Craniofacial Syndromes with Airway Anomalies: An Overview

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Abnormal craniofacial development can cause airway anomalies in the neonate at multiple levels (Table 1). While evaluating a neonate with a craniofacial syndrome, it is imperative that airway concerns are taken into account. This consideration is important for treating any immediate and evident airway problems and for identifying any nascent airway pathology to avert avoidable airway emergencies. In one study, 65 % of patients with craniofacial abnormalities required some airway management ranging from positioning to tracheotomy, and 80 % of interventions occurred within the first month of life [29]. This chapter provides an introduction to several craniofacial syndromes commonly associated with airway pathologies (Table 2). These syndromes will be discussed in detail in the subsequent chapters.

Nasal Cavity and Midface

Nasal obstruction can cause respiratory distress immediately after birth in the neonate who is an obligate nasal breather. It has been suggested that this phenomenon is due to the prominent soft palate and relatively higher epiglottis in the neonate with a resultant smaller oropharyngeal airway. The neonate can have cyclical breathing in which he/she initially has nasal obstruction, develops cyanosis and hypercapnia, and then begins to cry and ventilate orally. When the cyanosis subsides, the neonate calms and attempts to breathe nasally, thus starting the cycle over again. These cyanotic episodes and ineffective ventilation can result in death if not discovered quickly. Neonates gradually outgrow this sole reliance on nasal breathing by about 4–6 months of age. Obstruction at the nasal level is commonly due to nasal pyriform aperture stenosis, choanal stenosis or atresia, and midface hypoplasia.

Congenital Nasal Pyriform Aperture Stenosis

Etiology. Congenital nasal pyriform aperture stenosis (CNPAS), first described in 1989, is believed to occur when bony overgrowth of the nasal processes of the maxilla narrows or obstructs the nasal cavities [12]. CNPAS can occur in isolation, but there are frequently additional findings suggestive of a microform holoprosencephaly (HPE). The full spectrum of HPE has been linked to many chromosomal abnormalities.

Epidemiology. The true incidence of CNPAS is unknown but occurs less commonly than choanal stenosis or atresia.

Pathogenesis. HPE, the abnormal division of the forebrain, varies widely in severity. A single central maxillary incisor, present in approximately 60 % of CNPAS, is considered the least severe form of HPE [5, 43]. Additional findings linked with CNPAS can include abnormal development of the brain and the pituitary gland leading to endocrine dysfunction.

Clinical presentation. CNPAS causes symptoms of nasal obstruction, which develop shortly after birth. In mild cases, the patient may present with "noisy breathing," aggravated with feeding and agitation. In severe cases, cyclical breathing may be present with cyanotic episodes.

Diagnosis. The inability to pass a suction catheter larger than 5 Fr through the anterior nares is suspicious for CNPAS and should be confirmed by an otolaryngologist with nasal endoscopy. CT imaging can help evaluate for other contemporaneous midline defects such as a single central maxillary incisor (Fig. 1). A pyriform aperture width, as viewed on CT axial imaging, of less than 11 mm in a term infant is considered to be diagnostic for CNPAS [7]. Careful evaluation is

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necessary to distinguish CNPAS from choanal atresia, which can present in a similar fashion.

Management. Neonates with CNPAS often require airway monitoring in the intensive care unit. Conservative management, including support with special feeding techniques and monitoring until the airway grows, is indicated in mildly symptomatic neonates. Nasal decongestants, humidification, and nasal continuous positive airway pressure (CPAP) may be sufficient. Surgery to widen the nasal pyriform aperture, accessed through a sublabial incision, is often required in the more severely afflicted neonates. Some feel that CNPAS is associated with an overall narrowing of the width of bilateral nasal cavities. Thus, dilation of the nasal cavities with inferior turbinate outfracturing may be required with possible temporary nasal stent placement.

Table 1 Overview of sites of primary airway anomalies and associated craniofacial syndromes

Site of primary airway anomaly	Syndrome
Nasal Cavity and Midface	Congenital nasal pyriform aperture stenosis
	CHARGE syndrome
	Craniosynostosis syndromes (Crouzon, Apert, Pfeiffer)
Oromandibular	Stickler syndrome
	Treacher Collins syndrome
	Craniofacial microsomia
Laryngotracheal	Complete tracheal rings in Down syndrome (Trisomy 21)
	Tracheal cartilaginous sleeve in craniosynostosis syndromes

