Surgery of the Salivary Glands

3

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3.1 Introduction

The human salivary gland system can be divided into two distinct exocrine groups. The *major salivary glands*, which include the paired parotid, submandibular, and sublingual glands, and *the minor salivary glands*, which are hundreds of small glands lining the mucosa of the upper aerodigestive tract. The major function of the salivary glands is to secrete saliva, which plays a major role in lubrication, digestion, immunity, and the overall maintenance of homeostasis within the human body.

3.2 Embryology and Developmental Disorders

Development of the major salivary glands is thought to consist of three main stages [1, 2]. The *first stage* is marked by the presence of a primordial anlage (from the German verb *anlagen*, to set a foundation) and the formation of branched duct buds due to repeated epithelial cleft and bud development (Fig. 3.1). Ciliated epithelial cells form the luminal lining, while external surfaces are lined by ectodermal myoepithelial cells [3]. During the *second stage*, the early appearance of lobules and duct canalization take place resulting in the appearance of primitive acini and distal duct regions.

The *third stage* is marked by maturation of acini and intercalated ducts and reduced prominence of interstitial connective tissue.

The primordial *parotid gland* is the first to appear, during the sixth gestational week, when oral ectodermal outpouchings extend into the adjacent mesoderm and serve as the site of origin for growth of glands. After a short journey of

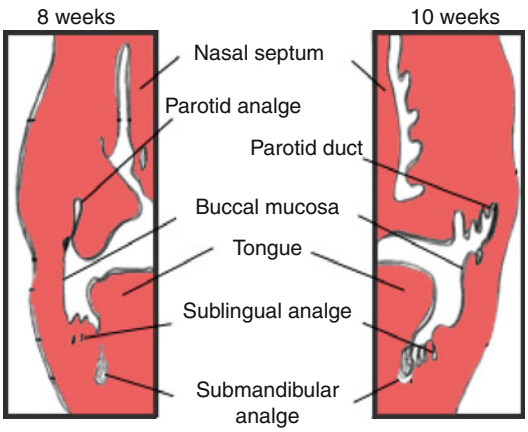

Fig. 3.1 Embryological development of the salivary glands

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M. Sakr (ed.), *Head and Neck and Endocrine Surgery: From Clinical Presentation to Treatment Success*, DOI 10.1007/978-3-319-27532-1_3

dorsal and lateral migration, the parotid gland resides in the preauricular region. The facial nerve arbitrarily divides the gland into superficial and deep lobes by the 10th week of gestation. A fully developed capsule from the nearby mesenchyme surrounds the gland by the 12th week [1].

During the sixth week of embryonic life, small buds appear in the floor of the mouth lateral to the tongue and extend posteriorly around the mylohyoid muscle into the submandibular triangle. These buds eventually develop into the *submandibular glands*. A capsule from the surrounding mesenchyme is fully formed around the gland by the third-gestational month [2].

During the ninth embryonic month, the *sublingual gland* anlage is formed from multiple endodermal epithelial buds in the paralingual sulcus of the floor of the mouth. Absence of a capsule is due to infiltration of the glands by sublingual connective tissue. Intraglandular lymph nodes (LNs) and major ducts also do not generally develop within sublingual glands. Upper respiratory ectoderm gives rise to simple tubuloacinar units. They develop into the *minor salivary glands* during the 12th intrauterine week [4].

Aside from heterotopic salivary glands, developmental disorders of these glands are rare. Reported congenital anomalies include aplasia (absence) [5–8], gland duplication [9], as well as congenitally atretic, imperforate, ectatic, and duplicated ducts [10, 11]. Agenesis may be associated with abnormalities of the lacrimal apparatus and may also be genetically transmitted [7]. Agenesis may be partial or total or unilateral or bilateral and may involve more than one salivary gland. Association with specific syndromes such as Levy-Hollister syndrome, Down syndrome, or Klinefelter syndrome has been reported. The true incidence of parotid agenesis is unknown since most of the cases are asymptomatic. Symptoms include dental caries, thirst, xerostomia, and gingival infections. Oral examination reveals absence of the papilla of Stensen's duct. When suspected, magnetic resonance imaging (MRI) is the imaging tool of choice to demonstrate glandular bed being replaced by fat. Congenital parotid fistula is another developmental disorder.

Tumorlike presentations of maldevelopment include rare hamartomas of the hard palate [12] and unusual cystic choristomas of the submandibular gland [13], which appear to be a mixture of epithelium of both ectodermal and endodermal derivation. The congenital salivary gland anlage tumor or congenital pleomorphic adenoma (PA) is thought to represent a hamartoma of minor salivary gland origin [14].

3.3 Histology

All glands in general are derived from epithelial cells and consist of *parenchyma* (secretory unit and associated ducts) and *stroma* (surrounding connective tissue that penetrates and divides the gland into lobules). Salivary glands are exocrine glands that secrete saliva through ducts from a flask-like, blind-ended secretory structure called *the salivary acinus*.

The acini of the *parotid gland* are lined exclusively by *serous* cells. The acini of the *submandibular gland* are also mainly serous (90 %) but also contain mucous as well as mixed acini. The *sublingual gland* is composed primarily of mucous acini. *Minor salivary glands* are either mucinous or seromucinous except for the serous *Ebner's glands* on the posterior aspect of the tongue. This histological description results in parotid thin watery, devoid of mucins, saliva; submandibular mixed saliva; and sublingual more viscous, mucin-rich, saliva [15].

The acini are drained by a series of ducts, the smallest of which are the intralobular intercalated ducts, which are comprised of an irregular myoepithelial cell layer lined with squamous or low cuboidal epithelium and in turn drain into the striated ducts. The striated ducts are also intralobular but lined by a different epithelial arrangement. Striated ducts drain into the interlobular ducts. In the major salivary glands, these ducts drain into major excretory ducts (*Stensen's* duct in the parotid gland, *Wharton's* duct in the submandibular gland, and *Bartholin's* duct in the sublingual gland), and the epithelium of these ducts changes to squamous as they exit through the oral mucosa. The *minor salivary gland* duct

system is simpler than that of the major salivary glands, where the intercalated ducts are longer and the striated ducts are either less developed or not present [15].

3.4 Physiology

The major function of the salivary glands is the production of saliva, which performs many functions including lubrication of the food bolus, maintaining the pH of the oral cavity within 6–7, maintaining the teeth integrity, fighting bacteria, aiding taste and digestion, as well as providing a continuous lavaging biofilm for the oral cavity [4].

The amount of saliva is affected by the total body fluid volume, and so dehydration decreases its amount and so one feels thirsty. Many agents and viruses are actively excreted in saliva. Mercury poisoning can manifest as stomatitis and lead poisoning by the gingival deposition of lead. The rabies and poliomyelitis viruses are excreted into saliva and can be transmitted in this manner. The two main triggers for salivary production are mastication and gustatory stimuli. Acidic foods are the best stimulus and sweet tastes the least. Olfaction is surprisingly a poor secretory stimulus.

3.4.1 Salivary Flow Rates

In normal circumstances the minimal total unstimulated salivary flow rate is defined as 0.1 mL per minute, and the minimal stimulated flow rate is 0.2 mL per minute. Maximal stimulated flow rate is 7 mL per minute. The 24-h volume of salivary secretion has been estimated to be 500–1,500 mL. Salivary flow in the unstimulated glands is produced primarily by the submandibular glands (65 %), with the parotid, sublingual, and minor glands providing 20 % and 7–8 % of the flow, respectively. Once stimulated, the relative contributions of the parotid and submandibular glands are reversed, with the parotid gland supplying greater than 50 % of the flow. The minor salivary glands, independent of stimulation, produce less than 10 % of the total flow.

Bilateral tympanic neurectomies (bilateral parasympathetic denervation) have been used for patients with ptyalism (drooling) with good initial results. Others, however, advocate bilateral parotid duct rerouting with or without bilateral submandibular gland excision for long-term management of drooling. Intraglandular botulinum toxin has been reported to have good results for patients with hyper-sialorrhea. Most resting salivary gland flow arises from the submandibular glands, and surgery should be focused on this gland to control uncontrolled sialorrhea. Salivary flow rates are independent of age. Xerostomia in the elderly is probably the result of systemic disease or medication side effects. Salivary gland hypofunction is defined as an unstimulated flow rate less than 0.1 mL per minute or a 50 % reduction below basal rates if they have been determined. Basal flow rates should be recorded after 15 years of age [4, 16].

