cells. Under normal circumstances, the thyroglossal duct obliterates by gestational week 5–10, with the superior portion becoming the foramen cecum and inferior portion forming a pyramidal lobe of the thyroid gland in 30% of the population (Rosa et al. 2008). TGDCs are a consequence of a duct that fails to obliterate. They may be found anywhere from tongue base to suprasternal notch, although the majority are found adjacent (60%) or superior (24%) to the hyoid bone (Foley and Fallat 2006). The development of the hyoid bone is particularly relevant to management of TGDCs, as anterior hyoid fusion occurs during decent of the thyroglossal duct. Histologic evaluation of excised thyroglossal tracts shows them to be lined by ductal epithelium and to frequently contain solid thyroid tissue. All are intimately associated with the hyoid, with 70% of tracts coursing anterior to the bone, 30% running in the posterior hyoid space, and rare cases passing through the substance of the hyoid bone (Mondin et al. 2008). Importantly, over 50% of

specimens have demonstrated arborization of the tract superior to the hyoid (Chandra and Palmer 2006).

Diagnosis and Management

The majority of TGDCs present as an asymptomatic, cystic midline neck mass identified within the first five years of life. These masses typically elevate with tongue protrusion or swallowing due to connections to the tongue base and hyoid (see Fig. 14a, b). Less frequent cases are those that come to clinical attention following suppurative infection, complaints of recurrent foul oral drainage from a patent foramen cecum, or symptoms of airway compression. Despite lack of skin involvement during normal thyroid development, up to 25% of thyroglossal defects exhibit a cutaneous draining sinus, likely from prior spontaneous or surgical drainage of a TGDC abscess (Foley and Fallat 2006). An important subset of TGDC patients (<2%) are those with median ectopic thyroid, where the thyroglossal tract contains the patient's only functional thyroid tissue. Median ectopic thyroid glands are usually hypofunctional and become hypertrophic as a result (Foley and Fallat 2006).

Controversy exists regarding the optimal workup for an uncomplicated TGDC. Most practitioners obtain ultrasound or CT imaging to define the anatomy of the lesion and confirm the presence of thyroid tissue in the normal location (see Fig. 15a, b). Fine-needle biopsy, frequently employed in the diagnosis of adult neck masses, typically provides nonspecific cytologic results. Due to the potential for median ectopic thyroid, some authors advocate routine radionucleotide scanning of all patients. Others have argued that these cases are apparent as they exhibit distinctly solid components on ultrasound as well as clinical hypothyroidism. Preoperative ultrasound and screening TSH level therefore represent a more cost-effective method of identifying patients who will require postexcision thyroid replacement therapy (Rosa et al. 2008).

Surgical extirpation remains the standard treatment for TGDCs. Classically, this has involved excision of the cyst, medial portion of the hyoid bone, and thyroglossal duct tract up to the foramen cecum as described by Sistrunk in 1920. Intraoral digital pressure on the tongue base may assist in this dissection, although it is not necessary to violate the mucosa to obtain complete resection (Mondin et al. 2008). The Sistrunk procedure avoids the frequent recurrence noted by earlier surgeons by addressing the ductal
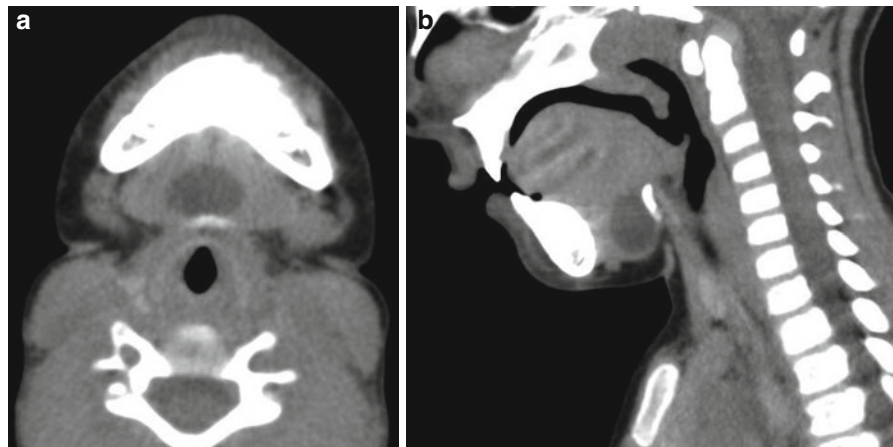
Congenital Cysts, Sinuses, and Fistulae,
Fig. 14 (**a**) Thyroglossal duct cyst adjacent to the hyoid. (**b**) Elevation of a thyroglossal duct cyst with tongue protrusion
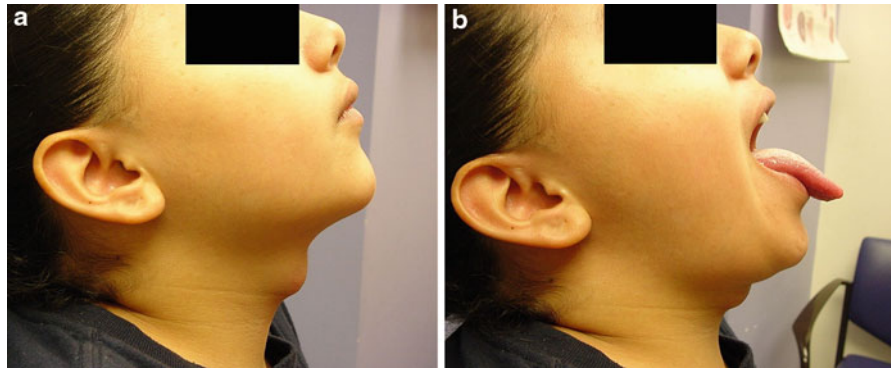
Congenital Cysts, Sinuses, and Fistulae,
Fig. 15 (**a**) Axial CT of a thyroglossal duct cyst located anterior to the hyoid bone. (**b**) Sagittal CT of a thyroglossal duct cyst located anterior to the hyoid bone

remnants adjacent to the hyoid or contained in accessory tracts within the tongue base musculature. A large meta-analysis of 950 patients treated with Sistrunk's procedure showed an overall recurrence rate of 6.6%. This compares favorably to the 20% recurrence when only the TGDC and medial hyoid are removed or the nearly 50% recurrence seen with simple incision and drainage (Mondin et al. 2008). Surgical management of a median ectopic thyroid is more controversial. When this represents a patient's only thyroid tissue, some practitioners will excise and autotransplant the frozen-section-confirmed solid component into the SCM, rectus, or quadriceps muscles. However, the frequent hypofunction of this tissue and risk of future malignant degeneration have led many to eschew reimplantation for planned thyroid hormone supplementation (Foley and Fallat 2006).

Congenital Germ Cell Layer Defects

Introduction

A subset of congenital head and neck cystic lesions are derived from defects in the organization of one or more of the three primary germ cell layers (ectoderm, mesoderm, and endoderm). Although a consequence of localized abnormal embryologic development, they may not be identified until adulthood in certain cases. Several theories have been advanced to explain the origin of these defects. Many are found along embryonic lines of fusion, suggesting possible entrapment of germ cell remnants during development. Alternatively, implantation of germ cells into adjacent tissues following intrauterine trauma or sequestration of isolated rests of pluripotent stem cells may lead to cystic abnormalities (Rosa et al. 2008). The identity and behavior

of these congenital cysts is determined by the number of germ cell layers involved.

Epidermoids

Epidermoid cysts are the simplest germ cell layer lesion, consisting of only a single layer of ectoderm. Histologically, these cysts are lined with stratified squamous or ciliated epithelium and usually contain keratin debris within the cyst lumen. Although often associated with an inflamed hair follicle, the cyst does not contain cutaneous adnexal structures, as these are of mesodermal origin. The presence of exposed keratin and/or recurrent inflammation/infection may produce a local granulomatous reaction. These lesions typically present in adults and are more commonly seen in males (Rosa et al. 2008). They have been found throughout the soft tissues of the head and neck, as well as involving bony structures of the paranasal sinuses and skull base. Superficial cysts are typically mobile, fluctuant, and nontender. Deeper lesions may be imaged with a combination of ultrasound, CT, and/or MRI. Treatment typically involves simple excision, with care taken to obtain complete cyst wall removal and minimize spillage of cyst contents. Marsupialization of paranasal sinus epidermoids has been described, but this requires long-term follow-up to surveil for recurrence (Chandra and Palmer 2006).

Dermoids

Dermoid cysts are the third most common congenital head and neck abnormalities, after thyroglossal duct and branchial anomalies. Dermoids may be found throughout the body, with 7% occurring in the head and neck. These may be classified into four groups based on anatomic location. Group 1 cysts occur in the periorbital region and constitute roughly 70% of head and neck dermoids. Group 2 lesions occur within the nasal dorsum and make up around 10%, while Groups 3 and 4 involve the submental and lower cervical regions of the neck, respectively, and together account for 20% of the total (Pryor et al. 2005). Histologic examination reveals both ectoderm-derived epithelium and mesoderm-derived structures such as hair follicles, sebaceous glands, smooth muscle, and adipose tissue. Dermoids are typically identified in childhood but may present in adults after years of accumulating keratin/sebaceous debris. Complete surgical excision is curative, although CT is advocated to rule out intracranial involvement of lesions adjacent to the skull base (Pryor et al. 2005).
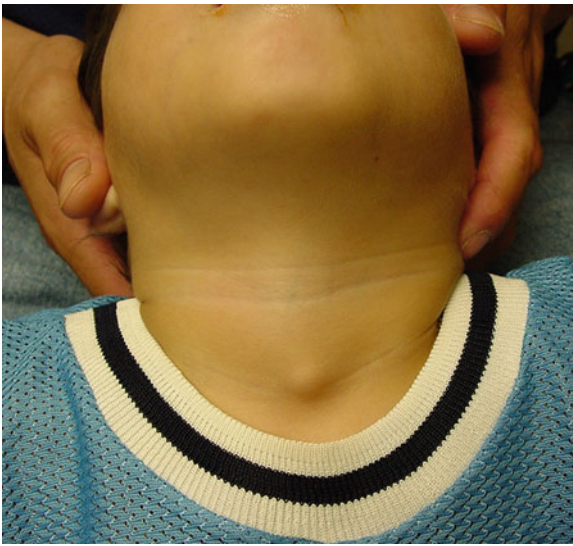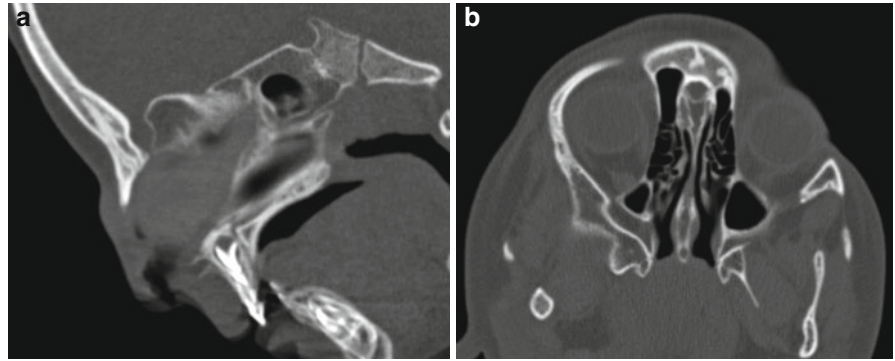

Congenital Cysts, Sinuses, and Fistulae, Fig. 16 Infected dermoid cyst of the nasal dorsum

Nasal dermoid cysts are typically identified as noncompressible swellings of the nasal dorsum located between the columella and glabella. A cutaneous sinus opening exhibiting both protruding hair and sebaceous drainage is common, as is recurrent infection of the cyst and surrounding soft tissues (see Fig. 16). Of paramount importance is characterization of a nasal dermoid's relationship to the contents of the cranial vault. Intracranial extension has been estimated to occur in 5–40% of cases and to significantly increase the risk of intracranial infection. A combination of CT and MRI is advocated to characterize the anatomy of the dermoid tract and allow for preoperative planning. Classic CT findings include an enlarged foramen cecum and bifid crista galli (see Fig. 17a, b). MRI is used to differentiate dermoid cysts, which give a high-intensity signal on T1-weighted images but do not enhance with contrast, from other skull base masses. Care must be taken to differentiate normal anatomic variants such as nonossification of the cribriform plate in neonates and fatty replacement of the crista galli in adolescents from intracranial dermoid extension. Nasal dermoids without intracranial involvement are excised using an open rhinoplasty approach, with the addition of a bicoronal flap and craniotomy in cases with intracranial attachments (Zapata and Kearns 2006).

Cervical dermoid cysts are frequently misdiagnosed as thyroglossal duct cysts (TGDCs) due to similar presentation and behavior (see Fig. 18). They are usually discovered as soft, superficial, midline masses adjacent to the hyoid. Lack of attachments to deep structures usually prevents dermoids from elevating

Congenital Cysts, Sinuses, and Fistulae,
Fig. 17 (**a**) Sagittal CT of a dermoid cyst of the nasal dorsum associated with a widened foramen cecum. (**b**) Axial CT of a dermoid cyst of the nasal dorsum associated with a widened foramen cecum. Note presence of bifid crista galli

Congenital Cysts, Sinuses, and Fistulae, Fig. 18 Dermoid cyst of the midline lower neck

Teratomas

Approximately 2–10% of congenital teratomas occur in the head and neck. They most commonly present in the cervical region but may also be found in the oral cavity or naso/oropharynx. These lesions often exhibit rapid growth and may cause obstruction of the airway or alimentary tract in the perinatal period. Polyhydramnios and pulmonary hypoplasia may result. Teratomas contain all three germ cell layers, although the extent of tissue maturity may vary from poorly to highly differentiated. Pediatric teratomas are almost exclusively benign, in contrast to those found in adults, which are frequently malignant and require aggressive treatment. Nevertheless, the former do exhibit a rate of malignant transformation, and complete excision, while sparing critical structures, is the treatment of choice (Rosa et al. 2008; Acierno and Waldhausen 2007).

Nasopharyngeal Cysts

Congenital cystic masses of the nasopharynx are rare lesions derived from defects of skull base development. Medial lesions include Thornwaldt's cysts and Rathke's pouch cysts/craniopharyngiomas while lateral cysts represent second branchial cleft cyst variants. Most nasopharyngeal cysts are discovered incidentally on imaging studies obtained for other reasons and only occasionally come to medical attention due to symptoms. Nasal airway obstruction is the most common symptom, although Eustachian tube dysfunction, chronic halitosis, rhinosinusitis, occipital headache, and CSF rhinorrhea have also been described. Physical exam is generally of limited value, and MRI is

with tongue movement or swallowing, although this finding may be difficult to reliably observe in young children (Foley and Fallat 2006). Infection of a cervical dermoid cyst is rare, although traumatic rupture may result in local granulomatous soft tissue inflammation. Ultrasound is the most useful imaging study to support the diagnosis. CT and fine needle biopsy may be employed to differentiate these cysts from malignant disease. Submental dermoids above the level of the mylohyoid may be excised transorally, while those located lower in the neck that cannot be definitively differentiated from TGDCs are removed with the Sistrunk procedure (Acierno and Waldhausen 2007).

typically the preferred imaging modality to characterize these lesions and their relationship to the adjacent tissue compartments (Salem et al. 2006).

Thornwaldt's cysts are believed to result as a consequence of abnormal notochord embryologic development. Until it degenerates during week six of gestation, the notochord follows a tortuous course between the developing skull base and the endodermal lining of the nasopharynx (Salem et al. 2006). Persistent attachment to this endodermal layer can tether the developing nasopharyngeal mucosa to the prevertebral tissues as the notochord regresses. This forms a nasopharyngeal bursa (of Luschka) in the midline above the superior constrictor muscle. Obstruction of this bursa leads to development of a Thornwaldt's cyst. Those that intermittently drain are termed *crusting* type and those that do not are *cystic* type. Autopsy and imaging incidence studies have shown nasopharyngeal bursas in 4–7% of the general population, with 0.2–5% exhibiting a Thornwaldt's cyst (Marom et al. 2009). They are typically only symptomatic if they become infected and/or obstructive. Treatment typically includes excision or marsupialization through an endonasal or transoral retrovelar approach, with overall low rates of recurrence. Histologic examination showing a lining of respiratory epithelium and lack of lymphoid follicles confirms the diagnosis and differentiates Thornwaldt's cyst from the more common lymphoid-rich adenoid retention cyst (Marom et al. 2009).

Rathke's pouch cysts and cystic craniopharyngiomas are derived from incomplete obliteration of the craniopharyngeal canal following formation of the anterior pituitary gland. They are located between the sellar floor and nasopharyngeal roof adjacent to the sphenoid sinus. The majority of these lesions remain intracranial with only large cysts extending into the nasopharyngeal lumen. These cysts may contain functional pituitary tissue and occasionally communicate with dura. Imaging of all masses in this area is critical to avoid inadvertent posttreatment hypopituitarism or CSF leak. CT imaging shows a low attenuation cystic structure with a bony skull base defect. On MRI, the cyst is T2 hyperintense and T1 isointense with peripheral contrast enhancement (Salem et al. 2006). Marsupialization may adequately treat simple Rathke's pouch cysts. Craniopharyngiomas, although benign, tend to impinge on skull base structures and require neurosurgical management

of the intracranial portion. In general, the significant morbidities associated with aggressive treatment have led to the adoption of a conservative approach, with limited surgical excision supplemented with intracystic injection of chemotherapy or stereotactic radiotherapy (Marom et al. 2009).

Thymic Cysts

Cystic remnants of thymus development are uncommon causes of congenital neck masses, with less than 100 cases reported. Most are identified in the left lateral neck of children and often have mediastinal connections. They are rarely symptomatic and are identified following resection by distinctive histology – Hassall's corpuscles, which are branching epithelial cords pathognomonic for mature thymic medullary tissue. These cysts are believed to represent vestiges of the thymic anlage, which descends into the superior mediastinum from the third (and possibly fourth) branchial pouches via the thymopharyngeal duct. This may be seen in a minority of thymic cysts with associated pyriform sinus tracts. Alternatively, thymic cysts may result from cystic degeneration of Hassall's corpuscles. Suspected thymic cysts should first be characterized by ultrasound, with CT or MRI subsequently used to identify mediastinal connections and define the cyst's relationship to deep neck structures (see Fig. 19). Most can be excised successfully from a cervical approach, but rare cases may require a sternotomy. It is critical to confirm the presence of a normal thymus prior to excision of a thymic cyst in children to avoid inadvertent iatrogenic immunodeficiency. Similarly, symptomatic thymic cysts in neonates should only be partially excised if normal thymus cannot be verified (Caluwe et al. 2002).

Bronchogenic Cysts

There are approximately 70 case reports of cervical cystic masses determined to be of bronchogenic origin. These lesions appear to derive from abnormal development of the airways and usually occur in the posterior mediastinum. However, due to abnormal migration during development, a minority may be found in the neck. Defects of the trachea or bronchi typically present as upper midline or lower lateral neck

Congenital Cysts, Sinuses, and Fistulae, Fig. 19 Left thymic cyst at the inferior pole of the left thyroid lobe with compression of the trachea

masses, respectively, with tracheal lesions being more common. Direct connection to the airway is rare. Most cases are asymptomatic, but airway compression, abscess formation, air embolism, and malignant transformation have been described (Bocciolini et al. 2006). Children are more likely to present with symptoms than adults, and most lesions are identified incidentally on routine chest X-ray. Surgical excision is usually straightforward and is the treatment of choice. The bronchogenic origin of these cysts is confirmed on pathologic identification of ciliated respiratory epithelium as well as cartilage plates, submucosal glands, and smooth muscle within the cyst wall (Ustundag et al. 2005).

Vascular Malformation

Vascular anomalies are an important part of the differential diagnosis of cystic head and neck masses, with an estimated prevalence in the general population of between 4% and 11%. Defects in endothelial development underlie these localized lesions of anomalous arterial, venous, capillary, or lymphatic structure. Usually identified in childhood, vascular malformations may present with cosmetic disfigurement and/or functional complications such as airway compromise. The large variety of congenital vascular anomalies with similar presentations has prompted recent clarification and reorganization of the numerous historic terms used to identify them. Currently, they are organized by clinical behavior and histopathologic characteristics. *Vascular tumors* are defined as benign neoplasms exhibiting unregulated cell growth, while *vascular malformations* describe errors in vascular development that have stable endothelial turnover (Greene 2011). The details of current classification and treatment controversies will be addressed elsewhere; however, it is important to consider these entities in the differential diagnosis of a cystic mass in the head and neck.

Hemangiomas

The term *hemangioma* has had varied meanings over the years, but currently refers to a group of benign neoplasms of vascular tissue. Within this group, the vast majority of lesions are properly termed *infantile hemangiomas* (IHs). These hemangiomas represent the most common neoplasm of childhood, affecting 10% of infants. They are most frequently seen in Caucasian and female infants, especially those born premature. Sixty percent of IHs are found in the head and neck. They typically are first noted approximately 2 weeks after birth, forming a firm red or purple lesion whose "footprint" shows minimal change while the lesion itself exhibits rapid growth (see Fig. 20a, b). The proliferative phase is usually complete by 8–12 months, after which the lesion slowly involutes to a fibrofatty scar by around 10 years of age. Although predominantly isolated and focal, IH may also exhibit a segmental presentation with broader and/or deeper anatomic involvement. In some patients, these segmental IHs are a key component of the PHACES syndrome, which includes *P*osterior fossa malformations, *H*emangiomas, *A*rterial cerebral anomalies, *C*ardiac defects, *E*ye abnormalities, and *S*ternal clefting (Greene 2011).

Apart from physical exam, MRI is the diagnostic modality of choice. IHs are hyperintense on T2 sequences, enhance with contrast, and demonstrate signal voids due to high flow. The soft tissue detail of MRI is particularly useful for lesions involving critical

Congenital Cysts, Sinuses, and Fistulae, Fig. 20 (a, b) Large infantile hemangiomas of the lower lip and lateral face


structures and for preoperative planning. Doppler ultrasound is emerging as a useful screening tool to initially characterize these lesions. Initially, IHs demonstrate diffuse hypoechoic structure, which typically develops into high-flow vascular lesions. Biopsy is rarely performed unless malignancy is suspected, with the marker Glut-1 used to confirm the diagnosis of IH (MacArthur 2006; Greene 2011).

Approximately 10–25% of patients with head and neck IH will experience complications: ulceration, bleeding, destruction of adjacent tissues causing cosmetic deformity, loss of vision, or airway obstruction. Traditional medical treatment for IH with complications consists of intralesional or systemic steroids, with antineoplastic agents such as vincristine reserved for lesions that fail to respond. In 2008, the beta-blocker propranolol was unexpectedly found to stimulate involution of IH with minimal side effects (Zimmerman et al. 2010). This agent has since become first-line treatment for IHs not amenable to observation. Surgery during the proliferative phase is generally reserved for medical therapy failures or to manage acute complications. Soft tissue reconstruction may be necessary following involution to address cosmetic or functional deficits (MacArthur 2006).

Lymphatic Malformations

Previously known as "lymphangiomas" or "cystic hygromas," lymphatic malformations (LMs) represent defects of lymphatic endothelial development. These congenital lesions are present at birth and tend to grow along with the patient. However, they may not be identified until adulthood, when rapid enlargement may occur in response to upper respiratory infections, trauma, or hemorrhage. The majority of LMs occur in the head and neck and show no gender predilection.
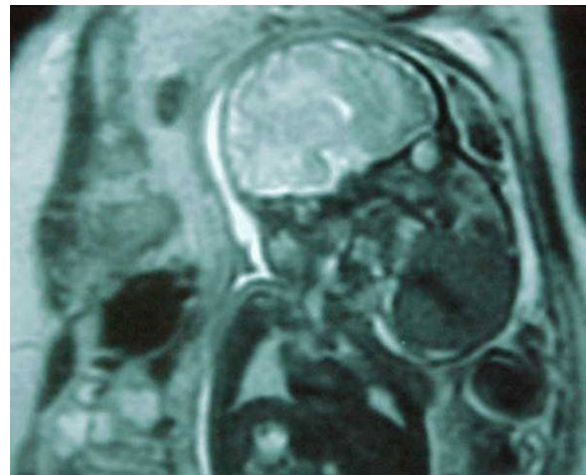
Congenital Cysts, Sinuses, and Fistulae, Fig. 21 Sagittal T2-weighted fetal MRI showing a large cervicofacial lymphatic malformation

They usually present as soft, compressible cystic masses that do not respect anatomic boundaries. Ultrasound identifies these lesions as low-flow and, along with MRI, can classify them as macro- or microcystic (Perkins et al. 2010). Imaging is also important to identify the relationship of these lesions to critical structures such as the airway (see Figs. 21 and 22).

A staging system based on laterality (uni- or bilateral) and relationship to the hyoid bone (supra- or infrahyoid) provides important prognostic information when forming a treatment plan. Although LMs are histologically benign, significant complications may arise from either their locally destructive/obstructive nature or by efforts to remove them. Best outcomes are predicted for unilateral and infrahyoid lesions. Macrocystic structure is also a good prognostic sign (Perkins et al. 2010).

Congenital Cysts, Sinuses, and Fistulae, Fig. 22 Infant following EXIT procedure with tracheostomy to secure the airway

Traditional treatment of LMs is surgical excision, although complete resection without compromise of vital structures can be difficult. In particular, microcystic disease tends to be infiltrative and to obscure normal anatomic landmarks. Subtotal and/or staged resection is frequently required, with recurrence and postoperative complications more significant with increased clinicoradiologic stage and microcystic structure. Sclerotherapy is a more recently developed alternative to surgery. Lesions are percutaneously drained and then infused with one of several sclerosing agents (bleomycin, doxycycline, OK-432). Care must be taken to anticipate acute postsclerotherapy tissue edema when treating LMs involving the orbit or aerodigestive tract. As with surgery, the extent of LM treatment must be weighed against the potential functional consequences of therapy (Perkins et al. 2010; Renton and Smith 2011).

Conclusion

When a pathologic cyst, sinus, or fistula is identified in the head and neck, congenital causes represent an important part of the differential diagnosis. An understanding of the developmental processes that produce such a lesion is the foundation upon which a comprehensive diagnostic workup and treatment plan should be built. This approach will allow the clinician to successfully address the disease process while minimizing functional compromises or the risk of disease recurrence.

References

Acierno S, Waldhausen J (2007) Congenital cervical cysts, sinuses and fistulae. Otolaryngol Clin North Am 40:161–176

Bocciolini C, Dall'olio D, Cunsolo E, Latini G, Gradoni P, Laudadio P (2006) Cervical bronchogenic cyst: asymptomatic neck mass in an adult male. Acta Oto-Laryngol 126:553–556

Caluwe D, Ahmed M, Puri P (2002) Cervical thymic cysts. Pediatr Surg Int 18:477–479

Chandra R, Palmer J (2006) Epidermoids of the paranasal sinuses and beyond: endoscopic management. Am J Rhinol 20(4):441–444

Deane S, Telander R (1978) Surgery for thyroglossal duct and branchial cleft anomalies. Am J Surg 136:348–353

Foley D, Fallat M (2006) Thyroglossal duct and other congenital midline cervical anomalies. Semin Pediatr Surg 15:70–75

Girvigian M, Rechdouni A, Zeger G, Segall H, Rice D, Petrovich Z (2004) Squamous cell carcinoma arising in a second branchial cleft cyst. Am J Clin Oncol 27:96–100

Greene A (2011) Management of hemangiomas and other vascular tumors. Clin Plast Surg 38:45–63

James A, Steward C, Warrick P, Tzifa C, Forte V (2007) Branchial sinus of the piriform fossa: reappraisal of third and fourth branchial anomalies. Laryngoscope 117:1920–1924

MacArthur C (2006) Head and neck hemangiomas of infancy. Curr Opin Otolaryngol Head Neck Surg 14:397–405

Mandell D (2000) Head and neck anomalies related to the branchial apparatus. Otolaryngol Clin North Am 33(6):1309–1332

Marom T, Russo E, Salem D, Roth Y (2009) Nasopharyngeal cysts. Int J Pediatr Otorhinolaryn 73:1063–1070

Mlynarek A, Hagr A, Tewfik T, Nguyen V (2003) Congenital mid-line cervical cyst: case report and review of literature. Int J Pediatr Otorhinolaryn 67:1243–1249

Mondin V, Ferlito A, Muzzi E, Silver C, Fagan J, Devaney K, Rinaldo A (2008) Thyroglossal duct cyst: personal experience and literature review. Auris Nasus Larynx 35:11–25

Nicoucar K, Giger R, Jaecklin T, Pope H, Dulguerov P (2010) Management of congenital third branchial arch anomalies: a systematic review. Otolaryngol Head Neck Surg 142:21–28

Pahlavan S, Haque W, Pereira K, Larrier D, Valdez T (2009) Microbiology of third and fourth branchial pouch cysts. Laryngoscope 120:458–462

Pereira K, Davies J (2006) Piriform sinus tracts in children. Arch Otolaryngol Head Neck Surg 132:1119–1121

Pereira K, Losh G, Oliver D, Poole M (2004) Management of anomalies of the third and fourth branchial pouches. Int J Pediatr Otorhinolaryn 68:43–50

Perkins J, Manning S, Tempero R, Cunningham M, Edmonds J, Hoffer F, Egbert M (2010) Lymphatic malformations: review of current treatment. Otolaryngol Head Neck Surg 142:795–803

Pryor A, Lewis J, Weaver A, Orvidas L (2005) Pediatric dermoid cysts of the head and neck. Otolaryngol Head Neck Surg 132(6):938–942

Renton J, Smith R (2011) Current treatment paradigms in the management of lymphatic malformations. Laryngoscope 121(1):56–59

Rosa P, Hirsch D, Dierks E (2008) Congenital neck masses. Oral Maxillofac Surg Clin North Am 20:339–352

Salem D, Duvillard C, Assous D, Ballester M, Krause D, Ricolfi F (2006) Imaging of nasopharyngeal cysts and bursae. Eur Radiol 16:2249–2258

Senel E, Kocak H, Akbiyik F, Saylam G, Gulleroglu B, Senel S (2009) From a branchial fistula to a branchiootorenal syndrome: a case report and review of the literature. J Pediatr Surg 44:623–625

Tan T, Constantinides H, Mitchell T (2005) The preauricular sinus: a review of its aetiology, clinical presentation and management. Int J Pediatr Otorhinolaryn 69:1469–1474

Triglia J, Nicollas R, Ducroz V, Koltai P, Garabedian E (1998) First branchial cleft anomalies. Arch Otolaryngol Head Neck Surg 124:291–295

Ustundag E, Iseri M, Keskin G, Yayla B, Muezzinoglu B (2005) Cervical bronchogenic cysts in head and neck region: review of the literature. J Laryngol Otol 119:419–423

Waldhausen J (2006) Branchial cleft and arch anomalies in children. Semin Pediatr Surg 15:64–69

Work W (1972) Newer concepts of first branchial cleft defects. Laryngoscope 82(9):1581–1593

Zapata S, Kearns D (2006) Nasal dermoids. Curr Opin Otolaryngol Head Neck Surg 14:406–411

Zimmerman A, Wiegand S, Werner J, Eivazi B (2010) Propranolol therapy for infantile haemangiomas: review of the literature. Int J Pediatr Otorhinolaryn 74:338–342

Congenital Cytomegalovirus and Sensorineural Hearing Loss

Albert H. Park
Division of Otolaryngology-ENT Head and Neck Surgery, Department of Surgery, University of Utah, Salt Lake City, UT, USA

Synonyms

Hearing (Sensorineural Hearing Loss – infection); Hearing (Sensorineural Hearing Loss – pediatric)

Introduction

Cytomegalovirus (CMV), a member of the beta-herpesvirus family is the most common infectious cause of sensorineural hearing loss (SNHL) in children. CMV may account for 40% of all nonsyndromic SNHL and at least one-third of SNHL in young children (Demmler 1991; Hicks et al. 1993). The cost associated with congenital CMV infection has been estimated to be $ 4 billion a year (Stratton et al. 2001).

Pathogenesis

Transmission to the fetus is more frequent in women who develop a primary infection during pregnancy compared to those with prior infection (Fowler et al. 1992). Approximately 25% of infants infected during a primary infection will develop long-term sequelae compared to 8% of infants whose mothers had serologic evidence of a prior infection (Fowler et al. 1992). Why the ear is one of the common targets for congenital CMV is not understood.

Animal models that can mimic CMV primary infections during pregnancy have been studied to determine the pathogenesis of congenital SNHL. Woolf et al. were the first to successfully inoculate newborn guinea pig pups via transplacental transmission of CMV (Woolf et al. 1989). They performed GPCMV injections of first and second trimester pregnant guinea pigs and demonstrated temporal bone involvement in 45% of infected neonates and an auditory deficit in 28% of the offspring. Other investigators have been able to detect labyrinthitis via the more sensitive PCR techniques and to measure neonatal auditory function over time using serial auditory brainstem response studies (Park et al. 2010). The results of those studies demonstrated similar characteristics of hearing loss seen in children with congenital CMV-induced sensorineural hearing loss. Unfortunately, the pathogenesis of CMV-induced SNHL is still poorly understood.

Clinical Presentation

Dahle et al. divided a large population of CMV infected children into two groups: symptomatic and asymptomatic (Dahle et al. 2000). Patients with the symptomatic form of this infection had intrauterine growth retardation, petechial/purpuric skin rash, jaundice, hepatosplenomegaly, microcephaly, and/or chorioretinitis. Patients without any clinically apparent symptoms were designated as asymptomatic. The number of children in the asymptomatic group was approximately three times greater than the number of children in the symptomatic group. A major finding of this large study was that a large portion of newborns with congenital CMV infection may present with only SNHL as their disability.

A characteristic of CMV-induced SNHL is that a late onset occurs in at least 50% of the cases, is

unilateral in about half of cases, and results in a profound loss in 23% (Barbi et al. 2003). Fowler et al. reported on 307 children with asymptomatic CMV infection (Fowler et al. 1997). Of the 22 children with SNHL, further hearing deterioration occurred in 50% with a median age at first progression at 18 months. Progression was noted as late as 6 years of age. Delayed-onset SNHL was observed in 18.2% children with the median age of detection at 27 months of age. Late onset hearing loss was reported to be as late as 5 years of age.

Diagnostics

The diagnosis of congenital CMV infection requires laboratory testing of neonatal samples within the first 3 weeks of life since postnatal exposure to CMV is not associated with SNHL (Barbi et al. 2003). Unfortunately, despite the Joint Committee on Infant Hearing's recommendation to diagnose SNHL within the first 90 days of life, many infants identified with SNHL are not diagnosed within 3 weeks of life (Position Statement 2007). In addition, many infants with congenital CMV do not present with clinical abnormalities at birth and have normal newborn screening results.

One approach to circumvent the limitations of early SNHL detection was reported by Barbi et al. in 2003 (Barbi et al. 2003). They extracted CMV DNA from archived dried-blood-spot (DBS) specimens from 130 children with greater than 40 dB hearing loss. The percentage of SNHL attributable to congenital CMV was 10% in infants whose SNHL had been diagnosed in the first 2 months of life and 34.2% in children with "idiopathic SNHL" diagnosed in early childhood.

Another approach is to perform universal screening of all newborns for congenital CMV infection. Traditional virus isolation from saliva or urine in tissue culture is considered the standard diagnostic method but is too labor and resource-intensive for mass screening (Boppana et al. 2010). Real-time polymerase chain reaction (PCR) technology is well-suited for large-scale screening since it does not require tissue culture facilities and is amenable to automation. Since DBS specimens are routinely collected for newborn metabolic screening there has been considerable interest in performing DNA CMV detection using PCR technology. Boppana et al. evaluated the sensitivity and specificity of single and two-primer DBS real-time PCR assays compared to saliva rapid culture in infants born between March 2007 and May 2008 at seven US medical centers (Boppana et al. 2010). The single-primer DBS PCR identified congenital CMV with a sensitivity of 28.3% and specificity of 99.9%; the two-primer DBS PCR assay identified congenital CMV with a sensitivity of 34.4% and a specificity of 99.9%. Their conclusion was that CMV testing with DBS PCR compared with saliva rapid culture had low sensitivity limiting its value as a screening tool.