Table 2 Specific airway concerns with craniofacial syndromes

Craniofacial syndrome	Specific airway concerns
Congenital nasal pyriform aperture stenosis	Narrow pyriform aperture width
	Can have associated narrow nasal cavities
CHARGE syndrome	Unilateral choanal atresia
	Bilateral choanal atresia
	Laryngomalacia
	Pharyngolaryngeal hypotonia
Craniosynostosis syndromes	Midface hypoplasia—nasopharyngeal and oropharyngeal obstruction
	Obstructive sleep apnea
	Nasal cavity stenosis
	Choanal atresia
	Tracheal anomalies—tracheal cartilaginous sleeve
Stickler syndrome	Macroglossia
	Micrognathia
Treacher Collins syndrome	Severe micrognathia
	Unilateral choanal atresia
	Bilateral choanal atresia
	Obstructive sleep apnea
Craniofacial microsomia	Mandibular hypoplasia
Down syndrome	Complete tracheal rings resulting in tracheal stenosis
	Subglottic stenosis
	Laryngomalacia
	Tracheobronchomalacia
	Macroglossia
	Midfacial hypoplasia
	Obstructive sleep apnea
	Pharyngeal hypotonia

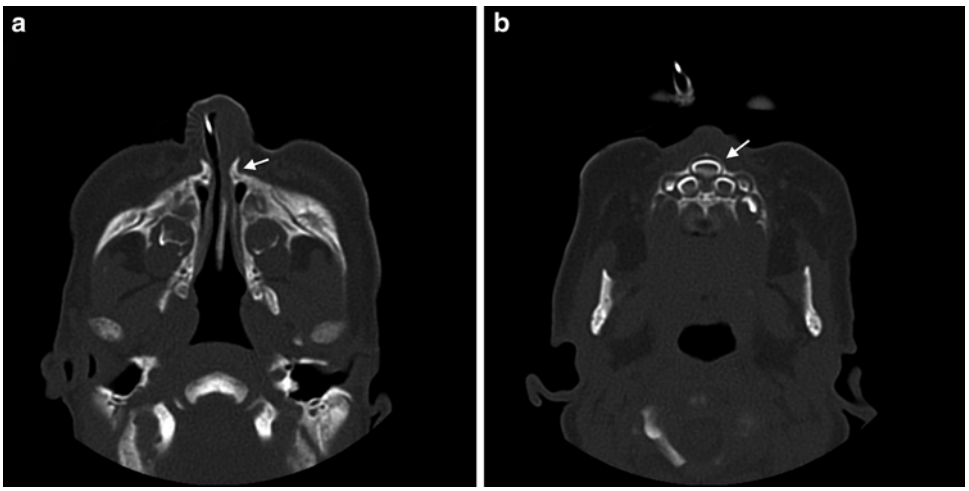

Fig. 1 Congenital nasal pyriform aperture stenosis (CNPAS). (**a**) Axial computed tomographic (CT) image showing a narrow 4 mm pyriform aperture width. (**b**) Concurrent single central maxillary incisor

Multidisciplinary considerations. A brain MRI and blood tests for pituitary hormone levels should be considered to assess for pituitary dysfunction. The need for consultation of specialists, such as endocrinology and neurology, depends on the constellation of HPE-associated findings. Developmental delay of variable severity may occur in children with HPE and patients should be followed long-term.

CHARGE Syndrome

Etiology. The CHARGE acronym stands for *C*oloboma of the eye, *H*eart defects, *A*tresia of the choanae, *R*estricted growth, *G*enital anomalies, and *E*ar anomalies. CHARGE syndrome, also known as Hall Hittner syndrome, was first described in 1979. CHARGE is associated with mutations in the *CHD7* gene, but approximately one-third of cases have no identified mutation [24]. Most cases arise *de novo* and represent a single occurrence in a family, but an autosomal dominant inheritance pattern is seen in familial CHARGE syndrome.

Epidemiology. Approximately between 1:8,500 and 1:12,000 [14, 24].

Pathogenesis. CHD7 gene mutations affect the protein involved in chromatin remodeling, which disrupts the regulation of gene expression [13].

Clinical presentation. Choanal stenosis or atresia can cause life-threatening respiratory distress in neonates (Fig. 2). Unilateral or bilateral choanal atresia is present in 50–60 % of patients [24]. Laryngomalacia is a major cause of upper airway obstruction and can be present in 8–37 % of patients with CHARGE [27]. Pharyngolaryngeal hypotonia can result in additional upper airway obstruction. Patients may also have cranial neuropathies involving cranial nerves V, VII, VIII, IX, and X [27]. Cardiovascular instability and feeding issues such as dysphagia and aspiration can present additional significant challenges in the neonatal period. As many as 80 % of children with CHARGE may have gastroesophageal reflux disease [27], which can further exacerbate airway obstruction.