3.5 Parotid Glands

The parotid gland is the largest of the major salivary glands and consists of two lobes: superficial and deep with regard to its relation with the facial nerve. It is wrapped around the mandibular ramus and secretes saliva through the parotid (*Stensen's*) duct and the oral cavity. The word "parotid" (*paraotic*) literally means around the ear.

3.5.1 Surgical Anatomy

The parotid gland is a paired organ, weighing about 15–30 g each. Its superficial lobe overlies the lateral surface of the masseter muscle and is bounded superiorly by the zygomatic arch, while its deep lobe is located in the pre-styloid compartment of the parapharyngeal space between the mastoid process posteriorly, the ramus of the mandible anteriorly, and the external auditory meatus (EAM) superiorly. Medially, the gland reaches to the styloid process. Inferiorly, the parotid tail extends down to about the anteromedial margin of the sternocleidomastoid (SCM) muscle.

Several structures run through the parotid gland. These are (1) the terminal segment of the external carotid artery (ECA), which gives the posterior auricular artery just before entering the gland and terminates by dividing into the superficial temporal artery and the maxillary artery; (2) retromandibular vein; (3) facial nerve which soon gives 5 branches inside the gland radiating forward superficial to the vein and artery; and (4) parotid lymph nodes (LNs).

3.5.1.1 Parotid Fascia

The deep cervical fascia continues superiorly to form the parotid fascia which is split into superficial and deep layers to enclose the parotid gland. The thicker superficial fascia extends up to the zygomatic arch, while the deep one extends to the stylomandibular ligament, which separates the superficial and deep parotid lobes. The parotid fascia forms a dense inelastic capsule.

3.5.1.2 Parotid Duct (Stensen's Duct)

The parotid gland drains its serous secretions through a long duct (Stensen's duct) that arises from the most anterior superficial portion of the gland and travels parallel and 1 cm below the zygoma, running on the lateral surface of the masseter, just deep to the skin, and then it finally dives at an angle of about 90° at the anterior border of the masseter to pierce the buccal pad of fat and the buccinator muscle and opens in the oral vestibule opposite the 2nd maxillary molar over the summit of a papilla [4, 17].

3.5.1.3 Accessory Parotid Gland

Accessory parotid tissue (lobe or gland) may sometimes exist and come to reside over the masseter muscle between the zygomatic arch and Stensen's duct. As proved histologically, this accessory glandular tissue secretes mucous in addition to serous secretions drained through a single short duct that joins the main duct [18].

3.5.1.4 Surface Anatomy of the Parotid Gland

The *anterior* border of the gland corresponds to a line that extends from the ear tragus to the posterior border of the masseter opposite the angle of the mouth, the *inferior* border from there to below and behind the angle of the mandible, the *posterior* border from there to the mastoid process, and the *superior* border from the mastoid process to the ear tragus. Surface anatomy of the *parotid duct* corresponds to the middle third of an imaginary line that extends from the tragus of the ear to the midportion of the upper lip.

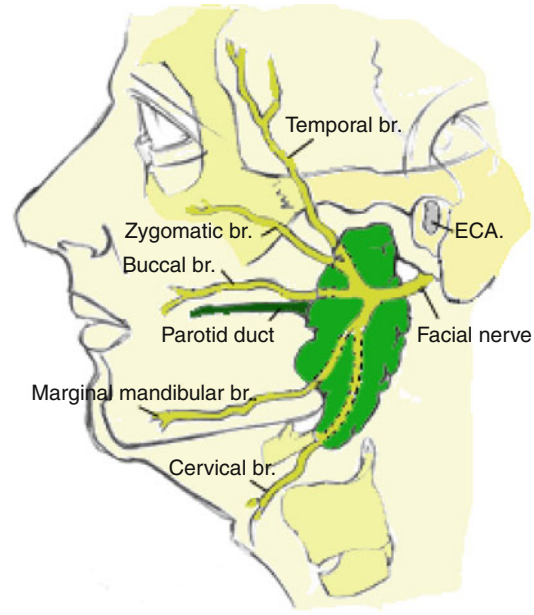

Fig. 3.2 Anatomy of the facial nerve. It divides first into two divisions: upper temporofacial and lower cervicofacial. The upper division gives off the temporal, zygomatic, and buccal branches, while the lower gives off the marginal mandibular and cervical branches

3.5.1.5 Nerve Supply

The facial nerve (CN VII) exits the skull base through the stylomastoid foramen, which is slightly posterolateral to the styloid process and anteromedial to the mastoid process. The nerve immediately gives off three motor branches for the posterior belly of the digastric, the stylohyoid, and the postauricular muscles. Its main trunk then enters the posterior portion of the gland. Inside the gland, at the pesanserinus (*Latin*: goose's foot), it divides into upper temporofacial and lower cervicofacial division approximately 1.3 cm from the stylomastoid foramen (Fig. 3.2). The temporofacial division gives off the temporal, zygomatic, and buccal branches, while the cervicofacial gives off the marginal mandibular and cervical branches.

The *temporal branch* passes with the superficial temporal vessels over the zygoma to supply the frontal belly of occipitofrontalis, orbicularis oculi, corrugator supercilii, and anterior and superior auricular muscles. The *zygomatic branch* passes over the periosteum of the zygomatic arch to supply the zygomatic, orbital, and infraorbital muscles. The *buccal branch* travels with the Stensen's duct to supply the buccinator, upper lip, and nostril muscles. The *marginal mandibular branch* travels along the inferior border of the parotid gland just deep to the platysma muscle but superficial to the posterior facial and retromandibular veins, to supply the lower lip and chin muscles. Running in the same plane is the *cervical branch*, which supplies the platysma muscle. All the muscles supplied by the facial nerve are muscles of facial expression.

The *great auricular nerve* (C2, C3) is a sensory branch of the cervical plexus that provides general sensation to the parotid gland and the skin of the posterior portion of the ear pinna and the ear lobule. It accompanies the external jugular vein along the lateral surface of the SCM muscle toward the tail of the parotid gland, and there it splits into anterior and posterior branches. It is often injured during parotidectomy leaving the ear lobule senseless. Its harvesting for facial nerve grafting may be needed when the latter is injured or sacrificed.

The *auriculotemporal nerve* (ATN) is a branch of the mandibular division of the trigeminal nerve (CN V). After exiting the foramen ovale, it runs parallel to the superficial temporal vessels and anterior to the external auditory canal to innervate the skin and scalp immediately anterior to the ear.

The *glossopharyngeal nerve* (CN IX) provides visceral secretory innervation to the parotid gland. The nerve carries preganglionic parasympathetic fibers from the inferior salivatory nucleus in the medulla through the jugular foramen. Then, a small branch of the CN IX (Jacobsen's nerve) reenters the skull through the inferior tympanic canaliculus and into the middle ear to form the tympanic plexus.

The preganglionic fibers then travel as the lesser petrosal nerve into the middle cranial fossa and out through the foramen ovale to synapse in the otic ganglion. Postganglionic parasympathetic fibers exit the otic ganglion to join the ATN in the infratemporal fossa. The ATN enters the substance of the gland from its deep aspect along the neck of the mandible and emerges from the gland just inferior to the root of the zygomatic arch. The ATN carries fibers that innervate the parotid gland for secretion of saliva (Fig. 3.3).