In a recent paper, Boppana et al. compared real-time PCR assays of liquid-saliva and dried-saliva specimens with rapid culture of saliva specimens obtained from 34,989 infants (Boppana et al. 2011). The ease of collection and high titers of CMV shed in the saliva of infected newborns has been cited as a potential advantage when compared to DBS PCR screenings. The dried-saliva assay was evaluated since it is simpler to collect. They noted that the liquid-saliva PCR assay resulted in a 100% sensitivity and 99.9% specificity, and the dried-saliva PCR assay had a 97.4% sensitivity and 99.9% specificity compared to a rapid culture of saliva specimens. These specimens may be potential screening tools for newborn CMV.

Differential Diagnosis

SNHL has many causes including genetic and environmental etiologies. Genetic factors account for at least 55% of all cases of profound SNHL. Mutations involving the *GJB2* gene that codes for subunits of the gap junction connexin 26 are the most common genetic anomaly, accounting for approximately 20% of congenital SNHL (Dent et al. 2004). Inner ear abnormalities which may or may not be associated with a known genetic etiology have been reported to make up approximately 20% of congenital SNHL (Park et al. 2000).

Until recently, much of the emphasis on diagnostic testing has focused on genetic testing or temporal bone imaging. Preciado et al. have advocated a stepwise diagnostic paradigm tailored to the severity of hearing loss involving either temporal bone CT scanning or GJB2 screening (Preciado et al. 2004). With our current knowledge of the high incidence of CMV-mediated SNHL and the potential advent of universal CMV testing, a new paradigm involving early CMV testing may be in the horizon. This approach may be more attractive from a cost aspect since PCR CMV testing is

less expensive than genetic testing or imaging. Early CMV testing may also obviate the risks from sedation required for imaging. The option of antiviral therapy also magnifies the importance of early CMV detection.

Therapy

One of the most exciting areas of CMV investigation has been in therapy. One provocative paper by Nigro et al. reported positive results from using passive immune globulin during pregnancy to prevent transmission of CMV from mother to the fetus (Nigro et al. 2005). Pregnant women with primary CMV infection were offered amniocentesis to look for fetal infection; if they had infection, they were offered treatment with CMV-specific hyperimmune globulin. A total of 31 women chose treatment, 14 refused and 10 chose early termination. Of the 31 treated women, 15 had abnormal fetal ultrasounds prior to treatment. At follow-up only one had a persistent abnormality. None of the infants with normal fetal ultrasounds had symptoms later. In contrast, seven of the 14 untreated women had abnormal fetal ultrasounds. None were normal at birth, and two died. A future randomized clinical trial is needed to determine the true efficacy of this approach.

Another approach utilizes the finding that preconceptual immunity to human CMV reduces the impact of congenital HCMV infection, resulting in a lower incidence of central nervous system sequelae (Fowler et al. 1992). An effective preconceptual vaccine against HCMV given to young women of childbearing age may prevent congenital HCMV infection and hearing loss. These findings, combined with the ubiquitous nature of this pathogen and the serious consequences of infection for the fetus, makes the development of vaccines that prevent congenital HCMV infection an important public health priority. In fact, an Institute of Medicine (IOM) report, "Vaccines for the 21st Century," characterized HCMV vaccines as the highest-level (Level 1) priority for vaccines in the new millennium (Stratton et al. 2001).

Pass et al. recently reported their phase II clinical trial comparing a recombinant CMV envelope glycoprotein B administered with MF59 adjuvant with placebo (Pass et al. 2009). They demonstrated an efficacy of 50% for this recombinant vaccine for protection against acquisition of a primary HCMV infection in young women. Kaplan-Meier analysis showed that the

vaccine group was more likely to remain uninfected during a 42-month period than the placebo group (p = 0.02). These results represented the first reported efficacy of any HCMV vaccine with prevention of infection as a primary study endpoint.

Finally, there has been much interest in using antiviral therapy for treating congenital CMV. Ganciclovir has been the most studied antiviral medication for this purpose. It is a nucleoside analog of guanosine and is structurally related to acyclovir. The National Institute of Allergy and Infectious Disease Collaborative Antiviral Study Group (CASG) presented a large, randomized controlled study of 6 weeks of intravenous ganciclovir compared with no treatment in infants with CNS involvement and age less than 30 days (Kimberlin et al. 2003). They found that infants treated with ganciclovir were more likely to have stable hearing compared to those infants who received no treatment. None of the treated infants had hearing deterioration at 6 months compared to 41% of the untreated infants. At the 1-year follow-up, 21% infants in the treated group had some hearing deterioration in the better ear compared with 68% in the untreated group.

Amir et al. reported their results in 23 infants with culture-proven congenital CMV treated with ganciclovir for 6 weeks followed by oral valganciclovir to age 12 months (Amir et al. 2010). None of the 25 ears with normal hearing developed worsening of their hearing at 1 year of age. For the 21 ears with hearing loss, 12 (57%) had improved hearing, eight (38%) had no change, and one (5%) had worse thresholds at 1-year follow-up. These preliminary results indicate potential efficacy with longer duration therapy.

The major toxicities associated with ganciclovir and valganciclovir are bone marrow depression, specifically neutropenia (Kimberlin et al. 2003). Twenty-nine of the 46 (63%) ganciclovir treated patients developed grade 3 or 4 neutropenia. Of the 29 ganciclovir treated patients developing neutropenia, 14 required dosage adjustment and 4 had the drug permanently discontinued. Neutropenia was observed only during the first 3 months of treatment, mainly during the intravenous ganciclovir administration in Amir et al.'s study (Amir et al. 2010). Renal toxicity has also been documented in the ganciclovir studies; however, these patients were frequently taking other nephrotoxic medications, making it difficult to ascribe the toxicity to ganciclovir (Michaels 2007). Animal studies have demonstrated impaired fertility and

carcinogenic properties following ganciclovir exposure in mice (Michaels 2007). No toxicity has been reported in any pediatric patient, despite its widespread use in pediatric transplantation.

In conclusion, any otolaryngologist who evaluates and treats pediatric hearing loss needs to be aware of ramifications of CMV-induced SNHL. It is entirely conceivable that maternal identification or newborn screening will provide early diagnosis and a means for effective treatment. Intrauterine CMV hyperimmune globulin, vaccination, or antiviral treatments may provide an effective method to control this important condition.

References

American Academy of Pediatrics, Joint Committee on Infant Hearing (2007) Year 2007 position statement: principles and guidelines for early hearing detection and intervention programs. Pediatrics 120:898–921

Amir J, Wolf DG, Levy I (2010) Treatment of symptomatic congenital cytomegalovirus infection with intravenous ganciclovir followed by long-term oral valganciclovir. Eur J Pediatr 169:1061–1067

Barbi M, Binda S, Caroppo S, Ambrosetti U, Corbetta C, Sergi P (2003) A wider role for congenital cytomegalovirus infection in sensorineural hearing loss. Pediatr Infect Dis J 22:39–42

Boppana SB, Ross SA, Novak Z et al (2010) Dried blood spot real-time polymerase chain reaction assays to screen newborns for congenital cytomegalovirus infection. JAMA 303:1375–1382

Boppana SB, Ross SA, Shimamura M et al (2011) Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. N Engl J Med 364:2111–2118

Dahle AJ, Fowler KB, Wright JD, Boppana SB, Britt WJ, Pass RF (2000) Longitudinal investigation of hearing disorders in children with congenital cytomegalovirus. J Am Acad Audiol 11:283–290

Demmler GJ (1991) Summary of a workshop on surveillance for congenital cytomegalovirus disease. Rev Infect Dis 13:315–329

Dent KM, Kenneson A, Palumbos JC et al (2004) Methodology of a multistate study of congenital hearing loss: preliminary data from Utah newborn screening. Am J Med Genet 125C:28–34

Fowler KB, Stagno S, Pass RF, Britt WJ, Boll TJ, Alford CA (1992) The outcome of congenital cytomegalovirus infection in relation to maternal antibody status. N Engl J Med 326:663–667

Fowler KB, McCollister FP, Dahle AJ, Boppana S, Britt WJ, Pass RF (1997) Progressive and fluctuating sensorineural hearing loss in children with asymptomatic congenital cytomegalovirus infection. J Pediatr 130:624–630

Hicks T, Fowler K, Richardson M, Dahle A, Adams L, Pass R (1993) Congenital cytomegalovirus infection and neonatal auditory screening. J Pediatr 123:779–782

Kimberlin DW, Lin CY, Sanchez PJ et al (2003) Effect of ganciclovir therapy on hearing in symptomatic congenital cytomegalovirus disease involving the central nervous system: a randomized, controlled trial. J Pediatr 143:16–25

Michaels MG (2007) Treatment of congenital cytomegalovirus: where are we now? Expert Rev Anti Infect Ther 5:441–448

Nigro G, Adler SP, La Torre R, Best AM (2005) Passive immunization during pregnancy for congenital cytomegalovirus infection. N Engl J Med 353:1350–1362

Park AH, Kou B, Hotaling A, Azar-Kia B, Leonetti J, Papsin B (2000) Clinical course of pediatric congenital inner ear malformations. Laryngoscope 110:1715–1719

Park AH, Gifford T, Schleiss MR et al (2010) Development of cytomegalovirus-mediated sensorineural hearing loss in a Guinea pig model. Arch Otolaryngol Head Neck Surg 136:48–53

Pass RF, Zhang C, Evans A et al (2009) Vaccine prevention of maternal cytomegalovirus infection. N Engl J Med 360:1191–1199

Preciado DA, Lim LH, Cohen AP et al (2004) A diagnostic paradigm for childhood idiopathic sensorineural hearing loss. Otolaryngol Head Neck Surg 131:804–809

Stratton KR, Durch JS, Lawrence RS (2001) Vaccines for the 21st century: a tool for decision making. National Academy Press, Washington, DC

Woolf NK, Harris JP, Koehrn FJ, Richman DD (1989) Congenital cytomegalovirus labyrinthitis and sensorineural hearing loss in Guinea pigs. J Infect Dis 160:929–937

Congenital Deafness

Congenital Hearing Loss

Matthew Ng[1] and Drew M. Horlbeck[2]
[1]Department of Surgery, Division of Otolaryngology, University of Nevada School of Medicine, Las Vegas, NV, USA
[2]Department of Surgery, Division of Pediatric Otolaryngology, Nemours Children's Clinic, Jacksonville, FL, USA

Definition

Hearing loss present at birth.

Cross-References

Congenital Laryngeal and Tracheal Anomalies

Amal Isaiah and Kevin D. Pereira
Department of Otorhinolaryngology-HNS, University
of Maryland School of Medicine, Baltimore,
MD, USA

Synonyms

Airway anomalies in the neonate; Congenital airway
disorders

Definition

Congenital laryngeal and tracheal anomalies refer to
a wide spectrum of disorders that present with symp-
toms related to functional restriction of the airway and
phonation.

Embryology

The complex laryngeal anatomy evolves through both
prenatal and postnatal stages of development. The
cephalic portion of the primordial pharyngeal appara-
tus evaginates to form the primitive larynx by the third
week of gestation. The laryngotracheal groove subse-
quently forms the primitive lower respiratory tract at
the ventral aspect of the foregut. The development of
the lower respiratory system begins at 26 days after
conception as the laryngotracheal groove (also known
as the respiratory primordium) at the ventral aspect of
the foregut. The laryngotracheal diverticulum
becomes separated from the foregut by the tracheoe-
sophageal folds that ultimately fuse to form the
tracheoesophageal septum. At this point, there is defin-
itive separation of the foregut into a ventral
laryngotracheal tube and the dorsal esophagus. Incom-
plete fusion of the tracheoesophageal folds leads to

persistent communication between the trachea and
the esophagus.

The arytenoids swellings appear from the sixth
branchial arch, near the cranial end of the
laryngotracheal tube. These approximate in the mid-
line and convert the aperture of the tube to a T-shaped
opening. Subsequent differentiation of structures leads
to formation of the arytenoids, corniculate cartilages,
and the aryepiglottic folds. Additional supraglottic
structures, including the epiglottic and the cuneiform
cartilages, have developed by this time, and as devel-
opment proceeds to completion, the thyroid cartilage is
formed from the fourth branchial arch, and the cricoid
and tracheal cartilages develop from the sixth bran-
chial arch. The superior and recurrent laryngeal nerves
complete their paths at the same time. Changes in
shape and form take place in the ensuing days, with
the cricoid becoming a complete ring and the epiglottis
achieving its postnatal concave shape. Continued
luminal invagination ensures that the laryngotracheal
tube becomes completely patent. By the sixth week of
gestation, the separation of the trachea and esophagus
is complete. The precursor cells then provide tissue
from which cartilage, muscle, and connective tissue
are formed. Since the developmental processes of the
larynx and the trachea are separate, tracheal
malformations may occur despite normal development
of the larynx and the bronchial tree.

Anatomy of the Larynx and the Trachea

The infant larynx is located higher in the neck com-
pared to adults. At 2 years, the larynx begins a slow
descent from its position high in the neck between C1
and C4 vertebrae, to finally assume a position between
the C4 and C7 vertebrae by 6 years. The tip of the
epiglottis rests behind the soft palate and, thus,
explains the preferential nasal breathing seen in chil-
dren. The shape of the epiglottis is more tubular or
omega shaped and is situated more posteriorly com-
pared to the adult.

The glottic segment of the larynx consists of the true
vocal cords, the anterior and posterior commissures,
and the vocal processes of the arytenoid cartilages. The
ventricle forms the boundary between the supraglottic
airway and the glottis. Posteriorly, the glottis consists
of the posterior third of the vocal cords, the posterior
commissure, the cricoid lamina, the cricoarytenoid

joints, the arytenoids, and the overlying mucosa. The posterior glottic width varies between 35% and 45% of the length of the glottis and approximately 50–65% of its area. The anterior glottis subserves the function of phonation and the posterior glottis, that of respiration.

The cuneiform cartilages are a pair of elastic cartilages, located within the aryepiglottic fold, without any direct contact with the arytenoid cartilages. The cricoid cartilage has a V-shaped portion superiorly, as opposed to a circular cross-section inferiorly. This configuration produces an elliptical shape within the subglottic lumen. The normal subglottic lumen measures 4.5–5.5 mm in the full-term neonate and about 1 mm less in premature neonates. In children, the subglottic region within the cricoid cartilage is regarded as the narrowest portion within the airway. The proximal subglottic airway is limited by the thyroid cartilage anteriorly and by the cricoid cartilage posterolaterally. The laryngeal ventricle extends from the true and false vocal cords in a craniocaudal dimension. Anteriorly, the ventricle forms a pouch termed the saccule.

The glottic lumen is pentagonal during inspiration and is narrower inferiorly, resembling a funnel. The tissues that make up infant larynx are softer and more pliable compared with the adult. Hence, any pathological conditions resulting in inflammation of the laryngeal mucosa may potentially result in substantial loss of airway diameter.

The trachea commences at the level of the of the cricoid cartilage and enters the superior mediastinum behind the sternum, dividing into two primary bronchi at the level of the sternal angle. The trachea is 4 cm long in the term infant. The diameter of the trachea varies from 3 to 4 mm in a term newborn and increases to 12–23 mm in the adult. The tracheal lumen is bound by 16–20 horseshoe-shaped cartilages, composed of C-shaped hyaline cartilages. Posteriorly, the membranous portion consists of the trachealis muscle along with elastic and fibrous tissue. The normal cartilaginous-to-membranous ratio is 4.5:1, with variations accounted for by changes in head and neck position and intrathoracic pressure.

Two depressions on the tracheal surface are formed by the left thyroid lobule and the aortic arch respectively. The tracheal lumen is lined by ciliated, pseudostratified columnar epithelium and lamina propria. Arterial supply is provided by inferior thyroid, thymic, and right bronchial arteries. Venous outflow is to the esophageal and inferior thyroid veins. The trachea is innervated by the vagus via the pulmonary plexus in combination with the cervical and dorsal ganglia providing sympathetic innervation.

Symptomatology

Presenting symptoms may vary depending on the site of pathology (Cotton and Myer 1999). Most symptoms are related to some form of respiratory obstruction and are usually a function of whether the lesion is supraglottic, glottic, or subglottic. Specific signs include stridor, muffled or abnormal cry, dyspnea, hoarseness, feeding problems, cyanosis, or sudden death. Stridor is usually inspiratory or biphasic when the location of obstruction is at the level of the larynx. Inspiratory stridor points to the supraglottic or glottis areas, while biphasic stridor generally originates from the subglottic or tracheal regions. Stertor, on the other hand, is related to obstructive pathology within the pharynx.

Diagnosis

The first step in assessment of a child with suspected laryngeal pathology is a thorough history and physical examination. Retractions, nasal flaring, or tachypnea highlight increased work of breathing. Specific attention needs to be paid to birth history, history of intubation, and medical problems. Details of intubation should also be obtained if available. Growth curves add to information about failure to thrive. An important aspect is also the relationship between feeding and airway symptoms.

A detailed head and neck examination is of prime importance. Voice evaluation should start with assessment for weakness, hoarseness, or aphonia. A flexible fiber optic laryngoscopy may be performed in a suitable setting if the patient is stable and can cooperate for the examination. Features that should be recorded are vocal cord mobility, reflux-related changes, sensation, anatomic abnormalities, and assessment of the airway lumen itself. Difficulty in intubation during a surgical procedure may also lead to a diagnosis. Other tools such as CT and MRI are not routinely performed for diagnosis of congenital laryngeal lesions. Airway fluoroscopy (AF) is useful in the

diagnosis of laryngomalacia and may be used in conjunction with rigid endoscopy. However, a recent study (Huntley and Carr 2010) demonstrated that airway fluoroscopy showed an inconsistent sensitivity, specificity, and positive and negative predictive value compared to FFL and DL with regard to specific lesions. AF had an overall sensitivity of 35%, specificity of 67%, positive predictive value of 78%, and negative predictive value of 23% when compared to FFL in diagnosing laryngomalacia. When compared to DL, AF had an overall sensitivity of 44%, specificity of 60%, positive predictive value of 67%, and negative predictive value of 38% when diagnosing laryngomalacia. The role of an AF in such a setting is generally relegated to ruling out synchronous airway lesions.

The next step in diagnosis is a direct laryngoscopic and bronchoscopic examination under general anesthesia, using rigid telescopes. If there is impending airway obstruction, a tracheostomy should also be discussed with the family prior to the procedure. Assessment should definitively include (1) location and length of stenosis (2) diameter of the endotracheal tube that can be safely inserted (3) cartilage-membrane ratio (4) reflux-related changes and (5) static obstructive lesions such as clefts, webs, and cricoarytenoid joint fixation. Rigid bronchoscopes should not be forced into a narrowed segment of the trachea. Esophagoscopy is useful in demonstrating esophageal malformations or external compressions from lesions such as vascular anomalies. Tracheoesophageal fistulae are located within the membranous portion of the trachea and may require angled telescopes for identification.

CT and MRI may provide useful information for tracheal anomalies, often in conjunction with three-dimensional reconstructions. MRI is specifically useful where cardiovascular anomalies are suspected. In children undergoing surgery for tracheal anomalies, an echocardiogram and, occasionally, cardiac catheterization are often useful for assessment of cardiac physiology. Angiograms are the gold standard for vascular anomalies.

Laryngomalacia

Laryngomalacia is the most common congenital laryngeal anomaly and accounts for most laryngeal

Congenital Laryngeal and Tracheal Anomalies, Table 1 Classification of findings in laryngomalacia

Type	Characteristics
1	Prolapse of the mucosa overlying the arytenoids
2	Foreshortened aryepiglottic folds
3	Posterior displacement of the epiglottis

problems (50–75%) in the newborn. There is a 2:1 male preponderance that has not been explained. Laryngomalacia is characterized by flaccidity and neuromuscular incoordination of supraglottic tissues that causes their collapse during inspiration.

Findings at the time of FFL in a child with laryngomalacia (Table 1) were classified to reflect the tissue causing the supraglottic obstruction (Olney et al. 1999).

At the level of the vocal folds, the aryepiglottic folds are shortened and intrude into the lumen with inspiration (Fig. 1a, b). These are restored to a normal position during expiration. In addition, there is anterior collapse of cuneiform and corniculate cartilages. In severe laryngomalacia, the ratio of length of AE folds to the length of glottis is 0.4 or less; in normal controls, this ratio increases to ≥0.5 (Manning et al. 2005).

Laryngomalacia often presents with symptoms of airway obstruction that may be mild to moderate in severity. Crying or agitation may exacerbate the symptoms. Retractions may also be observed. Other sequelae include feeding difficulties, failure to thrive, gastroesophageal reflux disorder (GERD), obstructive sleep apnea, and, in extreme circumstances, total airway obstruction and death. The pathophysiology of GERD in laryngomalacia is explained by negative intrathoracic pressure caused by inspiration against a prolapsed and obstructed supraglottis that pulls open the lower esophageal sphincter leading to reflux of gastric contents.

Clinical observation may show stridor that is primarily inspiratory. It is often high-pitched, seen first within the first few weeks after birth, and increases in severity in the ensuing months. It is worse when supine and improves when prone. In addition, it may disappear while asleep. A flexible fiber optic laryngoscopic exam is performed while awake, and the findings are usually diagnostic. Concomitant direct laryngoscopic and bronchoscopic evaluation should also be
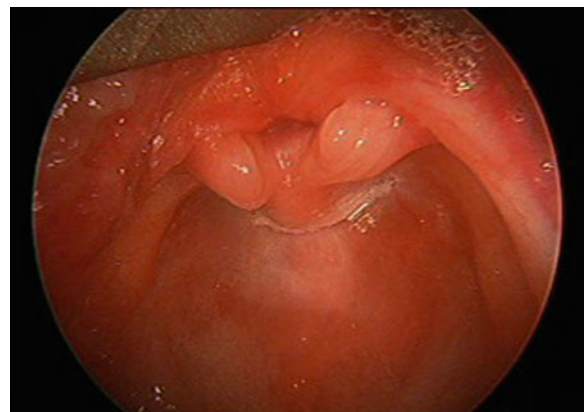
Congenital Laryngeal and Tracheal Anomalies,
Fig. 1 Pre- and postoperative (**a**, **b**) endoscopic evaluations of the airway show marked improvement in the airway caliber after supraglottoplasty (*Courtesy of Dr KD Pereira*)
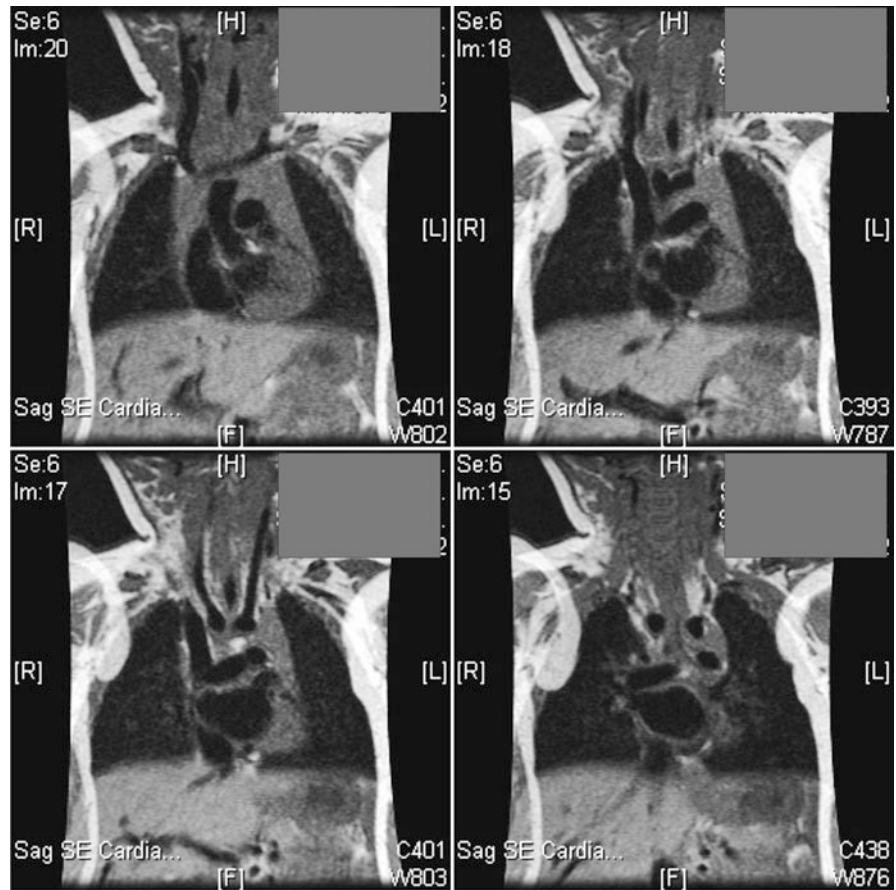
performed to identify synchronous airway pathology, although most, even if present, will not require intervention (Video 1).

The vast majority of children show resolution of symptoms by the age of 2 years. Treatment of concomitant reflux is important. 10–15% of the patients may develop medical problems such as failure to thrive, obstructive sleep apnea, and cor pulmonale resulting from chronic hypoxia. In these instances, surgical treatment may be indicated.

The history of surgical procedures dates back to 1922 when Iglauer first performed a partial epiglottectomy in order to remove the redundant tissue from the supraglottic larynx. Hasslinger (1928) reported endoscopic resection of AE folds in three infants using cupped forceps. However, the standard

Congenital Laryngeal and Tracheal Anomalies,
Video 1 Laryngomalacia_video.mpg (Courtesy of Dr KD Pereira)

of treatment continued to be tracheostomy until the resolution of obstructive symptoms and until the gradual advancement of endoscopic laryngeal surgery provided alternatives to tracheostomy.

Lane (1984) improved upon the original Hasslinger technique using Bellucci scissors and microcup forceps to reduce supra-arytenoid mucosa and incise the AE folds. Subsequently, Zalzal described *epiglottoplasty* wherein the lateral epiglottis, the AE folds, and the supra-arytenoid tissues were trimmed using microscissors. Seid popularized the use of CO_2 laser as an alternative to the cold knife technique for division of the AE folds. A review of the results of this procedure showed near-complete resolution of symptoms in 53% of instances (Roger et al. 1995). Relatively rare complications of the procedure include supraglottic stenosis, collapse of the supraglottic framework requiring tracheostomy, posterior glottic stenosis and cricoarytenoid joint fixation.

Laryngoceles

The laryngeal ventricle is a fusiform fossa bounded by the true and the false vocal folds. The anterior part of the ventricular roof converges into a cecal pouch termed the saccule. Laryngoceles are abnormal membranous dilatations of the saccule that communicate with the laryngeal lumen. While internal laryngoceles remain within the lumen of the larynx, external laryngoceles extrude through the thyrohyoid membrane, extending posterosuperiorly into the area of the false vocal cords and AE folds. Combined laryngoceles consist of external laryngoceles that coalesce with a symptomatic dilatation of the internal portion.

Symptoms of laryngoceles include intermittent hoarseness and shortness of breath that may increase with crying spells. A weak cry or aphonia may also be present. Sometimes, dysphagia is also reported.

The pathophysiology of laryngoceles is explained by local increase in pressure within the laryngeal lumen, although congenital or acquired factors may be implicated. Laryngoceles in newborns are unambiguously congenital. In infants and children, anatomical variations of the saccule may be implicated to a greater

degree. These may be acquired solely due to increased intralaryngeal pressures.

Direct laryngoscopy may reveal fullness in the region of the involved false vocal cords and the AE folds. Radiographic evaluation is necessary as these lesions may not be completely visualized under anesthesia. Soft tissue X-ray of the neck is likely to demonstrate a localized dilatation of the laryngeal lumen with increase in size during a Valsalva maneuver.

The operative technique adheres to the principle of adequate exposure for complete excision with minimal intralaryngeal trauma. A lateral horizontal skin incision is made at the superior margin of the thyroid cartilage followed by retraction of the strap muscles. The thyrohyoid membrane is identified and incised along the superior margin of the thyroid cartilage. At this point, the cyst bulges into view from its location within the paraglottic space. If the cyst protrudes through the neck, it may be followed through the thyrohyoid membrane. The cyst is dissected out, the base ligated, and the specimen is removed. It is important to preserve the superior laryngeal nerve during this procedure. With standard anesthetic techniques and careful handling of tissues, the procedure may be performed without the need for a tracheostomy.

Saccular Cysts

These are congenital cystic dilatations of the larynx and are formed in a manner similar to that of laryngoceles, except that the site of origin is the laryngeal saccule, and differ from the laryngocele in that its lumen is isolated from the interior of the larynx and is not air filled. They are entirely submucosal and are covered with normal mucous membrane.

Of the several mechanisms proposed to explain the formation of saccular cysts, the most widely accepted one is that these cysts result from a developmental failure to maintain the patency of the saccular orifice. While congenital saccular cysts result from atresia of the saccular orifice, inflammation, trauma, or tumors may occlude the saccular orifice with the same result.

The lateral saccular cyst extends posterosuperiorly into the false vocal cords and AE folds from the saccule. The anterior saccular cyst extends medially and
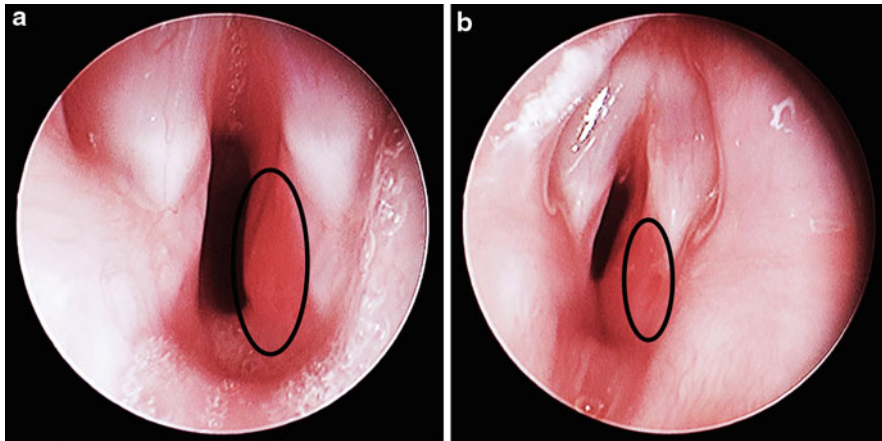
Congenital Laryngeal and Tracheal Anomalies, Fig. 2 Pre- and postoperative images (**a**, **b**) (Courtesy of Dr KD Pereira) of the supraglottic airway with congenital hemangioma. (**b**) shows regression after intralesional injection of corticosteroid. Techniques for treatment are primarily aimed at bypass of the obstruction with tracheostomy and reduction of size using radiation, corticosteroid injection, cryotherapy, sclerotherapy, and, more recently, use of laser to accelerate involution. Both CO_2 and potassium titanyl phosphate (KTP) lasers have been advocated for treatment. There is some evidence to favor the use of the KTP laser as the use of CO_2 lasers have been implicated in scar tissue formation leading to subglottic stenosis (Sie et al. 1994)

posteriorly from the saccule into the laryngeal lumen between the true and the false vocal cords.

Direct laryngoscopy may confirm the location of a saccular cyst that was initially evaluated by clinical examination and radiographic evaluation. Confirmation of diagnosis is made by excisional biopsy with cup forceps – and often – may be the only treatment required. Recurrence, on the other hand, is managed by repeated aspiration or unroofing with cup forceps or CO_2 laser.

Vascular and Lymphatic Malformations

Hemangiomas result from an anomalous development of blood vessels and are the most common benign tumors of the head and neck in infants. The natural history consists of an initial proliferative phase with rapid growth in the first 18 months of life. The involutional phase that follows may last for up to 10 years. These malformations present insidiously and also have preponderance toward resolution with time. They tend to cause the most severe symptoms between 1 and 6 months of life, due to the rapid growth during this time. Clinically, they present with attacks of stridor that are episodic and random, potentially related to the

distention of vascular spaces within the lesion. They can thus cause varying degrees of airway narrowing with unpredictable behavior of individual lesions. Lymphatic malformations result from abnormal development of lymphatic channels. Lymphatic malformations of the supraglottis are cystic malformations that result from abnormal development of lymphatic vessels. Lymphangiomas within the vallecula may compress the epiglottis and cause airway distress. Symptoms may include bleeding, changes in speech, dyspnea, and dysphagia. They have potential to cause airway obstruction from direct compression (Fig. 2a, b). These lesions may also cause bleeding, dyspnea, and/or dysphagia.

The differential diagnosis of an airway hemangioma in infants is similar to that of other structural lesions that can cause stridor due to luminal narrowing. These include laryngomalacia and tracheomalacia, laryngeal papilloma, granuloma, mucocele, cysts, and lymphangioma.

Traditionally, radiological diagnosis was made by inspiratory anteroposterior and lateral X-rays of the neck with special filters for better visualization of the upper airways. Rigid endoscopic findings may sometimes be equivocal, with atypical lesions or when the vertical extent of the lesion cannot be determined

accurately. In such instances, dynamic contrast-enhanced CT may be a useful adjunct (Koplewitz et al. 2005).

Improved pediatric laryngeal surgical techniques have rekindled an interest in surgical management of subglottic vascular lesions from the 1980s. The technique of submucosal excision of hemangiomas in conjunction with anterior cricoid split avoided the complications of subglottic stenosis and recurrent nerve paralysis. This approach is considered by some authors as the technique of choice for large lesions and lesions with extra-laryngeal extension (Hoeve et al. 1997).

Vocal Cord Paralysis

Vocal fold paralysis has been recognized as the second most significant cause of stridor and hoarseness in infants and children. Incidence between unilateral and bilateral cord paralysis is roughly equal. Narcy (Narcy et al. 1990) reports it as representing 23% of congenital laryngeal pathology, whereas Holinger and Fearon suggest lower figures of 10% and 6.5%, respectively (Holinger et al. 1997). Almost one-half of cases occur in association with other anomalies. Acquired paralysis is intimately related to congenital neurologic abnormalities (meningoceles, Arnold-Chiari malformation, Myasthenia Gravis, or Hydrocephalus) or the neurosurgical procedures used to treat them. Unilateral paralysis is most commonly seen in cardiovascular disorders such as tetralogy of Fallot, abnormalities of the great vessels, and persistent ductus arteriosus (PDA) and is more common on the left side. Laryngeal paralysis may be present at birth or may manifest itself in the first month or two of life.

Stridor is the most common presenting symptom and is often cited as the reason for failure of neonates to wean from nasal CPAP therapy. Ineffective cough, aspiration, recurrent pneumonia, and feeding difficulties are also commonly reported. Voice and cry, however, may be normal particularly in cases of bilateral vocal cord paralysis. Hoarseness and dysphonia are common in cases of unilateral vocal fold paralysis. Feeding difficulties may be encountered secondary to laryngeal penetration and aspiration.

Diagnostic procedures should be deferred until the airway is stabilized and secured. Ideally, this should be performed in the safe setting of an operating room with emergency instrumentation readily available. If the initial symptoms are not life-threatening, an awake flexible laryngoscopic examination should be performed for assessment of vocal cord function. Laryngeal EMG gives information about prognosis and may help differentiate this condition from bilateral cricoarytenoid joint fixation. In the latter, the laryngeal EMG evoked potentials are normal.

Concomitant imaging such as chest films is performed for diagnosis of associated cardiac and/or pulmonary abnormalities. Chest films, however, are useful for detecting associated cardiac or pulmonary anomalies, both of which are common in cases of unilateral paralysis. The course of vagus nerve should be described through CT or MR imaging. A barium swallow can provide evidence of subtle neurologic abnormalities, abnormalities of laryngeal sensation, and can document associated mediastinal anomalies such as vascular rings.

Management is contingent upon the status of the airway. Approximately 50% of children with bilateral cord paralysis require a surgical procedure such as tracheostomy. In cases of mild airway symptomatology with bilateral vocal fold paralysis, expectant close follow up is possible. In cases of Arnold-Chiari malformation, a VP shunt should be considered for urgent brainstem decompression. Vocal cord lateralization is recommended only after waiting for at least 1 year for return of function as spontaneous resolution is seen in about 48–64% of instances. During this time, serial laryngeal EMGs provide information on prognosis.