Diagnosis. Mutations in the *CHD7* gene are identified by genetic testing in approximately 67 % of individuals with a phenotype consistent with CHARGE [38]. Four major defining characteristics in CHARGE are ocular coloboma, choanal stenosis or atresia, cranial nerve dysfunction (varies from dysphagia, sensorineural hearing loss, hyposmia, or facial palsy), and anomalies of the middle or inner ear. The minor characteristics that are less specific but commonly seen in CHARGE are cardiovascular anomalies, growth delays, developmental delay and genital hypoplasia, which are more apparent in males. A clinical diagnosis can be made if an individual has four major characteristics or three major with one minor characteristic [10].

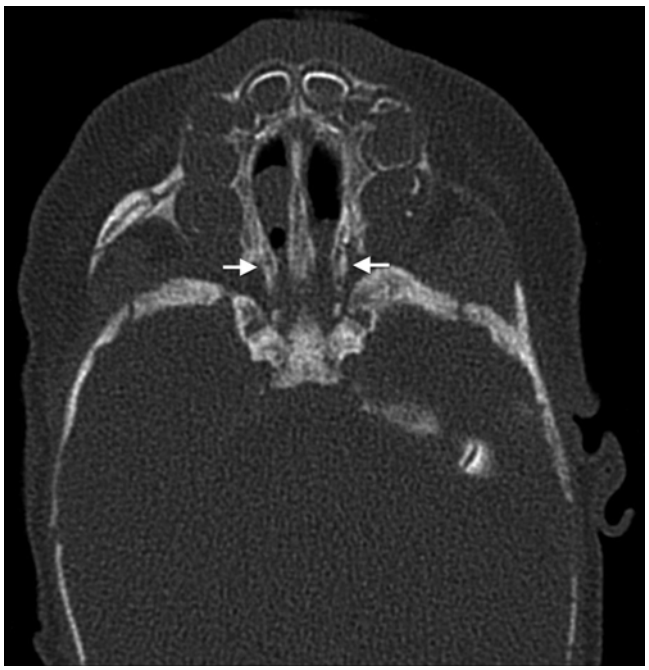

Fig. 2 Bilateral mixed membranous and bony choanal atresia in a patient with CHARGE syndrome

Management. Airway and cardiac evaluations are required immediately. Airway management may require intubation, transnasal or transpalatal surgical repair of choanal stenosis or atresia, or tracheotomy. A tracheotomy may need to be performed in as many as 10–60 % of patients [27]. A supraglottoplasty for management of severe laryngomalacia should be performed only after a thorough airway evaluation as children with CHARGE syndrome have poorer outcomes likely due to concurrent airway pathology. Feeding difficulties can be a major source of morbidity requiring speech and swallow therapy.

Multidisciplinary considerations. Specialist consultations of cardiology, otolaryngology, ophthalmology, audiology, and speech pathology services are usually needed. Individuals with CHARGE usually have feeding issues and variable learning disabilities worsened by dual visual and hearing impairment. Serial audiologic and ophthalmologic exams are recommended. Hypogonadism may disrupt progression into puberty.

Craniosynostosis Syndromes

Etiology. Mutations in the fibroblast growth factor receptor (*FGFR*) genes account for many craniosynostosis syndromes including Crouzon, Apert and Pfeiffer syndromes. *FGFR* genes encode different fibroblast growth factor receptors that

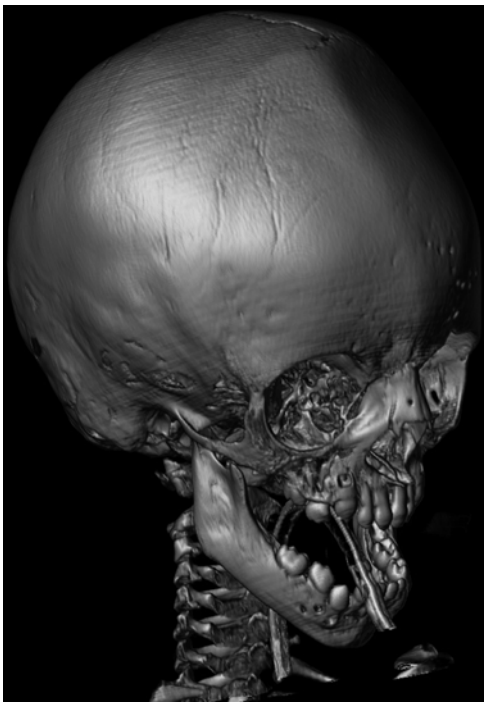

Fig. 3 Patient with Crouzon syndrome with premature fusion of the cranial sutures. Three-dimensional reconstructed image from CT images shows ridge in the midline of the frontal bone which results from early fusion of the metopic suture

regulate cell growth and embryonic development. The *FGFR* mutations are transmitted in an autosomal dominant inheritance pattern [36].

Epidemiology. Crouzon syndrome affects 16 per million newborns [15]. Apert syndrome affects between 1:65,000 and 1:88,000 newborns [3], and Pfeiffer syndrome affects 1:100,000 newborns [45].