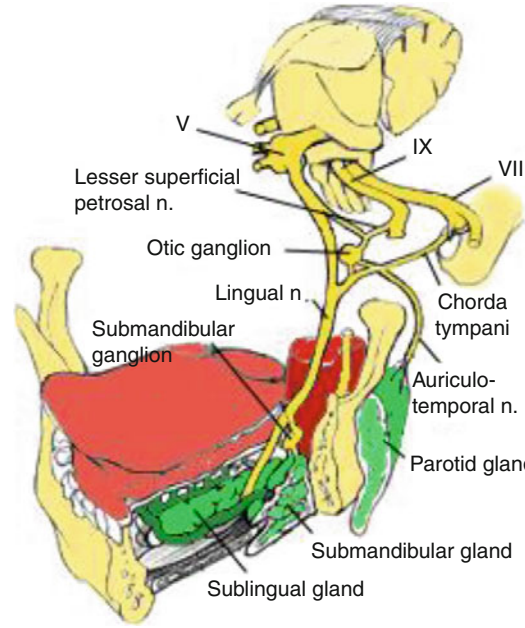

Fig. 3.3 Parasympathetic innervations of the salivary glands

Postganglionic sympathetic fibers innervate the salivary glands, sweat glands, and cutaneous blood vessels, mediating vasoconstriction, through the external carotid plexus from the superior cervical ganglion. Acetylcholine serves as the neurotransmitter for both postganglionic sympathetic and parasympathetic fibers. This physiologic coincidence allows for the occasional development of "gustatory sweating," also known as *Frey's syndrome*, following parotidectomy [19].

3.5.1.6 Arterial Supply

The parotid gland receives its blood supply through branches of the external carotid artery (ECA), mainly through the *posterior auricular artery*. The ECA travels parallel to the mandible under the posterior belly of digastric muscle. It then travels medial to the gland and splits into its two terminal branches: the superficial temporal

artery that leaves the superior portion of the gland and the maxillary artery that leaves the medial portion of the gland. The *transverse facial artery* is a branch of the superficial temporal artery that runs anteriorly between the zygoma and parotid duct to supply it together with the parotid gland and the masseter muscle.

3.5.1.7 Venous Drainage

The *retromandibular vein*, formed by the union of the maxillary and the superficial temporal veins, runs through the parotid gland just deep to the facial nerve. It drains into the external jugular vein. There are many variations as regards the surgical anatomy of the retromandibular vein.

3.5.1.8 Lymphatic Drainage

As a result of late encapsulation during embryological development, the parotid gland, unlike the submandibular and sublingual glands, contains intraparenchymal lymph nodes (LNs), with salivary gland structures, usually ducts and less frequency acini, in the intra- and peri-parotid LNs. Ninety percent of the nodes draining the parotid gland are located in the superficial layer between the gland and its capsule (3–20 nodes). These drain the parotid gland, external auditory canal, pinna, scalp, eyelids, and lacrimal glands. Deep LNs, residing on the lateral wall of the pharynx, drain the gland, external auditory canal, middle ear, nasopharynx, and soft palate. Both groups drain into level II of cervical LNs.

3.5.1.9 Parapharyngeal Space (PPS)

Tumors of the deep lobe of the parotid gland often extend medially into the PPS, which is shaped like an inverted pyramid, where the greater cornu of the hyoid bone serves as the *apex* and the petrous bone of the skull base as the *base*. The PPS is bound *medially* by the lateral pharyngeal wall, which consists of the superior constrictor muscles, buccopharyngeal fascia and tensor veli palatine. It is bounded *laterally* by the ramus of the mandible and the medial pterygoid muscle, *anteriorly* by the pterygoid fascia and the pterygomandibular raphe, and *posteriorly* by the carotid sheath and prevertebral fascia.

A line from the styloid process to the medial portion of the medial pterygoid plate divides the PPS into pre- and post-styloid compartments. The *pre-styloid* one contains the deep parotid lobe, internal maxillary and ascending pharyngeal arteries, and inferior alveolar, lingual, and ATNs. The *post-styloid* compartment contains the internal jugular vein (IJV), carotid artery, vagus nerve (tenth cranial nerve, CN X) all within the carotid sheath, as well as the cranial nerves IX, XI, and XII and the cervical sympathetic chain. Thus, neurogenic tumors or paragangliomas arising from these nerves lie in this post-styloid compartment [20].

Hints and Tips

- The parotid bed is an irregular space located between the ramus of the mandible, the EAM, the mastoid and styloid processes, the digastric, and SCM muscles.
- Structures entering the parotid gland exit from its posterior, superior, inferior, and anterior surfaces. The posterior auricular artery exits from the posterior aspect of the gland. The superficial temporal artery and vein, ATN, and temporal branches of the facial nerve are seen at the superior margin of the gland. Inferiorly, the retromandibular vein exits the parotid gland. Emanating from the entire facial margin of the gland are the terminal branches of the facial nerve, grouped into five major branches: the temporal, zygomatic, buccal, mandibular, and cervical branches.
- General sensation to the parotid gland is provided by the great auricular nerve of the cervical plexus. Sympathetic innervation is supplied by the carotid plexus, whereas secretomotor innervation is supplied by the glossopharyngeal nerve and delivered to the gland by the ATN.
- The gland cannot be moved over the deep structures and becomes more prominent when the patient clenches his teeth by contracting the masseter muscles.

3.5.2 Evaluation of the Parotid Gland

3.5.2.1 Clinical Evaluation

Despite the availability of modern technology in diagnosis of parotid gland disorders, great care should be taken during history taking and thorough physical examination as they still play important roles in the clinical diagnosis of the patient.

History Taking

Patients with parotid gland disorders usually complain of swelling, pain, *xerostomia* (dry mouth), foul taste, and occasionally *sialorrhea* (excessive salivation). Swelling and pain during meals followed by reduction in symptoms after meals may indicate partial stenosis of the duct. *Demographic data* (age and gender) are of considerable importance. The autoimmune disorder known as Sjogren's syndrome, for example, is common in menopausal women, while *mumps* usually occurs in children.

The *medical profile* of the patient may provide helpful clues to diagnosis. Dysfunction of the gland is often associated with certain systemic disorders such as diabetes mellitus (DM), atherosclerosis, hormonal imbalances, and neurologic disorders [21, 22]. A careful *dietary and nutrition* history should not be neglected, for patients who suffer from chronic dehydration due to bulimia or anorexia or during chemotherapy are at risk for parotitis.

Drug history of the patient should also be considered, for salivary function is often affected by certain drugs such as diuretics and other antihypertensive drugs, which may cause xerostomia [21, 22]. Since xerostomia is also a debilitating consequence of radiation therapy to the head and neck, history of *prior irradiation* should be sought.

Physical Examination

Initial clinical evaluation involves careful examination of the head and neck regions. Both extraoral and intraoral examinations should be carried out in a systematic way to avoid missing any crucial signs. Bimanual palpation (extraoral with one hand and intraoral with the palmar aspects of the fingertips of the other) must be also performed to properly examine the submandibular glands.

Inspection *Extraoral inspection* is performed with the patient facing in front of the examiner, three to four feet away. The examiner should inspect symmetry, color, pulsations, and discharging sinuses on both sides of the patient. Enlargement of the parotid gland may be unilateral or bilateral. *Parotitis* typically presents as preauricular swelling, but may not be visible if deep in the parotid tail or within the substance of the gland. Neurologic deficits should also be examined. Facial nerve paralysis in conjunction with a parotid mass, for example, should raise the suspicion of a *malignant* parotid neoplasm. *Intraoral inspection* is done using a torch or headlight. The orifices of the parotid (Stensen's) ducts are inspected opposite the second upper molar tooth and the two sides compared. Saliva may be seen pouring from the non-affected side only.

Palpation With the examiner standing in front of or behind the patient, the patient's head is inclined forward to maximally expose the parotid gland region. Size, tenderness, consistency, mobility, and other features of the parotid gland and associated masses can be easily evaluated with *extraoral and intraoral palpation* owing to the superficial anatomical location of the gland.

Auscultation Rare clinical entities, such as *hemangiomas* and other vascular anomalies, may be identified by auscultation.

3.5.2.2 Imaging

For patients with no specific symptoms (swelling and pain) and unclear physical signs, imaging studies can play an important role in clarifying the etiology of the gland disorder and assist in treatment selection and planning.

Sialography

Sialography is used to evaluate sialolithiasis (or other obstructive disorders) and inflammatory and neoplastic diseases. In this technique, 0.5 to 2 mL of a suitable radiopaque liquid such as

Hypaque (sodium diatrizoate) or Lipiodol is introduced into the duct system through a fine polythene catheter, or a blunt metal cannula, and a plain-film radiograph is taken. Sialography is contraindicated in case of iodine allergy and acute sialadenitis. Any filling defect (e.g., stone), retained sections (e.g., chronic sialadenitis), stricture (e.g., inflammation), extravasation (e.g., Sjogren's syndrome), or irregular borders (e.g., tumor) are noted. Fistulae and abscesses cavities can also be displayed with this technique.