Procedures used to increase the glottic diameter should be considered in conjunction with those to improve vocalization. Surgical widening of the glottis must balance voice and airway patency issues. Older techniques such as the Woodman procedure have been abandoned. CO_2 laser cordotomy and open arytenoidectomy, arytenoidopexy, arytenoid separation with cartilage grafting or laser arytenoidectomy, and cordectomy have been proposed as more efficacious alternatives. Decannulation rates of over 60% can be expected. Static reanimation procedures have been described. Phrenic to recurrent laryngeal nerve anastomosis, phrenic to posterior cricoarytenoid muscle, and omohyoid nerve muscle pedicles have all been utilized. Laryngeal pacing using electrical stimulation controlled by inspiratory effort is being described as

Congenital Laryngeal and Tracheal Anomalies, Fig. 3 Intraoperative photograph of a laryngeal web causing significant obstruction of the airway (Courtesy of Dr KD Pereira)
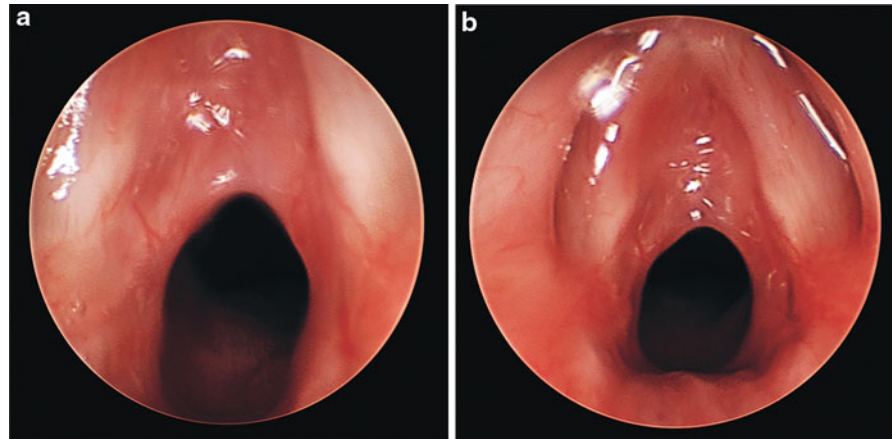
a novel technique for restoration of normal respiratory control of the glottis.

The basic tenet for management of unilateral vocal cord paralysis is watchful waiting. 70% of all cases resolve spontaneously and most within 6 months after onset. A speech therapy consult is recommended for auditory-verbal rehabilitation. Lateral augmentation procedures and thyroplasty techniques are not recommended in children, although a thyroplasty may play a role in older children who fail conservative measures and who also present with significant dysphonia.

Laryngeal Webs

Laryngeal webs form as a result of failure of laryngeal recanalization during embryonic development. 75% of webs that occur at the level of the glottis are composed of a membrane of differential thickness that partially occludes the lumen. Most webs are thick and fibrotic, and are located anteriorly with a concave posterior glottic opening, often extending toward the arytenoids and with an extension into the subglottis. Most webs are thick and fibrous with a subglottic extension. (Fig. 3a, b). 10% of webs are associated with other congenital anomalies that may be located more superiorly in the airway.

The most common symptom seen is vocal dysfunction, with or without an absent/husky voice. Vocal tone is characteristically falsetto. Air movement may be restricted to a degree that can produce complete aphonia. The diagnosis of this condition is usually clear on flexible laryngoscopy; however, airway films may aid in the diagnosis if subglottic or cricoid pathology is also present. Approximately 60% of patients require surgical intervention, and another 30–40% may require tracheostomy. Treatment is dependent on the thickness of the web and degree of airway obstruction. Thin membranous type I webs may be observed until 3–4 years of age and then divided with either CO_2 laser or cold knife. Mitomycin C may reduce recurrence. Some authors employ local flaps to prevent recurrence. Simple dilation is also employed. Other forms of management include endoscopic division with an attempt to prevent recurrence via placement of sutures through the divided edges. Rarely, a laryngofissure is performed to allow removal of redundant soft tissue, with or without the use of a keel. Posterior glottic webbing consists of thin membranous sheets of tissue present between the vocal cords posteriorly. Minor webs may respond to simple division and dilation; however, interarytenoid webs with significant posterior glottic stenosis may require cartilage grafts and placement of a stent.

Subglottic Hemangiomas

Subglottic hemangiomas are present at birth only 30% of the time, with the majority of cases presenting within the first few months of life. The initial period of rapid growth is followed by a period of stability that may continue for 2–3 years after birth. Most lesions spontaneously regress. Symptoms typically follow the same pattern of growth and involution, with majority

Congenital Laryngeal and Tracheal Anomalies, Fig. 4 Airway endoscopic examination of a 6-month child with *circled area* demonstrating subglottic hemangiomas (**a**). (**b**) shows same area after injection of intralesional triamcinolone
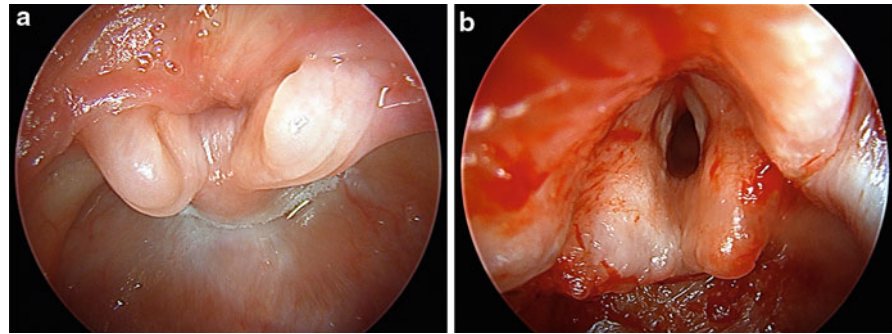
of infants presenting with stridor by the age of 6 months. Stridor may be inspiratory or biphasic. Cough, hoarseness, croup-like symptoms, and occasional hemoptysis may be seen. Cutaneous hemangiomas occur in approximately 50% of children with subglottic hemangiomas. It is thus important to perform a thorough search for skin lesions.

A direct airway endoscopic exam (Fig. 4) is usually necessary for a diagnosis, although a biopsy may not be required. Lesions typically have a bluish or reddish hue and are most commonly seen. Rigid endoscopy should be performed to make the definitive diagnosis; however, biopsy is not always necessary. The lesion is typically a compressible symmetric bluish or reddish submucosal mass typically seen in the posterolateral subglottis. Neck and chest films may show asymmetric narrowing, although similar findings are seen in croup, subglottic cysts and stenosis, or RRP. A contrast-enhanced CT facilitates clear demarcation of the lesion and assessment of cervical or mediastinal extension.

Treatment options are aimed at increasing the airway luminal diameter while preventing recurrence and sequelae of the procedure itself. The treatment modalities that have been described include laser ablation using the CO_2 or KTP laser, tracheostomy, external beam radiation, radioactive gold grain implantation, cryotherapy, sclerosing agents, corticosteroid therapy (systemic or intralesional), and open surgical excision. The most common intervention is CO_2 laser ablation. A recent report documented 20% rate of subglottic stenosis after this treatment modality. Laser excision may be combined with intralesional injection of corticosteroids (triamcinolone, 1–2mg/Kg/day). Long-term side effects from this therapy include growth retardation, cushingnoid appearance, and sepsis directly

related to suppression of HP axis. Children with large subglottic hemangiomas causing severe airway obstruction, necessitating tracheostomy, may benefit from an open procedure. This may be performed in a single-stage procedure requiring postoperative intubation for 7–10 days. Initial use of propranolol for most hemangiomas in the head and neck has found promise when used orally, with reports suggesting successful treatment with the agent alone, often circumventing the need for surgery or the use of long-term corticosteroids. The exact mechanism is unknown, although theories include vasoconstriction, downregulation of growth factors, or cellular apoptosis (Maturo and Hartnick 2010).

Posterior Laryngeal Cleft

The laryngeal cleft arises at approximately 35 days of gestation from failure of rostral development of the tracheoesophageal septum. Failure of the interarytenoid tissue or cricoid cartilage to fuse in the posterior midline will likely result in a laryngeal cleft. In severe cases, the cleft extends inferiorly into the thoracic trachea with possible extension into the mainstem bronchi.

The incidence is less than 0.1%, and the majority of cases are sporadic, with a strong association seen with other anomalies such as tracheoesophageal fistulae. Laryngeal clefts are also seen in Pallister-Hall syndrome, Opitz-Frias, and G-syndrome. Respiratory distress is usually precipitated by feeding and is often associated with cyanosis. Stridor is typically inspiratory, with collapse of supraglottic structures into the laryngeal lumen causing obstruction.

The diagnosis is obtained by careful history and assessment of symptoms specifically related to airway obstruction and aspiration. Radiographic evaluation is performed with water-soluble contrast material only. Aspiration pneumonia may be diagnosed by chest films. Direct laryngoscopic examination in the OR is required for confirmation of diagnosis and for delineation of the vertical extent of the lesion. Attention should be paid to the posterior glottic and interarytenoid areas.

Benjamin and Inglis describe type I clefts as supraglottic, interarytenoid clefts. Type II clefts are partial cricoid clefts. Type III clefts are complete cricoid clefts with or without extension into the esophagus, and type IV clefts are complete laryngotracheoesophageal clefts.

Surgical repair must be undertaken in symptomatic clefts, and a tracheostomy is often necessary to ensure a safe airway. Type I clefts can sometimes be managed nonsurgically with speech and feeding therapy aimed toward decreasing aspiration. Symptoms of GERD must be strictly controlled. When conservative measures fail to prevent aspiration, endoscopic or open repair of the cleft may be possible. Small clefts are managed by injection of Gelfoam or endoscopic interposition grafts. Type II and III clefts can be approached through lateral cervical or posterior pharyngotomy approaches. In revision surgery, an anterior approach is advantageous as the scarring from previous posterior or lateral approaches may place the superior and inferior laryngeal nerves at risk.

Successful management is thus based on (1) precise delineation of the cleft with concomitant stabilization of the airway, (2) control of other coexisting anomalies, (3) treatment of GERD, and (4) asymmetric closure to minimize scar formation.

Subglottic Stenosis

Subglottic stenosis (SGS) may be classified (Potsic et al. 1997) based on (1) cause: congenital or acquired and (2) anatomic characteristics: hard/soft, degree of stenosis, and location of narrowed segment. Congenital SGS is very uncommon although it is the third most common congenital airway problem after laryngomalacia and vocal cord paralysis. Congenital SGS is related to failure of the laryngeal lumen to recanalize properly during embryogenesis. SGS is considered congenital if there is no history of any form of laryngeal trauma including intubation. Subglottic stenosis is defined as a subglottic lumen 4.0 mm or less in diameter at the level of the cricoid in a full-term infant. In a premature infant, this number is below 3.5 mm in the stenotic area.

Congenital SGS is divided broadly into cartilaginous and soft tissue (cartilaginous), based on histopathological appearance. Membranous SGS is usually circumferential and consists of fibrous soft tissue thickening caused by increased fibrous connective tissue or hyperplastic submucous glands that may involve the vocal folds. The cartilaginous type usually results from a thickened or deformed cricoid cartilage that forms an anterior subglottic shelf that extends posteriorly, allowing only a small posterior opening. Other malformations exist, such as an elliptical cricoid leaving a slit-like opening or a trapped first tracheal ring. Membranous SGS is usually less severe compared to the cartilaginous type. Congenital SGS demands a search for other associated anomalies (Fig. 5, Video 2).

The severity of congenital subglottic stenosis is related to the degree of subglottic narrowing. Symptoms can range from mild, with a picture of recurrent croup, to severe with respiratory distress starting from birth. Children with subglottic stenosis usually present with stridor and/or respiratory distress. Symptoms include irritability, restlessness, dyspnea, tachypnea, and cyanosis. The stridor is typically biphasic. Children with mild congenital SGS who are otherwise asymptomatic may have signs of respiratory distress when there is a concomitant UTI or on physical exertion. It is thus important to perform airway endoscopic examination in any child with recurrent croup in order to rule out congenital SGS. The evaluation of SGS includes a complete history and physical examination. The standard for diagnosis is direct laryngoscopic and bronchoscopic examination under general anesthesia. Radiographic evaluation may be valuable, with the subglottis appearing narrowed and peaked – often described as the steeple sign. Fluoroscopic examination may reveal vascular malformations and GERD that may exacerbate symptoms. A CT or MRI is not routinely indicated. Dual-channel pH probe testing is useful for evaluation of GERD. GERD should be treated prior to surgical treatment.

Congenital Laryngeal and Tracheal Anomalies, Fig. 5 Intraoperative photographs (**a**, **b**) (Courtesy of Dr KD Pereira) show narrowed subglottic luminal diameters in congenital subglottic stenosis
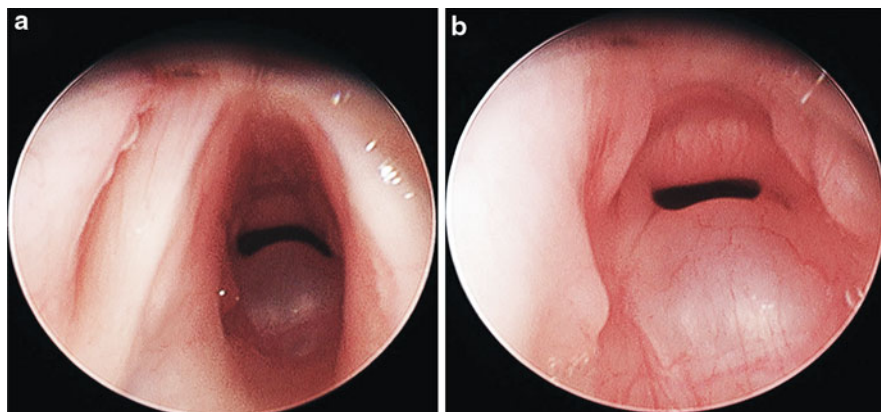
Congenital Laryngeal and Tracheal Anomalies, Video 2 Subglottic_stenosis.mpg (Courtesy of Dr KD Pereira)

Congenital Laryngeal and Tracheal Anomalies, Table 2 Myer-Cotton grading of degree of obstruction in subglottic stenosis

Grade	Degree of obstruction
I	0–50% of luminal obstruction
II	51–70% of luminal obstruction
III	71–99% of luminal obstruction
IV	100% obstruction, no detectable lumen

including rigid bronchoscopes, laryngeal forceps, and angioplasty catheters.

Myers and Cotton devised a staging procedure based on severity of circumferential stenosis (Myer et al. 1994). The system consists of four grades and is shown in the table below (Table 2).

The subglottis and the glottis should be further evaluated for presence of any fixation, scarring, granulation, edema, and paralysis. The vertical and luminal extent of the stenotic segment should be assessed.

Mild stenosis (Cotton-Myer grades I and II) usually do not require surgical intervention. Surgery is reserved for instances where the child continues to have intermittent or persistent stridor. In cases that do require surgery, endoscopic techniques such as CO_2 laser resection of a membranous web can be performed. A popular technique is the use of CO_2 laser to make four radial incisions followed by dilation. However, laser is known to cause recurrence of stenosis in mature stenosis and should be carefully used, possibly in conjunction with mitomycin C in order to prevent fibrotic reaction. Factors associated

In a child with mild to moderate obstruction, a flexible fiber optic nasopharyngoscopy and laryngoscopy should be performed. Flexible examination may be substituted by formal bronchoscopic examination in the OR setting in a child with severe symptoms. Flexible examination should rule out pyriform aperture stenosis and choanal atresia with attention to the adenoid pad. The endoscope should then be advanced for assessment of the supraglottis. In addition, the true cords should be assessed for edema and erythema. Rigid laryngoscopy and bronchoscopy is the single test that offers the best visualization of the subglottis and the tracheobronchial tree. Measurements are done either subjectively or by using various instruments

with failure of these endoscopic techniques include previous attempts at endoscopic repair, circumferential scarring, loss of cartilaginous support, exposure of cartilage during laser excision leading to chondritis, severe bacterial infection, posterior inlet scarring with arytenoid fixation, combined laryngeal or tracheal stenosis, or vertical scar length >1 cm.

Grade III or IV stenosis may require some form of open surgical procedure, as these typically are the result of a cartilaginous stenosis. Several techniques have been described.

The anterior cricoid split (ACS) procedure was originally described for a neonate who has had multiple failed extubations instead of performing a tracheostomy (Cotton and Seid 1980). This procedure may also be performed in older children in whom a tracheostomy has already been performed. Indications were later expanded to include patients with congenital subglottic stenosis. Criteria as established by Cotton include extubation failure on two occasions or more due to laryngeal pathology, weight >1,500 g, no assisted ventilation for 10 days prior to evaluation, O_2 requirements <30 %, no CHF for 1 month prior to evaluation, no acute respiratory tract infection, and no antihypertensive medications 10 days prior to evaluation. The procedure may be performed only after confirmation of the diagnosis via an endoscopic examination. In principle, the procedure involves a vertical midline incision through the cricoid and the first two tracheal rings and may be extended into the lower thyroid cartilage.

A vertical midline incision is made through the cricoid cartilage and first two tracheal rings as well as the lower thyroid cartilage. This is followed by placement of stay sutures that are applied to either side of the cricoid cartilage and reapproximation of the skin after insertion of a drain. This allows the cartilages to spring open and allow edematous mucosa to drain, increasing airway size. The child is then left intubated, sedated, and paralyzed in the ICU for 7–14 days.

Laryngotracheoplasty (LTP) is shown to have higher success rates for treatment of symptomatic SGS when compared with ACS. The procedure may be performed with a tracheostomy and stenting using dedicated stents (Teflon, ETS Poirot, or silastic [Montgomery] stents). Alternatively, an endotracheal tube may be used to stent the larynx and the trachea. Success of LTR is determined by the surgical procedure, including possible need for stenting, choice of type and

length of stent, and duration of stenting. The key to a successful outcome in surgical repair of laryngotracheal stenosis in children is the choice of surgical procedure, including possible need for stenting, choice of type and length of stent, and duration of stenting. Choosing the appropriate method for stenting requires careful consideration of the consistency of stenosis, altered anatomy, size, location, and stability of grafts when used for surgical repair and host tissue healing factors (Zalzal 1988). An accepted and popular method is use of autogenous costal cartilage for grafting. Auricular, hyoid, and thyroid cartilage may also be used. Although use of bone grafts may provide good tensile strength, cartilage has much less resorption over time. If anterior luminal augmentation is performed, it is important to adhere to standard principles that include (a) lesion should not involve the glottis, (b) alternate procedures may be considered if cricoid cartilage is structurally insufficient, (c) the perichondrium should be oriented in the same direction as the lumen, and (d) use of large external flange prevents the prolapse of the graft into the airway.

In posterior glottic stenosis or posterior glottic stenosis that extends into the glottis, the cricoid is divided both anteriorly as well as posteriorly. Although a complete laryngofissure is suboptimal, this may potentially be necessary. Superiorly, the incision is extended to the interarytenoid area and inferiorly to the membranous trachea. An appropriately sized graft is then sutured in place without any tessellation within the lumen, to prevent aspiration. Maximum acceptable level of distraction is 0.05–1 mm/1 year of age, up to a maximum of 1 cm. Long-term stenting (3–6 months) may be required. Once the graft is sutured in, a decision must be made whether the procedure is single- or two-staged. If a two-staged procedure is considered, the strap muscles in the neck must be separated, providing adequate exposure and subsequent closure providing adequate blood supply to the outer surface. The latter is recommended for severe stenosis, history of reactive airway, or poor pulmonary function (Walner et al. 1999).

The first cricotracheal resection (CTR) with thyrotracheal anastomosis was performed by Conley in 1953 for a case of laryngeal chondroma. After being popularized by Ogura and Powers (1964) as a technique for treatment of traumatic stenosis, it rapidly became the treatment of choice in adults with

Congenital Laryngeal and Tracheal Anomalies, Fig. 6 Inspiratory (**a**) and expiratory (**b**) MRI images (Courtesy of Dr KD Pereira) of the airway in tracheomalacia, illustrating the dynamic collapse of the airway with changes in intrathoracic pressure
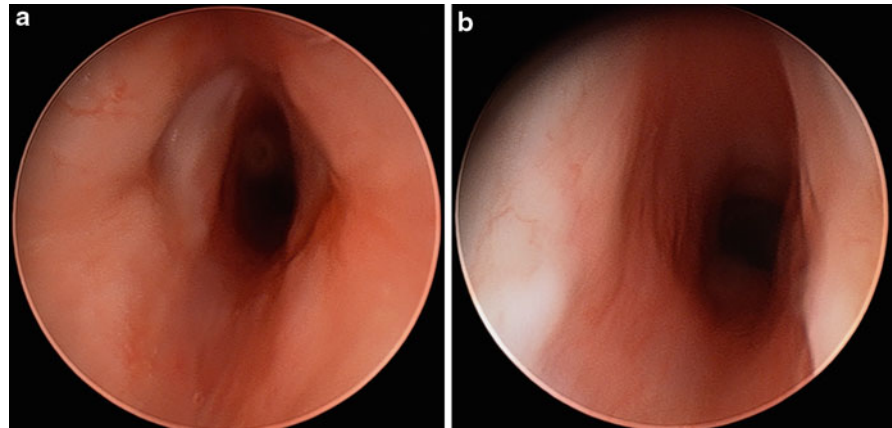
acquired subglottic stenosis from intubation-related injury. Until recently, this procedure was not widely accepted in pediatric patients due to the risk of anastomotic dehiscence and recurrent laryngeal nerve injury and disturbance of the normal growth of the larynx. The first successful CTR performed in a child was subsequently performed in 1978 (Monnier et al. 1993).

Tracheal Anomalies

Tracheal Agenesis

This is an extremely rare anomaly with an incidence <1:50,000. Although it is not compatible with prolonged life, a diagnosis may be made by an inability to produce an audible cry, and intubation is nearly always unsuccessful. However, if a TEF is present, accidental esophageal intubation may temporarily improve respiratory status. Antenatal USG may reveal presence of hyperechoic lungs. Due to the complexity of this defect, a surgical algorithm does not exist. Survival is exceedingly rare. It is expected that tissue engineering may offer some promise through the provision of cartilaginous reconstruction of the airway using cultured chondrocytes.

Tracheobronchomalacia

Tracheomalacia (TM) refers to decreased tensile strength of the trachea, due to reduction and/or atrophy of the longitudinal elastic fibers of the pars membranacea, or impaired cartilage integrity, such that the airway is structurally weak. Thus, due to increased compliance, the normal intrathoracic trachea

dilates with inspiration and narrows with expiration, due to the difference between intrathoracic and intraluminal pressures. If the mainstem bronchi are also involved, the term used is tracheobronchomalacia. Primary (Fig. 6) or secondary (Figs. 7 and 8) tracheobronchomalacia (TBM, Table 3) represents one of the commonest causes of significant airway collapse leading to obstruction. Here, mucosal defects lead to increased airflow resistance and, consequently, the work of breathing. Management is often complicated by mucosal defects leading to increase in airflow resistance and work of breathing. This condition may spontaneously resolve in 1–2 years. Permanent measures are indicated in children who have ALTEs, recurrent pneumonia, or those who cannot be weaned from long-term ventilation. The condition may also result from vascular compression. Rarely, a primary disorder such as dyschondroplasia or polychondritis may lead to TBM.

The mainstay of treatment in the past was tracheostomy and long-term ventilation. In addition, long tracheostomy tubes were developed that could potentially pneumatically stent the distal trachea. CPAP is also an effective treatment for infants with moderate to severe TBM. The major disadvantages, however, are related to delayed speech and language development, intermittent respiratory obstruction, and developmental delays.

In treatment of vascular anomalies causing TBM, aortopexy has been described as a useful surgical technique. The ascending aorta may be exposed via a right-sided anterior thoracotomy within the third intercostal space (Applebaum and Woolley 1990). Sutures are placed on the aortic wall, opposing the aorta to the
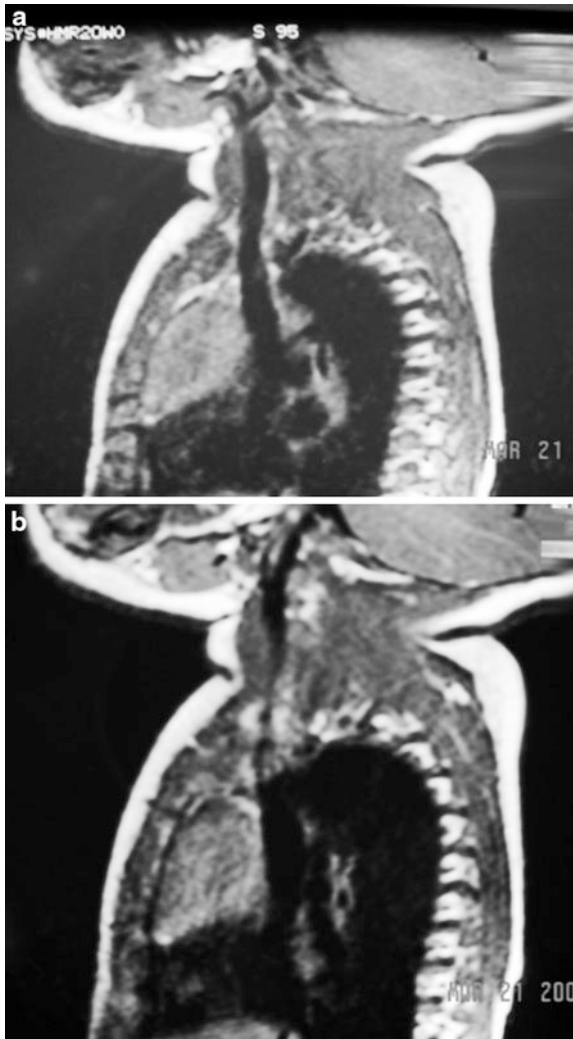
Congenital Laryngeal and Tracheal Anomalies, Fig. 7 T1 MRI images (Courtesy of Dr KD Pereira) of the chest show static compression of the airway from an aberrant aortic arch
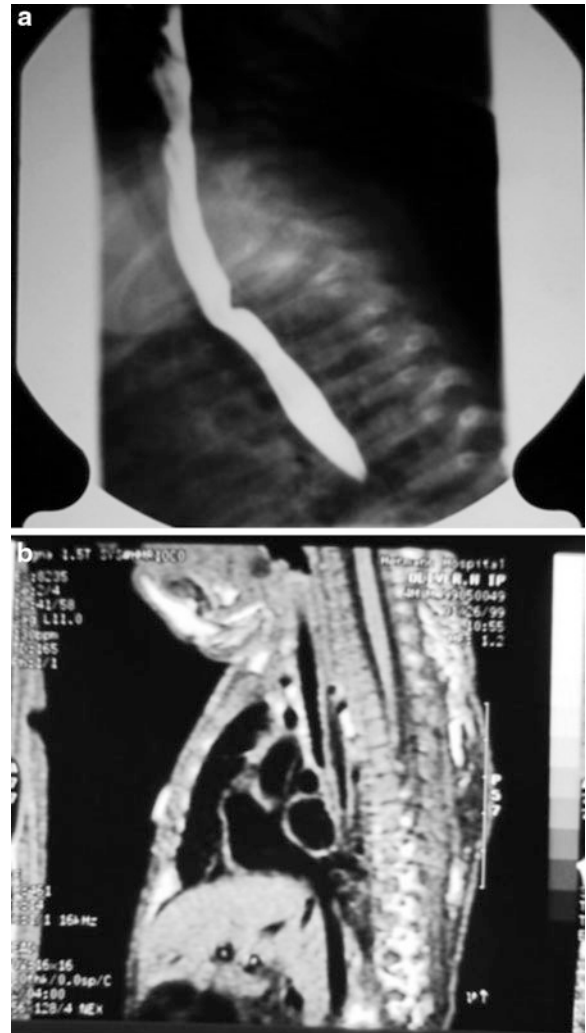
Congenital Laryngeal and Tracheal Anomalies, Fig. 8 Barium swallow exam (**a**) of the airway and equivalent MRI (**b**) show static compression of the trachea from an aberrant course of the left subclavian artery (Courtesy of Dr KD Pereira)

posterior sternum. Thus, the mechanical fixation of the aorta widens the anteroposterior extent of the trachea, preventing collapse. Additional surgical procedures may also be required.

Support can be provided either by suturing rigid support material directly to the membranous trachea through a posterolateral right thoracotomy or by applying it to the circumference of the trachea through an anterior cervical or median sternotomy approach. Hagl and colleagues described bronchoscopically guided, external tracheobronchial suspension within a ring-reinforced PTFE prosthesis, which reduced the degree of collapse of the trachea or mainstem bronchi in infants without the need for resection. Stenosis-free tracheobronchial reexpansion was achieved in all patients, as seen on repeated bronchoscopies during hospitalization and thereafter. All patients were extubated within 1–12 days after the operation. In animal studies and in limited human studies, this procedure did not affect the growth of the trachea adversely. However, it is an invasive procedure that may not treat distal bronchial lesions adequately and may not be well tolerated by patients who have complicated conditions (Sandu and Monnier 2007).

Congenital Laryngeal and Tracheal Anomalies, Table 3 Etiology of acquired tracheobronchomalacia

Esophageal atresia with TEF	
Extrinsic compression	Vascular causes (innominate, aortic arch ring, pulmonary artery sling, aberrant right subclavian)
	Cardiac causes (enlarged left atrium, enlarged pulmonary arteries or veins)
	Cysts (lymphatic, thymic cysts, bronchogenic)
	Neoplasms (teratoma, neuroblastoma)
	Infections
Prolonged intubation	
Chondrodysplasias	
Post-traumatic	

Congenital Tracheal Stenosis (CTS)

CTS is a potentially life-threatening anomaly characterized by the absence of membranous portion of the trachea either focally or in a generalized fashion. Tracheal stenosis is defined as reduction in the anatomic luminal diameter of the trachea by more than 50% (Dunham et al. 1994). The formation of complete or near-complete tracheal rings arises from disproportionate growth of the cartilage relative to the posterior tracheal pars membranacea. In addition to near-complete tracheal rings, the infant may also be affected by a vertical fusion of the tracheal cartilage (tracheal cartilaginous sleeve). Defective development of the cervical splanchnic mesenchyme may account for the presence of complete tracheal rings and the frequent association of mediastinal and cervical chondrogenic anomalies like a foreshortened neck and trachea, pulmonary agenesis, and abnormal vasculature (Voland et al. 1986).

CTS is classified into three principal types (Hoffer et al. 1994): (1) generalized hypoplasia, (2) funnel-like narrowing, and (3) segmental stenosis. The stenotic segment is most often composed of completely circular "O" rings of cartilage. Alternatively, disorganized cartilages, ridges, or plates of cartilage may occur. Type I CTS is the term used for a trachea that is mostly stenotic. Type II CTS is a funnel-like stenosis, variably located and of differing lengths. Type III CTS is a short, segmental stenosis, sometimes below an anomalous right upper lobe bronchus, and type IV CTS occurs when there is an anomalous right upper lobe bronchus with a "bronchus" leading to horizontally branching bronchi to the rest of the lung.

In resection and reconstruction of the trachea, it is of paramount importance to prevent anastomotic tension and circumvent the danger of postoperative obstruction secondary to edema. Delicate handling of tissue is important. It is preferable to use 5-0 interrupted polyglactin 910 (Vicryl) sutures due to ease of handling and strength; in addition, they also reduce the incidence of granulation tissue formation. In large numbers of cases, polyglactin 910 sutures are ideal as tracheal anastomotic sutures in terms of ease of use, strength, minimal reactivity, and, most importantly, absence of long-term complications such as granulomas, suture erosion into the lumen, and anastomotic separation and stenosis.

Other Anomalies

The term tracheal bronchus includes bronchial anomalies arising within the trachea or the main bronchus and directed toward the upper lobe territory. The anomalous bronchus usually exits the right lateral wall of the trachea, less than 2 cm above the major carina, and can supply the entire upper lobe or its apical segment. A tracheal bronchus may be displaced or may be supernumerary. Right tracheal bronchus has a prevalence of 0.1–2% and left tracheal bronchus a prevalence of 0.3–1%, in bronchographic and bronchoscopic studies. Patients are usually asymptomatic, but the diagnosis of tracheal bronchus should be considered in cases of persistent or recurrent upper lobe pneumonia, atelectasis or air trapping, and chronic bronchitis. Bronchiectasis, focal emphysema, and cystic lung malformations may coexist. Most of these bronchial branching anomalies are well diagnosed on chest CT as small areas of hypoattenuation arising directly from the trachea. Most patients who have tracheal bronchus do not require treatment; however, in symptomatic patients, surgical excision of the involved segment may be necessary.

Congenital fistulous tracts between biliary and respiratory tracts are extraordinarily rare. These patients present with a cough alone and subsequently progresses often to pneumonia. Respiratory problems begin with cough and progress to intractable pneumonia. The most common location of the fistula is at the level of the carina but may have left and right bronchial connections. Fluid appearing yellow may be identified bronchoscopically. Contrast will identify a long paraesophageal tract connecting to a hepatic duct. This condition has also been seen in a young adult. Excision of the intrathoracic segment with closure at the carina (or bronchus) and at the diaphragmatic level cures this problem.

Tracheal webs may be seen in neonatal or juvenile trachea at the cricoid level, though laryngeal webs are more commonly seen at the level of the glottis. Tracheal webs are usually short and are generally treated endoscopically by laser or a short tracheal resection with end-to-end anastomosis.

Tracheobronchomegaly (Mounier-Kuhn disease) is usually recognized as a congenital disorder, but most patients do not present with symptoms until much later in life. The condition is very rare and is thought to be caused by the absence of the trachealis muscle. The anterior tracheal wall may become indented as the rings fold backward.