Pathogenesis. Mutations in the *FGFR* protein affect the development of bone cells and cause premature fusion of the sutures of the skull (Fig. 3). Craniosynostosis can cause airway obstruction from midface hypoplasia or tracheal abnormalities.

Clinical presentation. An abnormally shaped skull is apparent at birth in a neonate with craniosynostosis. The degree of airway compromise secondary to midface hypoplasia is variable, and almost half of children with Crouzon, Apert and Pfeiffer syndromes develop obstructive sleep apnea [6]. Nasal cavity stenosis or choanal atresia may also be present in this population. Additionally, neonates with Crouzon, Apert and Pfeiffer syndromes may have stridor and respiratory distress secondary to tracheal abnormalities, which are discussed later in this chapter. In one large retrospective review, children with craniofacial synostosis syndromes had the highest rate of tracheotomy at 48 % [39].

Diagnosis. Genetic testing is available, but a clinical diagnosis is frequently possible for most of the *FGFR*-related craniosynostosis syndromes based on facial features, distinguishing anomalies of the hands and feet, and the cranial sutures affected. These three craniosynostosis syndromes share common features of maxillary hypoplasia, shallow orbits causing proptosis, wide set eyes and a beaked nose. Apert syndrome is notable for syndactyly of the fingers and toes whereas normal hands and feet are typical for Crouzon syndrome [4, 16, 35]. Individuals with Pfeiffer syndrome tend to have partial syndactyly and medially displaced, broad and short thumbs and big toes [30, 45].

Management. Expansion of the cranial vault and midface advancement require staged surgeries. Tracheotomy may be needed for airway management especially when multiple surgeries are often needed to address the craniofacial abnormalities. Midface advancement can help alleviate obstruction of the nasopharyngeal and oropharyngeal airway. Choanal atresia repair or nasal splints may be needed to address nasal obstruction. Adenotonsillectomy may partially alleviate OSA if hypertrophy of these structures develops later in childhood.

Multidisciplinary considerations. Long-term care should be managed by a craniofacial team involving neurosurgery, plastic surgery, otolaryngology, ophthalmology, genetics, and developmental pediatrics. Intellectual disability affects individuals in certain types of *FGFR*-related craniosynostosis. Cognitive function is normal in Crouzon syndrome, but variable intellectual disability is common in Apert and Pfeiffer syndromes [23]. Individuals with craniosynostosis may require lifelong monitoring for hydrocephalus.

Oromandibular

An underdeveloped mandible can cause upper airway obstruction due to the resulting posterior or downward displacement of the tongue.

Stickler Syndrome

Etiology. Stickler syndrome is a group of connective tissue disorders characterized by distinctive orofacial features, hearing loss, premature degenerative joint disease, progressive myopia, and retinal detachment [41]. The subtypes of Stickler syndrome (types I through V) are associated with mutations in the genes *COL2A1*, *COL11A1*, *COL11A2*, *COL9A1*, and *COL9A2*, respectively, with types I through III being most common [41]. The inheritance pattern could be either autosomal dominant or recessive depending on the subtype.

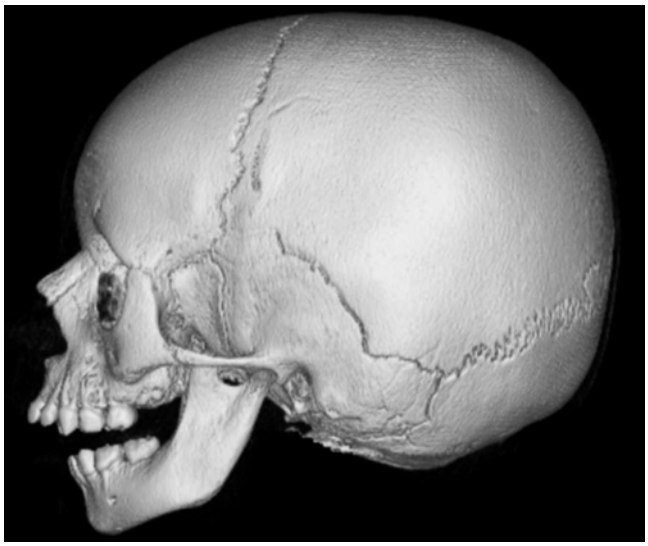

Fig. 4 Patient with Pierre Robin sequence. Three-dimensional reconstructed image from CT images shows retrognathia

Epidemiology. The estimated incidence of Stickler syndrome is between 1:7,500 and 1:9,000 [35]. Approximately 35 % of newborns with Pierre Robin sequence develop features of Stickler syndrome.

Pathogenesis. Mutations in any of these genes affect the production of collagen types II, IX, and XI. Connective tissues containing these collagen fibers do not develop normally.