Computed Tomography (CT)

The parotid gland has low attenuation due to its high fat content and is therefore easily discernible by CT scanning. The advantage of CT imaging is the two-dimensional view of the salivary gland, which can elucidate relationships to adjacent vital structures, differentiate intrinsic from extrinsic disease, and assess the draining cervical LNs. It is also extremely valuable in defining abscess formation versus phlegmon. However, it is limited in evaluating the ductal system unless combined with simultaneous sialography (CT sialography) [23]. Differences between intrinsic and extrinsic parotid gland masses, however, are often difficult to assess especially when present in the parapharyngeal space (PPS) [24].

Magnetic Resonance Imaging (MRI)

Compared with CT, MRI provides better contrast resolution, exposes the patient to less harmful radiation, and yields detailed images on several different planes without patient repositioning. It is more often used for assessment of parapharyngeal space abnormalities especially in discriminating between deep lobe parotid tumors and other lesions, such as schwannoma and/or glomus vagale. However, MRI is inferior to CT scanning for the detection of calcification and early bone erosion. Chronic inflammation of the salivary glands and calculi are *not* indications for MRI.

3.5.2.3 Endoscopic Examination (Sialendoscopy)

Sialendoscopy is a minimally invasive technique that inspects the salivary glands using narrow-diameter, rigid fiber optic endoscopes, introduced under direct vision through the ductal orifice after its dilatation with a lacrimal probe [25]. It is well tolerated, with minimal complications, and has thus opened up a new frontier for evaluation and treatment of salivary gland disorders [26]. Direct inspection of the glandular duct and hilum is performed during lavage of the duct. Thus, in one setting, at the time of diagnosis, treatment of benign lesions can be performed [27]. Through a CO_2-laser papillotomy, sialolithectomy can be easily performed. Pharmacotherapy and laser ablation can also be performed. This relatively new technique has shown much promise in the diagnosis and treatment of chronic obstructive sialadenitis (COS) and sialolithiasis.

3.5.2.4 Biopsy

Fine-needle aspiration cytology (FNAC) is an accurate investigation for the diagnosis of a parotid mass in up to 93 % of cases [25–27]. It allows for improved patient selection for surgery since it can identify disorders such as reactive lymph nodes that might mimic parotid tumors clinically. The information gained by FNAC is thus useful for patient counseling and for surgical timing and planning. Open biopsy of the lip should be considered when the diagnosis of Sjogren's disease is contemplated.

3.5.3 Parotid Injuries and Fistulae

Successful treatment of parotid injuries depends on early recognition and appropriate early intervention. Sequelae of inadequate diagnosis and treatment include parotid fistula and sialocele formation, which are inconvenient for the patient and more difficult to treat than the initial injury.

A parotid fistula is a communication between the parotid gland (*glandular fistula*) or duct (*ductal fistula*) and the skin externally (*external fistula*) or the oral cavity internally (*internal fistula*). A sialocele is a collection of saliva beneath the skin that occurs if the duct leaks but no fistula forms or when the glandular substance, but not the duct, is disrupted.

3.5.3.1 Etiology

Causes of the fistula include: (1) penetrating or blunt injury in the region of the parotid gland, (2)

improper incision and drainage or spontaneous rupture of a parotid abscess (or sialocele), (3) intraoperative iatrogenic injury, (4) complication of parotid duct cannulation for sialography, and (5) malignant tumors invading the surface [28].

3.5.3.2 Clinical Presentation

Males are twice as likely to experience parotid duct injury as females, and the mean age of patients with parotid duct injury is approximately 30 years.

History

Important aspects of history of the wound include the circumstances surrounding the injury, precipitating cause, exact mechanism and site of injury, time of occurrence, and treatment initiated prior to presentation.

Other important aspects of the history include tobacco, alcohol, or drug use; tetanus immune status; and comorbid conditions that may place the patient at a higher risk for infection such as diabetes mellitus and immunosuppression.

Physical Examination

An internal fistula constitutes no consequences and requires *no treatment*. However, an external fistula connected with large ducts causes extreme discomfort every time the patient has a meal, smells, or even thinks of food, due to excessive outpouring of saliva on the cheek causing skin excoriation. A sialogram will determine whether the fistula is ductal or glandular.

A thorough clinical examination is necessary for proper evaluation of the overall state of health, comorbidities, nutritional status, and mental status of the patient. Important signs or symptoms related to the wound include pain, fever, edema, discharge, and/or odor. Important aspects of wound assessment include location, shape, size, type (blunt or penetrating), depth, drainage (quality, character, odor), presence of a foreign body (e.g., glass, tooth fragments), loss of tissue, tenderness, asymmetry, surrounding skin (erythema, edema, crepitus), and status of the facial nerve.

An injury classification system that divides the parotid duct into 3 regions has been devised for parotid duct injuries.

- Site A: Posterior to the masseter muscle or intraglandular (*glandular*)
- Site B: Overlying the masseter muscle (*masseteric*)
- Site C: Anterior to the masseter muscle (*pre-masseteric*)

3.5.3.3 Treatment

Various treatment modalities to treat the parotid fistula have been advocated, if *conservative measures* fail. *Tympanic neurectomy* involves drilling into the temporal bone and disruption of the tympanic nerve, which carries parasympathetic secretory nerve fibers to the parotid gland [29, 30]. This technique aims at reducing salivary flow and causing spontaneous fistula resolution. Although popular in the past, this method tends to be abandoned due to short-term and poor results due to reinnervation of the gland with time [31].

Radiation has been used in the past to suppress the gland, but use of radiation for benign disease is now avoided. Some authors advocate use of *anticholinergics* to suppress glandular function during healing, but this is not a frequently used modality. *Three operative techniques* have been popularized over time. These include repair of the duct over a stent, ligation of the duct, and fistulization of the duct into the oral cavity.

Medical Therapy

Wound care is the cornerstone of therapy. Prophylactic antibiotics should be administered and continued for 5–7 days, but it should be noted that antibiotics cannot avert or cure infections in the setting of poor wound care. In rare cases, human saliva contains and occasionally transmits *Clostridium tetani.* Accordingly, all patients should be assessed for their tetanus immune status and immunization should be updated as appropriate.

Some authors choose to use anticholinergic agents to suppress glandular function during healing or in an attempt to close a fistula or resolve a sialocele spontaneously. A commonly used agent is propantheline bromide (Pro-Banthine), which inhibits the action of acetylcholine at the postganglionic nerve endings of the parasympathetic nervous system (adult dose 15 mg PO qid half an hour prior to meals).

Sialocele and salivary fistula can frequently be managed nonoperatively with antibiotics, pressure dressings, and serial aspiration. Anticholinergic medications and the injection of botulinum toxin represent additional measures before resorting to surgical therapies such as tympanic neurectomy or parotidectomy [32].

Surgical Therapy

Copious irrigation of the wound with normal saline solution has been shown to decrease the incidence of wound infection. *Careful debridement* of devitalized tissue, particulate matter, and clot is necessary to reduce the infection risk and to improve the cosmetic result. Clean, surgically created wound margins allow for faster wound healing and better scarring.

Head and neck wounds, less than 12 h old and not obviously infected, being in a cosmetically sensitive area, may be *closed directly* with a low incidence of infection. The low infection rate is probably related to the excellent regional blood supply and infrequency of edema in these areas. For a good cosmetic result, closure is performed in a simple interrupted fashion, using fine stitches and avoiding layered closure with buried sutures.

The most important initial step for proper surgical repair is the identification of key structures, namely, the buccal branches of the facial nerve (with the aid of a nerve stimulator intraoperatively if available) and the parotid duct itself. If the buccal branch was transected, repair it with fine sutures (8–0 to 10–0 monofilament is appropriate) under microscopic aid. The distal end of the parotid duct is identified by a Silastic tube, placed via cannulation of the intraoral papilla. The proximal parotid duct can usually be identified by the flow of saliva into the wound, with gentle pressure over the gland if necessary. Once all key structures are identified, a decision is made regarding which repair technique to employ.