Cross-References

▶ Emergency Airways
▶ Emergent Airway
▶ Imaging of Pediatric Neck and Airway
▶ Larynx, Neurological Disorders
▶ Pediatric Inflammatory Airway Disorders
▶ Radiologic Evaluation of Larynx
▶ Subglottic and Tracheal Stenosis in Adults

References

Applebaum H, Woolley MM (1990) Pericardial flap aortopexy for tracheomalacia**. J Pediatr Surg 25(1):30–32
Cotton RT, Myer CM (1999) Practical pediatric otolaryngology. Lippincott-Raven, Philadelphia
Cotton RT, Seid AB (1980) Management of the extubation problem in the premature child. Anterior cricoid split as an alternative to tracheotomy. Ann Otol Rhinol Laryngol 89(6 Pt 1):508
Dunham ME, Holinger LD, Backer CL, Mavroudis C (1994) Management of severe congenital tracheal stenosis. Ann Otol Rhinol Laryngol 103(5 Pt 1):351
Hasslinger F (1928) Zur pathogenes, diagnostik und therapie des stridor congenitus. Ztschr Hals-Nasen-u Ohrenh 21:223–35
Hoeve LJ, Küppers GLE, Verwoerd CDA (1997) Management of infantile subglottic hemangioma: laser vaporization, submucous resection, intubation, or intralesional steroids? Int J Pediatr Otorhinolaryngol 42(2):179–186
Hoffer ME, Tom LWC, Wetmore RF, Handler SD, Potsic WP (1994) Congenital tracheal stenosis: the otolaryngologist's perspective. Arch Otolaryngol Head Neck Surg 120(4):449
Holinger LD, Lusk RP, Green CG (1997) Pediatric laryngology and bronchoesophagology. Lippincott-Raven, Philadelphia
Huntley C, Carr MM (2010) Evaluation of the effectiveness of airway fluoroscopy in diagnosing patients with laryngomalacia. Laryngoscope 120(7):1430–1434
Koplewitz BZ, Springer C, Slasky BS, Avital A, Uwyyed K, Piccard E, Bar-Ziv J (2005) CT of hemangiomas of the upper airways in children. Am J Roentgenol 184(2):663–670
Manning SC, Inglis AF, Mouzakes J, Carron J, Perkins JA (2005) Laryngeal anatomic differences in pediatric patients with severe laryngomalacia. Arch Otolaryngol Head Neck Surg 131(4):340
Maturo S, Hartnick C (2010) Initial experience using propranolol as the sole treatment for infantile airway hemangiomas. Int J Pediatr Otorhinolaryngol 74(3):323–325
Monnier P, Savary M, Chapuis G (1993) Partial cricoid resection with primary tracheal anastomosis for subglottic stenosis in infants and children. Laryngoscope 103(11):1273–1283
Myer CM 3, O'connor DM, Cotton RT (1994) Proposed grading system for subglottic stenosis based on endotracheal tube sizes. Ann Otol Rhinol Laryngol 103(4 Pt 1):319
Narcy P, Contencin P, Viala P (1990) Surgical treatment for laryngeal paralysis in infants and children. Ann Otol Rhinol Laryngol 99(2):124–128
Olney DR, Greinwald JH Jr, Smith RJH, Bauman NM (1999) Laryngomalacia and its treatment. Laryngoscope 109(11):1770–1775
Potsic WP, Cotton RT, Handler SD (1997) Surgical pediatric otolaryngology. George Thieme, New York
Roger G, Garabedian EN, Denoyelle F, Triglia JM (1995) Severe laryngomalacia: surgical indications and results in 115 patients. Laryngoscope 105(10):1111–1117
Sandu K, Monnier P (2007) Congenital tracheal anomalies. Otolaryngol Clin North Am 40(1):193–217
Sie KC, McGill T, Healy GB (1994) Subglottic hemangioma: Ten years' experience with the carbon dioxide laser. Ann Otol Rhinol Laryngol 103(3):167
Voland JR, Benirschke K, Saunders B (1986) Congenital tracheal stenosis with associated cardiopulmonary anomalies: report of two cases with a review of the literature. Pediatr Pulmonol 2(4):247–249
Walner DL, Cotton RT, Willging J, Bove KE, Toriumi DM (1999) Model for evaluating the effect of growth factors on the larynx. Otolaryngol Head Neck Surg 120(1):78–83
Zalzal GH (1988) Use of stents in laryngotracheal reconstruction in children: indications, technical considerations, and complications. Laryngoscope 98(8):849–854

Congenital Mixed Hearing Loss

Brian S. Chen, Scott E. Bevans and James V. Crawford
Department of Otolaryngology, Madigan Healthcare System, Tacoma, WA, USA

Synonyms

Acquired hearing loss; Conductive and sensorineural hearing loss; Genetic mixed hearing loss; Mixed hearing loss

Definition

Congenital mixed hearing loss is that which is present at birth or develops during the first month of life and is comprised of both conductive and sensorineural components. Mixed hearing loss that occurs later in life is considered *acquired* mixed hearing loss and is discussed in another entry. There is significant crossover between these two types of hearing loss; however, there are some entities that are specific to each. ▶ Conductive hearing loss occurs when the outer or middle ear fail to transmit sound wave energy to the inner ear. ▶ Sensorineural hearing loss is secondary to a problem with converting the mechanical energy into an electrical signal. The error may occur in the inner ear (cochlea) or in the pathway of transmission to the auditory cortex.

Etiology

Congenital hearing loss (conductive, sensorineural, and mixed) occurs in approximately 1.4 per 1,000 neonates in America (CDC 2011). Of these, 50% are caused by environmental insults in utero and 50% are caused by inherited defects. Genetic hearing loss can be further broken down into non-syndromic and syndromic associations (70% and 30%, respectively). Furthermore, 80% of the non-syndromic congenital hearing loss is a result of autosomal recessive genetic mutations (Table 1) (Yildirim and Yilmaz 2006).

Congenital Mixed hearing comprises only a small subset of ▶ congenital hearing loss. At the time of this publication, there are no published statistics, to our knowledge, on the prevalence of congenital mixed hearing loss. However, it can be inferred that it is less than 15% of all congenital hearing loss (<15 in 200,000 neonates), as it most commonly occurs within the category of congenital syndromic hearing loss.

A mixed hearing loss, by definition, must include impairment to both the conductive and sensorineural parts of the hearing pathway. The conductive component comes from pathology associated with the external or middle ear. This includes all components from the auricle to the oval window of the cochlea. The sensorineural component comes from pathology to the inner ear through the auditory pathway to the brain. Table 2 presents a list of congenital ear abnormalities, which of course is not all encompassing.

Any combination of a conductive and sensorineural congenital abnormality from Table 2, in theory, would cause a mixed hearing loss. Additionally, there are distinct congenital syndromes associated with mixed hearing loss. These will be discussed later in the differential diagnosis portion of this entry.

It is important to emphasize the embryology behind ear development and highlight some key steps to help better understand congenital malformations. The ▶ auricle develops from the fusion of six mesenchymal proliferations, called hillocks, at the dorsal ends of the first and second pharyngeal arches surrounding the first pharyngeal cleft (Sadler 2004). The first pharyngeal cleft forms the external auditory meatus and canal. Improper fusions of the hillocks result in abnormal auricles, microtia, or even anotia. The exact mechanisms behind these abnormalities are unknown; however, isoretinoin, thalidomide, and mycophenolate mofetil have an associative relationship with microtia (Murakami et al. 2010).

The tympanic membrane has three layers and is formed by the in-growth of the first pharyngeal cleft (ectodermal epithelial lining) and the out-growth of the first pharyngeal pouch (endodermal lining) with remaining mesenchyme in between (fibrous layer). Failure of the first cleft to recanalize at 6 months of fetal life results in canal ▶ atresia or stenosis. It is important to understand that in severe cases of ▶ atresia, the middle ear space and structures are often involved. For this reason, the Jahrsdoerfer classification is often helpful to evaluate the severity of middle ear abnormalities and help judge the likely success of atresia repair (Rodriguez et al. 2007).

The middle ear cavity itself is endoderm in origin. It is derived from the first pharyngeal pouch during week 3 of gestation from the tubotympanic recess. This recess develops from expansion of the first and possibly the second pharyngeal pouch. The ossicles are developed from the differentiation of neural crest mesenchyme of the middle ear, and lined by the epithelium of the first pharyngeal pouch. This development starts during the fourth to sixth week. Initially the neural crest mesenchyme forms cartilaginous models of the ossicles which slowly ossify by 30 weeks and the mesenchyme resorbs, allowing the ossicles to be free (Rodriguez et al. 2007). Any impairment during this maturation process may cause ossicular chain abnormalities (e.g., fixation, complete absence or shortening, ankylosis, or malformation).

Congenital Mixed Hearing Loss, Table 1 Breakdown of congenital deafness

Congenital deafness					
Genetic (50%)					Environmental (50%)
Non-syndromic (70%)				Syndromic (30%)	(Infectious, metabolic, etc.)
AR (80%)	AD (15%)	X-linked (3%)	Mitochondrial (2%)	(Branchio-oto-renal, Pendred, Usher, Waadrenburg, Jervell and Lange-Nielsen syndrome, etc.)	

Congenital Mixed Hearing Loss, Table 2 Congenital ear anomalies (Huang et al. 2012; Rodriguez et al. 2007; St. Martin and Hirsch 2008)

Congenital ear anomalies		
Conductive hearing loss External ear	Middle ear	Sensorineural hearing loss Inner ear
Microtia	Atresia	Michel's aplasia
Anotia	Ossicular chain abnormalities	Cochlear aplasia
Atresia	Absent ossicle	Cochlear hypoplasia
External auditory canal stenosis	Malleus head fixation	Mondini malformation
	Absence of long process of incus	Enlarged vestibular aqueduct
	Malformed stapes (from aberrant facial nerve)	Semicircular canal dysplasia
	Stapes ankylosis	Cochleosaccular dysplasia
	Stapes fixation	Infections (in utero)
	Atresia of the oval or round window	Internal auditory canal stenosis
	Persistent Stapedial Artery	
	Congenital cholesteatoma	
	High riding jugular bulb	

Lastly, the inner ear development starts during the fourth week of gestation with the otic placodes, a pair of surface sensory placodes in the head. The placodes eventually invaginate to form otocysts which later give rise to a ventral component (forming the ▶ saccule and cochlear duct) and a dorsal component (forming the ▶ utricle, semicircular canals, and endolymphatic duct) (Sadler 2004). Together these epithelial structures form the membranous labyrinth. Although the exact mechanisms are complex, it is important to understand that disruptions during this very complicated developmental process may cause incomplete development of one or all parts of the inner ear. Systemic diseases such as cretinism or infections in utero tend to favor disruption of the ▶ Organ of Corti, causing hearing loss that is sensorineural. In cretinism, oftentimes the ossicles are also effected creating a mixed hearing loss picture (Pellitteri et al. 2010). Common infectious pathogens include maternal toxoplasmosis, rubella, CMV, and syphilis.

Clinical Presentation

As implied in its name, congenital mixed hearing loss is present at birth or develops during the first month of life. Ideally, this is discovered during the first few days of life with a failed newborn hearing screen. In areas where universal screening is not mandated, patients may present later in life when they are of school age and having difficulty hearing in school. Oftentimes, pediatricians will be the first to detect an abnormality and initiate the workup with an ▶ audiogram. At this point, it may be difficult to differentiate between a congenital and an ▶ acquired hearing loss.

Diagnostics

The first consistent opportunity to detect hearing loss is after birth via a newborn hearing screen. In the past, hearing screening was only conducted when known risk factors were present (craniofacial anomalies, family history of hereditary hearing loss, NICU admission >2 days, intrauterine infection, or other syndromes associated with hearing loss). Over the past decades, there has been a greater push to mandate universal newborn hearing screening. Groups such as the Joint Committee on Infant Hearing (JCIH), Centers for Disease Control and Prevention (CDC), and American Academy of Pediatrics (AAP) recommend universal newborn screening (Wrightson 2007). In fact, the 2009 National Centers for Disease Control and Prevention's Early Hearing Detection and Intervention (EHDI) program reported 97.4% screening in all documented US births, a considerable improvement from previous years (CDC 2011).

The two main screening modalities in infants are ▶ otoacoustic emissions (OAEs) and acoustic brainstem responses (ABRs). Specifically, ▶ transiently evoked otoacoustic emissions (TEOAEs) and automated acoustic brainstem responses (AABRs) are used. TEOAEs evaluate the function of the peripheral auditory system through a small probe placed in the ear canal which delivers a click stimulus. The ▶ outer hair cells of the cochlea transmit a physiologic response to these clicks which is detected by a microphone in the same ear probe. These responses are then compared to emission norms and a pass or fail report is generated. AABRs are able to measure the auditory function from the eighth nerve and auditory brainstem by using electrodes placed on the patient's forehead and neck, with the ears being covered with earphones. A series of clicks are emitted through the earphones, and the brain wave responses are measured and compared to normal response templates.

There currently is no evidence supporting the use of AABRs over TEOAEs. At our institution, all newborns on the postpartum floor receive ▶ distortion product otoacoustic emissions (DPOAEs) and all neonates admitted to the NICU receive AABRs and DPOAEs. DPOAEs are very similar to TEOAEs, except in that two tones or frequencies are delivered instead of one. If a newborn fails their initial DPOAE testing, they receive a repeat exam at 1 month of age. Failure at the second test warrants an ABR. If any NICU patient fails either exam, they will be referred to an audiologist for a formal examination with an ABR (see the auditory/vestibular testing entry for more details). Mixed hearing losses can be detected on formal ABRs. As the patients are followed through life, and binaural subjective data can be obtained, traditional audiograms should be pursued (pictured below in Fig. 1).

Once hearing loss is identified, a congenital hearing loss evaluation algorithm should be used. Currently there is no consensus on a standard workup, however many have been proposed. First, a thorough history and physical should be conducted. Emphasis on maternal infections or systemic illnesses during pregnancy as well as a family history of hearing loss should be delineated in the history. The physical exam should assess for syndromic facial characteristics (e.g., branchial clefts, auricle abnormalities, thyroid goiters, facial symmetry). Thorough ophthalmologic examination should be included due to the high prevalence of concurrent ophthalmologic problems. Additionally, hearing-impaired children are so heavily reliant on visual input. Experts generally agree that an EKG (abnormalities present in Jervell Lange-Nielsen Syndrome), Connexin 26 screening (most common cause of autosomal recessive non-syndromic hearing loss), and radiographic workup should also be considered (De Leenheer et al. 2010).

A high-resolution computed tomography (HRCT) scan of the temporal bones is the imaging study of choice for most congenital hearing loss because most anatomic causes are due to abnormalities of the middle or inner ear (St. Martin and Hirsch 2008). Abnormalities of the ossicles to include fused, malformed, or absent ossicles, lateral chain fixation, and facial nerve abnormalities are particularly important when looking for either a conductive or mixed hearing loss etiology. Inner ear malformations such as a mondini malformation, Michel's aplasia, round or oval window atresia, and internal auditory canal stenosis can also be visualized on HRCT studies.

Differential Diagnosis

Even after a thorough evaluation, a child with congenital mixed hearing loss may still not have a firm diagnosis. Direct visualization of the middle ear space in the operating room may be necessary later in life. Additionally, the presence of a middle ear effusion in
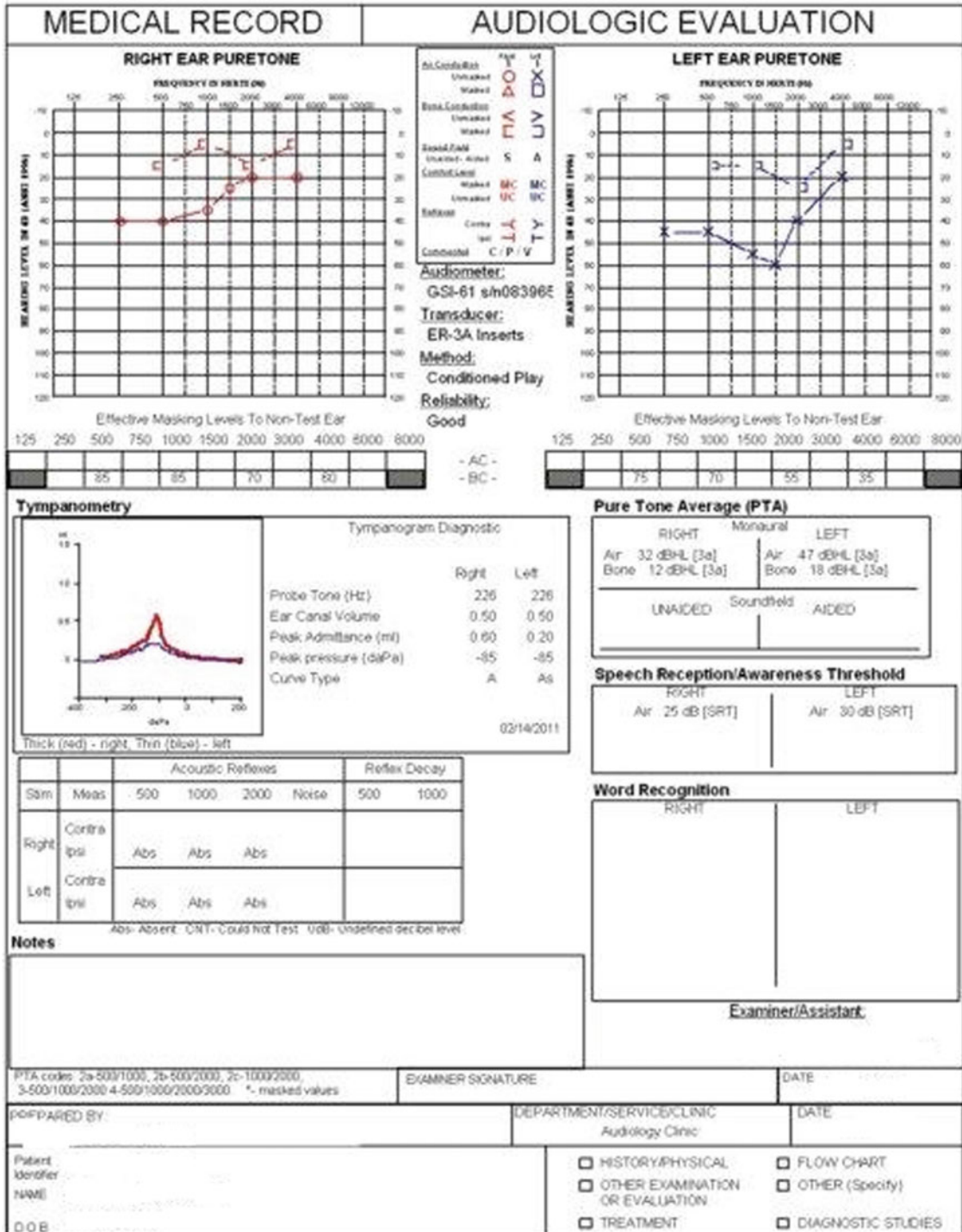
Congenital Mixed Hearing Loss, Fig. 1 This is an audiogram of a 4-year-old child we identified and have been following since birth. There is right-sided conductive hearing loss and a left-sided mixed hearing loss. The etiology at this time still remains unclear

the setting of congenital sensorineural is not congenital mixed hearing loss, but rather acquired, and is discussed in another entry. Listed below are the more common conditions that have congenital mixed hearing loss associations. However, it is important to remember that the incidence of these conditions is very low.

Congenital Cretinism

Cretinism is a condition of physical and mental growth retardation due to untreated congenital hypothyroidism. Congenital hypothyroidism is most frequently due to iodine deficiency which has been largely eliminated in the developed world. Progressive mixed hearing loss is reported in one half to nearly all children with endemic cretinism (Meyerhoff 1979). Hearing loss with hypothyroidism may be conductive, sensorineural, or mixed. It tends to be more severe and mixed in congenital than in adult hypothyroidism. Oftentimes, there are ossicular chain abnormalities and edema of the eustachian tube mucosa causing a conductive hearing loss. The sensorineural hearing loss is a result of the myxedematous changes in the ▶ organ of corti and ▶ tectorial membrane. In adults, severe myxedema may cause bilateral symmetric and progressive sensorineural hearing loss.

CHARGE Association

CHARGE association refers to the presence of four of the six listed congenital anomalies that occur in random which include *c*olobomas, *h*eart defects, choanal *a*tresia, *r*etarded growth (neurological), *g*enital hypoplasia, and *e*ar anomalies (Edwards et al. 1995). It is associated with mutations in chromosome 8. Among the ear anomalies, CHARGE includes the external, middle, and inner ear malformations which can cause a conductive, sensorineural, or mixed hearing loss. In the external ear, there can be wide and short pinnas and cup deformities. In the middle ear, Wright et al. describe absence of stapedial muscles, absence of the oval window, aberrant course of the facial nerve, and dehiscence of the facial nerve canal. In regard to the inner ear, Wright also describes a Mondini-type malformation of the cochlea in addition to multiple anomalies of the vestibule (Wright et al. 1986). CHARGE can also be associated with lateral semicircular canal dysplasia which can cause an isolated conductive, sensorineural, or mixed hearing loss (Johnson and Lalwani 2000). A CT scan, in particular, is useful to help delineate these middle and inner ear abnormalities.

Branchio-Oto-Renal (BOR) Syndrome

BOR is an autosomal dominant syndrome with an estimated prevalence of 1:40,000 caused by a mutation in the *EYA1* gene. BOR presents with a spectrum of clinical manifestations to include second branchial clefts; hearing loss; malformations of the outer, middle, and/or inner ear; and renal anomalies ranging from mild hypoplasia to complete agenesis (Kemperman et al. 2004). CT scans are also helpful to visualize cochlear hypoplasia or dysplasia, large vestibular aqueducts, ossicular chain abnormalities, and cochlear nerve hypoplasia which are commonly found with this syndrome (St. Martin and Hirsch 2008).

Treacher Collins Syndrome

▶ Treacher Collins Syndrome, also known as Franceschetti syndrome or mandibulofacial dysostosis, is a rare autosomal dominant congenital disorder associated with a TCOF1 gene, and is characterized by craniofacial deformities such as absent zygomas, malformed small ears, auditory pits, down slanting palpebral fissures, and micrognathia. Hearing loss in these patients is conductive 55% of the time in concert with a high proportion of high-frequency sensorineural hearing loss.

Hemifacial Microsomia

Hemifacial microsomia is a craniofacial disorder that occurs in 1 in 5,600 births which is also commonly known as ▶ Goldenhar syndrome, oculoauriculovertebral sequence, oculoauriculovertebral dysplasia, and "first and second branchial arch" anomalies. The involvement of the ear can be highly variable. External and middle ear anomalies of this syndrome include a flattened helical rim of the pinna, preauricular skin tags, microtia, external canal atresia, ossicular chain abnormalities, and anotia (Carvalho et al. 1999). Although the inner ear is not classically affected, there seems to be an increasing association of sensorineural hearing loss.

Klippel-Feil Syndrome

Klippel-Feil syndrome (KFS) is a congenital abnormality of the vertebrae characterized by vertebral malformations of the atlas and axis resulting in

a short neck, low posterior hair line, and limited neck mobility. KFS also has extraskeletal manifestations to include renal, cardiac, neural tubes, cleft palate, and ear abnormalities. Yildirm et al. described a spectrum of ear findings to include low-set ears, microtia, and numerous ossicular malformations (deformed caput mallei, rudimentary incus head, shortened incus, stapes footplate fixation) causing conductive hearing loss. Mondini deformities are also common, causing a sensorineural hearing loss (Yildirim et al. 2008).

Prophylaxis

Fifty percent of congenital hearing loss is caused by inherited genetic defects and are largely unpreventable; therefore, prophylaxis does not apply after birth. For the other 50% of cases caused by environmental issues, appropriate prenatal care cannot be overemphasized. Good prenatal care will serve to detect (or prevent via vaccinations) infectious etiologies such as TORCHES infections. Prenatal care will also serve to educate mothers on avoiding teratogens (e.g., thalidomides and retinoic acid). Early health screening can also detect maternal metabolic and endocrine issues.

Therapy

The main therapy for congenital hearing loss is bilateral amplification. The push for early detection and intervention has become standard of care, and ensures normal or near-normal speech, language, and social skill development in children. The Joint Committee on Infant Hearing (JCIH), in their published position statement in 2007, emphasized early hearing screening and amplification within 1 month of detection. Depending on the severity of hearing loss, different types of hearing amplification (nonsurgical and surgical) are available. Middle ear explorations as a neonate are not recommended. Some patients may benefit from a middle ear exploration with concomitant ossicular chain reconstruction to help their conductive loss, but this should not be considered until later in life.

Medical Therapy

Congenital mixed hearing loss secondary to congenital cretinism may be one of the few disease processes that are amenable to medical therapy. Even in these populations, 10% of deafness still persist after T_4 therapy (Pellitteri et al. 2010).

Hearing Amplification

Hearing aids are small electroacoustic devices that simply amplify and modulate sound for the wearer. Due to the constant advances in technologies, hearing aids are discrete, powerful, and provide better quality of life for patients with hearing loss than ever before. For congenital hearing loss, in particular, any newborn child with hearing loss greater than 20 dB should be fitted for hearing amplification. Hearing aids come in various varieties. The behind the ear (BTE) hearing aids are most appropriate for children under the age of 7 as their ear canals are perpetually increasing in size. In the ear (ITE) and completely in the canal (CIC) aids tend to be less appropriate. In addition, these smaller hearing aids are more easily lost and are potential airway foreign bodies which are a safety issue for children.

Frequency Modulation (FM) systems should also be encouraged in hearing losses of 55 dB and above to improve the speech-to-noise ratio. A receiver attached to the child's hearing aid and a microphone worn by the caregiver can improve feedback issues in infants who have poor head control and mobility (Norton et al. 2010).

Implantable Devices

In patients with auricular abnormalities, such as microtia or atresia, ▶ bone-anchored hearing aids (BAHA) should be considered because hearing aids may be poor fitting. BAHAs work by rerouting sound directly to bone via a sound processor and an osseointegrated implant that is located behind the ear. The sound processor detects sound waves, enhances the signal, and converts it into vibrations that are transmitted through the abutment implanted into the skull. This allows sound energy to bypass the outer and middle ear malformations and be transmitted directly to the inner ear for conversion to sensorineural input.

Disadvantages of BAHAs include the complications that occur to the skin surrounding the transducer and osseointegrated abutment. Meticulous skin care is required to prevent overgrowth or breakdown of skin around the implant. Poor osseointegration and need for revision implants can also be an issue. Lastly, BAHAs

can have poor cosmesis in patients who wear their hair short. The clear benefit of BAHAs, however, is its reversibility and ability to bypass the conductive components of hearing.

Implantation is limited to the cortical thickness of the skull, so most patients are unable to implant until about 3–4 years of age (Snik et al. 2008). In the meantime, the BAHA can be attached to a special disk held in place by a steel headband of an elastic headband called the BAHA Softband. This can be used bilaterally if necessary with no impact on speech and language development. The BAHA Softband is also a great modality to trial the efficacy of a BAHA prior to implantation in older patients (Cochlear 2011).

Cochlear Implantation

▶ Cochlear implantation (CI) is an excellent modality for profound sensorineural hearing loss when hearing aids and BAHAs are of little benefit (please refer to the entry on surgically implanted devices for more information). CIs can bypass the conductive components of hearing and can directly stimulate nerve hearing which is beneficial for congenitally mixed hearing loss patients. Major contraindications for CI are inner ear or eighth nerve abnormalities; so CT temporal bones and an MRI of the internal auditory canals are imperative for preoperative planning.

Middle Ear Implantable Devices

There are several middle ear implantable devices on the market. Most are indicated for sensorineural hearing loss, but work in Europe has shown significant benefits in patients with mixed hearing loss. ▶ Vibrant Sound Bridge (VSB) is an example of an active middle ear implant that utilizes a floating mass transducer on the round window, oval window, or medial ossicular chain to transmit sound wave energy into the inner ear. For this reason, it is also an excellent device for patients who have middle and/or external ear abnormalities. Sound is picked up from a microphone on the audio processor which is a removable device worn on the skull behind the ear. This device transforms the sound energy into an electrical signal and transmits it across the skin to an implanted receiver which then relays the signal down to the floating mass transducer resting in the middle ear. This is an excellent option for patients

who have failed BAHAs or hearing aids. Recently, an international committee convened in Frankfurt, Germany and deemed the Vibrant Sound bridge "appropriate for application in subjects under age 18, when the subjects satisfy the inclusion criteria, including having adequate anatomy to allow placement of the VSB and when weighed against and compared to other potential therapies" (Cremers et al. 2010). The exact lower age limit for implantation, however, is still in question. Please refer to the ▶ Hearing Aid entry for more details.

With any of the above modalities, close follow-up with audiologist for aid adjustments is vital to normal speech and language development.

Prognosis

Congenital mixed hearing loss, with the exception of hearing loss caused by congenital hypothyroidism, is a permanent condition and often progressive. Emphasis should be made on early detection and intervention to minimize the sequelae (speech and language development) of this disease process.

Cross-References

▶ Acquired Mixed Hearing Loss
▶ Acute Otitis Media
▶ Atresiaplasty
▶ Audiometry
▶ Auditory System Exam
▶ Autoimmune Sensorineural Hearing Loss
▶ Bone-Anchored Hearing Aid in Pediatrics
▶ Bone-Anchored Hearing Aid in Single-Sided Deafness
▶ Bone-Anchored Hearing Aids in Conductive and Mixed Hearing Loss
▶ Boney Lesions of the Temporal Bone (Fibrous Dysplasia)
▶ Cartilage Tympanoplasty
▶ Cholesteatoma, Acquired
▶ Chronic Otitis Media
▶ Cochlea, Anatomy
▶ Cochlear Implantation, Revision – Adult
▶ Cochlear Implants (CIs)
▶ Conductive and Mixed Hearing Losses, Use of Vibrant Soundbridge

References

Carvalho GJ, Song CS, Vargerrik F, Lalwani AK (1999) Auditory and facial nerve dysfunction in patients with hemifacial microsomia. Arch Otolaryngol Head Neck Surg 125:209–212

Centers for Disease Control and Prevention. Hearing Loss in Children. http://www.cdc.gov/ncbddd/hearingloss/index.html. Accessed 28 June 2011

Cochlear. http://www.cochlearamericas.com. Accessed June 28 2011

Cremers CW et al (2010) International consensus on Vibrant Soundbridge implantation in children and adolescents. Int J Pediatr Otorhinolaryngol 74:1267–1269

De Leenheer EMR, Janssens S, Padalko E, Loose D, Leroy BP, Dhooge IJ (2010) Etiological diagnosis in the hearing impaired newborn: proposal of a flow chart. Int J Perdiatr Otorhinolaryngol 75:27–32

Edwards BM, Van Riper LA, Fileny PR (1995) Clinical manifestations at CHARGE Association. Int J Pediatr Otorhinolaryngol 33:23–42

Huang BV, Zdanski C, Castib M (2012) Pediatric sensorineural hearing loss, Part 2: syndromic and acquired causes. Am J Neurorardiol 33(3):399–406

Johnson J, Lalwani AK (2000) Sensorineural and conductive hearing loss associated with lateral semicircular canal malformation. Laryngoscope 110:1673–1679

Kemperman MH et al (2004) Evidence of progression and fluctuation of hearing impairment in branchio-oto-renal syndrome. Int J Audiol 43:523–532

Meyerhoff WL (1979) Hypothyroidism and the ear: electrophysical, morphological, and chemical considerations. Laryngoscope 89:1–25

Murakami CS, Quatela VC, Sie KCY, Shvidler J (2010) Microtia reconstruction. In: Flint: Cummings otolaryngology: head & neck surgery, 5th edn. Mosby, Philadelphia, pp 2741–2751

Norton SJ, Bhama PK, Perkins JA (2010) Early detection and diagnosis of infant hearing impairment. In: Flint: Cummings otolaryngology: head and neck surgery, 5th edn. Mosby, Philadelphia, pp 2718–2725

Pellitteri PK, Ing S, Jameson B (2010) Disorders of the thyroid gland. In: Flint: Cummings otolaryngology: head and neck surgery, 5th edn. Mosby, Philadelphia, pp 1735–1749

Rodriguez K, Shah RK, Kenna M (2007) Anomalies of the middle and inner ear. Otolaryngol Clin North Am 40:81–96

Sadler TW (2004) Langman's medical embryology. Lippincott, Baltimore

Snik A, Leijendeckers J, Mylanus E, Cremers C (2008) The bone-anchored hearing aid for children: recent developments. Int J Audiol 47:554–559

St. Martin MB, Hirsch BE (2008) Imaging of hearing lodd. Otolaryngol Clin North Am 41:157–178

Wright CG, Brown OE, Meyerhoff WL, Rutledge JC (1986) Auditory and temporal bone abnormalities of CHARGE association. Ann Otol Rhinol Laryngol 95:154–161

Wrightson AS (2007) Universal newborn hearing screening. Am Fam Physician 75:1349–1352

Yildirim AB, Yilmaz M (2006) An overview of hereditary hearing loss. ORL 68:57–63

Yildirim N, Arslanoglu A, Mahirogullari M, Sahan M, Ozkan H (2008) Klippel-Feil and associated ear anomalies. Am J Otolaryngol 29:319–325

Congenital Unilateral Lower Lip Paralysis

Carlos M. Rivera-Serrano[1,2] and Barry M. Schaitkin[1]
[1]Department of Otolaryngology, Facial Nerve Center, School of Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA, USA
[2]Department of Surgery, Division of Plastic Surgery, University of Florida College of Medicine, Gainesville, FL, USA

Synonyms

Congenital hypoplasia of the depressor anguli oris muscle. Asymmetrical crying facies. Partial unilateral facial paresis, Partial unilateral facial paralysis.

Definition

Congenital unilateral lower lip paralysis (CULLP) is a *congenital* condition characterized by inversion and decreased depression of the affected lower lip while opening the mouth, which is noticed when the infant cries. CULLP is rare variation of *complete unilateral congenital facial paralysis (CUFP)*, and is caused by congenital palsy of the marginal mandibular branch of the ▶ facial nerve due to abnormal development, or hypoplasia of the depressor anguli oris muscle (Kobayashi 1979; Pape and Pickering 1972). Since the depressor anguli oris muscle is present in most cases, the term "CULLP" has been preferred by some authors (Roedel et al. 1998). Some authors have also included facial nerve compression as a possible etiology for this condition (Sapin et al. 2005).

- Congenital: Existing at or before birth
- Congenital facial paralysis (CUFP): Complete congenital loss or impairment of motor function of the entire hemi-face due to a lesion of the neural or muscular systems

Etiology

Genetic conditions have been associated with both unilateral and bilateral facial palsy. Holmich et al. reported a case of familial congenital facial paresis in five generations. They reported that the paresis varied in location ("i.e., two right-sided and three left-sided, one side unknown"). Electromyographic studies revealed absent voluntary activity of the depressor labii inferioris muscle in the primary patient of the study. They concluded that the findings suggested either absence of the depressor labii inferioris muscle, or absent voluntary activation due to brainstem pathology (Holmich and Medgyesi 1994). Derangements on chromosome 22q11 and two separate loci on 3q4 and 10q have been suggested for being responsible of CULLP. The underlying mechanism of theses malformations is unclear, but may be secondary to a disrupted migration of neural crest cells during early embryogenesis (before the second month) (Pratap et al. 2007).

CULLP has been associated with other congenital anomalies such as cardiac defects. Caylar reported cases of CULLP associated with congenital cardiac anomalies, and coined the term "cardiofacial syndrome" (Caylar 1967, 1969). Therefore, we believe it is prudent to investigate congenital heart problems in patients presenting with CULLP, although the senior author has never found a cardiac anomaly on ECHO in this patient population.

Clinical Presentation

Inversion and decreased depression of the affected lower lip while opening the mouth is noticed when the infant cries. In general, there is no functional deficit secondary to the paralysis (Kobayashi 1979).

Diagnosis

Diagnosis of congenital unilateral lower lip paralysis is clinical. No electromyographic or neurographical test are required (Pratap et al. 2007). It is important to notice that this syndrome is associated with other birth defects.

Differential Diagnosis

The findings are isolated and diagnostic of the condition, easily separating it from cases of complete unilateral congenital ▶ facial paralysis (CUFP).

Therapy

Multiple surgical techniques have been employed with different outcomes. The ideal time for intervention is controversial. Some authors recommend early interventions (preschool) while others recommend doing it later in life; however, most recommend intervening before adolescence (Pratap et al. 2007). "Passive treatments" have been proposed to balance the face by weakening the unaffected side. These include selective marginal mandibular neuronectomy, botulinum toxin injections, and excision of the depressor anguli oris muscle. Some authors have also used bidirectional fascial grafts to restore the aesthetic appearance, and even more invasive microneurovascular free tissue transfer (Udagawa et al. 2007; Pratap et al. 2007; Kubota et al. 2009; Chen and Tang 2007; Tulley et al. 2000). The lesion is very well tolerated and no treatment of something minimal is recommended. Static repositioning is possible during grade school age.

Prognosis

The paralysis is permanent and irreversible if the condition is due to abnormal development of the facial nerve or to hypoplasia of the depressor anguli oris muscle. If the etiology of the paralysis is secondary to trauma during delivery, some recovery is generally expected.

Epidemiology

Some authors have reported that the incidence of "asymmetric crying facies" is 1 in 160 live births; however, traumatic events (facial nerve compression during delivery) were included in the calculation of this number. CULLP is a rare disease, and the true incidence and prevalence is unclear.