Clinical presentation. Common orofacial findings include the Pierre Robin sequence of macroglossia, cleft palate, and micrognathia (Fig. 4). Some neonates may present with airway distress requiring intubation in severe cases of micrognathia. Cleft palate occurs in about 40 % and causes feeding difficulties [37]. Additional facial characteristics, such as a hypoplastic flattened midface with a depressed nasal bridge, are more prominent in younger children than in adults [40]. Hearing loss affects approximately 63 % of individuals and is predominantly sensorineural (67.8 %) from abnormal collagen in the inner ear [1]. A mixed or conductive hearing loss is common in individuals with a cleft palate from chronic Eustachian tube dysfunction. Common eye problems include myopia and vitreous abnormalities. The different subtypes of Stickler syndrome have specific associated features for each genotype, but phenotypic variability is common even within families with the same genotype.

Diagnosis. Genetic testing is available, but the diagnosis is considered when this combination of orofacial, ocular, auditory, and musculoskeletal manifestations are present.

Management. The feeding and airway problems present in the neonatal period often require care coordination to determine the timing of cleft palate repair and airway management. Airway management is aimed at relieving base of tongue obstruction at the level of the oropharynx. Non-operative management includes prone positioning, oral airway placement, nasopharyngeal stenting, and short-term intubation. Operative management includes tongue-lip adhesion and mandibular distraction osteogenesis [34]. Tracheotomy is reserved for severe airway obstruction.

Multidisciplinary considerations. Long-term care should be coordinated by a craniofacial team including plastic surgery, oromaxillofacial surgery, otolaryngology, and genetics. Children with Stickler syndrome should have an eye exam performed annually by a vitreoretinal specialist and a hearing test biannually until age five then annually thereafter [35]. Screening for mitral valve prolapse should be performed during routine physicals. Contact sports should be avoided due to the underlying risk of retinal detachment.

Treacher Collins Syndrome

Etiology. Abnormal development of the facial bones and soft tissues is a hallmark of Treacher Collins syndrome. Three genes have been identified. Mutations in the *TCOF1* gene account for more than 80 % of cases, often arise *de novo* and have an autosomal dominant inheritance pattern [22]. Mutations in the *POLR1C* or *POLR1D* genes account for about 8 % of cases [22].

Epidemiology. Approximately between 1:10,000 and 1:50,000 [42].

Pathogenesis. Mutations in these genes reduce the production of ribosomal RNA, which is essential in the assembly of proteins that regulate cell function and cell death. Abnormal cellular death disrupts the development of the facial bones and soft tissues bilaterally. It is not known why the abnormal development is limited to structures originating from the nasal placode and the first and second branchial arches [32].

Clinical presentation. There is significant phenotypic variability in Treacher Collins syndrome. Symmetrical characteristic features are apparent at birth. The underdevelopment of the zygoma causes downward slanting eyes, a prominent appearing nose, and a convex-appearing facial profile bilaterally. Severe mandibular hypoplasia can cause airway distress in the neonate. Choanal atresia, either unilateral or bilateral, can be present and exacerbate neonatal respiratory distress. More than half of children with Treacher Collins syndrome develop obstructive sleep apnea [31]. Microtia, notching of the lower eyelids, and the paucity of medial lower eyelashes

are also classic findings. Conductive hearing loss is common from anomalies of the outer ear (microtia and aural atresia) and middle ear (ossicular anomalies and hypoplasia of the middle ear). The inner ear is rarely affected [22].

Diagnosis. Distinguishing clinical features and radiographic findings (malar hypoplasia, hypoplasia of the zygoma on CT scan or X-rays) are sufficient for diagnosis. Genetic testing is available.

Management. An airway evaluation is often required to assess for obstruction secondary to micrognathia. Airway management is aimed at relieving base of tongue obstruction at the level of the oropharynx. Non-operative management includes prone positioning, oral airway placement, nasopharyngeal stenting, and short-term intubation. Operative management includes tongue-lip adhesion and mandibular distraction osteogenesis [34]. Tracheotomy is reserved for severe airway obstruction and provides a secure airway for the multiple surgeries that are usually needed to address the craniofacial abnormalities. Bilateral choanal atresia may require early neonatal surgical repair, whereas surgical repair of unilateral choanal atresia usually can be delayed. Swallowing difficulties present in the neonatal period and may require speech and swallow therapy.

Multidisciplinary considerations. Long-term care should be coordinated by a craniofacial team including plastic surgery, oromaxillofacial surgery, orthodontics, and otolaryngology. Ophthalmologic care and hearing amplification are often necessary. Intellect is usually normal although children are at risk for developmental delay from hearing loss and visual problems. Dental anomalies and malocclusion are addressed at an older age.