Distal lacerations, occurring at site C, may be treated in several ways. If the *papilla is uninjured*, the proximal portion may be dissected free and reimplanted into the papilla. If the *papilla is injured* or if the proximal duct does not reach the papilla, the duct may be reimplanted (under magnification) into the oral mucosa posterior to the papilla, using fine interrupted absorbable sutures with meticulous approximation of duct epithelium to oral mucosa. If the distal injury is too short to be reimplanted into the oral mucosa without undue tension, then the best decision is to ligate the proximal duct.

Injuries occurring over the masseter muscle, at site B, are the most common injuries to the parotid duct and may be treated by *repair or ligation*. If enough *length remains*, primary anastomosis over a Silastic stent, using a single layer of interrupted fine sutures (8–0 to 10–0 monofilament) is performed under magnification. If a portion of the duct is *damaged* beyond repair or is missing, the proximal and distal duct should be ligated. Reports of attempts to use a vein graft (saphenous) in such cases have generally found such attempts unsuccessful. Sialendoscopy-assisted repair of a transected Stensen's duct in zone B has been reported [33].

Injuries of the proximal duct near the parotid substance, at site A, are usually best treated by duct *ligation* as the amount of proximal duct remaining is usually insufficient to result in a useful repair. Laceration of the gland itself without disruption of the parotid duct may be repaired with fine absorbable sutures (5–0 or 6–0 Vicryl).

A drain in the wound bed is recommended to drain any residual salivary leak and prevent early sialocele formation. Drains are removed once drainage is minimal and the skin has become adherent to the operative site. *Postoperatively*, a compression dressing is placed over the operative field postoperatively for several days. If ductal injury required ligation of the proximal duct, marked temporary swelling of the gland followed by rapid glandular atrophy is expected. If leaking of saliva occurs as in the development of a fistula or sialocele, the pressure dressing should be continued or reinstituted. Intermittent aspiration of sialoceles has led to resolution in many cases. Anticholinergics may be used to temporarily decrease salivary flow in order to effect wound healing. In the case of a *chronic* parotid duct fistula, an intraoral diversion technique to reestablish salivary flow in case of a nonfunctional parotid duct punctum has been described. The fistula tract and the surrounding ellipse of skin are passed in the oral cavity and sutured to the buccal mucosa with 4–0 chromic sutures without

need for stenting [34]. Alternatively, chronic fistula and sialocele have been medically managed with botulinum toxin [35].

3.5.3.4 Complications

Persistent Salivary Fistula If the fistula occurs in the oral cavity, it is of no consequence and requires no further therapy. If the fistula occurs to the overlying skin, the patient experiences saliva dripping down the cheek. Initial expectant management, with or without anticholinergic medications, has led to resolution in many cases. Other cases have required surgical excision of the fistula tract with repair of the duct or superficial parotidectomy. *Sialocele* usually resolves with intermittent aspiration and compression and rarely requires drain placement. Anticholinergics may be beneficial in the treatment of sialoceles. Duct ligation may lead to early edema of the gland with accompanying pain from stretching of the capsule. This usually subsides spontaneously within 1–2 weeks as atrophy of the gland occurs. Infection of the remaining glandular substance may occur as a late complication of duct ligation. *Sialadenitis* may result from manipulation of the intraoral papilla or from sialography and may require drainage and antibiotics. *Facial nerve injury* and sensory nerve injury may occur when surgery is conducted in the region of the parotid duct, particularly in cases where trauma and blood extravasation have discolored the tissues and disrupted tissue planes.

3.5.4 Parotid Calculus

Parotid stones are much less common than submandibular stones (20 % versus 80 %, respectively). However, recent studies showed some rapprochement between these figures. This is attributed to a number of factors such as the difference in the composition of the saliva produced by each gland and the dependence of the submandibular (Wharton's) duct, which hinders easy drainage of its viscid secretions. Parotid stones are composed of organic substances such as cellular debris, mucopolysaccharides and glycoproteins, and inorganic substances such as different calcium and magnesium salts. The organic substances are mainly found as the core of the stone, while the inorganic substances are in its periphery. Apatite is the most frequent component present throughout the calculus. The annual growth rate of an established stone is about 1 mm per year. Their shape is either rounded or irregular and the average size is about 3.2 mm. Clinical presentations of a parotid stone vary from being *asymptomatic*, to intermittent obstructive parotitis, to an acute abscess. Parotid stones are usually imaged through sialography being mostly radiolucent [36].

Stones present in the gland or within the collecting ducts are treated with parotidectomy, while those present near the papilla may be treated with longitudinal incision of the duct releasing the stone. The advent of external lithotripsy in the early 1990s [37] paved the way for conservative treatment of all calculi, with a success rate of 40 % in the submandibular gland and 75 % in the parotid. Unfortunately, results were discouraging, specifically in patients with large calculi [38–41].

Interventional sialendoscopy, first described in the 1990s, offered much less invasive therapeutic options and became popular with technological improvements in the years after 2000 [42–47]. It can be used to retrieve stones from the ducts (Fig. 3.4) as well as dilating strictures.

Nevertheless, success rates of interventional sialendoscopy with intraductal laser fragmentation and basket extraction of calculi remained possible in only 80 % of patients [42]. Unsuccessful treatment of the remaining 20 % of patients was attributed not only to large-sized calculi (6 mm and larger) but also due to associated ductal stenosis [48]. In such cases, the only solution was to remove the gland, with its associated significant morbidity [38–40].

3.5.5 Inflammatory Disorders (Sialadenitis)

3.5.5.1 Viral Infections

Mumps [49]

Mumps is a specific acute viral infection due to a paramyxovirus, an RNA virus that belongs to the influenza and parainfluenza family. In 85 % of cases, it affects the school-age children under the

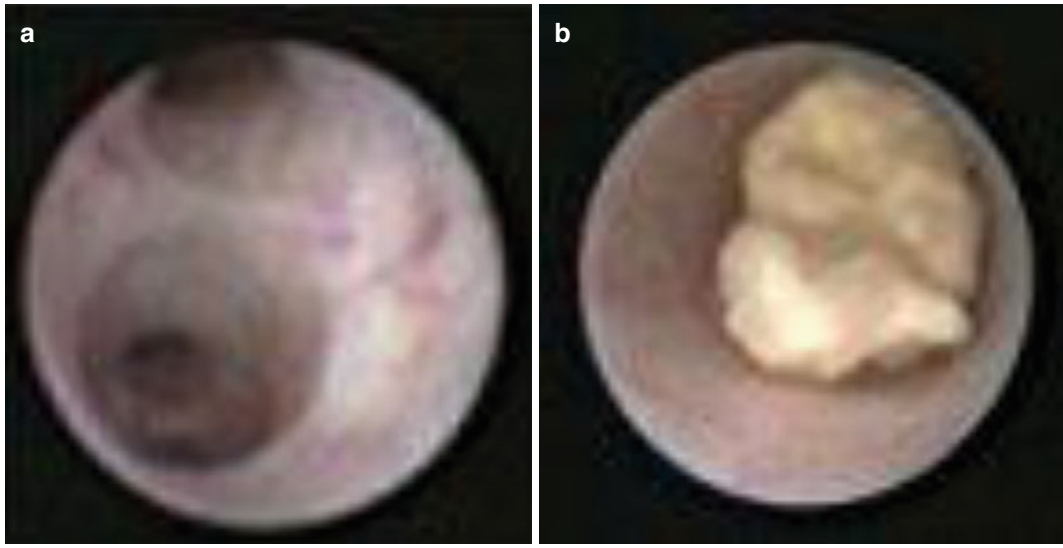

Fig. 3.4 Sialendoscopy showing interior of the parotid (Stensen's) duct (**a**) and intraductal stones (**b**)

age of 15 years, with an incubation period of 2–3 weeks. The illness starts by 1–2 days of prodromal influenza-like syndrome (discomfort, loss of appetite, nausea, chills, fever, sore throat, and headache), followed by the appearance of the characteristic face swelling. The patient is infectious from 3 days before the onset of salivary swellings to 7 days after, through airborne droplets of infected saliva. A single episode of infection confers lifelong immunity. Fortunately, this condition has been mostly eradicated as a result of vaccination.

The swelling, which usually starts unilateral and in a few days becomes bilateral, lasts from a couple of days to 1 week (Fig. 3.5). The virus causes fever and is considered the most common cause of acute painful profuse swelling of the parotid gland.