References

Caylar GG (1967) An "epidemic" of congenital facial paresis and heart disease. Pediatrics 40:666

Caylar GG (1969) Cardiofacial syndrome: congenital heart disease and weakness, a hitherto unrecognized association. Arch Dis Child 44:69

Chen CK, Tang YB (2007) Myectomy and botulinum toxin for paralysis of the marginal mandibular branch of the facial nerve: a series of 76 cases. Plast Reconstr Surg 120(7):1859–1864

Holmich LR, Medgyesi S (1994) Congenital hereditary paresis of ramus marginalis nervus facialis in five generations. Ann Plast Surg 33:96–99

Kobayashi T (1979) Congenital unilateral lower lip palsy. Acta Otolaryngol 88:303–309

Kubota Y, Kuroki T, Koizumi T, Udagawa A (2009) Bidirectional fascia graft for congenital unilateral lower lip palsy in an adult. J Plast Reconstr Aesthet Surg 62:e121–e122

Pape KE, Pickering D (1972) Asymmetric crying faces: an index of other congenital anomalies. J Pediatr 81:21–30

Pratap A, Agrawal A, Bhatta N, Shakya VC (2007) Congenital unilateral lower lip palsy and eventration of diaphragm. Singapore Med J 48:e209–e211

Roedel R, Christen HJ, Laskawi R (1998) Aplasia of the depressor anguli oris muscle: a rare cause of congenital lower lip palsy? Neuropediatrics 29(4):215–219

Sapin SO, Miller AA, Bass HN (2005) Neonatal asymmetric crying facies: a new look at an old problem. Clin Pediatr (Phila) 44(2):109–119

Schaitkin BM (2003) Facial paralysis in children. In: Bluestone CD (ed) Pediatric otolaryngology, vol 2. Elsevier Health Sciences, Philadelphia, PA

Tulley P, Webb A, Chana JS, Tan ST, Hudson D, Grobbelaar AO, Harrison DH (2000) Paralysis of the marginal mandibular branch of the facial nerve: treatment options. Source Raft Institute of Plastic Surgery, Mount Vernon Hospital, Northwood, Middlesex, UK. Br J Plast Surg 53(5):378–385

Udagawa A, Arikawa K, Shimizu S et al (2007) A simple reconstruction for congenital unilateral lower lip palsy. Plast Reconstr Surg 120:238–244

Conservation Laryngeal Surgery

Brett T. Comer[1] and Thomas J. Gal[2]
[1]Department of Otolaryngology-Head and Neck Surgery, Community Howard Regional Health, Kokomo, IN, USA
[2]Department of Otolaryngology-Head and Neck Surgery, University of Kentucky, Chandler Medical Center, Lexington, KY, USA

Synonyms

Hemilaryngectomy; Organ-preservation laryngeal surgery; Partial laryngectomy; Subtotal laryngectomy

Definition

Conservation Laryngeal Surgery: An all-encompassing term referring to a variety of open and transoral surgical procedures that result in the removal of less tissue than a ▶ total laryngectomy while attempting to maximize oncologic and functional outcomes for the patient. These procedures are generally reserved for earlier (e.g., stage I/II) cancers or localized recurrent cancers, though some specific exceptions exist.

Purpose

The primary goal of oncologic surgical resections is primary tumor control to prevent persistence, recurrence, or metastasis. Preservation of the four main functions of the larynx – respiration, airway protection, deglutition, and phonation – were traditionally considered secondary goals. In this light, ▶ total laryngectomy was the surgical standard for ▶ malignant laryngeal neoplasms. As surgical and nonsurgical therapies evolved for cancers in these regions, head and neck surgeons realized that adequate oncologic results could be achieved via more conservative laryngeal surgery techniques, while preserving some or all of the functions of the laryngeal apparatus (Bron et al. 2005; Mendenhall et al. 2004; Silver et al. 2009; Tuna et al. 2009). ▶ Total laryngectomy evolved to be reserved for either very advanced primary tumors of these locations with extensive tissue destruction, for recurrent tumors of these locations after prior surgery and/or adjuvant therapy such as chemotherapy and radiation, or for the crippled larynx. While many tumors for which conservation or partial laryngeal surgical procedures are indicated may be treated with nonsurgical therapy, specifically chemoradiation, these procedures continue to play a selective role in the management of these tumors.

For ▶ head and neck cancer staging purposes, the larynx has traditionally been divided into the supraglottis, the glottis, and the subglottis. Supraglottic structures develop from the 3rd and 4th branchial arches (the buccopharyngeal analogue), while glottic and subglottic structures arise from the 5th and 6th arches (the tracheobronchial analogue). The fusion creates an embryologic barrier at the level of the ventricle (Tufano et al. 2004). The supraglottis extends
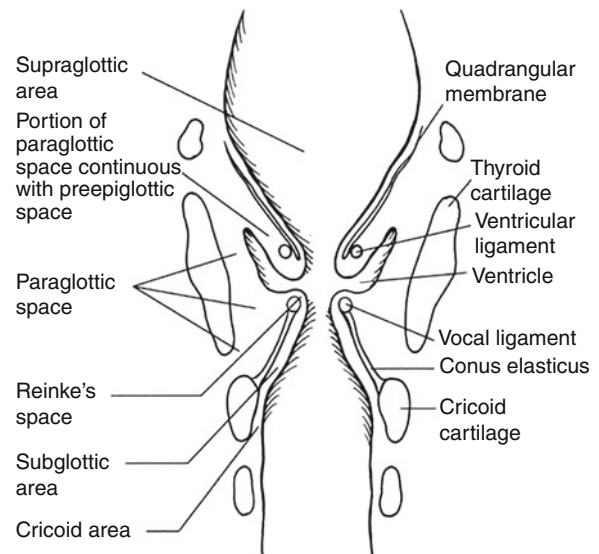
Conservation Laryngeal Surgery, Fig. 1 Tissue barriers within the larynx (Figure borrowed, with permission, from Cummings Otolaryngology, 4th edn)

superiorly from the tip of the epiglottis to the lateral recess of the ventricle, but does not include the mucosa of the tongue base. Subsites of the supraglottis include the suprahyoid epiglottis (lingual and laryngeal surfaces), the infrahyoid epiglottis, the false vocal folds, the arytenoid cartilages, and the aryepiglottic folds. The glottis begins at the lateral recess of the ventricle and extends to 1 cm inferior to the level of the true vocal fold midpoint. The subglottis begins superiorly at the inferior portion of the glottis and extends to the inferior aspect of the cricoid cartilage. Of note, an area referred to as the hypopharynx extends from the circumvallate papillae of the tongue to the apex of the pyriform sinuses and lies lateral and posterior to the aforementioned laryngeal subsites. The hypopharyngeal structures, along with the tongue base, hyoid bone, thyrohyoid membrane, thyroid cartilage, and cricothyroid membrane provide the anterior, lateral, and posterior anatomic limitations to the larynx (Smith and Fried 2006).

The embryologic development results in several structures that initially may impede or prevent cancer spread throughout the different portions of the larynx, and may also help predict likely paths of spread (Fig. 1). For instance, the quadrangular membrane and triangular membrane, or conus elasticus, are developmental fascial barriers to tumor spread. The quadrangular membrane is a membrane that traverses

from the epiglottic petiole and aryepiglottic folds to the margin of the false vocal fold. The conus elasticus is a membrane that has, as its medial margin, the thyroarytenoid muscle, and traverses inferior-obliquely to the cricoid cartilage. Lateral to both of these structures lay the paraglottic spaces, which traverse from the supraglottis inferiorly to the subglottis and may allow tumor growth secondary to lack of natural impedences. Borders of the paraglottic spaces include the quadrangular membrane, the medial wall of the piriform sinus, the conus elasticus, and the thyroid cartilage. Similarly, the preepiglottic space is the anatomic space bounded superiorly by hyoepiglottic ligament and vallecula, anteriorly by thyrohyoid membrane, and posteriorly by epiglottis and thyroepiglottic ligament. The preepiglottic space is considered to be in continuity with the paraglottic spaces (Thawley et al. 1999). Because of the aforementioned natural barriers and pathways, laryngeal cancers tend to spread through typical patterns, with earlier tumors confined to anatomic or embryologic compartments (Kirchner 1987; Kirchner and Carter 1987).

Principle

The techniques for conservation laryngeal surgery include transoral endoscopic surgery via laser or endoscopic instruments, laryngofissure with cordectomy, vertical hemilaryngectomy, and horizontal hemilaryngectomies. A thorough discussion of each type of conservative laryngeal surgery is far beyond the scope of this entry, and the reader is referred to separate entries in this encyclopedia such as ▶ transoral laser resection for laryngeal malignancy and ▶ supraglottic laryngectomy for a more thorough discussion of these topics. However, all conservative laryngeal surgical procedures are based on several principles as have been described previously (Tufano et al. 2004):

1. Local tumor control is imperative. Incomplete resection results in persistence or recurrence, and may necessitate postoperative adjuvant therapy or total laryngectomy.
2. The three-dimensional extent of the tumor should be known via preoperative diagnostic imaging of the larynx and via clinical examination. The proper conservative laryngeal surgical technique, if indicated, can be chosen based on this knowledge.
3. The ▶ cricoarytenoid unit is the basic functional unit of the larynx and at least one unit must be preserved in order to allow for speech and swallowing without tracheostomy postoperatively. The cricoarytenoid unit includes the arytenoid cartilage, the cricoid cartilage, associated musculature, and the ipsilateral superior and recurrent laryngeal nerves.
4. In order to obtain the best functional outcomes, some nondiseased tissue may need to be removed.

Informed Consent

Patients who undergo conservative laryngeal surgery do so presumably because functional outcomes will be maximized without sacrificing oncologic outcomes relative to ▶ total laryngectomy. Therefore, expectations are often elevated. As with any surgical procedure, informed consent is a critical component of patient education and care. Patients should be informed of the range of surgical and/or organ preservation strategies for head and neck cancer available based on the type, location, and extent of each particular cancer. Additionally, patients should be made aware of the relative risks, benefits, and alternatives of each approach. Specifically, patients must be informed about potential voice, swallowing, and aspiration difficulties that could be encountered in either the acute or extended postoperative period. Patients should be thoroughly counseled on and even offered nonsurgical therapy, specifically radiotherapy +/− chemotherapy. It is also recommended that preoperative consent for ▶ total laryngectomy be performed in the event that intraoperative conversion is deemed necessary based on findings.

Patients who undergo conservation laryngeal surgery may or may not have had preoperative radiation, tracheostomy, and/or percutaneous gastrostomy tube (PEG) placement. Conservation laryngeal surgery may lead to anatomic alterations and edema that may either prevent decannulation in the short term or may necessitate intraoperative or postoperative tracheostomy. In some instances, patients cannot be decannulated or may require permanent gastrostomy. Depending on the extent of surgery, some degree of chronic aspiration may be experienced, so patients should be well informed about realistic expectations regarding both short-term and long-term swallowing and aspiration.

Surgical Procedures

Conservation laryngeal procedures can broadly be grouped into open versus transoral approaches. Variations of some of the more common open approaches for conservative laryngeal surgery will be discussed, with the understanding that endoscopic/transoral variations exist with the same goals of oncologic control and improved functional outcomes. Additionally, the nomenclature behind the various conservative laryngeal surgery approaches can be daunting. Due to the variations in nomenclature, the terms "vertical hemilaryngectomy" and "horizontal hemilaryngectomy" will serve as the two basic starting points.

Surgical Variations

Most open conservation laryngeal procedures begin with tracheostomy placement in anticipation of postoperative edema and aspiration. A separate incision is then made over the thyroid cartilage, and the strap muscles are divided. From this point in the surgery, the approaches vary as below.

Vertical Hemilaryngectomy

Vertical hemilaryngectomy, also known as *vertical partial laryngectomy*, involves a vertical incision through the thyroid cartilage and paraglottic space and is typically used for T_1 or T_2 tumors. This incision is called a layngofissure. A more lateral or posterior incision may then be made based on the extent of tumor, and horizontal incision used to connect the two. The diseased soft tissue, margins, and the excised portion of the thyroid lamina are removed. Reconstruction can be performed via numerous methods, including direct suturing, a mucosal and/or strap muscle flap, or secondary intention. The vertical hemilaryngectomy traditionally removes a true vocal fold and false vocal fold, with variations as listed below:

The *frontolateral vertical hemilaryngectomy* is used for lesions that involve or are close to the anterior commissure of the true vocal folds. In this case, the vertical thyrotomy or laryngofissure is made through the thyroid lamina of the less involved side so that a portion of the opposite true vocal fold can also be removed in addition to the more diseased side.

The *posterolateral vertical hemilaryngectomy* is used for lesions that involve the ipsilateral arytenoid mucosa. The posterior extend of resection will remove
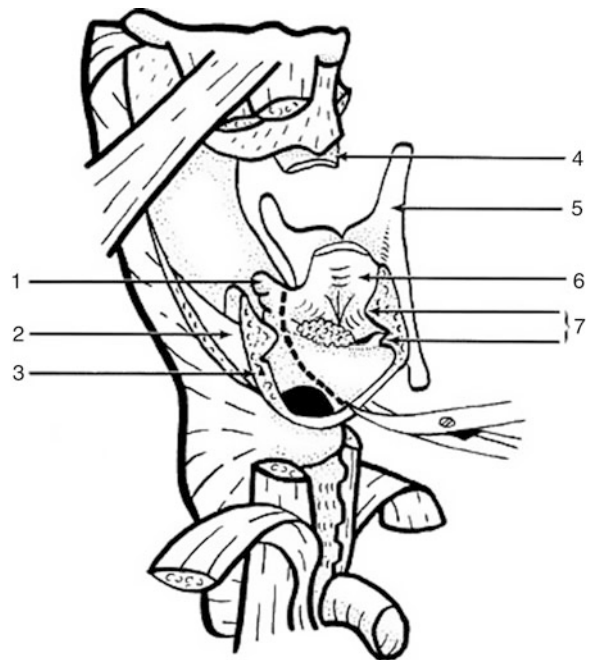
Conservation Laryngeal Surgery, Fig. 2 Supracricoid partial laryngectomy with cricohyoidoepiglottopexy – exposure of malignancy. *1* Arytenoid; *2* internal thyroid perichondrium; *3* vocal process; *4* inferior aspect of transected epiglottis; *5* thyroid cartilage; *6* petiole of the epiglottis; *7* false and true vocal cords (Figure borrowed, with permission, from Cummings Otolaryngology, 4th edn)

all or part of the ipsilateral arytenoid cartilage and mucosa.

The *extended vertical hemilaryngectomy* is simply removal of additional tissue, such as the entire hemilarynx or a portion of the thyroid cartilage.

Horizontal Hemilaryngectomy

Supracricoid laryngectomy is a subtype of horizontal hemilaryngectomy in which both true vocal folds, false vocal folds, paraglottic spaces, the entire thyroid cartilage, and up to one arytenoid are removed. A cricohyoidpexy or cricohyoidepiglottopexy is performed to reconstruct the glottis in order to facilitate swallowing rehabilitation postoperatively (Fig. 2).

Supraglottic laryngectomy is a subtype of horizontal hemilaryngectomy in which the epiglottis, preepiglottic space, false vocal folds, upper portion of the thyroid cartilage, and, at times, the hyoid bone are removed (Fig. 3). This procedure can be extended to
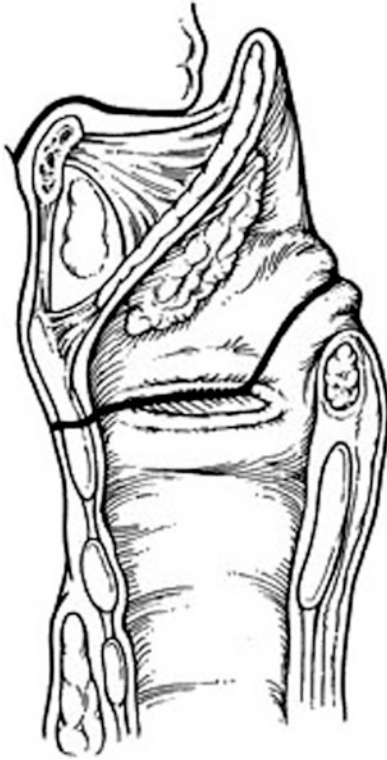
Conservation Laryngeal Surgery, Fig. 3 Limits of resection of a supraglottic laryngectomy (Figure borrowed, with permission, from Cummings Otolaryngology, 4th edn)

include structures such as an arytenoid cartilage. As with the supracricoid laryngectomy, a pexy may need to be performed to reduce the risk of long-term post-operative airway obstruction and dysphagia.

Complications

As with any surgical procedure, complications of conservation laryngeal surgery include bleeding, infection, wound breakdown and fistula formation, and the risks of anesthesia. These risks may be associated with whether an open or transoral approach is used (Karatzanis et al. 2010). Conservation laryngeal surgery can also be complicated by poor voice, swallowing, and/or aspiration outcomes. Patients should be informed that an intraoperative or postoperative tracheostomy could be necessary pending the degree of edema and function of the glottic apparatus. The same could be said for placement of either a nasogastric, orogastric, or PEG tube for feeding access.

Functional Outcomes

Functional outcomes with conservation laryngeal surgery are generally encouraging, with a majority of patients able to be decannulated and not need long-term feeding access (Bron et al. 2005; Mendenhall et al. 2004; Silver et al. 2009; Tuna et al. 2009). The reader is referred to the specific entries for each type of conservative laryngeal surgery.

Modern Approaches to Conservative Laryngeal Surgery

As with most surgical procedures, technology continues to improve, allowing surgeons to obtain similar oncologic outcomes to more traditional techniques while improving functional outcomes. Many of the procedures listed above can be performed transorally. This is accomplished with the exposure of the larynx using a wide variety of surgical laryngoscopes, with the resection being performed with a CO_2 laser. Not only can smaller glottic or supraglottic tumors be removed in this manner, but the procedure may be extended to a complete supraglottic or vertical laryngectomy. While there are extensive applications for transoral laser partial laryngeal surgery, they are limited by the inability to resect cartilage when indicated or when reconstruction is necessary. Another evolving field of interest in conservation laryngeal surgery, particularly for supraglottic tumors, is ▶ transoral robotic surgery (TORS) using the da Vinci robot.

Indications/Contraindications

Conservation laryngeal surgery is generally indicated for primary T_1 or T_2 cancers of the supraglottis and glottis. A limited number of exceptions exist for more advanced cancers, such as $T_3N_0M_0$ supraglottic cancer based on preepiglottic space involvement (Lima et al. 2006). In addition, some centers are using conservation laryngeal surgical methods for limited cancer recurrences after failure of other modalities (Marchese-Ragona et al. 2005; Marioni et al. 2006; Piazza et al. 2007).

The list of contraindications for conservation laryngeal surgery is extensive, and can generally be divided into oncologic contraindications and functional contraindications. In terms of oncologic contraindications, conservation laryngeal surgical procedures should not

be used if the extent or location of tumor precludes adequate removal with anything short of a nonsurgical modalities or total laryngectomy. Generally, this involves most stage III and stage IV tumors. Exceptions to this exist as mentioned above.

In terms of functional outcomes, if the expected functional outcomes of the laryngeal apparatus are no better than those achieved with total laryngectomy, then conservation laryngeal surgery is contraindicated. An additional consideration relates to the patient's general pulmonary status – preoperative pulmonary function may indicate that a patient cannot tolerate any amount of aspiration, even for the short-term. In cases such as this, conservative laryngeal surgery may be contraindicated. Because of the breadth of possible tumor location(s) and extent, and because of the wide range of possible surgical techniques, decisions should be made by the surgeon on a case-by-case basis. The traditional indications and contraindications for the more common types of conservation laryngeal surgeries are listed below:

Vertical Hemilaryngectomy

Indications	Contraindications
T_1 or T_2 tumors	Fixed true vocal fold (implying T3 disease)
	Involvement of the posterior commissure/ interarytenoid area
	Bilateral arytenoid invasion
	Bulky transglottic lesions
	Thyroid cartilage invasion
	>10 mm anterior subglottic extension or >5 mm posterior subglottic extension
	Lesions beyond superior free edge of false vocal folds

Supraglottic Hemilaryngectomy

Indications	Contraindications
Tumor limited to the epiglottis, false vocal fold, or aryepiglottic fold	Fixed true vocal fold
"Extended" includes an arytenoid, the valleculae, base or tongue, or medial pyriform sinus wall	Thyroid cartilage invasion
	Paraglottic space invasion
	Interarytenoid or arytenoid cartilage invasion
	Epliglottic petiole invasion
	Pyriform sinus apex invasion
	Impaired tongue base mobility
	Poor pulmonary function

Supracricoid Hemilaryngectomy

Indications	Contraindications
Glottis and anterior commissure invasion	≥10 mm anterior subglottic or ≥5 mm posterior subglottic extension
Ventricle invasion	True vocal fold and arytenoid fixation
True vocal fold mobility impairment	Base of tongue involvement
Thyroid cartilage invasion	Significant preepiglottic space or vallecular invasion
Paraglottic or transglottic invasion	Interarytenoid involvement
Moderate preepiglottic space invasion	Poor pulmonary function

Advantage/Disadvantage

Advantages of Conservation Laryngeal Surgery

The advantages of conservation laryngeal surgery relate to improved functional outcomes with avoidance of ▶ total laryngectomy. Outcomes with regard to voice, aspiration, and swallowing are the most important. Many patients are able to be decannulated or avoid tracheostomy all together and preserve some degree of voice. Others can either avoid a PEG tube or have their feeding tube removed. In cases of primary surgery, a patient may be able to avoid postoperative radiation pending pathologic results.

Disadvantages of Conservation Laryngeal Surgery

The disadvantages of conservative laryngeal surgery usually relate to functional outcomes that are poorer than expected or predicted. Examples include inability to decannulate, inability to remove a PEG tube, or chronic aspiration leading to recurrent pneumonia. These patients may necessitate ▶ total laryngectomy for a crippled larynx, and thus have theoretically undergone an extra surgical procedure. From an oncologic perspective, intraoperative findings or pathologic results may indicate that a ▶ total laryngectomy, postoperative radiation, and/or postoperative chemotherapy may be necessary. Therefore, in retrospect, the patient may have undergone an extra surgical procedure. Alternatively, primary organ preservation therapy with chemoradiation may be more appropriate under these circumstances.

Cross-References

References

Bron LP, Soldati D, Monod ML et al (2005) Horizontal partial laryngectomy for supraglottic squamous cell carcinoma. Eur Arch Otorhinolaryngol 262:302–306

Karatzanis AD, Psychogios G, Zenk J et al (2010) Evaluation of available surgical management options for early supraglottic cancer. Head Neck 32(8):1048–1055

Kirchner JA (1987) Two hundred laryngeal cancers: patterns of growth and spread as seen in serial section. Laryngoscope 103(4):474–482

Kirchner JA, Carter D (1987) Intralaryngeal barriers to the spread of cancer. Acta Otolaryngol 103(5–6):503–513

Lima RA, Freitas EQ, Dias FL et al (2006) Supracricoid laryngectomy with cricohyoidoepiglottopexy for advanced glottis cancer. Head Neck 28(6):481–486

Marchese-Ragona R, Marioni G, Chiarello G et al (2005) Supracricoid laryngectomy with cricohyoidopexy for recurrence of early-stage glottic carcinoma after irradiation. Long-term oncological and functional results. Acta Otolaryngol 125:91–95

Marioni G, Marchese-Ragona R, Pastore A et al (2006) The role of supracricoid laryngectomy for glottis carcinoma recurrence after radiotherapy failure: a critical review. Acta Otolaryngol 126:1245–1251

Mendenhall WM, Werning JW, Hinerman RW et al (2004) Management of T_1–T_2 glottic carcinomas. Cancer 100(9):1786–1792

Piazza C, Peretti G, Cattaneo A et al (2007) Salvage surgery after radiotherapy for laryngeal cancer. Arch Otolaryngol Head Neck Surg 133(10):1037–1043

Silver CE, Beitler JJ, Shaha AR et al (2009) Current trends in initial management of laryngeal cancer: the declining use of open surgery. Eur Arch Otorhinolaryngol 266:1333–1352

Smith RV, Fried MP (2006) Advanced cancer of the larynx. In: Bailey BJ, Johnson JT (eds) Head and neck surgery – otolaryngology, 4th edn. Lippincott Williams & Wilkins, Philadelphia, pp 1757–1777

Thawley SE, Sessions D, Deddins A (1999) Surgical therapy of supraglottic tumors. In: Thawley SE, Panje WR, Batsakis JG, Lindberg RD (eds) Comprehensive management of head and neck tumors, 2nd edn. Elsevier, Philadelphia, pp1006–1035

Tufano RP, Weinstein GS, Laccourreye O (2004) Conservation laryngeal surgery. In: Cummings CW et al (eds) Otolaryngology, head and neck surgery, 4th edn. Mosby, Philadelphia

Tuna B, Katilmis H, Ozturkcan S et al (2009) Outcome of conservation surgery for laryngeal carcinoma: an 8-year trial. Eur Arch Otorhinolaryngol 266:1681–1686

Constant Current Stimulation

Angela E. Downes and A. Samy Youssef
Department of Neurosurgery, University of South Florida, Tampa, FL, USA

Definition

Current delivered to the nerve that is maintained at a constant level despite changes in electrode impedance and is subject to the wide variations in the degree of shunting of the nerve.

Cross-References

Constant Voltage Stimulation

Angela E. Downes and A. Samy Youssef
Department of Neurosurgery, University of South Florida, Tampa, FL, USA

Definition

Current delivered to the nerve from a constant voltage stimulator that depends on the impedance of the nerve itself, regardless of the amount of any shunting of the nerve by blood, cerebrospinal fluid, or irrigation.

Cross-References

C

Consumption

▶ Otologic Manifestations of Tuberculosis, Diagnosis and Treatment

Contrast Injection

▶ Angiography

Contrast Study

▶ Angiography

Cottle Maneuver

▶ Nasal Function (Rhinometry, Rhinomanometry), Evaluation

Countersink

Abdul Aleem Kadar
Otolaryngology-Head and Neck Surgery, Jinnah
Postgraduate Medical Centre, Karachi, Sindh, Pakistan

Definition

A hole drilled during BAHA surgery with the top part enlarged so that the head of a screw or bolt will lie flush with or below the surface.

Cross-References

▶ Bone-Anchored Hearing Aids (BAHAs)

Cranial Base

▶ Skull Base Neoplasms

Cranial Facial

▶ Craniofacial Resection

Cranial Fossa

▶ Skull Base Neoplasms

Cranial Nerve 7

▶ Facial Nerve Imaging, CT and MRI

Cranial Nerve Monitoring – *VIII, IX, X, XI*

Amir Ahmadian, Angela E. Downes and
A. Samy Youssef
Department of Neurosurgery, University of
South Florida, Tampa, FL, USA

Synonyms

Brainstem evoked potential monitoring; Hearing preservation; intra-operative monitoring; Lower cranial nerves

Introduction

Intraoperative neurophysiologic monitoring of cranial nerves has become an integral part of any cranial base

procedure. The preservation of cranial nerve function after removal of a skull base tumor is a fundamental goal of surgery. However given the fragile nature of these nerves, intraoperative damage may not be noticed; therefore real-time or continuous monitoring is strongly recommended when possible. There are many factors that may affect cranial nerve function; these include: mechanical manipulation/retraction, trans-section, post-surgical edema/inflammation and regional vasoconstriction. The VIII cranial nerve is the cranial nerve at greatest risk during cerebellopontine angle surgery. Injury of the lower cranial nerves IX–XI can profoundly affect a patient's quality of life. In this entry, the modern techniques of intraoperative monitoring of cranial nerves VIII, IX, X and XI with emphasis on preservation of functional integrity are reviewed.

Anesthesia

As described in the facial nerve section, anesthesia induced physiological variations may affect intraoperative monitoring reliability. ▶ EMG and ▶ CNAP monitoring are the most vulnerable to physiological changes since baseline-recoding patterns may be affected or altered. Long acting paralytics and certain neuro-active inhaled anesthetics should be avoided, as they may inhibit ▶ EMG recording. Nitrous oxide and Isofurane may be used at a low dose with concomitant narcotics to maintain anesthesia. Induction should be performed with fast acting neuromuscular blockade agents. Twitch monitor is used to confirm reversal of paralysis prior to intraoperative monitoring of cranial nerves.

VIII: Vestibulocochlear Nerve

The vestibulocochlear nerve (VIII) is particularly vulnerable during surgical approaches to cerebellopontine angle (CPA) tumors (i.e., Vestibular schwannoma and CPA meningiomas) or microvascular decompression of posterior fossa cranial nerves. Only the auditory portion of the nerve can be monitored using far-field (brain stem auditory evoked potentials - ▶ BAEP) or near-field (cochlear nerve action potential - ▶ CNAP) techniques.

The first report of intraoperative auditory nerve monitoring was by Levine et al. in 1978 (Levine et al.

1978). Since then, ▶ hearing preservation has been a feasible task in CPA surgeries. In patients with CPA lesions and serviceable hearing, a ▶ hearing preservation approach (middle fossa or retrosigmoid transmeatal) is necessary.

Direct Cochlear nerve action potential (▶ CNAP) and brain stem auditory evoked potential (▶ (BAEP) can be used for real-time functional monitoring. The brain stem auditory evoked potential (▶ BAEP) is a more widely used technique in which an auditory stimulus is delivered to the ipsilateral ear. In large tumors causing brain stem compression with no serviceable ipsilateral hearing, ▶ BAEP may be recorded from the contralateral ear as a measure of brain stem function. ▶ BAEP patterns are generally resistant to sedation and general anesthesia. After induction of general anesthesia, a soft ear mold attached to a 12 in. plastic tube is placed and sealed inside the ear canal. For fast-auditory brain stem response, a needle connected to the positive grid of the differential amplifier is inserted transcutaneously at the vertex, and a ground electrode is inserted 3 cm anterior to the vertex. A needle connected to the negative grid of the differential amplifier is placed in the pre-tragal area or mastoid tip area. A brief click or tone is delivered in an intensity level of 90–100 dB and at a rate of 31–51 pulses per second. Baseline responses for each ear are recorded before the beginning of surgery and used as baselines through the case. The classic ▶ BAEP comprises 5–7 peaks, all occurring within 10 ms of the click; the first five peaks, I-V, are the main peaks used in clinical practice. Waves IV and V are generated at the upper pons and lower midbrain. ▶ Wave V tends to be the most robust and is the most closely monitored during surgery. Change in the "▶ wave I" to "▶ wave V" latency greater than 0.5 ms represents disruption of auditory pathway (Legatt 2002).

The recording for direct-▶ CNAP is done after exposure of the cochlear portion of the vestibulo-cochlear nerve. A teflon-coated silver wire electrode with attached cotton pledget is placed on the cochlear nerve. Before the beginning of surgery, a negative and a ground electrodes are placed on the contralateral mastoid tip and vertex, respectively. A baseline ▶ CNAP pattern is obtained and continuously monitored. Any change in the baseline wave pattern suggests functional stress or disruption allowing the surgeon to make appropriate microsurgical changes to maintain baseline patterns (Colletti et al. 1994).

Intraoperative electrocochleography (▶ ECOG) is another near-field technique that has been advocated by some neurotologists to directly monitor the cochlear nerve (Winzenburg et al. 1993). ▶ ECOG monitoring generally requires transtympanic electrode placement because electrode placement in the external ear does not yield large enough amplitude. A perforation is made in the tympanic membrane for cotton wick or needle electrode placement. Electrode placement outside the surgical field is a major advantage of ▶ ECOG over ▶ CNAP.

IX, X, & XI: Glossopharyngeal, Vagus and Spinal Accessory Nerves

The lower cranial nerves are at risk during posterior fossa surgery for large tumors located in the cerebellopontine angle, petroclival region, jugular foramen, brain stem and the foramen magnum. Experience from intraoperative neurophysiologic monitoring of the facial nerve was syllogistically applied in the lower cranial nerves in order to preserve their functional and anatomical integrity.

Stimulation Technique
A constant current stimulation technique is applied with square wave pulses of 30 Hz frequencies, 100 μs duration and an intensity of 0.5 mA (direct nerve stimulation) or 0.05 mA (stimulation of brain stem nuclei).

Recording Technique
The glossopharyngeal nerve has multiple functions and carries motor, sensory and autonomic fibers. It emerges from the medulla to exit the cranial vault via the jugular foramen. Glossopharyngeal nerve monitoring can be challenging. Intraoperative EMG monitoring of the motor fibers can be performed by both needle and surface electrode recordings of the stylopharyngeus muscle. Needle EMG electrode is placed in the soft palate midway between the uvula and posterior tonsillar pillar (2–3 mm deep) for direct recording of stylopharyngeus muscle (Schlake et al. 2001). Husain et al. have described surface recording for the stylopharyngeus by mounting surface electrode on a laryngeal mask airway (LMA) (Husain et al. 2008). The CN IX EMG response is of low amplitude, difficult to follow reliably and therefore is

recommended to be done in conjunction with vagus nerve (CN X) monitoring (Loftus and Traynelis 1994). The lack of laryngeal muscle (CN X) response with low amplitude EMG of posterior pharyngeal muscles (CN IX & CN X) suggest glossopharyngeal activity (Topsakal et al. 2008).

CN X monitoring can be performed by both surface and needle electrodes recording at the level of the false vocal cords. The recurrent laryngeal nerve (RLN), superior laryngeal nerve (SLN) or the inferior laryngeal nerve (ILF) (branches of CN X) can be selectively monitored. Endotracheal tube (ETT) mounted with surface electrodes recording can be performed. Blind percutaneous placed electrodes are the least reliable and not recommended. However, laryngoscopically placed needle electrodes (thyroarytenoid muscle for RLN and cricothyroid muscle for SLN) are the most reliable and sensitive method. A pair of needle electrodes is placed in to the ipsilateral "true vocal cords" (vocalis muscle) in a distance of 2–3 mm.

Cranial nerve XI (spinal accessory nerve) exits the cranial vault via the jugular foramen with CN X. Its motor fibers innervate the sternocleidomastoid and the trapezius muscles. The spinal accessory nerve can be monitored with percutaneous needle electrode insertion into the trapezius muscle. For optimum EMG amplitude, electrodes can be placed 2–3 cm lateral to the midpoint between the acromion and C7 spinous process.

Data Acquisition
Loudspeaker monitoring offers an immediate feedback to the surgeon by transmitting ▶ EMG signals to a speaker. Spontaneous muscle activity (▶ SMA) can be in the form of "▶ bursts" or "▶ trains." Short-lasting bursts are muscular discharges that represent contact activity. Long-lasting ▶ bursts outlast surgical manipulations and are considered warning signals. Non-rhythmic discharges or "▶ trains" that persist for a long time are predictive of nerve damage and postoperative deficits. Evoked compound muscle action potentials (▶ CMAP) describe the synchronous activation of a group of motor neurons within a nerve bundle by brief electrical stimulation producing activity in the target muscle. The ▶ CMAP latencies and amplitudes can be compared to the patient's baseline values more than normative reference values.

Discussion

Postoperative hearing loss in a previously hearing ear leaves the patient with some sort of a permanent handicap and is perceived as a setback for microsurgery. ► Hearing preservation is defined as preservation of hearing within normal and social hearing classification, i.e. pure tone audiometry (PTA) ≤50 dB and speech discrimination score (SDS) ≥50% according to guidelines of the American Academy of Otolaryngology-Head and Neck surgery (1995). The surgical approach used is either middle fossa approach or retrosigmoid transmeatal approach. Intraoperative cochlear nerve monitoring has been traditionally performed with ► BAEP. However, direct cochlear nerve action potential has been used in multiple centers and is theoretically the most ideal technique since surgical manipulations resulting in reduced activity or de-synchronization of high-frequency nerve fibers can be detected as a change of amplitude or latency of the wave. Both ► CNAP and ► ECOG have the advantage of being near-field techniques in which electrodes are placed close to the eighth nerve or cochlea. Larger amplitude signals are produced; acquisition takes only 2–3 s (in contrast to minutes with ► BAEP), and thus allowing near real-time feedback to the surgeon. Several studies have reported that ► CNAP and ► ECOG are more reliable than ► BAEP while others failed to prove their superiority in terms of ► hearing preservation (Piccirillo et al. 2008).