Craniofacial Microsomia

Etiology. Craniofacial microsomia is characterized by the abnormal development of structures derived from the embryologic first and second branchial arches and results in maxillary and mandibular hypoplasia. The term craniofacial microsomia is used broadly to encompass a spectrum of syndromes with asymmetric facial development including hemifacial microsomia and Goldenhar syndrome. No frequently occurring genetic mutation has been identified. One suspected cause may be a disruption of the blood supply to the first and second branchial arches early in pregnancy. Several environmental risk factors including maternal diabetes, multiple gestation, exposure to vasoactive drugs, and the use of assisted reproductive technology have been associated with craniofacial microsomia [9].

Epidemiology. The incidence for craniofacial microsomia is estimated to be between 1:3,000 and 1:5,000, and it is the second most common facial birth defect after cleft lip and palate [9]. The reported male-to-female ratio is approximately between 1.2:1 and 1.6:1 [26, 33].

Pathogenesis. The asymmetric facial anomalies in craniofacial microsomia are due to the disruption of the embryologic development of the nerves, muscles, blood vessels, cartilages, and bones derived from the first and second branchial arches.

Clinical presentation. Craniofacial microsomia commonly affects only one side of the face, but approximately 10–15 % have bilateral involvement to varying degrees causing facial asymmetry [26]. The ratio of right-to-left sided involvement is 3:2 [19]. One classification system, *OMENS-Plus*, is used to rate the severity of *O*rbital distortion, *M*andibular hypoplasia, *E*ar anomaly, *N*erve involvement, *S*oft tissue deficiency, and extra-craniofacial anomalies ("*Plus*") [21, 44]. Mandibular hypoplasia is the most apparent feature and can cause respiratory distress (Fig. 5). The common ear anomalies include preauricular skin tags, microtia, anotia, or external auditory canal atresia. Facial nerve palsy is the most frequently observed nerve anomaly. Soft tissue deficiencies of the face and macrostomia can occur. Cleft lip and/or palate affect approximately 25 % of individuals [26]. Additional craniofacial abnormalities and extra-craniofacial abnormalities, such as vertebral, renal, limb, cardiac, and central nervous system deformities, have been associated with craniofacial microsomia [19].

Diagnosis. The distinctive facial findings characteristic for craniofacial microsomia help distinguish it from other craniofacial syndromes. Facial asymmetry is one key component of craniofacial microsomia that separates it from the symmetrical anomalies seen in Treacher Collins syndrome.

Management. In severe cases of mandibular hypoplasia, the initial neonatal airway management is aimed at relieving base of tongue obstruction at the level of the oropharynx. Non-operative management includes prone positioning, oral airway placement, nasopharyngeal stenting, and short-term intubation. Operative management includes tongue-lip adhesion and mandibular distraction osteogenesis. Tracheotomy is reserved for severe airway obstruction and provides a secure airway for the multiple surgeries that are usually needed to address the craniofacial abnormalities.

Multidisciplinary considerations. Long-term care should be coordinated by a craniofacial team including plastic surgery, maxillofacial surgery, orthodontics, and otolaryngology.

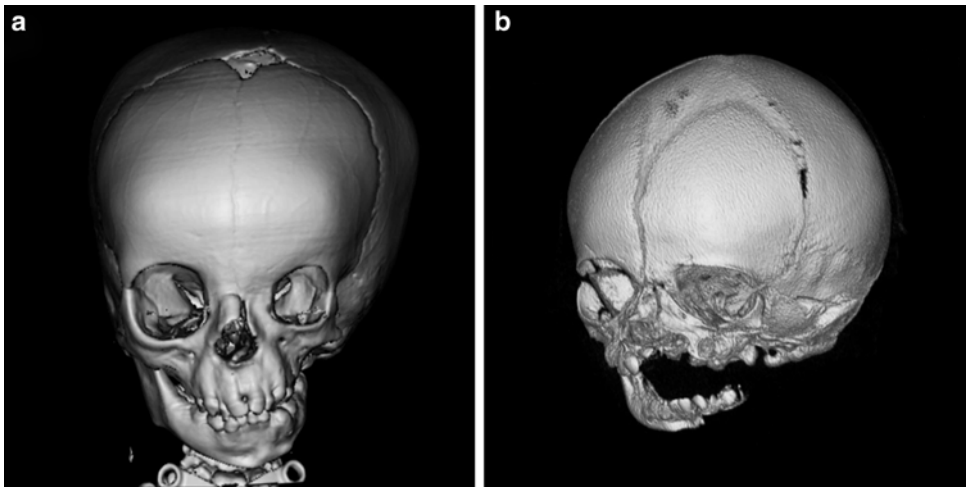

Fig. 5 Craniofacial microsomia. (**a**) Three-dimensional reconstructed image from CT images shows left sided maxillary and mandibular hypoplasia resulting in facial asymmetry and airway narrowing-note the tracheotomy tube flange in the inferior aspect of the image. (**b**) Three-dimensional reconstructed image from CT images from another patient shows left sided mandibular body, ramus, and condylar agenesis

Feeding difficulties may require additional support. Hearing amplification may be necessary if the ear anomalies cause hearing loss, which can be conductive, sensorineural, or mixed. Intellect is usually normal although children are at risk for developmental delay from hearing loss. Further surgeries to improve facial asymmetry, ear anomalies, and jaw malocclusion are usually performed at an older age.