The gland is soft and tender, but never suppurates. Impingement on the auriculotemporal and great auricular nerves causes much pain as the gland is pressured during mastication. Symptoms usually resolve within 5–10 days.

Mumps may be complicated by pancreatitis, orchitis, and oophoritis. It might be a cause of abortion during the first trimester of pregnancy because of fetal endocardial fibroelastosis. Sensorineural deafness (1/20,000) and meningoencephalitis are rare but are more likely to occur in adults.

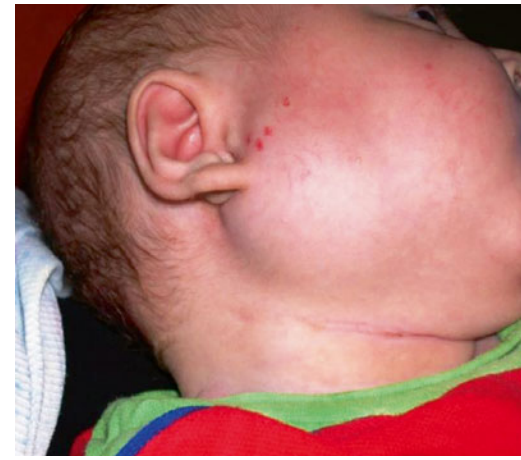

Fig. 3.5 Mumps in a 10-month child with a smooth enlargement of the right parotid gland

Laboratory findings include leukocytopenia with relative lymphocytosis. Serum amylase peaks in the 1st week and normalizes by the 2nd or 3rd week. Soluble antibodies directed against the nucleoprotein core of the virus appear within the final week of infection and disappear within 8 months. Antibodies directed against the outer surface appear several weeks after soluble antibodies, and persist for 5 years. Mumps is a self-limited disease that requires rest and symptomatic treatment only, which includes antibiotics, sialagogues, and rehydration.

Non-Mumps

Parotitis with the same clinical picture as that described for mumps can be caused by other viral agents, namely, Coxsackie A and B, parainfluenza types 1 and 3, echovirus, and lymphocytic choriomeningitis virus.

Human Immunodeficiency Virus (HIV)-Associated Sialadenitis [50, 51]

The presentation of HIV-associated sialadenitis is in the form of chronic, bilateral enlargement of parotid glands where the glands are painless, hard, and nodular. The disease is more common among children than among adults. The condition may be associated with xerostomia and xerophthalmia, being so similar to the classical Sjogren's syndrome in adulthood. Although both conditions share similar histological characteristics, HIV-associated sialadenitis is usually associated with a negative autoantibody screen. Multiple glandular cysts causing gross parotid swelling and facial disfigurement are another pattern of presentation. Thirty percent of HIV-infected children have been reported to have enlargement of their parotid glands. In addition, patients with HIV are more susceptible to infection with cytomegalovirus (CMV) and adenoviruses as causative agents for non-mumps parotitis.

Useful imaging tools include ultrasound (US), computed tomography (CT), and MRI. The latter two demonstrate the characteristic "Swiss cheese" appearance of multiple large cystic lesions (Fig. 3.6). They can also guide fine-needle aspiration, which reveals serous fluid with the presence of lymphocytes and macrophages. As the parotid gland contains many LNs at different levels, they might be enlarged as the HIV virus mainly affects the lymphoid tissue. The sole indication of surgery might be to improve the appearance.

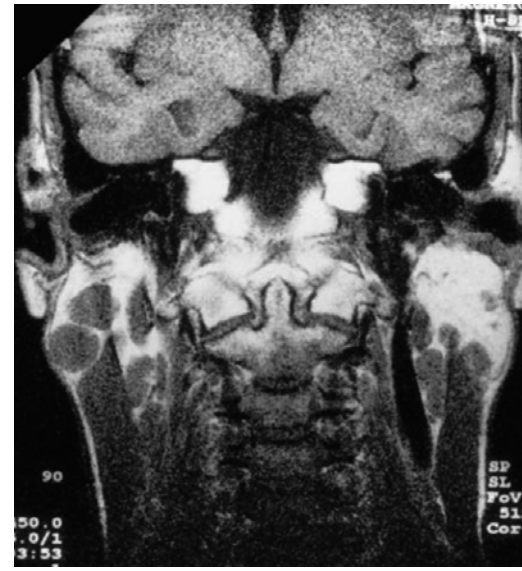

Fig. 3.6 MRI showing the characteristic Swiss cheese appearance of multiple large cystic lesions

3.5.5.2 Bacterial Infections

Acute Suppurative Parotitis (Abscess) [52]

The infective organism can be any of the following bacteria: *Staphylococcus aureus*, *Streptococcus viridans*, Penicillin-resistant coagulase-positive staphylococcus, *Streptococcus pneumoniae*, beta-hemolytic streptococcus, methicillin-resistant *Staphylococcus aureus* (MRSA), or gram-negative germs, such as *E. coli*. Studies have shown the presence of 30–40 % of anaerobic bacteria: bacteroides, peptostreptococcus, and fusobacteria. In Southeast Asia, *Pseudomonas pseudomallei* has been reported. In many cases the infection is a mixed one.

Ascending retrograde infection spreads from an infected dry mouth through the duct into the gland, or it may be blood-borne. One or more of the following factors that cause dehydration and/or electrolyte imbalance are usually evident: septicemia, obstruction of Stensen's duct by a stone, after major surgery, or bad oral hygiene. However, sometimes the condition is totally idiopathic. Parotids are affected more frequently than submandibular glands. One of the possible reasons is that the bacteriostatic activity of the saliva secreted by the parotid gland is inferior to that secreted by the submandibular gland as the former is predominantly serous and thus lacks the protective constituents (IgA, sialic acid, and lysosomes) seen in mucinous secretions of the other salivary glands.

The patient generally complains of anorexia, fever, tachycardia, and malaise. Over several

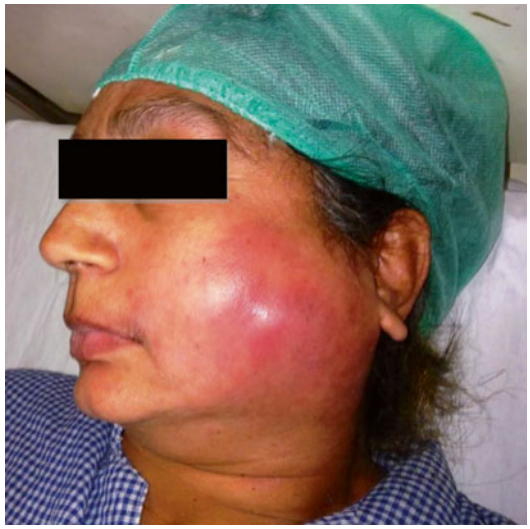

Fig. 3.7 Large left parotid abscess with erythematous, edematous, and tethered overlying skin

hours, the local condition starts with a swelling which is very tender, hot, and with throbbing pain that is exacerbated by mastication. The gland size may reach 3–4 times larger than that of the normal gland, which is usually diffuse but may localize to the lower pole. The skin overlying the gland is red, edematous, and tethered (Fig. 3.7). Movements of the ipsilateral temporomandibular joint (TMJ) are restricted and painful. The upper deep cervical LNs are enlarged and tender.

The parotid gland, being enclosed in a dense capsule, is liable to fulminating inflammation and necrosis due to increased tension within this tightly closed fascial compartment. Fluctuation is difficult to elicit and is never waited for. Pus may exude from the duct orifice on massage of the gland, which is in spite of being painful at the moment; it relieves the pressure inside the ductal system and thence the pain. Diseases of the parotid gland cause pain to be referred to the ear, the TMJ, and the external auditory meatus. This is due to the overlapping of sensory branches of various nerves serving the regions of the parotid bed, ear, and TMJ. Infections of the parotid gland may be confused with toothache as a result of trigeminal nerve (CN V) involvement. An inflamed parotid papilla (parotid duct orifice in the oral cavity) provides clue to diagnosis.

A parotid abscess may be complicated by local spread in the form of cellulitis, chronicity due to inadequate management, development of a fistula, septicemia, and rupture into the external auditory meatus or along the carotid sheath. The patient shows increased white blood cell count, and culture and sensitivity should be done from the pus. Sialography is contraindicated during acute infection and US may be needed; however, the diagnosis is mostly done on clinical grounds.