Intraoperative injury of one or more of the lower cranial nerves can result in dysphonia, dysarthria, dysgeusia, dysphagia and the risk of aspiration. Postoperative functional and anatomical integrity of lower cranial nerves during skull base surgery is the ultimate goal of intraoperative nerve monitoring. Two different modalities of ► EMG signals can be monitored: first the spontaneous muscle activity (► SMA) and second, compound muscle action potentials (CAMP). ► SMA in the form of long-lasting bursts is a warning sign and reflects nerve irritation. Non-rhythmic long-lasting bursts or "► trains" signify nerve lesion and predict postoperative deficit. CAMP technique serves two goals: identification of location and course of the nerve and determination of the functional integrity of the nerve through measurement of the latencies and amplitude of response pre and post tumor resection in addition to along the intracranial course of the nerve.

Delayed postoperative functional decline of cranial nerve can commonly occur in the setting of intact intraoperative recordings. Edema and microvascular vasoconstriction have been suggested as an etiology for delayed dysfunction. Peri-operative steroids and calcium channel blockers (i.e., nimodipine) have been shown to improve outcomes. Scheller et al. suggest that prophylactic administration of a combination of neuroprotective vasoactive agents (nimodipine + hydroxyethyl starch) is superior as compared to intraoperative administration. However no recommended guidelines or consensus have been endorsed and a short course of postoperative steroids have been a common practice by most surgeons.

Summary

Maintaining functional integrity of cranial nerves during skull base surgery is imperative. Although modern monitoring technologies and advances in microsurgical techniques have greatly decreased surgical morbidity, maintaining functional integrity of cranial nerves during complex skull base remains challenging. Intraoperative neurophysiologic monitoring has stood the test of time in preserving the functional integrity of cranial nerves and must be a crucial part of a surgeon's technological armamentarium in order to minimize postoperative morbidity.

Cross-References

► Audiometry
► Cochlear Nerve, Anatomy
► Electromyogram
► EMG
► Evoked EMG
► Hearing Testing, Auditory Brainstem Response (ABR)
► Jugular Foramen, Approaches
► Lateral Skull Base Surgical Approaches
► Vestibular and Central Nervous System, Anatomy

References

(1995) Committee on Hearing and Equilibrium guidelines for the evaluation of hearing preservation in acoustic neuroma (vestibular schwannoma). American Academy of Otolaryngology-Head and Neck Surgery Foundation, INC. Otolaryngol Head Neck Surg 113:179–180

Colletti V, Bricolo A, Fiorino FG, Bruni L (1994) Changes in directly recorded cochlear nerve compound action potentials during acoustic tumor surgery. Skull Base Surg 4:1–9

Husain AM, Wright DR, Stolp BW, Friedman AH, Keifer JC (2008) Neurophysiological intraoperative monitoring of the glossopharyngeal nerve: technical case report. Neurosurgery 63:277–278; discussion 278

Legatt AD (2002) Mechanisms of intraoperative brainstem auditory evoked potential changes. J Clin Neurophysiol 19:396–408

Levine RA, Montgomery WW, Ojemann RG, Pringer MFB (1978) Evoked potential detection of hearing loss during acoustic neuroma surgery. Neurology 28:339

Loftus CM, Traynelis VC (1994) Intraoperative monitoring techniques in neurosurgery. McGraw-Hill, Health Professions Division, New York

Piccirillo E, Hiraumi H, Hamada M, Russo A, De Stefano A, Sanna M (2008) Intraoperative cochlear nerve monitoring in vestibular schwannoma surgery – does it really affect hearing outcome? Audiol Neurootol 13:58–64

Schlake HP, Goldbrunner RH, Milewski C, Krauss J, Trautner H, Behr R, Sorensen N, Helms J, Roosen K (2001) Intraoperative electromyographic monitoring of the lower cranial motor nerves (LCN IX-XII) in skull base surgery. Clin Neurol Neurosurg 103:72–82

Topsakal C, Al-Mefty O, Bulsara KR, Williford VS (2008) Intraoperative monitoring of lower cranial nerves in skull base surgery: technical report and review of 123 monitored cases. Neurosurg Rev 31:45–53

Winzenburg SM, Margolis RH, Levine SC, Haines SJ, Fournier EM (1993) Tympanic and transtympanic electrocochleography in acoustic neuroma and vestibular nerve section surgery. Am J Otol 14:63–69

Cranial Nerve VII Rehabilitation

▶ Static Facial Paralysis Rehabilitation

Cranial Tumor

▶ Skull Base Neoplasms

Craniocervical Junction, Abnormalities

Chris Sanders Taylor[1] and Francesco T. Mangano D. O. F.A.C.O.S.[2]
[1]Department of Neurological Surgery, University of Cincinnati, Cincinnati, OH, USA
[2]Division of Pediatric Neurosurgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Synonyms

Craniovertebral junction

Definition

1. Craniocervical Junction: The junction of the base of the skull and the cervical spine including the occipital bone surrounding the foramen magnum (occiput), C1 (atlas), C2 (axis), and the intervening tendons and ligaments.

Introduction

The craniocervical junction (CCJ) is a term used to describe the interface between the skull and cervical spine, and more specifically it includes the occipital bone surrounding the foramen magnum and the first and second vertebrae. It is of note that this junction contains and provides protection for the transition of the lower brain stem, the medulla, to the cervical spinal cord. In addition the articulations of the skull, C1, and C2 play a vital role in the range of motion of the head. Hence, abnormalities at this junction may manifest in decreased range of motion if the bony elements are fused, or neurologic dysfunction if instability or stenosis causes compression of the brainstem, spinal cord, or nerve roots. The breadth of topics related to this anatomical region is extensive and is not our focus here. This chapter will focus primarily on three topics: Chiari malformations, segmentation anomalies, and congenital disorders. Chiari malformations are defined by varying degrees of cerebellar and brainstem

herniation into the cervical canal resulting in patient presentations ranging from no symptoms to significant neurologic compromise. These malformations are associated with many craniocervical abnormalities and treatment generally requires decompression of the CCJ. Bony segmentation abnormalities may have pathology that results in limited range of motion and spinal instability. The instability can result in pain, subluxation of the joint, and neurologic compression secondary to spinal canal compromise. Some congenital disorders may result in ligamentous laxity that contributes to pain, instability, and possible neurologic compromise.

Anatomy of the Craniocervical Junction

The CCJ includes the bony and ligamentous attachments of the base of the skull surrounding the foramen magnum, C1, the atlas, and C2, the axis (Figs. 1, 2, 3). Roughly 2–4 cm in diameter, the foramen magnum is the outlet for the cervical spinal cord, and the occipital bone composes the bone surrounding this portion of the skull. The occipital condyles and the superior surface of the lateral masses of C1 articulate in a ball and socket fashion to form the occipital cervical junction. Primarily flexion and extension movement of the head occurs at this joint and the range of motion is approximately 24°, proportionally greater than at lower cervical vertebrae for this movement (Steinmetz et al. 2010). C1 is a ring shaped vertebrae lacking a vertebral body and it consists of two lateral masses located slightly more anterior and connected by a smaller anterior and larger posterior bony arch. The inferior articular surface of the lateral masses of C1 articulates with the superior articular processes of C2, which differs from the lower cervical vertebrae in that the pedicle/superior articular process of C2 is an extension of the vertebral body. The dens/odontoid process is a superiorly projecting bony prominence of C2 averaging 38 mm in length and 9 mm in diameter that arises from the body and articulates with the anterior arch of C1(Clark and Benzel 2004). The articulations of C1 and C2 allow 20°–40° of lateral rotation in each direction, accounting for a significant proportion of this movement in the cervical spine (Steinmetz et al. 2010).

The ligaments supporting the craniocervical junction include a continuation of spinal ligaments from the cervical, thoracic, and lumbar spine in addition to specialized ligaments found only at this junction. The anterior and posterior longitudinal ligaments span the length of the ventral and dorsal vertebral bodies throughout the spine. The anterior longitudinal ligament attaches to the ventral aspect of the body of C2 and is continuous with the atlanto-occipital membrane, which attaches to the anterior margin of the foramen magnum. The posterior longitudinal ligament continues along the dorsal aspect of the C2 vertebral body and attaches to the anterior margin of the foramen magnum as the tectorial membrane. Ventral to the tectorial membrane, but dorsal to the dens, lies the cruciate ligament. This ligament is composed of a longitudinal portion that connects the body of C2 to the base of the skull and a transverse portion that spans the tubercles of C1, holding the dens in place against the anterior arch of the C1. Finally, two alar ligaments attach the tip of the dens to the occipital condyles and the apical ligament attaches the dens to the anterior aspect of the foramen magnum. This complex arrangement of ligaments and articulations allows a significant proportion of the movement of cervical spine.

Chiari Malformations

The Chiari malformations are four categories of hindbrain abnormalities. Hans Chiari, an Austrian-born pathologist, originally described the first three malformations in 1891 followed by further description and classification of the fourth malformation in 1896. Julius Arnold, a German pathologist, and John Cleland, a Scottish scientist, were cited in Chiari's works for previous descriptions of hindbrain anomalies, but Chiari is generally given credit for identifying the malformations. The Chiari I malformation consists of cerebellar tonsillar herniation and is often associated with other CCJ abnormalities, whereas Chiari II (Arnold-Chiari malformation) often involves vermian, medullary, and fourth ventricle herniation. Chiari III is defined by herniation of the cerebellum and often includes an encephalomeningocele. Chiari IV differs in that no herniation is present and it is defined by cerebellar aplasia. The Chiari IV malformation has a very poor prognosis and death ensues during infancy. Chiari I and II are the most clinically significant malformations seen in the clinical setting and result in varying degrees of cerebellar and brainstem

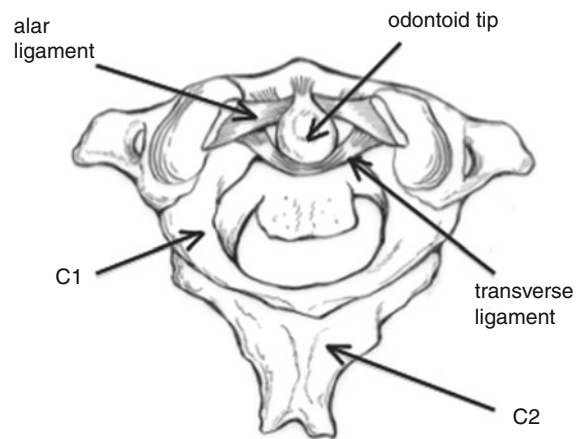**Craniocervical Junction, Abnormalities, Fig. 1** Midsagittal view of the craniocervical junction
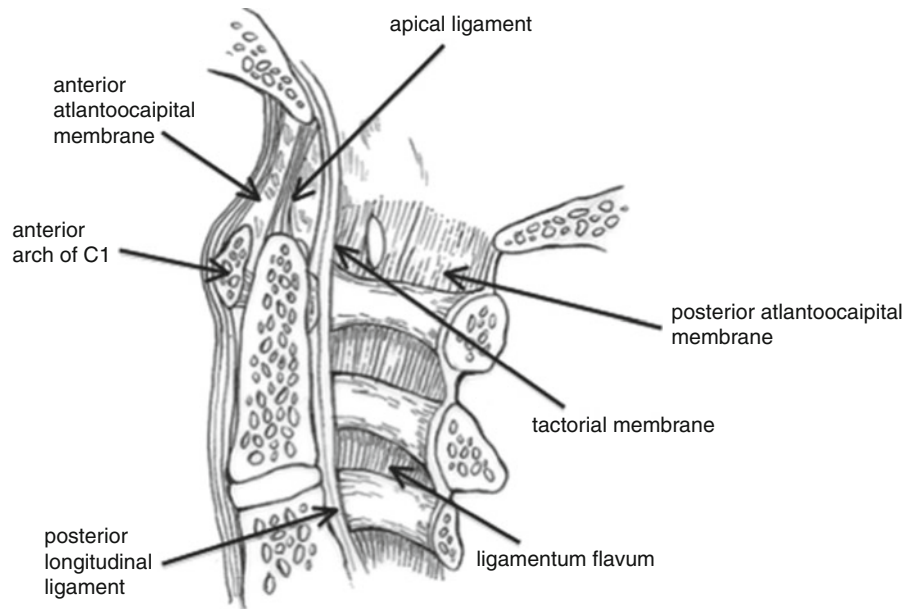
herniation into the craniocervical junction and at times the upper cervical spine.

The Chiari I malformation is defined by symptomatic cerebellar tonsillar herniation below the foramen magnum (Fig. 4). This malformation is associated with both skull and craniocervical junction anomalies and often presents with a small posterior fossa. In addition syringomyelia, a dilation of the central canal of the spinal cord, may occur in 30–70% of patients. Hydrocephalus is seen in 7–9% of patients (Guinto et al. 2004). The malformation is often diagnosed in early adulthood and presents with a wide range of signs and symptoms. Pain (mainly headaches) is present in 70% of cases, followed by weakness, numbness, and loss of temperature sensation in half of the patients (Paul et al. 1983) (Table 1). The headache is often suboccipital and exertional but may also be generalized or extend into the neck. Signs of the malformation include cerebellar compression resulting in ataxia and nystagmus, medullary compression resulting in dysarthria and lower cranial nerve dysfunction, and cervical cord compression resulting in long tract signs including weakness, spasticity, sensory loss, and hyperreflexia.

MRI of the brain and spinal cord is the modality of choice during the initial evaluation to measure the extent of tonsillar ectopia, and to evaluate for hydrocephalus and syringomyelia. Cine-mode MRI is a more recent sequence that is used to evaluate the
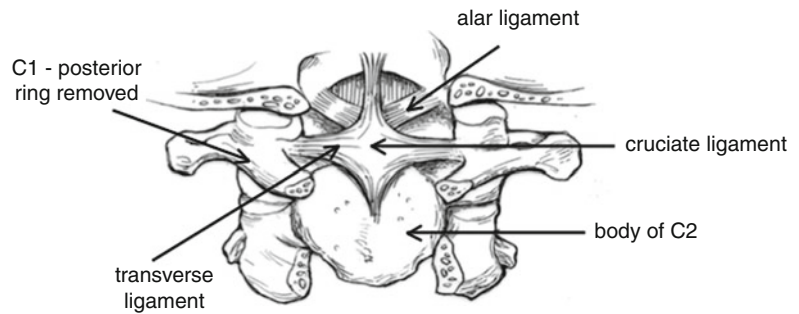

Craniocervical Junction, Abnormalities, Fig. 2 Superior view of C1 and C2

dynamic flow of CSF anterior and posterior to the craniocervical junction. Decreased flow has been shown to correlate clinically with preoperative symptoms, and outcome studies have shown a 2.5 time risk reduction of recurrent symptoms if absence of flow is noted both anteriorly and posteriorly (McGirt et al. 2006). However there are significant false positive and negative findings associated with the test. Other imaging modalities, such as ultrasound, CT, and skull X-rays can also be useful depending on the patient's age at the time of symptom occurrence. Treatment of

Craniocervical Junction, Abnormalities, Fig. 4 Sagittal T2 MRI sequence of Chiari type 1 malformation. The *arrow* points to the cerebellar tonsils herniated through the foramen magnum to the arch of C1. Note the paucity of CSF anterior and posterior to the medulla and cerebellar tonsils, respectively

Craniocervical Junction, Abnormalities, Table 1 Common signs and symptoms of Chiari I malformation

Symptoms	Signs
Headache (suboccipital)	Hyperactive reflexes
Numbness/weakness	Upper/lower extremity weakness
Visual symptoms	Sensory loss/dysesthesia
Dysarthria/dysphagia	Cerebellar signs
Dizziness	Nystagmus

Chiari I malformations is primarily dependent on the patient's symptoms. Generally several millimeters of tonsillar herniation are required for symptoms, and in one study descent of 3 mm demonstrated 96% sensitivity (Barkovich et al. 1986). Classically 5 mm of tonsillar herniation has been described as pathognomonic. Symptomatic patients with greater than 5 mm of tonsillar herniation are considered for intervention. Those with 3–5 mm of herniation may be considered for treatment based upon symptom severity. Periodic clinical and neurologic exams are generally appropriate for patients that are asymptomatic or have mild symptoms.

Chiari II malformations are almost exclusively associated with patients with myelomeningocele. In this population the great majority (>90%) also have hydrocephalus. Pathologically, Chiari II is characterized by not only cerebellar tonsil herniation, but also varying degrees of cerebellar vermis, brainstem, and fourth ventricular descent into the cervical canal. There is often a medullary kink in addition to a peaked tectum, commonly referred to as tectal beaking. The torcula, or confluence of the venous sinuses, is often low and the cranial nerves travel in a more cephalad direction. In comparison to Chiari I, Chiari II malformations present symptomatically from cervical pathology in infancy or early childhood. One third of the patients present before the age of five and outcomes are worse in the first few months of life (Oakes and Tubbs 2003). Very young children typically present with signs of brainstem compression and cranial nerve traction resulting in varying degrees of dysarthria, dysphagia, and apnea. Apnea can be secondary to vocal cord paresis or medullary compression, the former presenting with stridor and the latter

with central apnea and bradycardia. In older children and young adults, symptoms present more similarly to Chiari I with a mixed presentation including headache, ataxia, weakness, and sensory changes. The Chiari II malformation is often diagnosed by prenatal ultrasound or at birth given its strong association with myelomeningocele. MRI is the diagnostic imaging modality of choice and should include the complete neuroaxis. Particular attention is paid to the degree of cerebellar herniation, brainstem compression, and amount of CSF present surrounding the neural structures at the craniocervical junction. Symptomatic Chiari II patients may be a neurosurgical emergency given that compression can result in apnea, bradycardia, and death. Given the high frequency of hydrocephalus, a ventriculoperitoneal shunt malfunction must always be ruled out prior to proceeding to decompressive surgery. These patients are followed by multidisciplinary clinics that include pediatrics, physical therapy and rehabilitation, urology, orthopedics, and neurosurgery until adulthood in most tertiary centers. As symptoms progress or recur, evaluation for treatment is similar to patients with other Chiari type malformations.

Surgical treatment of Chiari malformations entails a suboccipital craniotomy usually accompanied by bilateral C1 laminectomies that may be extended lower into the cervical spine if necessary. Following the bony decompression surgical practices vary. Some surgeons perform a durotomy with duraplasty, whereas others may cut dural bands and evaluate tonsillar motion with intraoperative ultrasound to assist with decision-making. Once a durotomy is performed, coagulation and shrinkage of the herniated tonsils is generally completed. Outcomes have varied but generally 80% of patients show improvement to resolution of their symptoms (Paul et al. 1983; Sindou et al. 2002).

Congenital and Developmental Osseous Abnormalities

Although there are many bony abnormalities of the craniocervical junction, this chapter focuses on several of the more common entities (Table 2). Aplastic/hypoplastic abnormalities include condylar hypoplasia, aplasia of the atlas arches, and dens hypoplasia. Segmentation abnormalities such as

Craniocervical Junction, Abnormalities, Table 2 Selected craniocervical abnormalities

|	
1. Occipital bone malformations	a. Proatlas segmentation failure
	b. Occipital condyle hypoplasia
	c. Basilar invagination/impression
2. Atlas malformations	a. Aplasia of the atlas
	b. Hypoplasia of the atlas
	c. Atlas arch defects/clefts
	d. Assimilation of the atlas
3. Axis malformations	a. Atlantoaxial segmentation failure
	b. Basilar invagination
	c. Dens abnormalities i. Os odontoideum ii. Ossiculum terminale persistens iii. Dens hypoplasia

assimilation of the atlas and Klippel-Feil syndrome will be reviewed in addition to abnormalities of C2, such as os odontoideum, basilar impression/invagination, and ossiculum terminale persistens. Symptomatic presentation of these abnormalities is generally related to suboccipital and cervical pain. Other symptoms depend on the degree of neural compression and lack of segmentation. Abnormalities of segmentation may result in a limited range of motion, short necks, and head tilting, whereas neural compression may present with varying degrees of weakness, spasticity, and sensory abnormalities.

In occipital condyle hypoplasia, both the condyles and skull base can have a flattened appearance and the skull base may ascend (Smoker and Khanna 2008). Basilar invagination, or upward displacement of the dens into the foramen magnum, commonly occurs with condylar hypoplasia because of the decreased occipital cervical space. Clinically, the hypoplasia can limit motion at this joint and neural compression can occur from the basilar invagination. Atlas aplasia or hypoplasia may occur to varying degrees. The posterior arch is most commonly involved and complete aplasia varies in presentation from asymptomatic to frank instability. In contrast to aplasia, posterior arch hypoplasia may result in a narrowed neural canal, and this condition can present with spinal stenosis and neural compression. Although complete arch hypoplasia has been described, more commonly clefts are noted. Posterior arch clefts have been reported in 4% of autopsies with 97% being midline (Gehweiler et al. 1983).

Anterior arch anomalies are much less commonly reported at 0.1%, and in one series they were associated with posterior arch anomalies in greater than 80% of patients (Smoker and Khanna 2008). Clinically isolated clefts are rarely significant. Finally, odontoid hypoplasia and aplasia are both rare and may result in cervical instability.

Segmentation anomalies result from varying degrees of failure of segmentation from the occipital and spinal sclerotomes. Derived from upper axial somites, the CCJ sclerotomes begin chondrification in the sixth week of gestation and eventually form the upper cervical vertebrae and a portion of the occipital bone (David et al. 1998). Proatlas segmentation anomalies are bony abnormalities involving the lower occipital sclerotomes including the foramen magnum and clivus. In a series of 72 patients 66% presented with clival or medial occipital condyle anomalies, 37% with anterolateral anomalies, and 17% with posterior anomalies (Menezes and Fenoy 2009). These segmentation failures present most commonly with neural compression manifested as spastic paresis and often present with cranial nerve palsies (Menezes 2008). In some cases there is failure of the proatlas segment of the dens to separate from the clivus resulting in a bony prominence protruding into the neural canal with the arch of C1 located over the body of C2. Failure of separation of the fourth occipital sclerotome and first spinal sclerotome results in assimilation of the atlas, which has been reported in less than 1% of the population and can be bilateral or unilateral, focal or segmental (Burwood and Watt 1998) (Figs. 5, 6). Although often asymptomatic, when assimilation is accompanied by segmentation abnormalities of lower cervical vertebrae, the increased motion at the atlantoaxial complex can result in instability. If there is unilateral assimilation, torticollis can be seen. In both proatlas segmentation failures and assimilation of the atlas, hindbrain herniation has been reported in 30–40% of cases (Menezes 2008).

Klippel-Feil is a syndrome diagnosed with multiple segmentation failures of the cervical vertebrae and is described as a constellation of findings, which includes a low hairline with a short, often webbed neck and limited range of motion (Figs. 7, 8). The syndrome is divided into three types. Type 1 refers to cervical and upper thoracic fusion, type 2 is the most common and is limited to the cervical spine, and type 3 consists of a combination of cervical and lower thoracic/lumbar
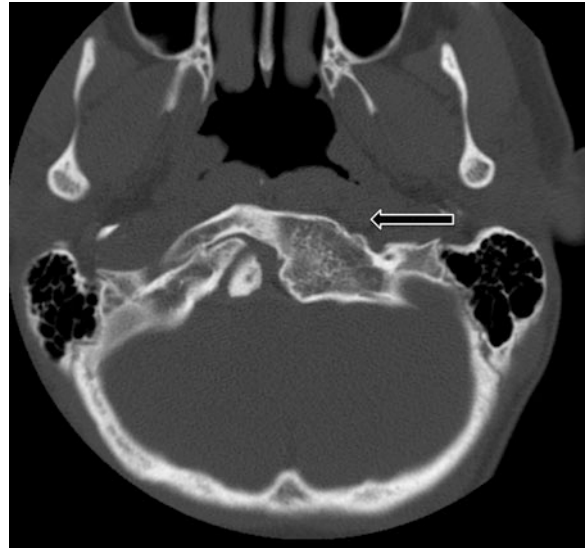
Craniocervical Junction, Abnormalities, Fig. 5 Axial CT of atlanto-occipital assimilation. The *arrow* illustrates the fusion of the occipital condyle to the lateral mass and arch of C1
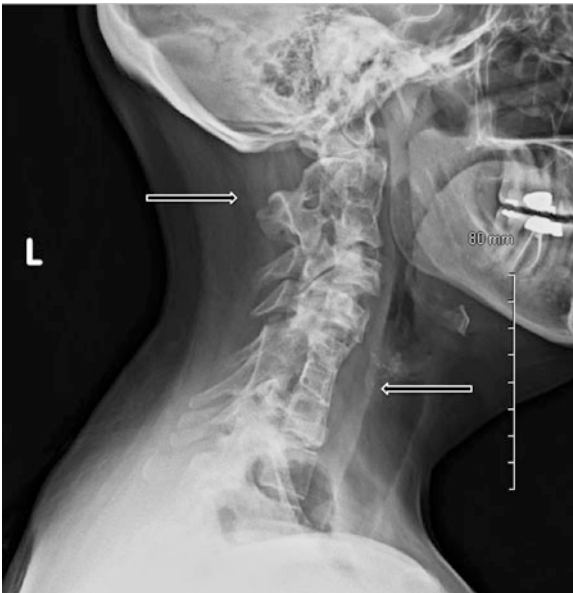

Craniocervical Junction, Abnormalities, Fig. 6 Coronal CT of atlanto-occipital assimilation. The *arrow* again highlights the fusion of the occipital condyle to the lateral mass of C1

fusion (Thomsen et al. 1997). The syndrome is often associated with scoliosis, hemivertebrae, cervical ribs, and Sprengel's deformity, which is a raised or malpositioned scapula. Abnormalities of the genitourinary and cardiovascular system are common, and in addition cleft palate/lip, facial palsies, and deafness are also associated (Smith and Griffin 1992).

Abnormalities of the dens include os odontoideum, ossiculum terminale persistens, and hypoplasia/aplasia. Os odontoideum is a bony separation of the dens defined by a smooth corticated ossicle overlying an odontoid peg (Fig. 9). There is no consensus about the etiology, but currently it is believed that os odontoideum is either congenital or traumatic in origin. There have been reports of identical twins with the defect, but the theory of early trauma and a nonunion of a type II odontoid fracture has become the popular explanation (Arvin et al. 2010). The defect can lead to instability at the C1-2 joint, and the clinical presentation may range from asymptomatic to cervical pain, neural compression, and neurologic dysfunction. Vertebrobasilar ischemia due to vertebral artery compression has been described concurrently. The natural history is yet to be elucidated but some authors prefer fusing all defects while others follow until neurologic symptoms or signs of instability present. As compared to os odontoideum, ossiculum terminale persistens is a small free ossicle from the tip of the dens and is favored to be congenital as opposed to a result of nonunion odontoid fracture. There is argument whether the separation occurs at one of the secondary ossification centers instead of a failure of segmentation, as the cephalad tip of the dens originates from the lowest occipital sclerotome. Regardless, ossiculum terminal persistens has little clinical significance when isolated and is rarely reported to result in atlantoaxial instability (Liang et al. 2001).

Basilar invagination refers to odontoid protrusion into the foramen magnum (Figs. 10, 11, 12). Primary invagination is seen with flattening and/or hypoplasia of the clivus, occipital condyle hypoplasia, assimilation of the atlas, and hypoplasia of the atlas (Smith et al. 2010). Secondary basilar invagination is referred to as basilar impression and results from a disease process affecting the bones/ligaments such as Paget's disease, osteogenesis imperfecta, rheumatoid arthritis, rickets, and achondroplasia (Clark and Benzel 2004). A large series found neck pain, weakness, paresthesias, and bowel and bladder dysfunction as common presenting symptoms, and 37–50% of the patients had a low hairline and short neck (Goel et al. 1998). Symptoms are a result of the upward displacement of the dens in addition to the flattened clivus producing not only brainstem

Craniocervical Junction, Abnormalities, Fig. 7 Lateral X-ray of congenital C2-3 and C6-7 fusion, highlighted by the superior and inferior *arrows*, respectively
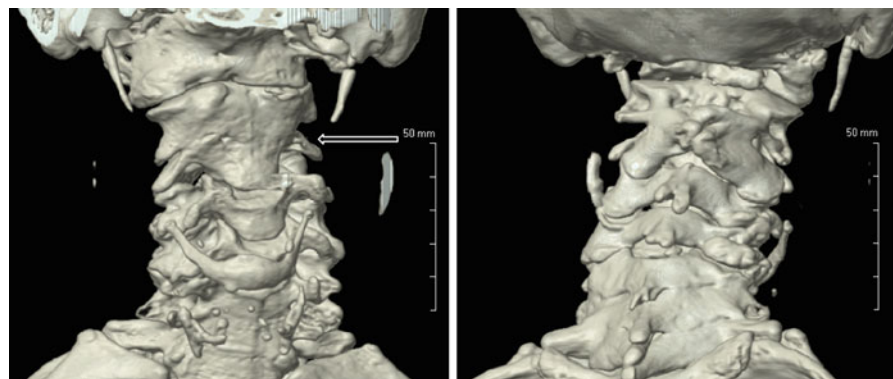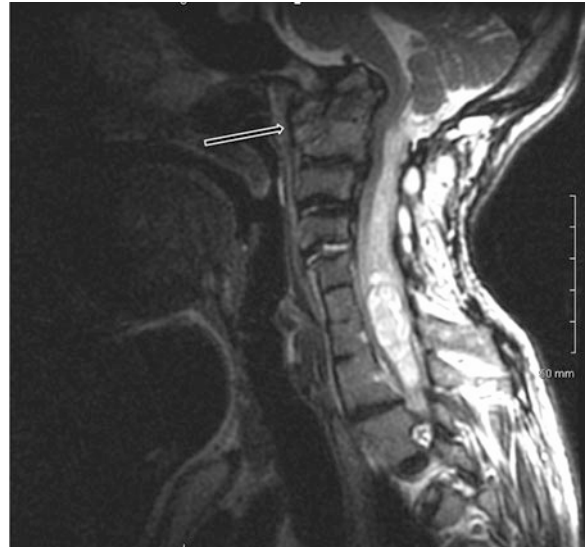

Craniocervical Junction, Abnormalities, Fig. 8 3D CT reconstruction of congenital C2-3 and C6-7 fusion. The *arrow* points to the C2-3 fusion

Craniocervical Junction, Abnormalities, Fig. 9 Sagittal CT of Os odontoideum in a child. The *arrow* points to the displaced corticated ossicle of the dens. Note the anterior subluxation of C1 on C2

Craniocervical Junction, Abnormalities, Fig. 10 Sagittal T2 MRI of basilar invagination in an adult. The *arrow* points to the dens, which protrudes through the foramen magnum. Note the flattened clivus

compression, but also traction on the cranial nerves with possible cranial palsies.

Diagnosis of the above abnormalities is often confirmed with imaging after the patients present with specific symptoms. However, many are diagnosed incidentally on imaging after a trauma or other non-related workup. Historically diagnoses were made with X-rays; however, CT and MRI have become the imaging modalities of choice and allow more direct and defined visualization. CT provides superior bony anatomy and vascular anatomy, whereas MRI is helpful in determining the ligamentous relationships and degree of neural compression. Other helpful modalities include 3D reconstructions of CT's, flexion extension CT, and MRI sequences. The latter two are helpful in defining the degree of dynamic stability/instability of the abnormality. Treatment depends on the degree of neural compression and the stability of the occipital cervical junction. If the instability is symptomatic an attempt at cervical traction is reasonable to reduce the defect. This obviates the need for decompression prior to fusion. Fusion techniques vary and common current options for C1-2 fusion include transarticular screws or C1 lateral mass and C2 pedicle
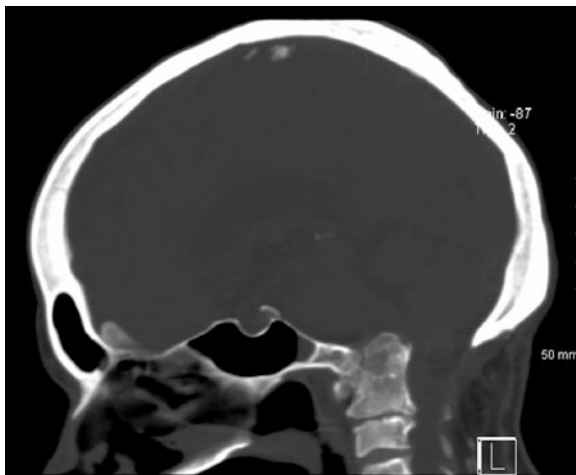

Craniocervical Junction, Abnormalities, Fig. 11 Sagittal CT of basilar invagination in a child. The *arrow* highlights the non-fused dens protruding into the foramen magnum

screws with rod fixation and grafting. If irreducible, neural compression may be relieved either ventrally or dorsally, depending on the location of the primary compression. Anterior decompression techniques depend on the pathology, but transoral approaches are often used for exposure. Dorsally, suboccipital decompression and laminectomy is commonly performed.

Craniocervical Junction, Abnormalities, Fig. 12 Sagittal CT of basilar invagination in a child

Infectious and Congenital Disorders Affecting Craniocervical Stability

Inflammatory, developmental, and traumatic etiologies may also lead to craniocervical pathology and possibly instability. Various bony disorders that result in softening can lead to basilar impression, such as osteogenesis imperfecta, achondroplasia, Hurlers syndrome, osteomalacia, rickets, and Paget's disease (Smith et al. 2010). Ligamentous instability can result from infection, including Grisel's syndrome and tuberculosis. Down's syndrome and mucopolysaccharidoses are congenital disorders associated with ligamentous laxity. Finally, trauma and neoplasms can result in instability and CCJ pathology.

Grisel's syndrome is defined as a nontraumatic atlantoaxial subluxation possibly secondary to otolaryngology procedures or infection of the head and neck (Richter and Bower 2006). Although multiple theories exist, it is currently believed to result from infectious spread from the pharynx to the cervical spine. A recent systematic review including 48 peer-reviewed publications found a 48% incidence related to infection, with 83% of those cases involving an upper respiratory tract infection. Thirty-one percent of cases were reported to be postoperative in which 78% occurred after adenotonsillectomy (Karkos et al. 2007). Presentation is typically associated with severe neck pain, limited range of motion, and torticollis. Diagnosis is confirmed with imaging and a needle biopsy may be beneficial if an infectious mass is identified. Antibiotics are administered and a cervical collar is placed for mild subluxations, whereas cervical traction and possible fusion may be needed for gross dislocations (Yu et al. 2003).

Down's syndrome is the most common chromosome abnormality and is characterized by mental retardation and characteristic facies in addition to multiple other features. Down's syndrome is also associated with other conditions including early onset Alzheimer's disease, congenital heart disease, and also craniovertebral instability. Craniovertebral instability occurs between 8% and 63% of children with C1-2 instability seen in 10–30%, although very few are symptomatic (1–2%) (Hankinson and Anderson 2010). In 64 patients with Down's syndrome followed by Menezes for symptomatic cervicomedullary compression, 47% had atlantoaxial subluxation and 63% had occipital cervical instability. Rotatory subluxation was seen in 47% of patients and os odontoideum was present in 19% (Menezes 2000). If symptomatic or unstable by clinical or imaging criteria, fusion may be indicated.