Laryngotracheal

Anomalies of the laryngotracheal complex can complicate management of the airway when using standard options such as intubation or tracheotomy. A select few anomalies are discussed below.

Complete Tracheal Rings in Down Syndrome (Trisomy 21)

Etiology. Complete tracheal rings causing tracheal stenosis have been associated with Down syndrome [8, 11, 47]. No specific factor has been identified that causes the formation of complete tracheal rings. Down syndrome occurs when an individual has three copies of chromosome 21 instead of the normal two copies. This occurs most commonly from a random nondisjunction error in cell division that results in an egg or sperm with an extra chromosome. Less commonly, Down syndrome can occur from translocation (inheriting an extra copy of chromosome 21 that is attached to another chromosome) or from mosaicism (an error of cell division that occurs during embryonic development resulting in only some cells carrying three copies) [18].

Epidemiology. Down syndrome is the most common chromosomal abnormality and affects approximately 1 in 600–800 newborns [8]. The incidence of complete tracheal rings in children with Down syndrome is unknown.

Pathogenesis. It is unclear how the extra copy of chromosome 21 results in intellectual disability and the diverse effects on multiple organ systems. Laryngotracheal airway anomalies in Down syndrome include complete tracheal rings, subglottic stenosis, laryngomalacia, tracheal bronchus, and tracheobronchomalacia [8, 46]. Tracheal stenosis from complete tracheal rings can involve either a short-segment or a long-segment of the tracheobronchial tree (Fig. 6).

Clinical presentation. Down syndrome is associated with a characteristic facies including low-set ears, up-slanting palpebral fissures, a flat nasal bridge, and a tendency to protrude the enlarged tongue. Discussion of the numerous medical issues commonly associated with Down syndrome is beyond the scope of this book. Respiratory difficulty in a newborn should raise the concern for tracheal stenosis, particularly when there is a history of a difficult intubation or persistent airway instability after intubation. Respiratory symptoms can range from mild stridor with exertion to the complete inability to ventilate necessitating the use of extra-corporeal membrane oxygenation (ECMO).

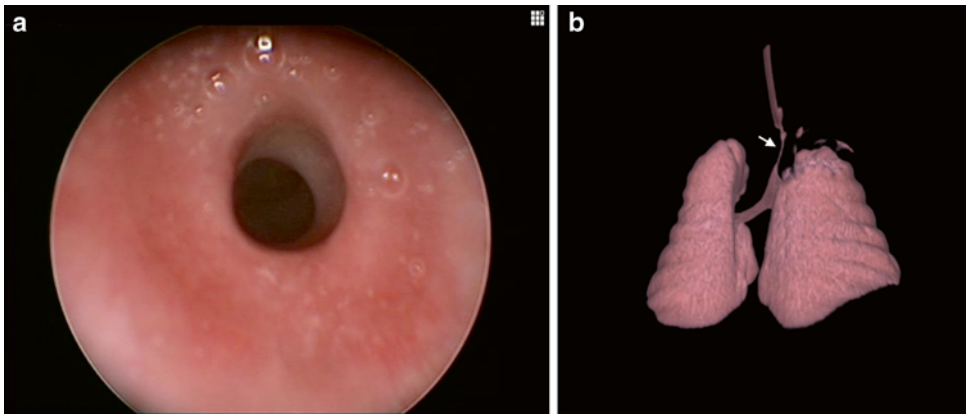

Fig. 6 Complete tracheal rings and tracheal stenosis. (**a**) Endoscopic view of airway during bronchoscopy shows complete tracheal rings with the absence of trachealis muscle posteriorly and a narrowed tracheal lumen. (**b**) Three-dimensional image of trachea and lungs reconstructed from CT images from a patient with long segment tracheal stenosis. Note the segment of the distal trachea marked with the arrow where the airway narrows to 1 mm

Diagnosis. Down syndrome can usually be diagnosed based on clinical findings, and chromosomal analysis is available for uncertain cases. Prenatal testing for Down syndrome is widely available. If tracheal stenosis is suspected, a tracheobronchoscopy is essential to evaluate the airway for complete tracheal rings or other airway anomalies. Tracheobronchoscopy permits characterization of the type, location, length, and severity of stenosis under dynamic conditions. Additionally, CT or MRI imaging can provide helpful information about the airway and evaluate for other cardiovascular anomalies [2].