Prophylaxis against the development of such suppuration is considered much safer through adopting good oral hygiene, preventing dehydration, and early adequate correction of electrolyte imbalance. As an early treatment of any inflammatory condition affecting the parotid gland, one should use warm local fomentations, intravenous antibiotics, anti-inflammatory agents, and analgesics. When suppuration ensues (known by throbbing pain, hectic fever, aspirated pus, or US-identified abscess formation), formal drainage under general anesthesia becomes necessary.

Decompression of the Parotid (Hilton's Method) Do not wait for fluctuation. Under general anesthesia, a *vertical* incision is done in the skin down to the parotid capsule. The capsule in then incised *transversely* along the course of the branches of the facial nerve to avoid their injury. Pus is evacuated, a drain is put in the lower part of the incision for 24–72 h, and then closure is achieved. Complications of this procedure include parotid fistula and facial nerve injury. Alternatively, the skin incision may be made low to avoid damage to the lower branch of the facial nerve.

Chronic Pyogenic Parotitis

Chronic bacterial sialadenitis is rare in the parotid gland. It may result from improper treatment of acute parotitis, presence of stones in the duct, or stenosis of the Stensen's duct [53].

Actinomycosis

Actinomycosis affects LNs adjacent to salivary glands, mimicking a salivary gland infection. The pathogen is *Actinomyces israelii*, *A. propionica*, *A. viscosus*, or *A. odontolyticus*. Infection may be acute, subacute, or chronic. The *acute* form is

associated with suppuration, the *subacute* with a slightly tender and tumorlike mass attached to the mandible, and the *chronic* with marked induration that may be misdiagnosed as a neoplasm. The finding of pollen grain like "sulfur granules" on clinical examination or "sulfur grounds" on pathological evaluation is pathognomonic of this condition. Treatment of the acute phase is surgical, with eventual drainage of the exudates and administration of broad-spectrum antibiotics [54].

Cat-Scratch Disease

A disease caused by infection with a gram-negative bacillus called *Bartonella henselae*. The disease originally involves LNs adjacent to salivary glands, which may be secondarily involved by continuous spread. The disease is due to contact with cats, and children or young adults are the most often involved. Laboratory tests include specific PCR or serology. Antibiotics do not seem to shorten the course of the disease but may be given as prophylaxis against secondary bacterial infection. The affected LNs disappear spontaneously within a few months [55, 56].

3.5.5.3 Recurrent Parotitis of Childhood

This is a distinct clinical entity of unknown etiology and unsure prognosis. It is the most frequent nonviral disorder of salivary glands in children [57]. Suggested etiologies include congenital malformation of the parotid ducts, primary or secondary infections, and local manifestations of systemic immunological disease.

The clinical picture comprises fever, malaise, rapid swelling of one or both parotid glands, and pain which is made worse by mastication. This usually lasts from 3 to 7 days followed by a quiescent period of weeks to several months. The condition may rarely start as early as 4 months of age, but usually children present between the ages of 3 and 6 years and usually resolve around puberty. The diagnosis is made by obtaining typical history and findings of the clinical examination. Sialography may be confirmatory. It shows a characteristic punctate sialectasis likened to a "snowstorm" (Fig. 3.8) which persists until adult life. Sialendoscopy may show diffuse

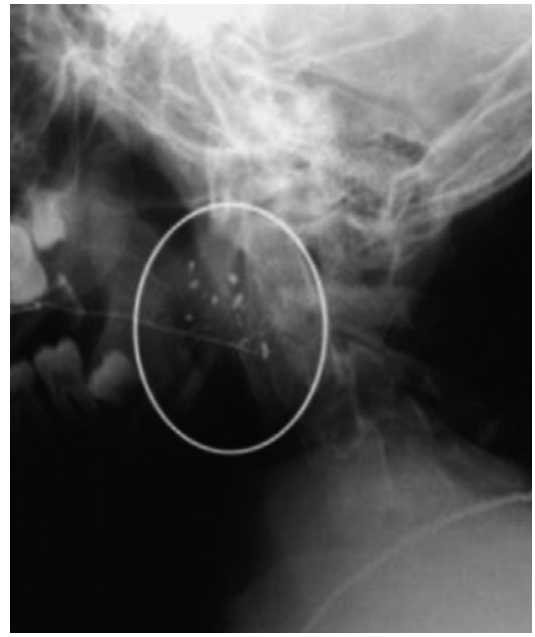

Fig. 3.8 Sialography showing a characteristic punctate sialectasis (snowstorm appearance)

reduction of the caliber of Stensen's duct, associated sometimes with multiple localized stenosis and may be salivary calculi. Endoscopy may also show sialectasia (dilated ductules and acini). Sialendoscopy has proven recently to be effective therapeutically through injection of antiseptic solutions in some cases [57].

No specific treatment is available; however, therapeutic options include good oral hygiene, prophylactic low-dose antibiotics for several months or even years especially if recurrence is frequent, anti-inflammatory agents, sialendoscopy, and total conservative parotidectomy [58].

3.5.5.4 Papillary Obstructive Parotitis

Although there are many recognized causes of obstructive parotitis, however, papillary obstruction due to trauma to the parotid papilla through either an overextended upper denture flange or a fractured upper molar tooth is merely the most common of all. Subsequent edema and then fibrosis of the papilla obstruct salivary flow, especially at mealtimes, in intermittent and then chronic forms, respectively. Thus, the patient suffers from an intermittent painful swelling of the

parotid, accumulating over minutes after the start of his meal. If stenosis ensues, the symptoms will not resolve except by a papillotomy. Obstructive parotitis is less common than obstructive submandibular sialadenitis.

3.5.5.5 Granulomatous Sialadenitis

Granulomatous sialadenitis can result from tuberculosis, mycosis, sarcoidosis, or duct obstruction from calculi or malignant tumors. In the latter instance, the granulomas result from rupture of ducts and may contain small pools of mucin.

Tuberculosis (TB)

Mycobacterium tuberculosis and atypical mycobacterium both affect LNs adjacent to salivary glands or intraglandular LNs. The patient may suffer from one or more of the systemic manifestations of TB such as low-grade fever, night sweating, and anemia. The gland is firm and nodular but may become cystic with sinuses and little pain. Polymerase chain reaction (PCR) is the best preoperative laboratory diagnostic tool, but diagnosis is only confirmed with histopathology following parotidectomy, if needed. Specific treatment of this condition includes multidrug therapy for an average of 1 year together with exposure to direct sunlight, good aeration, and well-balanced nutrition to enhance general health and immunity [59, 60].

Sarcoidosis

Sarcoidosis is a systemic disease involving multiple organs. Its etiology remains unclear, but several hypotheses have been made, including autoantigens and infectious organisms. It resembles TB but with no caseation. Salivary glands are usually affected and specifically the parotid glands. Symptoms include swellings and xerostomia. Sometimes, the disease my present as a mass, and the diagnosis is only made after surgical excision of the presumed tumor: the *sarcoid pseudotumor*. Laboratory diagnosis is made through amylase, kallikrein, and the ACE test. Radiological and histological evidences of noncaseous epithelial granulomas are confirmatory. Corticosteroids are the best therapeutic option. *Heerfordt's syndrome* is a rare form of sarcoidosis that involves parotid swelling, anterior uveitis, facial palsy, and fever (uveoparotid fever). It affects young patients in their third decade [61].

3.5.5.6 Autoimmune Sialadenitis

Mikulicz Disease (MD)

It is an autoimmune disease, which is characterized by chronic, symmetrical, bilateral enlargement of all salivary and lacrimal glands. The disease almost always occurs in association with another underlying disease such as TB, leukemia, syphilis, or systemic lupus erythematosus (SLE). Sometimes patients may experience recurring fever. Patients with MD are at higher risk of developing lymphomas. Some believe that it should be considered a form of Sjogren's syndrome (SS). Actually the main clinical difference between MD and SS is the preservation of the lacrimation and salivation in MD due to much less gland cell apoptosis than that found in SS [62].