References

Arvin B, Fournier-Gosselin M, Fehlings MG (2010) Os odontoideum. Neurosurgery 66(Suppl):A22–A31

Barkovich AJ, Wippold FJ, Sherman JL, Citrin CM (1986) Significance of cerebellar tonsillar position on MR. AJNR Am J Neuroradiol 7(5):795–799

Burwood RJ, Watt I (1998) Assimilation of the atlas and basilar impression: a review of 1,500 skull and cervical spine radiographs. Clin Radiol 25(3):327–333

Clark CR, Benzel EC (2004) The cervical spine. Lippincott Williams & Wilkins, Philadelphia

David KM, McLachlan JC, Aiton JF, Whiten SC, Smart SD, Thorogood PV, Crockard HA (1998) Cartilaginous development of the human craniovertebral junction as visualised by a new three-dimensional computer reconstruction technique. J Anat 192:269–277

Gehweiler JA Jr, Daffner RH, Roberts L Jr (1983) Malformations of the atlas vertebra simulating the Jefferson fracture. AJR Am J Roentgenol 140(6):1083–1086

Goel A, Bhatjiwale M, Desai K (1998) Basilar invagination: a study based on 190 surgically treated patients. J Neurosurg 88(6):962–968

Guinto G, Zamorano C, Dominguez F et al (2004) Chiari malformation: Part I. Contemporary. Neurosurgery 26(25):1–7

Hankinson TC, Anderson RCE (2010) Craniovertebral junction abnormalities in Down syndrome. Neurosurgery 66(Suppl): A32–A38

Karkos PD, Benton J, Leong SC, Mushi E, Sivaji N, Assimakopoulos DA (2007) Grisel's syndrome in otolaryngology: a systematic review. Int J Pediatr Otorhinolaryngol 71(12):1823–1827

Liang C-L, Lui C-C, Lu K, Lee T-C, Chen H-J (2001) Atlantoaxial stability in ossiculum terminale. J Neurosurg Spine 95(1):119–121

Martin MD, Bruner HJ, Maiman DJ (2010) Anatomic and biomechanical considerations of the craniovertebral junction. Neurosurgery 66(Suppl):A2–A6

McGirt MJ, Nimjee SM, Fuchs HE, George TM (2006) Relationship of cine phase-contrast magnetic resonance imaging with outcome after decompression for Chiari I malformations. Neurosurgery 59(1):140–146; discussion 140–146

Menezes AH (2000) Developmental and acquired abnormalities of the craniovertebral junction. In: Crockard A, Hayward R, Hoff JT (eds) Neurosurgery, the scientific basis of clinical practice. Blackwell Science, Oxford, pp 1120–1145

Menezes AH (2008) Craniocervical developmental anatomy and its implications. Childs Nerv Syst 24(10): 1109–1122

Menezes AH, Fenoy KA (2009) Remnants of occipital vertebrae. Neurosurgery 64(5):945–954

Oakes WJ, Tubbs RS (2003) Chiari malformations. In: Winn HR (ed) Youman's neurological surgery: a comprehensive guide to the diagnosis and management of neurological problems, 5th edn. WB Saunders, Philadelphia

Paul KS, Lye RH, Strang FA, Dutton J (1983) Arnold-Chiari malformation. Review of 71 cases. J Neurosurg 58(2): 183–187

Richter GT, Bower CM (2006) Cervical complications following routine tonsillectomy and adenoidectomy. Curr Opin Otolaryngol Head Neck Surg 14(6):375–380

Sindou M, Chávez-Machuca J, Hashish H (2002) Craniocervical decompression for Chiari type I-malformation, adding extreme lateral foramen magnum opening and expansile duroplasty with arachnoid preservation. Technique and long-term functional results in 44 consecutive adult cases – comparison with literature data. Acta Neurochir 144(10):1005–1019

Smith BA, Griffin C (1992) Klippel-Feil syndrome. Ann Emerg Med 21(7):876–879

Smith JS, Shaffrey CI, Abel MF, Menezes AH (2010) Basilar invagination. Neurosurgery 66(Suppl):A39–A47

Smoker WRK, Khanna G (2008) Imaging the craniocervical junction. Childs Nerv Syst 24(10):1123–1145

Steinmetz MP, Mroz TE, Benzel EC (2010) Craniovertebral junction. Neurosurgery 66(Suppl):A7–A12

Thomsen MN, Schneider U, Weber M, Johannisson R, Niethard FU (1997) Scoliosis and congenital anomalies associated with Klippel-Feil syndrome types I-III. Spine 22(4):396–401

Yu KK, White DR, Weissler MC, Pillsbury HC (2003) Nontraumatic atlantoaxial subluxation (Grisel syndrome): a rare complication of otolaryngological procedures. Laryngoscope 113(6):1047–1049

Craniofacial Dysostosis

▶ Congenital Craniofacial Malformations and Their Surgical Treatment

Craniofacial Microsomia

▶ Congenital Craniofacial Malformations and Their Surgical Treatment

Craniofacial Resection

Rui P. Fernandes[1], Daniel Petrisor[1] and Iman Naseri[2]
[1]Division of Oral and Maxillofacial Surgery, College of Medicine, University of Florida, Jacksonville, FL, USA
[2]Division of Otolaryngology, College of Medicine, University of Florida, Jacksonville, FL, USA

Synonyms

Anterior Skull Base Surgery, Approach; Anterior/extended craniofacial resection; Cranial facial; Craniofacial surgery

Definition

The term "craniofacial surgery" encompasses a range of surgical approaches to various areas of the skull base for access resection.

Purpose

Craniofacial surgery involves a dynamic range of surgical practices that have undergone a vast evolution due to improved understanding of the involved conditions in addition to various advances in technology. These transformations have altered both clinical implications and changed the techniques of surgery.

Benign and malignant craniofacial tumors are infrequent, making up less than 10% of the neoplasms in the

head and neck (Pittman and Zender 2010). Malignant neoplasms of the nasal cavity and paranasal sinuses account for 3% of tumors, and only about 0.5% of all head and neck malignancies (Cantu et al. 2006). Tumors involving the paranasal sinuses account for a small subset that warrants surgery. These tumor types most commonly affect Caucasians in the fifth to seventh decades of life (Mantravadi and Zender 2010). Most malignant tumors of the anterior skull base and sinonasal region are of epithelial origin, with squamous cell carcinoma being the most common. Others include esthesioneuroblastoma, sinonasal undifferentiated carcinoma (SNUC), minor salivary gland carcinoma, and melanoma. Benign neoplasms in this area include angiofibroma, chondromas, osteomas, inverted papilloma, and odontogenic tumors (Mantravadi and Zender 2010; Pittman and Zender 2010).

In the past, patients undergoing craniofacial surgery for tumors had poor outcomes both in terms of survival and morbidity. Many of these tumors were often characterized by late presentation, thus posing a management challenge. Tumor resection surgery often did not allow appropriate tumor visualization for en bloc resection and the application of basic oncologic principles (Smith et al. 1954; Ketcham et al. 1963). By the same token, boundaries regarding surgery remain unclear as to the limits of resectability (Flint 2010). Prior to the rise of other treatment modalities such as radiation and chemotherapy, many tumors were considered unresectable with poor outcomes. Today, these previously unresectable lesions are now highly treatable due to the advent of new imaging techniques, radiation and chemotherapeutic regimens, and advances in technologies that have improved surgical access.

Indication: Tumors that require craniofacial surgery arise from the anterior and middle cranial base. They also include tumors extending into this area but originate in the nasal cavity, paranasal sinuses, infratemporal, pterygopalatine, and parapharyngeal regions.

Craniofacial surgery is typically performed for two main categories of diagnoses. They involve nonneoplastic genetic and congenital diseases and anomalies, mostly in the pediatric population. The remaining category involves surgery for tumor resection. In this entry, we will focus mainly on craniofacial surgical modalities geared for a range of benign and malignant tumors.

Principle

The various conditions that require craniofacial surgery are numerous and often span multiple systems. Therefore, the considerations involving in the care of such patients typically requires parallel management by a diverse range of clinical disciplines. This is essential to ensure the best outcome for each patient.

Similar to many other tumors of various locations, a thorough clinical history and examination is vital, and may clarify the location and the degree of tumor involvement. Possible symptoms for craniofacial tumors include nasal airway obstruction, epistaxis, anosmia, facial pain, facial paresthesias, epiphora, and others that may be initially diagnosed as common conditions such as migraines, allergic rhinitis, or sinusitis, leading to a delay in diagnosis and treatment (Mantravadi and Zender 2010). For example, diplopia, proptosis, extraocular movement restriction, paresthesia in the V2 trigeminal distribution, and epiphora are signs that may represent invasion of the orbit and the adjacent nasolacrimal system. These external changes, among other similar types, all refer to the late manifestations of tumour involvement.

Radiographic workup including computed tomography (CT) and magnetic resonance imaging (MRI) has become an essential step in the initial workup of craniofacial tumors. CT imaging is useful for evaluating the extension of tumors into surrounding structures. Detailed visualization of the skull base requires thin sections (1.5 mm or less) allowing three-dimensional reconstruction to help in surgical planning. Additionally, stereo-lithographic modeling may be utilized for intraoperative assistance. Image-guided navigation may also be used as additional help for intraoperative guidance for identification of important landmarks.

Magnetic resonance (MR) imaging may be used to identify the relationship of a tumor to the surrounding soft tissue structures including vasculature. Angiography (CTA/CTV, MRA/MRV) may be helpful, and often essential, in evaluating vascular tumors to delineate the extent of involvement, relation to major vascular structures, and tumor blood supply (Mantravadi and Zender 2010). In order to prevent postsurgical artifact, the radiological examination should be completed prior to any formal biopsy. Despite the above techniques available in tumor imaging, histopathologic tissue evaluation may not be attainable due to

tumor location and lack of access. Therefore, preoperative imaging is a small part of the puzzle, to be combined with the history, examination, and other related tests including laboratory workup in the management of craniofacial tumors.

Preoperative endoscopic examination of the nasal cavity and nasopharynx may provide clues regarding a tumor's origin, extent, and vascularity. Various medical conditions including cardiopulmonary instability may obviously prevent surgical candidacy. Therefore, a complete preoperative medical workup of the cardiovascular system and any other medical conditions is necessary as such operations are often demanding in terms of time and cardiopulmonary stress that is exerted both intraoperatively and in the postoperative period.

Choice of Treatment/Planning

Many tumors involving the anterior skull base are surgically treated using various craniofacial approaches and often yield low morbidity (Kedeshian 2001; Ganly et al. 2005). When such tumors are deemed unresectable, concurrent chemoradiotherapy may aid in improving survival (Adelstein et al. 2003).

One of the most important steps in the successful management of patients with craniofacial conditions is proper communication to ensure the adequacy of the patient's understanding and expectations. It is often necessary to include the patient's spouse or family members in discussions during the pretreatment phase. An important consideration that may alter treatment selection between surgical and nonsurgical management includes the goal of achieving optimal prognosis and survival, especially for carcinomas.

A common result in the sequelae of craniofacial surgery is change in the appearance of the patient in relation to resultant surgical site defect. Due to the obvious location, surgery for craniofacial tumors may alter the facial symmetry and harmony (Thaller et al. 2007). Planning for surgical reconstruction must address the underlying skeletal structure and the surgeon should be mindful of possible aesthetic or functional deficiencies. Such deficiencies may have profound effects both physically and psychologically. These may include unsightly scars, diplopia, speech or swallowing defect, epiphora, anosmia, wound breakdown, and infection. It is crucial to optimally plan each

surgical routine both in terms of technique and mutual understanding among the surgeon and patient. Surgery remains the cornerstone in the treatment of many benign and malignant craniofacial tumors. The surgical approach selected should allow the surgeon to have optimum visualization and access to the tumor in order to ensure safe and complete excision and tumor-free margins.

Surgical Approaches

Endoscopic Approach

Endoscopic approaches geared for excision of tumors involving the paranasal sinuses and anterior skull base have been adopted by many surgeons in the last decade due to technological advances with optics and instrumentation that allow safe access of the tumor excision. Comparatively, in terms of 5-year survival and locoregional control, the outcomes for transnasal endoscopic approach have been shown to be similar to the traditional open approach for low-stage malignancies (Higgins et al. 2011). Most of the endoscopic approaches are endonasal. However, there are other similar approaches, like endoscopic trans-maxilllary, and/or trans-oral route. In planning a resection of such tumors, one must keep in mind the basic oncologic principles guiding tumor resection. Minimally invasive approaches such as endoscopic endonasal technique may be preferred by patients, but should be offered with caution, especially in the presence of a malignancy. Therefore, meticulous planning should be undertaken in terms of the particular approach to the tumor and its deep and lateral extent, in addition to the morbidity and risks to surrounding anatomy and neurovascular structures.

The endonasal endoscopic approach is used for a variety of benign and malignant tumors involving the midline skull base, nasal cavity, and paranasal structures. Tumors in the mid-sagittal plane are easier to resect than their counterparts which may be further away from this mid-sagittal point. This is simply because of the gradual decrease in the amount of access which can be established when the target is away from the midline as depicted in Fig. 1. Posteriorly, the trans-sphenoidal corridor serves as a highly practical region to access various anterior and even mid-skull base lesions.

Craniofacial Resection, Fig. 1 The extent of endoscopic endonasal access to the anterior skull base: *Arrows* indicate the anteroposterior access via the mid-sagittal plane, and the two coronal views depict the lateral limits with horizontal arrows and a box at two different coronal locations
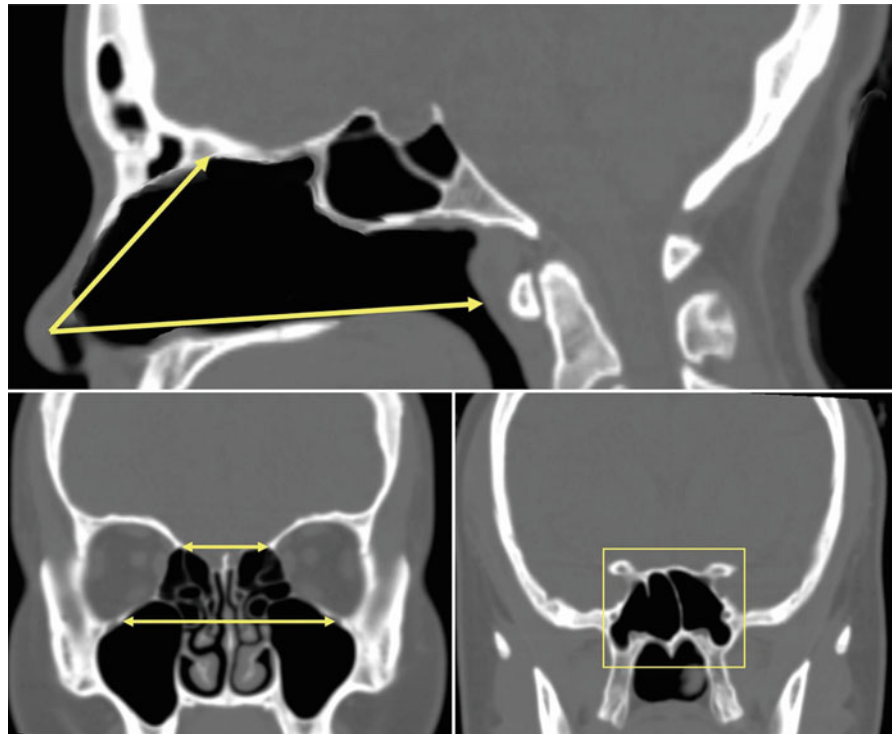
The endoscopic approach may also be combined with open approaches to ensure complete tumor excision. Various combined open approaches include Caldwell-Luc access via sublabial incision, or a brow versus Lynch-type incision to access the frontal or ethmoid sinus.

Direct Approach

The direct approach may be utilized in cases where the tumor involves the overlying skin. In these cases, skin resection allows a more direct approach for tumor clearance. There is often a need to sacrifice adjacent structures such as nerves, vessels, as well as others including periorbital tissue or an orbital exenteration, in cases of direct tumor involvement.

In cases where there is direct involvement of the supraorbital nerve with intracranial extension with or without erosion of the orbital roof, a direct approach may be used. If a resection is performed with adequate soft tissue margins, the orbital exenteration is performed first, and in so doing, the orbital roof is exposed. The neurosurgical resection can be carried out via the transorbital route. Orbital osteotomies are

often necessary to allow access to the cranial vault. Following the completion of the dural resection and resection of the brain, a dural repair may be performed through the same approach, followed by either local or free tissue reconstruction of the defect. This direct approach may be used in any case where the tumor extends to the overlying tissue and the incorporation of the tissue resection would offer adequate access for best oncologic resection.

Coronal Approach

The coronal approach (also named bi-coronal or bi-frontal) to tumors in the craniofacial region is preferred by many craniofacial surgeons and it is widely used. It often provides a suitable access to the lateral aspects of the paranasal sinuses, including the frontal sinus overlying the orbital roof, in addition to excellent access to the midline facial and anterior skull base (via an anterior cranial fossa craniotomy) (Fig. 2).

In order to fully understand the coronal technique, a thorough understanding of the scalp anatomy is required. The scalp is made up of several layers. The skin is the first layer, deep to the skin is the
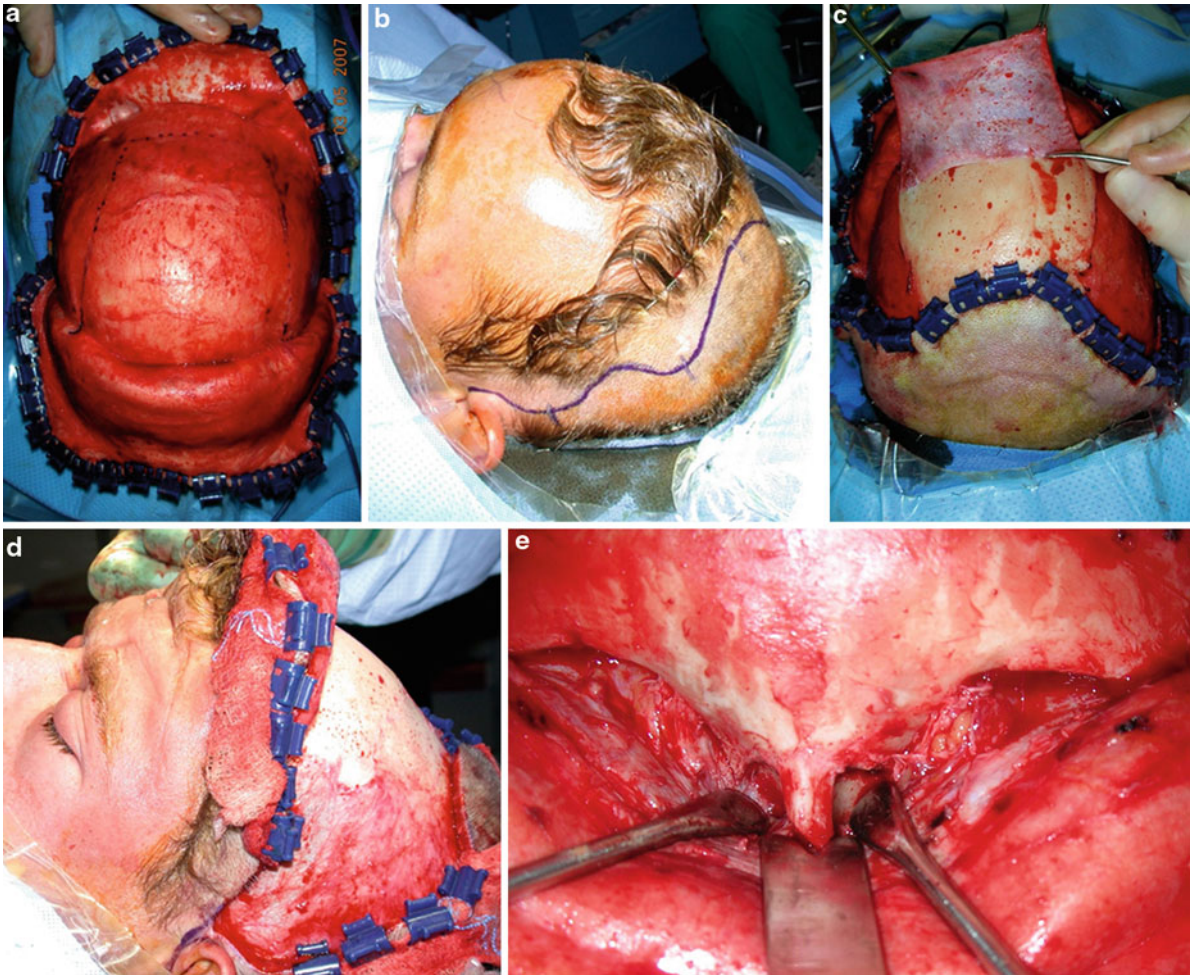
Craniofacial Resection, Fig. 2 (**a**) Coronal approach with a planned pericranial flap for possible use post resection; (**b**) Curvilinear incision planned to minimize the visibility of the scar postoperatively, note the extension of the incision to the preauricular region; (**c**) Reflected coronal flap with exposure of the frontal sinus; (**d**) lateral view of the coronal flap being reflected, note the intact temporalis muscle and the transition of the incision to the deep layer in order to protect the facial nerve; (**e**) exposure of the nasal root, medial canthus, and medial orbital region via the coronal approach

subcutaneous layer followed by the aponeurosis and the loose areolar tissue and finally the pericranium. Depending on the location, anterior or lateral, the anatomy varies due to the location of the respective muscle layers. In the lateral aspect, the temporalis muscle is encountered, while anteriorly the frontalis muscle. The blood supply to the scalp is also dependent on the location. Anteriorly, the main blood supply comes from the supraorbital arteries and veins, and medially by the supratrochlear artery. Laterally, the superficial temporal artery ascends in the preauricular region before splitting into an anterior and a posterior branch. Posterior to the ear, the postauricular artery supplies part of the scalp, then eventually completes various anastomoses to the occipital artery. The arterial supply is mirrored on the contralateral side. The main motor branch encountered is the frontal branch of the facial nerve. This branch has a predictable location as it extends from the main trunk of the nerve to eventually innervate the frontalis muscle. The nerve travels approximately 8 mm anterior to the tragus of the ear in an anterior-superior fashion. It innervates the

Craniofacial Resection, Fig. 3 (**a**) Lateral rhinotomy approach; (**b**) Extension of the lateral rhinotomy to include orbital exenteration due to tumor extension into the orbit
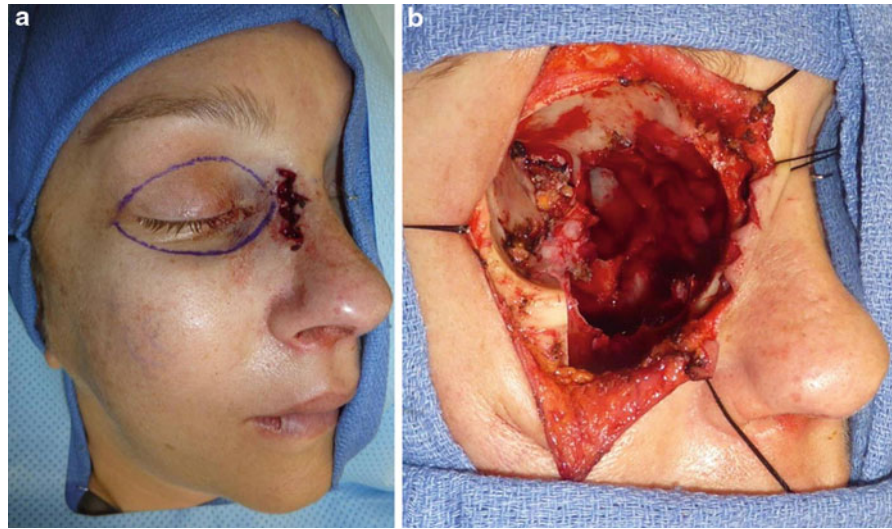
frontalis muscle anterior to a line drawn from the tragus to 2 cm in front of the lateral orbital rim. It lies deep to the superficial layer of the deep temporal fascia. The sensory nerves are the supraorbital nerves and the zygomaticotemporal nerves.

Flap Design: The coronal flap may be designed in many forms depending on the age, gender of the patient as well as tumor location. In males with male pattern baldness, the location of the incision is further posterior so as to help camouflage the incision, while in younger males, the location may be more anterior. Many forms have been described; a wavy pattern, a repeating series of "V"s, or a repeating curve. However, the choice of the coronal flap design is largely surgeon dependent.

Surgical Technique: The incision for the coronal approach is placed 4–5 cm into the hair line in men who are not balding and for most women, but may be placed farther posteriorly in balding men or those with receding hair lines at the widow's peak and lateral temporal regions (Ellis and Zide 2006). The incision is extended down to the level of the tragus in the preauricular crease. This allows exposure of the zygomatic arch, temporomandibular joint, and/or the infraorbital rims. The posterior skin flap is elevated just enough to allow for sufficient pericranial flap harvest for reconstruction while the anterior dissection is carried out in the subperiosteal plane anteriorly to the superior orbital rims (Smith and Ducic 2004; Mantravadi and Zender 2010). Careful attention must

be given to preserve the supratrochlear and supraorbital vasculature, which supply the pericranial flap when elevating at the supraorbital rims. The supraorbital neurovascular bundle is located in a notch or foramen along the medial third of the superior orbital rim. If the bundles is fully encompassed by bone within a foramen, it may be released by angled bone cuts with an osteotome on both sides of the artery and nerve through the supraorbital rim. Raney clips are applied to the incision edges on the anterior and posterior skin flaps for hemostasis (Ellis and Zide 2006). Dissection is carried out laterally and inferiorly at the zygomatic arch deep to the superficial layer of the temporalis fascia as the temporal branch of the facial nerve is always lateral to this layer (Ellis and Zide 2006).

Lateral Rhinotomy Approach

The lateral rhinotomy approach is a suitable technique for the ablation of a wide variety of lesions in the midface (Fig. 3). This approach affords excellent exposure for tumors arising from the nasal cavity, paranasal sinuses, nasal septum, lateral nasal wall, nasal roof, medial and inferior orbital walls, sphenoid sinus, nasopharynx, clivus, and the medial aspect of the infratemporal fossa with minimal postoperative deformity (Weisman 1995; Mantravadi and Zender 2010). The main disadvantage to this approach is that it offers limited access to lesions that extend bilaterally.

The incision for the lateral rhinotomy is made along the ala of the nose and along the sidewall toward

the medial canthus. The incision is extended to reflect the nasal mucosa and the bones along the medial wall of the maxillary sinus. The extent of the dissection will be dependent on the location of the tumor and the desired access.

Midface Degloving Approach

The midface, or midfacial, degloving approach avoids facial skin incisions, and resulting facial scars, while providing access to the nasal cavity and paranasal sinuses. A maxillary vestibular incision is usually placed approximately 3–5 mm superior to the mucogingival junction and can extend from the first molar on one side to the first molar on the contralateral side, leaving a cuff of unattached mucosa on the alveolus to facilitate closure (Ellis and Zide 2006). A subperiosteal dissection should be carried out superiorly to the level of the piriform aperture. Next, intranasal freeing is accomplished by bilateral incision of the nasal floor along the piriform, intercartilaginous incision, and a complete transfixion incision through the membranous septum. Finally, the soft tissue envelope over the nose and midface is dissected in a subperiosteal and subperichondrial fashion up to the level of the ethmoid sinuses, thus degloving the nose, nasal radix, and ethmoid region.

Although this approach has the benefit of a lack of scar in the face, the surgeon has to balance it with the potential for diminished visualization along the superior aspect of the orbital rims as well as the superior and posterior aspect of the maxillary sinuses.
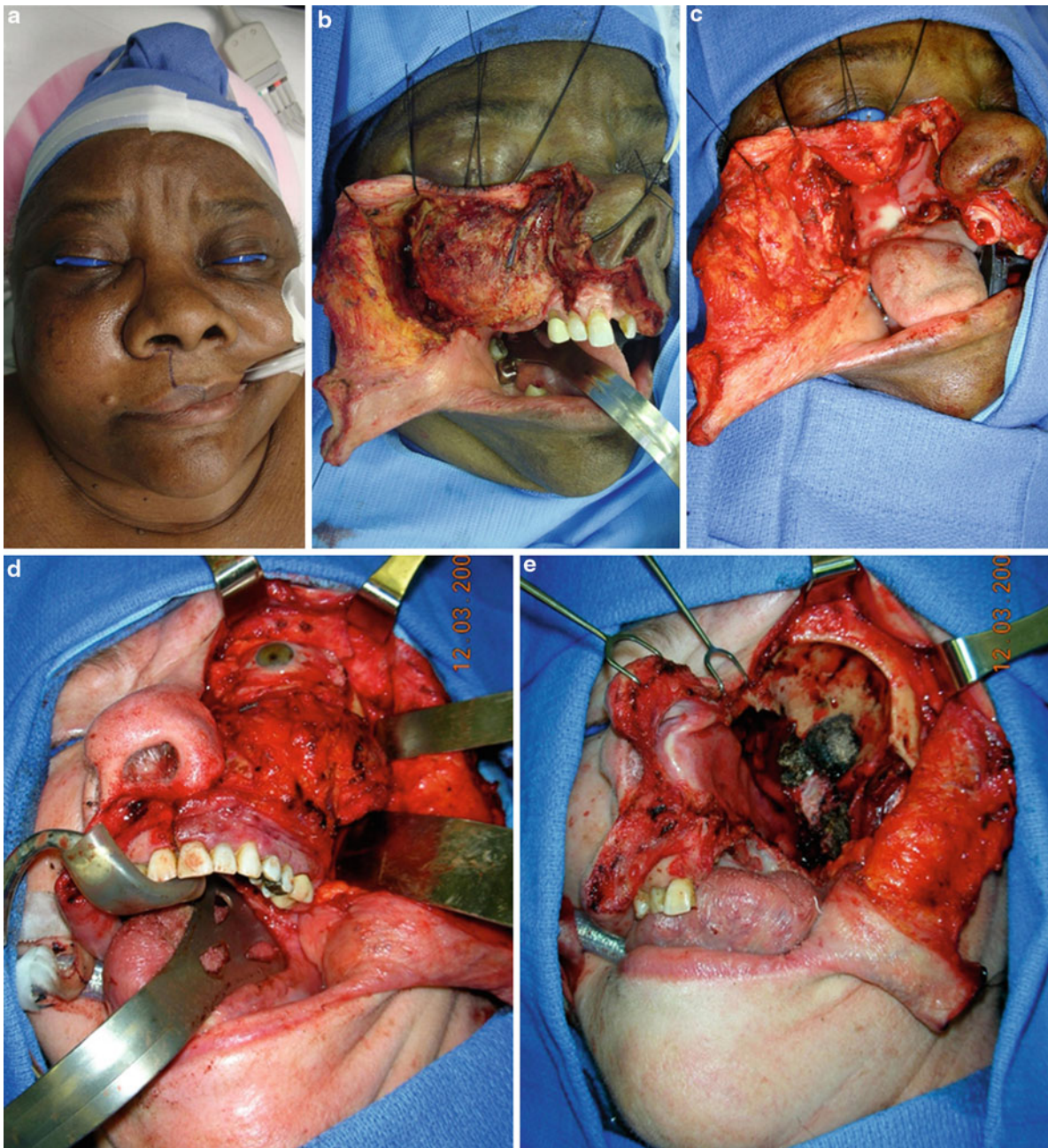
Weber–Ferguson Approach

The Weber–Ferguson approach combines the incisions of a lateral rhinotomy incision with an infraorbital incision (Bryce and Gates 1984). This incision has now evolved into a modified version which improves upon the cosmetic outcome (Fig. 4). The modified Weber–Ferguson incision extends from the upper lip along the philtrum up toward the nasal sill and laterally along the ala of the nose. It extends superiorly along the nasal sidewall toward the medial canthus. Once along the medial canthus, the incision can be extended using several methods: through the subconjunctival approach, subcilliary or in a lower eyelid crease toward the lateral canthus. The amount of extension of the incision will be dependent on the degree of needed exposure. The lip incision is a full thickness one and extends to the depth of the upper vestibule and

superiorly to the piriform rim. The nasal mucosa may be protected and reflected or an incision can be made depending on the location of the tumor and the planned resection. Once the flap is reflected laterally, the infraorbital nerve is encountered and is divided. The entire infraorbital rim is exposed and the integrity of the orbital floor is evaluated. If the floor is found to be intact, the orbital contents may be spared. The dissection is carried out laterally to expose the zygomatic buttress, and arch. Exposure along the arch is facilitated by the release of the masseter muscle attachment from the arch. In this region, the lateral aspect of the maxilla is exposed. The exposure is at times made more difficult by the extravasation of the buccal fat pad into the defect. If the buccal fat pat is displaced into the surgical field, a wide malleable retractor can be used to restrain the fat pad out of the field.

Preauricular/Temporomandibular Approach

The preauricular approach or temporomandibular approach may be used to access tumors in the infratemporal region and the middle cranial fossa region. The incision for this approach begins along the superior aspect of the helix of the ear and inferiorly along the tragus and lobule of the ear. The incision is then extended in the neck along a crease toward the midline of the neck. Once a subplatysmal flap is elevated, it is combined with the suprasmas preauricular dissection. The flap is reflected and dissection is extended toward the inferior border of the mandible, while protecting the marginal branch of the facial nerve. The fascia anterior to the sternocleidomastoid muscle is reflected and dissection extended toward the carotid sheath. The vessels are then dissected and a vessel loop is placed along the internal jugular vein and the carotid artery. The loop along the carotid artery may be placed after the bifurcation with one on the external carotid and the other on the internal. This precautionary action is to improve hemostatic control in case significant bleeding is encountered later on during tumor dissection. The masseter muscle is elevated and reflected off the mandible until the sigmoid notch is encountered. If the location of the tumor is toward the deep pharynx and toward the cranial base, a vertical subsigmoid osteotomy is then marked and two 4 hole, 2.0 mandibular plates are contoured and applied to the mandible along the osteotomy. The plates are then removed and kept on the back table for later use. The osteotomy is completed and the proximal mandible is reflected by first detaching the insertion of the medial
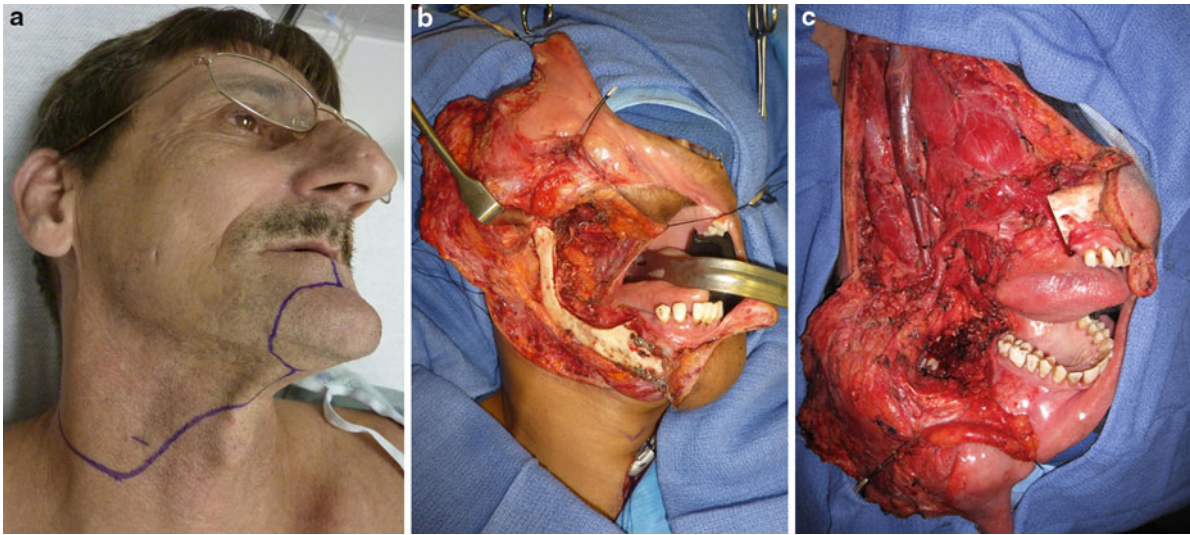
Craniofacial Resection, Fig. 4 (**a**) Markings for a modified Weber–Ferguson approach with a subcilliary extension; (**b**) Reflected flap laterally exposing the tumor with perforation of the anterior wall of the maxillary sinus; (**c**) Resected tumor with inclusion of the orbital floor but with preservation of the globe; (**d**) Modified Weber–Ferguson incision with extension into the supraorbital area for a planned resection including an orbital exenteration; (**e**) Craniofacial resection with orbital exenteration

pterygoid muscle. The reflection of the proximal mandible gives a significantly improved view of the surgical bed. In cases where the tumor is along the deep parotid, the main branch of the facial nerve is identified about 4 mm above the posterior belly of the digastric and along the same plane. This combined exposure allows the surgeon to have an unimpeded view of the infratemporal, deep pharyngeal space to carry out the resection.