Management. Respiratory distress secondary to tracheal stenosis can range from mild to life threatening. In one institution's experience, the overall mortality rate was 21 % for all children with tracheal stenosis in the study period [2]. Observation with medical management may be sufficient in mild cases, and symptoms will improve as the affected airway grows over time. In severe cases, intubation or tracheotomy may help provide temporary airway stability. When surgical repair is necessary, a partial tracheal resection with end-to-end anastomosis is preferred for short-segment stenosis; whereas, slide tracheoplasty is preferred for long-segment stenosis.

Multidisciplinary considerations. Otolaryngology should be consulted for a complete airway evaluation in symptomatic children with Down syndrome because airway compromise may be multifactorial. Obstructive sleep apnea later in childhood is commonly multifactorial due to macroglossia and midface hypoplasia in addition to adenotonsillar hypertrophy. Cardiothoracic surgery should be consulted in cases that may require intraoperative cardiopulmonary bypass. Long-term, children with Down syndrome require care coordination to monitor and support special needs including developmental and intellectual delay, hearing loss, immune compromise, endocrine dysfunction, and monitoring for leukemia.

Tracheal Cartilaginous Sleeve in Craniosynostosis Syndromes

Etiology. Tracheal cartilaginous sleeve (TCS), a rare airway malformation in which the normally discrete tracheal rings are replaced by a continuous cartilaginous segment, has been associated with multiple craniosynostosis syndromes but most commonly in Crouzon, Pfeiffer and Apert syndromes [25]. Please refer to the earlier section for an overview of mutations in the fibroblast growth factor receptor (*FGFR*) gene in these craniosynostosis syndromes.

Epidemiology. The incidence of TCS in *FGFR*-related craniosynostosis syndromes is unknown but is rare.

Pathogenesis. Mutations in the *FGFR* protein affect the development of bone cells and cause premature fusion of the sutures of the skull. The premature fusion of preformed cartilaginous structures is the suspected cause of the additional anatomic abnormalities in craniosynostosis [28]. In TCS, the continuous cartilaginous segment is formed by the vertical fusion of either C- or O-shaped cartilaginous tracheal rings. TCS can affect a few tracheal rings in length, involve the entire trachea or even extend into the bronchial airways. The diagnosis of TCS in children with craniosynostosis portends a poor prognosis with a reported 90 % mortality rate by age 2 years of age [28].

Clinical presentation. Upper airway obstruction from midface hypoplasia is frequently present in the craniosynostosis population and may necessitate tracheotomy. TCS may in fact first become apparent at the time of tracheotomy. In other patients, biphasic stridor, cough, recurrent croup, failure to thrive and cyanotic episodes may necessitate an endoscopic airway evaluation, which can reveal TCS. TCS greatly diminishes the normal elasticity present in the tracheal airway, and the trachea may not grow adequately to support the ventilation needs as a child grows [20].

Diagnosis. Previously reported TCS cases have been diagnosed postmortem, during endoscopic airway evaluation and during tracheotomy. Persistent airway distress in a neonate with craniosynostosis should raise suspicion for TCS when significant midface and pharyngeal obstruction have been ruled out. Endoscopy findings include the visible absence of discrete tracheal rings, complete or almost complete absence of the posterior membranous septum, little tracheal motion with respiration, and an abnormal carina [17, 20].

Management. In a neonate with craniosynostosis, a thorough airway evaluation is required to evaluate for multiple levels of obstruction from possible choanal stenosis or atresia, midface hypoplasia, and tracheal anomalies. Tracheotomy may help to increase life expectancy, but the rigidity of the involved segment appears to be a risk factor for the tendency to form granulation tissue [25]. Intraluminal granulation tissue can be problematic and may require the need for multiple bronchoscopic interventions to prevent secondary airway obstruction [20, 25]. Short-segment TCS may be amenable to tracheal resection with primary anastomosis.

Multidisciplinary considerations. Craniosynostosis syndromes often require collaboration between the neurosurgeon, otolaryngologist, and plastic surgeon.

Summary

Children with craniofacial syndromes may have several airway anomalies that contribute to airway obstruction at multiple levels. A comprehensive airway evaluation is essential for identifying the possible causes of obstruction and for formulating an optimal plan to manage the compromised neonatal airway. Being familiar with the characteristic airway anomalies in these syndromes serves as a useful guide, but there must be an awareness of the diverse phenotypic variability that exists in these syndromes. A familiarity of possible airway anomalies that can occur with craniofacial syndromes can allow clinicians to anticipate potential airway issues and institute earlier evaluation and management.

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