Craniofacial Resection, Fig. 5 (**a**) Markings for a lip-split mandibulotomy for resection of tumor extending into the skull base; (**b**, **c**) Intraoperative exposed mandible with tumor, and resultant defect after resection of the tumor and composite resection of the mandible

Mandibular Swing (With Lip Split)

The mandibular split approach is done when the planned craniofacial resection necessitates a better view of the posterior aspect of the maxilla along the pterygoids and infratemporal space (Fig. 5). The planned incision extends from the midline of the lower lip deep to the labiomental crease and then laterally along the menton in a circular fashion to the midline of the submandibular area. The incision is then extended along the neck in a circular aspect within a cervical crease curving posterior-superior toward the mastoid. The flap is reflected deep to the platysma muscle toward the inferior border of the mandible. The facial vessels are ligated and divided taking care to reflect the marginal mandibular branch of the facial nerve superiorly. The fascia along the inferior border of the mandible is reflected, therefore freeing the mandible. The lip incision is extended from the skin toward the mucosa, taking care to cauterize the labial vessel. The mucosa incision is extended to the buccal vestibule. An osteotomy is then marked anterior to the mental foramen and between the roots of the canine and first premolar. A 2.0 or greater mandibular plate is fashioned to the inferior aspect of the mandible and another superior to it in tension-band manner. The plates are secured and then removed and placed on the back table for later use. The lingual mucosa is reflected with the periostium and the osteotomy is

completed. The mucosa along the lingual aspect of the floor of mouth is incised taking care to protect the lingual nerve and submandibular duct toward the retromolar region. Once this is completed, the mylohyoid muscle is divided and the mandible is reflected laterally. This allows the visualization of the parapharyngeal space.

Combined Lip-Split and Weber–Ferguson Approach

This combined approach is preferred for providing the best open approach to tumors of the maxillary sinus with extension to the anterior wall, orbital floor, or into the pterygoid bone (cannot include those extending into the pterygoid muscles). This approach employs the two previously described techniques to better visualize the tumor and increase the safety of the resection by allowing better access to the great vessels (Fig. 6). Once both flaps are reflected, the resection can be performed in an oncologically safe manner while preserving the integrity of uninvolved vessels and nerves.
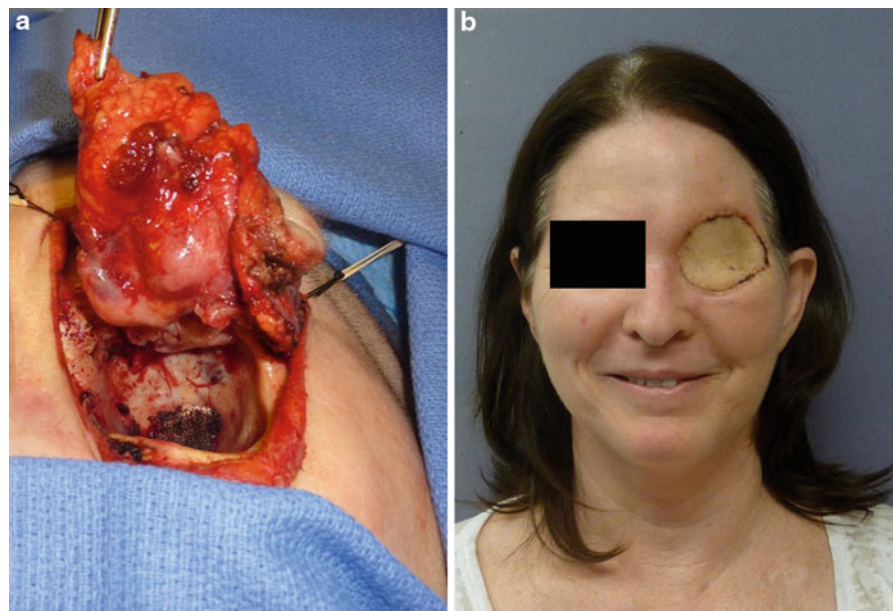
Reconstruction

Craniofacial reconstruction has previously been limited by the reaches of regional flaps and the surgical resection of complex cranial defects. One of the main
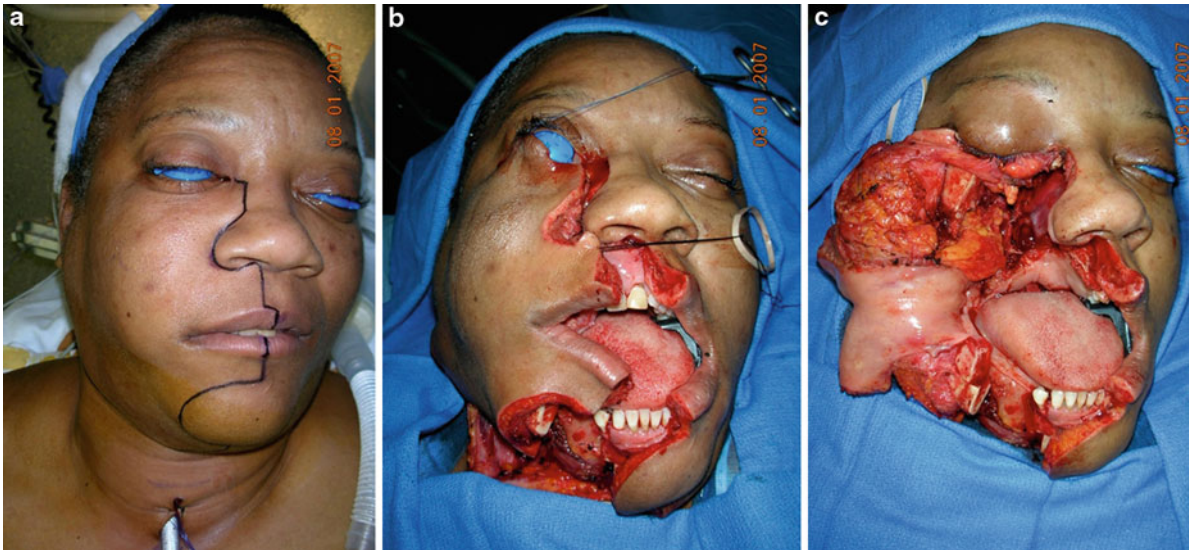
Craniofacial Resection, Fig. 6 (**a**) Planned combined approaches for a large tumor with extension to the orbital floor and posteriorly to the posterior maxilla with extension to the pterygoid region; (**b**) Incision and osteotomy completed; (**c**) combined approach following resection of the tumor

Craniofacial Resection, Fig. 7 (**a**) Direct transorbital approach with orbital exenteration; (**b**) Final aesthetic outcome after reconstruction using fasciocutanous radial forearm flap

advances in the management of patients with craniofacial tumors, aside from the developments in endoscopic surgery, has been the continued improvement and perfection of free tissue transfer (Fig. 7). The ability to predictably reconstruct these complex and often large defects has significantly allowed the ablative surgeon greater flexibility in redefining the boundaries of resectable disease.

The most often utilized flaps in reconstruction of craniofacial defects are the soft tissue flaps. These flaps

range from the simple fasciocutaneous radial forearm flaps, muscle flaps, and perforator flaps to complex chimeric perforator flaps. Several authors have reported their experience in the reconstruction of craniofacial defects (Chang et al. 2001; West et al. 2006). The published success rate of microvascular flaps is above 95% (Bui et al. 2007). The high success rate and dependability of free tissue transfer for head and neck reconstruction has significantly diminished the fear of using this reconstructive method for patients with craniofacial resection and has allowed surgeons to tackle larger and more complex tumors.

Postoperative Care

The postoperative care of patients undergoing surgery for craniofacial tumors is mainly related to the extent of surgical resection and the violation of surrounding anatomic areas due to gross involvement by the tumor. In the presence of intracranial extension, for example, there will be a need for dural repair, possibly requiring ventricular shunting or a lumbar drain. Therefore, the postoperative care regimen should include frequent neurologic examinations and related surveillance including imaging to evaluate for possible intracranial hemorrhage, pneumocephalus, and other possible complications.

A major aspect of postoperative monitoring in all patients following craniofacial resection revolves around monitoring the wound and the reconstructive method. In those patients reconstructed with free tissue transfer, they can be divided into two groups for monitoring: those with buried flaps and those with an external skin flaps. In those patients with deep flaps, the postoperative surveillance will be carried out by the use of internal Doppler monitoring systems such as the Cook device (Cook Vascular®, Vandergrift, Pennsylvania). The perfusion to the flap should be monitored on an hourly basis for the first 48 h and then every 2 h for the next 24 h. The experience of the authors suggests that the flaps which are found to be without issues after 72 h will survive while those that have any vascular compromise would be apparent by that time.

Role of Radiation and Chemotherapy

In the past, unresectable tumors were treated with radiation therapy as the mainstay of treatment, and carried a poor survival rate of about 25% (Vokes et al. 1993; Adelstein et al. 2003). In the past 30 years, survival rates have steadily improved with the advent of technology and multimodality treatment approaches (Marcial et al. 1990; Adelstein et al. 1993). In the early period of radiation delivery to the head and neck, large doses were used in wide fields of delivery. With improvements in cross-sectional imaging, improved tumor localization was made possible, and with better geographic localization of the tumor, improvements in focused radiation treatment have led to improved locoregional control and related morbidities (Peters 2007).

The role of chemotherapy in the management of head and neck tumors has undergone exhaustive investigation, leading to increased acceptance in the past decade. Among the treatment regimens, it has been shown that concurrent chemotherapy and radiation carries a survival benefit. No data has shown differences between single and multi-agent chemotherapy. Additionally, there is no evidence to demonstrate benefit from induction chemotherapy in the treatment of head and neck tumors (Fu 1997).

Advantage/Disadvantage

The main advantage of all craniofacial surgery is that it provides essential access to tumors requiring excision, as it ensures adequate exposure while maintaining the effective "footprint" as small as possible, to preserve function and aesthetic outcomes.

Despite the availability of the multiple methods used in craniofacial surgery, all of them carry inherent disadvantages. A surgeon's knowledge of such disadvantages is crucial, as they may equate to possible risks, which have to be clearly conveyed to the patients undergoing surgery. Whether the craniofacial approach uses a direct approach incision, coronal or endoscopic, they all disrupt the natural anatomy in some way. During the operation, disadvantages may be limited access/visualization, resulting in incomplete

tumor removal, or inability to control hemorrhage. Postoperative results may include wound breakdown, functional and aesthetic deficiencies. Therefore, surgeons must carefully select their surgical approach based on tumor type and location, in addition to careful perioperative patient workup in order to ensure the best final outcomes.

Cross-References

▶ Endoscopic Surgery of Skull Base
▶ Esthesioneuroblastoma

References

Adelstein DJ, Kalish LA et al (1993) Concurrent radiation therapy and chemotherapy for locally unresectable squamous cell head and neck cancer: an Eastern Cooperative Oncology Group pilot study. J Clin Oncol 11(11):2136–2142

Adelstein DJ, Li Y et al (2003) An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. J Clin Oncol 21(1):92–98

Bryce D, Gates GA (1984) Current therapy in otolaryngology – head and neck surgery. Mosby, Philadelphia

Bui DT, Cordeiro PG et al (2007) Free flap reexploration: indications, treatment, and outcomes in 1193 free flaps. Plast Reconstr Surg 119(7):2092–2100

Cantu G, Riccio S et al (2006) Craniofacial resection for malignant tumours involving the anterior skull base. Eur Arch Otorhinolaryngol 263(7):647–652

Chang DW, Langstein HN et al (2001) Reconstructive management of cranial base defects after tumor ablation. Plast Reconstr Surg 107(6):1346–1355; discussion 1356-7

Ellis E, Zide M (eds) (2006) Surgical approaches to the facial skeleton, 2nd edn. Lippincott Williams & Wilkins, Philadelphia

Flint PW (2010) Cummings otolaryngology head & neck surgery. Mosby Elsevier, Philadelpha

Fu KK (1997) Combined-modality therapy for head and neck cancer. Oncology (Williston Park) 11(12):1781–1790, 1796; discussion 1796, 179

Ganly I, Patel SG et al (2005) Craniofacial resection for malignant paranasal sinus tumors: report of an international collaborative study. Head Neck 27(7):575–584

Higgins M, Thorp B, Rawlings BA, Han JK (2011) Outcome results of endoscopic vs craniofacial resection of sinonasal malignancies: a systematic review and pooled-data analysis. Int Forum Allergy Rhinol 1(4):255–261

Kedeshian P (2001) Skull base: anterior and middle cranial fossa. In: Shah JP (ed) Cancer of the head and neck, vol 1. BC Decker, New York

Ketcham AS, Wilkins RH et al (1963) A combined intracranial facial approach to the paranasal sinuses. Am J Surg 106: 698–703

Mantravadi AV, Zender C (2010) Craniofacial approaches to the anterior skull base. Operative Tech Otolaryngol 21:181–187

Marcial VA, Pajak TF et al (1990) Concomitant cisplatin chemotherapy and radiotherapy in advanced mucosal squamous cell carcinoma of the head and neck. Long-term results of the Radiation Therapy Oncology Group study 81-17. Cancer 66(9):1861–1868

Peters LJ (2007) Changes in radiotherapeutic management of head and neck cancer: a 30-year perspective. Int J Radiat Oncol Biol Phys 69(2 Suppl):S8–S11

Pittman AL, Zender C (2010) Total maxillectomy. Operative Tech Otolaryngol 21:166–170

Smith JE, Ducic Y (2004) The versatile extended pericranial flap for closure of skull base defects. Otolaryngol Head Neck Surg 130(6):704–711

Smith RR, Klopp CT et al (1954) Surgical treatment of cancer of the frontal sinus and adjacent areas. Cancer 7(5):991–994

Thaller S, Garri JI, Bradley JP (2007) Craniofacial surgery. CRC Press, Boca Raton

Vokes EE, Weichselbaum RR et al (1993) Head and neck cancer. N Engl J Med 328(3):184–194

Weisman R (1995) Lateral rhinotomy and medial maxillectomy. Otolaryngol Clin North Am 28(6):1145–1156

West CA, Towns G et al (2006) Reconstruction of skull base and dura using rectus abdominis muscle combined with a vascularised fascial perforator flap. J Plast Reconstr Aesthet Surg 59(6):631–635

Craniofacial Surgery

▶ Craniofacial Resection

Craniovertebral Junction

▶ Craniocervical Junction, Abnormalities

Cricoarytenoid Articulation

▶ Cricoarytenoid Unit

Cricoarytenoid Joint

▶ Cricoarytenoid Unit

Cricoarytenoid Unit

Manish D. Shah[1] and Adam M. Klein[2]
[1]Department of Otolaryngology-Head and Neck Surgery, University of Toronto, Toronto, ON, Canada
[2]Department of Otolaryngology-Head and Neck Surgery, Emory University School of Medicine, Atlanta, GA, USA

Synonyms

Cricoarytenoid articulation; Cricoarytenoid joint

Definition

A diarthrodial articulation between the cricoid and arytenoid cartilages that functions to control true vocal fold movement, facilitating phonation, respiration, and airway protection.

Embryology

The arytenoid and cricoid cartilages are derived from the sixth branchial arch. The cricoid and the majority of the arytenoid consist of hyaline cartilage formed from the branchial arch mesoderm. The vocal process of the arytenoid, in contrast, forms from the mesoderm of the floor of the pharynx and consists of elastic cartilage, forming an embryonic fusion plane between it and the body of the arytenoid (Sadler 2010).

Anatomy

Cartilages

The cricoid cartilage has a signet-ring shape – the inferior border is essentially horizontal, whereas the superior border slopes superiorly from anterior to posterior. The posterior lamina is 2–3 cm in height compared to 0.5–0.7 cm anteriorly.

The arytenoid cartilage resembles a pyramid with four angles: (1) anterior angle (vocal process) for attachment of the vocal ligament, (2) lateral angle (muscular process) for attachment of the posterior cricoarytenoid (PCA) and lateral cricoarytenoid (LCA) muscles, (3) posterior angle to which the cricoarytenoid ligament attaches, and (4) the superior angle, which is the apex.

The cricoid facet is teardrop shaped and convex along both its long and short axes. It inclines at 30°–60° toward the anterolateral end (Wang 1998). This contour allows for an inferior and medial rotation of the vocal process toward the end of adduction. Wang (1998) studied both male and female adult larynges and found that the mean long axis dimension of the cricoid facet was 7.4 mm (range 5.4–9.0 mm) and that the mean short axis dimension was 4.2 mm (range 3.0–5.7 mm).

The arytenoid cartilage facet is also teardrop shaped but concave along its long axis, which rests perpendicular to the long axis of the cricoid facet (Wang 1998; Kasperbauer 1998). Wang's study (1998) found that the mean long axis dimension of the arytenoid facet was 5.0 mm (range 4.5–5.7 mm) and that the mean short axis measured 4.8 mm (range 3.5–5.8 mm).

Several other studies found similar dimensions for the cricoid and arytenoid facets (Maue and Dickson 1971; Sellars and Sellars 1983; Storck et al. 2010a). Wang (1998) did report that there can be shape and size asymmetry from right to left. There is, however, conflicting data as to whether there is a difference in facet size between male and female larynges (Wang 1998; Storck et al. 2010a).

Ligamentous Attachments

The conus elasticus is attached to the superior inner border of the cricoid cartilage and is continuous with the vocalis ligament superiorly. It attaches to the vocal process and to the posterior aspect of the body of the arytenoid. The quadrangular membrane attaches to the anterior surface of the body of the arytenoid and extends to the epiglottis, forming the aryepiglottic and false vocal folds.

The cricoarytenoid (CA) ligament (previously known as the posterior cricoarytenoid ligament) is a thick, fan-shaped ligament that originates from the superior rim of the posterior cricoid, just lateral to the

Cricoarytenoid Unit,
Fig. 1 Anatomy of the
cricoarytenoid ligament.
(**a**) Axial section through the
glottic larynx at the level of the
cricoarytenoid joint; *arrow
head* – true vocal fold; *arrow*
cricoarytenoid ligament.
(**b**) Paramedian sagittal
section showing the posterior
aspect of the cricoarytenoid
ligament (*arrow*). *T* thyroid
cartilage, *A* arytenoid
cartilage, *C* cricoid lamina,
G glottis, *TA* thyroarytenoid
muscle (Reprinted from
Reidenbach 1995)
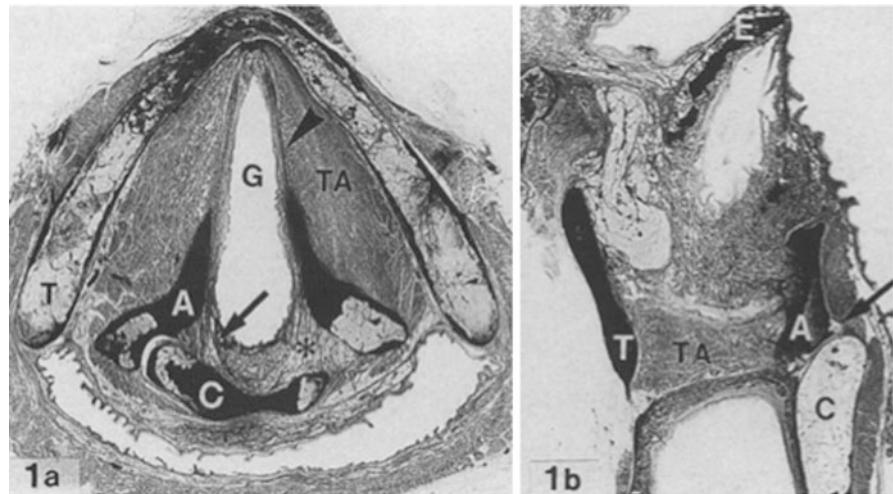
midline (Fig. 1) (Wang 1998; Paulsen et al. 2000). It consists of collagenous fibers interspersed with adipose tissue. Its dorsal component attaches to the posterior aspect of the arytenoid, and the medial component attaches to the medial aspect of the arytenoid (Wang 1998; Reidenbach 1995).

Deep and lateral to the CA ligament lies the posterior capsular ligament, which attaches to the posterior margins of the cricoid and arytenoid cartilage facets (Wang 1998). The anterior capsular ligament lies deep to the conus elasticus and attaches to the medial cricoid facet and the medial arytenoid facet (Wang 1998).

Joint Capsule

The CA joint is a diarthrodial joint – the articulating surfaces are surrounded by a wide and lax joint capsule lined with synovium. There are large, highly vascularized synovial folds projecting in to the joint cavity. The capsule wall is thin and is reinforced posteromedially by the cricoarytenoid ligament (Wang 1998; Paulsen et al. 2000).

Muscular Attachments

The PCA muscle originates from the posterior surface of cricoid lamina. It has two segments – lateral vertical fibers that insert onto the upper surface of the muscular process of the arytenoid and medial oblique fibers that insert on the posterior surface of the muscular process. It is the only muscle that actively opens the glottis, thus facilitating inspiration.

The thyroarytenoid (TA) muscle is also divided into two components. The external component extends from inner surface of thyroid cartilage and inserts on the lateral surface of the arytenoid. The internal or medial component (vocalis muscle) has the same origin but attaches to the lateral and inferior aspect of the vocal process of the arytenoid cartilage. Contraction of the TA shortens, slackens, and thickens the true vocal fold, contributing to phonation.

The LCA muscle originates from the upper and outer aspect of the anterolateral cricoid arch and inserts on to the anterior aspect of the muscular process and arytenoid body. It is the primary adductor of the true vocal folds, thus facilitating phonation and airway protection.

The interarytenoid (IA) muscle is located on the posterior surface of the arytenoids and has oblique and transverse components. The oblique fibers are more superficial and originate from the posterior aspect of one arytenoid and connect to the apex of the other. The transverse fibers arise from the posterolateral aspect of one arytenoid and insert in a similar location on the other. The IA muscle regulates medial compression of the arytenoid bodies, contributing to phonation and airway protection.

Biomechanics

The study of CA joint motion has been limited due to the joint's inaccessibility for direct study, the small amplitude of movements, and the limited spatial and

Cricoarytenoid Unit,
Fig. 2 Side (**a**), front (**b**), and top (**c**) views of 3D-rendered high-resolution CT images of the arytenoid and cricoid cartilages, showing the relative positions during phonation (*yellow*) and respiration (*blue*).
(**a**) Arytenoid cartilages "sliding" along the longitudinal cricoarytenoid joint axis (*red line*).
(**b**) "Rocking" of the arytenoid cartilages around the longitudinal cricoarytenoid joint axis (*red line*).
(**c**) "Rotation" of the arytenoid cartilages around an axis perpendicular to the longitudinal cricoarytenoid joint axis (*blue line*). MP_R muscular process, respiratory position, MP_P muscular process, phonatory position, VP_R vocal process, respiratory position, VP_P vocal process, phonatory position (Reprinted from Storck et al. 2010b)
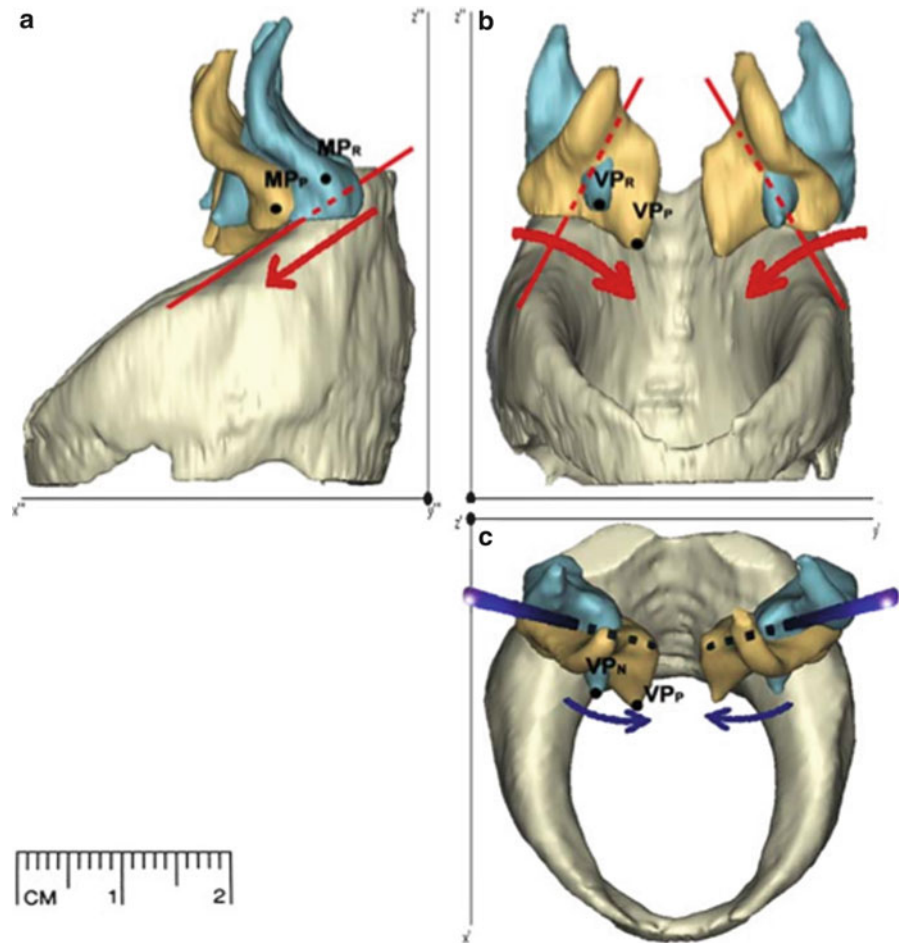
temporal resolution of current imaging modalities. Although many studies have attempted to characterize CA joint motion, no single description is well accepted. We do know that the joint's motion is a smooth, continuous, and complex process (Wang 1998; Storck et al. 2010a).

One of the most often quoted descriptions of CA joint motion is that of Sellars and Sellars (1983). They subclassified CA joint motion using three vector descriptors: (1) "rocking" – movement of the arytenoid around the longitudinal CA joint axis; (2) "sliding" for the movement of the arytenoid along the longitudinal CA joint axis; and (3) "rotating" – movement around an axis perpendicular to the CA

joint axis. Subsequent studies (Wang 1998; Storck et al. 2010a) support that movement does occur in these three vectors (Fig. 2).

Abduction and adduction of the vocal folds are not simple lateral and medial movements. During abduction, the vocal process moves predominantly laterally but also a small amount superiorly (Wang 1998). There is negligible anteroposterior motion. The arytenoid facet articulates with the posterosuperior surface of the cricoid facet (Wang 1998). During adduction, the vocal process moves predominantly medially but also inferiorly. The arytenoid facet articulates with the anteroinferior portion of the cricoid facet.

The various ligamentous structures of the larynx are also important in regulating arytenoid joint motion. The conus elasticus limits abduction and adduction along with preventing superior displacement of the vocal process during adduction, while the vocalis prevents posterior displacement of the vocal process (Wang 1998). The CA ligament seems to play an important role in maintaining CA joint position during abduction, with the posterior component acting as a stabilizer (Wang 1998). This strong ligament also prevents anterior displacement (Kasperbauer 1998; Reidenbach 1995). The posterior capsular ligament limits anterior and superior displacement of the vocal process during adduction. Both the anterior and posterior capsular ligaments limit lateral excursion of the body of the arytenoid during abduction (Wang 1998). These ligaments reinforce the otherwise lax and delicate joint capsule medially and posteriorly.

Cross-References

▶ Hoarseness and Pediatric Voice Disorders

References

Kasperbauer JL (1998) A biomechanical study of the human cricoarytenoid joint. Laryngoscope 108:1704–1711

Maue WM, Dickson DR (1971) Cartilages and ligaments of the adult human larynx. Arch Otolaryngol 94:432–439

Paulsen FP, Jungmann K, Tillmann BN (2000) The cricoarytenoid joint capsule and its relevance to endotracheal intubation. Anest Anal 90:180–184

Reidenbach MM (1995) The cricoarytenoid ligament: its morphology and possible implications for vocal cord movements. Surg Radiol Anat 17:307–310

Sadler TW (2010) Langman's medical embryology, 11th edn. Lippincott, Philadelphia

Sellars I, Sellars S (1983) Cricoarytenoid joint structure and function. J Laryngol Otol 97:1027–1034

Storck C, Juergens P, Fischer C et al (2010a) Biomechanics of the cricoarytenoid joint: three-dimensional imaging and vector analysis. J Voice 25(4):406–410

Storck C, Juergens P, Fischer C et al (2010b) Three-dimensional imaging of the larynx for pre-operative planning of laryngeal framework surgery. Eur Arch Otorhinolaryngol 267:557–563

Wang RC (1998) Three-dimensional analysis of cricoarytenoid joint motion. Laryngoscope Suppl 86:1–17

Cricothyroidotomy

Carrie M. Bush[1] and Melanie W. Seybt[2]
[1]Department of Otolaryngology, Medical College of Georgia, Augusta, GA, USA
[2]Department of Otolaryngology, Medical College of Georgia, Georgia Health Sciences University, Augusta, GA, USA

Definition

An incision made through the skin and cricothyroid membrane to establish a patent airway.

Cross-References

▶ Tracheostomy, Complications

Cross-Facial Nerve Grafting (CFNG), Procedure

Ryan Collar and Kofi Derek O. Boahene
Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Synonyms

7-7 transfer; Facial paralysis; Nerve grafting

Definition

Cross-facial nerve grafting is a means of coupling the paralyzed side of the face with the unparalyzed side by recruiting axons through a grafted nerve conduit. Axons growing from the donor unparalyzed side through a long nerve graft to the contralateral side reinnervated the weak or paralyzed facial muscles.

Principle

Successful CFNG allows for coordinated and volitional mimetic movement through rerouting facial

nerve axons from the unaffected side to the paralyzed side through a donor nerve conduit.

Indication

CFNG is used primarily as the *first stage prior to free muscle transfer*, or in *conjunction with other nerve transfer procedures such as hypoglossal or masseter nerve transfer* (Chan and Byrne 2011). It can also be used to upgrade the innervation into a partially innervated facial muscle.

CFNG plus free muscle transfer is indicated for patients with *complete irreversible paralysis* whose electromyography (EMG) demonstrates silent motor endplates not amenable to reinnervation (O'Brien et al. 1990). The advantages and disadvantages of this surgical approach are often deliberated against those of the temporalis tendon transfer (Byrne et al. 2007; Boahene et al. 2011) for this patient population.

CFNG with hypoglossal transfer is employed for patients *with complete reversible* paralysis, whose motor endplates are likely to respond to new axonal ingrowth (Terzis and Tzafetta 2009). In the author's practice, CFNG for *complete reversible paralysis* is most commonly used for patients with an unfavorable outcome following Bell's palsy, or those status-post resection of cerebellopontine angle (CPA) tumors where the nerve is believed to be intact. The timing of nerve transfer procedures is controversial for this population due to competing interests: allowing sufficient time for all possible facial nerve recovery, and surgically delivering axons to paralyzed muscles before endplate atrophy, i.e., the paralysis becomes irreversible. Key factors predictive of recovery include the time between insult and initial recovery, and the rate of recovery thereafter (Pietersen 2002; Rivas et al. 2011). Our institution may offer CFNG plus hypoglossal transfer to these patients 6 months after facial nerve injury if they remain House-Brackman VI and EMG shows no volitional potentials. In this situation, the CFNG is placed in conjunction with hypoglossal transfer wherein the facial nerve is anastamosed end-to-side with the hypoglossal nerve (with intentional hypoglossal axonal injury). The hypoglossal transfer provides axonal input to the denervated motor end plates, and confers excellent facial tone at rest. In many patients, hypoglossal-facial crossover also yields some level of commissural excursion that is activated by tongue movement. In a second procedure, the CFNG is used to "supercharge" those branches of the facial nerve responsible for excursion, allowing for spontaneous volitional smile (Terzis and Tzafetta 2009).

Contraindication

Bilateral facial paralysis, systemic peripheral neuropathy.

Advantages/Disadvantages

The major advantage of CFNG procedures is the potential for true spontaneous volitional movement. The major disadvantage is the small number of available axons and the need to sacrifice a functioning facial nerve branch on the non-paralyzed side, although this maneuver may sometimes enhance symmetry. The number of axons present in the donor facial nerve has been demonstrated to ultimately predict the outcome on the paralyzed side, with greater than 900 axons being a favorable count (Terzis et al. 2009). This requires a robust nerve proximal to the smallest terminal branches, considering that the entire facial nerve contains approximately 7,000 axons (Buskirk 1945).

References

Boahene KD, Farrag T, Ishii L, Byrne P (2011) Minimally invasive temporalis tendon transposition. Arch Facial Plast Surg 13:8–13

Buskirk CV (1945) The seventh nerve complex. J Comp Neurol 82:303–326

Byrne PJ, Kim M, Boahene K, Millar J, Moe K (2007) Temporalis tendon transfer as part of a comprehensive approach to facial reanimation. Arch Facial Plast Surg 9:234–241

Chan JY, Byrne PJ (2011) Management of facial paralysis in the 21st century. Facial Plast Surg 27(4):346–357, Epub 2011 Jul 26

O'Brien BM, Pederson WC, Khazanchi RK, Morrison WA, MacLeod AM, Kumar V (1990) Results of management of facial palsy with microvascular free-muscle transfer. Plast Reconstr Surg 86:12–22

Pietersen E (2002) Bell's Palsy: the spontaneous course of 2,500 peripheral facial nerve palsies of different etiologies. Acta Otolaryngol 549(Suppl):4–30

Rivas A, Boahene KD, Bravo HC, Tan M, Tamargo RJ, Francis HW (2011) A model for early prediction of facial nerve recovery after vestibular schwannoma surgery. Otol Neurotol 32:826–833

Terzis JK, Tzafetta K (2009) The babysitter pocedure: minihypoglossal to facial nerve transfer and cross facial nerve grafting. Plast Reconstr Surg 123:865–876

Terzis JK, Wang W, Zhao Y (2009) Effect of axonal load on the functional and aesthetic outcomes of the cross-facial nerve graft procedure for facial reanimation. Plast Reconstr Surg 124:1499–1512

Cross-Lip Flap

Eric J. Dobratz
Department of Otolaryngology, Eastern Virginia
Medical School, Norfolk, VA, USA

Synonyms

Lip-switch flap

Definition

Composite transfer of skin, muscle, and mucosa based on a pedicle containing the inferior or superior labial vessels. This permits reconstruction of the lip with similar tissue from the opposing lip. Cross-lip flaps are often indicated for defects involving one-third to two-thirds of the lip.

Cross-References

▶ Abbe Flap
▶ Estlander Flap

CSF Leak

▶ Cerebrospinal Fluid Rhinorrhea, Evaluation and Management
▶ Sinus Surgery, Complications

C-Train

Angela E. Downes and A. Samy Youssef
Department of Neurosurgery, University of South
Florida, Tampa, FL, USA

Definition

Facial EMG pattern characterized by continuous irregular activity that is composed of overlapping components ranging in amplitude from 20 to $\geq$5,000 μV.

Cross-References

▶ Intraoperative Neurophysiologic Monitoring of the Facial Nerve (VII)

Cutaneous Apudoma

▶ Merkel Cell Cancer of Head and Neck

Cutaneous Flap

Lynn L. Chiu-Collins[1], Amit D. Bhrany[2] and
Craig S. Murakami[3]
[1]Facial Plastic Surgery, San Francisco Plastic Surgery
& Laser Center, San Francisco, CA, USA
[2]Department of Otolaryngology-Head and Neck
Surgery, Facial Plastic and Reconstructive Surgery,
University of Washington, Seattle, WA, USA
[3]Department of Otolaryngology-Head and Neck
Surgery, Virginia Mason Medical Center, University
of Washington, Seattle, WA, USA

Definition

Cutaneous flap: Flap consisting of skin alone.

Cross-References

▶ Advancement Flaps

Cutaneous Lymphatic Drainage Patterns

▶ Lymphatic Spread from Cutaneous Neoplasms of
Head and Neck

Cutaneous Neuroendocrine Tumor

▶ Merkel Cell Cancer of Head and Neck

Cystic Hygroma

▶ Imaging for Parapharyngeal Space Tumors,
Lymphatic Malformation
▶ Vascular Anomalies of Head and Neck

Cystic Teratomas

▶ Heterotopias, Teratoma, and Choristoma