Sjogren's Syndrome (SS)

This disease is an autoimmune one involving the parotid glands more frequently than the submandibular glands. Females are affected more than males (10:1). It leads to xerostomia and keratoconjunctivitis sicca due to progressive destruction of both salivary and lacrimal glands. The diseased gland is occasionally enlarged and is occasionally painful. Secondary bacterial ascending infection may occur as a result of dry mouth. Histologically, SS is characterized by massive progressive lymphocytic infiltration, acinar cell destruction, and ductal epithelial cell proliferation affecting all salivary and lacrimal glands. This is the *primary* SS. *Secondary* SS differs in that it is associated with a connective tissue disorder, symptoms are less severe, and the incidence of lymphomatous transformation (most commonly monocytoid B-cell lymphoma) is also less [62].

There is no known specific treatment available to stop Sjogren's syndrome, and thus management is totally symptomatic. Artificial tears and periodic ophthalmological examination is mandatory to avoid corneal ulcerations. Artificial salivary substitutes are available and their importance

increases in the dentate patient where fluoride should be added as well. Usually the patient consumes a large amount of water daily carrying a bottle of water with him all the time [63].

3.5.5.7 Benign Lymphoepithelial Lesion (Myoepithelial Sialadenitis, MESA)

This disease mostly affects females over 50 years of age. Patients present with a diffusely enlarged, firm, and often painful parotid gland, which is bilateral in 20 % of cases. Sialography shows sialectasia, which ranges from punctuate to cavitary. Management is usually parotidectomy to establish a final diagnosis. Histopathological examination of the excised gland carries the very same previously described histopathological features of Sjogren's syndrome, and so the differentiation between both is only done on clinical grounds. Prolonged follow-up of such patients is mandatory as 20 % of them will develop lymphoma at a certain time [64].

3.5.5.8 Other Autoimmune Sialadenitis

Wegener's granulomatosis is an autoimmune disease characterized by upper and lower respiratory and renal disease. The most common salivary gland to be involved is the parotid gland [61]; however, this occurs in less than 1 % of the cases [65]. *Kimura's disease* occurs typically in young Asian males and is characterized clinically by painless lymphadenopathy of the head and neck region, including peri-parotid and intra-parotid LNs [61, 64, 66]. *Chronic sclerosing sialadenitis* presents as a firm localized swelling of the salivary gland mimicking a neoplasm, most commonly involving the submandibular gland. It may be associated with autoimmune extra-salivary disease such as primary sclerosing cholangitis and idiopathic retroperitoneal fibrosis [64].

3.5.6 Sialadenosis (Sialosis)

Sialadenosis is a noninflammatory disorder causing diffuse enlargement of salivary glands, usually the parotid glands and less commonly the submandibular [64, 67, 68], and minor salivary glands [69].

3.5.6.1 Clinical Presentation

Sialadenosis is frequently bilateral and has an equal sex distribution. Most of the patients are between 40 and 70 years of age. There is a painless, soft, and diffuse enlargement of both parotid glands giving the patient a striking facial feature, known as the "*hamster-like appearance*".

3.5.6.2 Etiology

Causes of sialadenosis can be categorized as: (1) *nutritional* (alcoholism, cirrhosis, bulimia, kwashiorkor, and pellagra), (2) *endocrine* (DM, thyroid disorders, gonadal dysfunction), and (3) *neurochemical* (vegetative state, lead and mercury poisoning, iodine, thiouracil, isoproterenol) [64, 68]. However, in many cases no underlying disorder can be detected.

3.5.6.3 Pathogenesis

The proposed pathogeneses include prolonged malnutrition with resultant glandular atrophy and fatty replacement. Sialadenosis is also thought to be a neurosecretory disorder. Diabetic neuropathy may be the clue causing acinar cell atrophy, in some cases. Ultrastructural and animal experimental studies point to a disturbance in the autonomic innervation of salivary glands. This is considered to be the initiating factor for sialadenosis [67, 68, 70–72].

3.5.6.4 Pathology

Grossly, there is only diffuse enlargement of the affected gland. Histologically, the condition is characterized by acinar hypertrophy and fatty infiltration [73]. Zymogen granules are increased in size and number by light and electron microscopy [71]. No inflammation or fibrosis can be detected, which differentiates sialadenosis from sialadenitis. While amyloidosis may also present with diffuse enlargement of the salivary glands, histologically, there will be interstitial fibrosis as well as the characteristic pale amyloid deposition that can be demonstrated with a Congo red stain [74].

3.5.6.5 Treatment

Treatment is in the form of controlling the underlying disorder or withdrawing the incriminated drug. There is usually little morbidity

Table 3.1 Cystic parotid lesions

Bilateral
Warthin's tumor
Benign lymphoepithelial lesions of HIV
Sjogren's syndrome
Sialocele
Unilateral
Warthin's tumor
Sialocele
First branchial cleft cyst: parotid lymphoepithelial cyst
Necrotic LN(s) especially SCC
Infected LN(s)

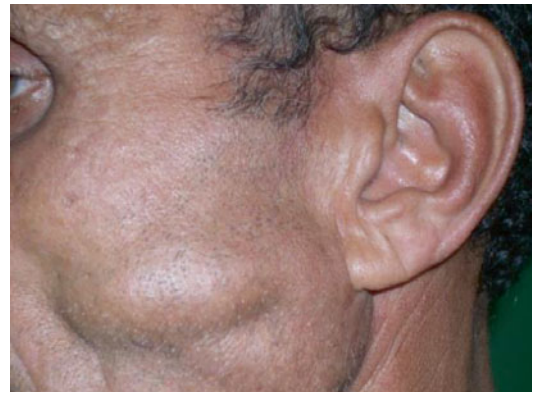

Fig. 3.9 Left parotid duct ectasia

associated with the condition itself, and surgery is resorted to only in case of significant cosmetic complaint.

3.5.7 Cystic Parotid Lesions

Cysts of the parotid gland represent a clinical dilemma. The differential for cystic parotid lesions is summarized in Table 3.1. Apart from the cystic forms of benign and malignant neoplasms, cysts of the parotid gland may be the presentation of a variety of diseases. Such nonneoplastic cysts are uncommon and represent 2–5 % of all salivary gland lesions [75]. A first branchial arch anomaly must be considered when one encounters a case of parotid cyst [76].

Disruption of the parotid duct or parenchyma results in extravasation of saliva into the glandular or peri-glandular tissues forming what is known by *sialocele*. The cause might be either facial trauma or surgery especially when Surgicel is used.

Parotid duct cysts are also known as sialocysts, simple cysts, and retention cysts and result from obstruction due to various causes [74, 77, 78]. They are true cysts lined by epithelium, unlike *mucocele*, which is lined by granulation tissue [77]. Parotid duct cysts should not be confused with duct ectasia (Fig. 3.9).

Duct cysts are unilocular and may grossly contain mucoid material or sialoliths in long-standing cases. Histologically, they are lined by a cuboidal, columnar, or squamous epithelium, though oncocytic metaplasia may be seen in older patients. However, these cysts are not associated with lymphoid elements [64]. Prognosis is excellent. Complications are rare and include superimposed infections. Recurrence is also rare and results from incomplete excision [64].

Dermoid cysts [78] and *hydatid* cysts [79] have also been reported in the parotid, yet they are exceptionally rare.

3.5.8 Tumors of the Parotid Glands

3.5.8.1 WHO Histological Classification of Tumors of Salivary Glands

Benign Epithelial Tumors

- Pleomorphic adenoma (PA) (mixed salivary tumor)
- Myoepithelioma
- Basal cell adenoma
- Warthin's tumor (adenolymphoma, papillary cystadenoma lymphomatosum)
- Oncocytoma
- Canalicular adenoma
- Sebaceous adenoma
- Lymphadenoma
  - Sebaceous
  - Non-sebaceous
- Duct papilloma
  - Inverted duct papilloma
  - Intraductal papilloma
  - Sialadenoma papilliferum
- Cystadenoma

Malignant Epithelial Tumors
- Acinic cell carcinoma
- Mucoepidermoid carcinoma (MEP)
- Adenoid cystic carcinoma (ACC)
- Polymorphous low-grade adenocarcinoma (PLGA)
- Epithelial-myoepithelial carcinoma
- Clear-cell carcinoma, not otherwise specified
- Basal cell adenocarcinoma
- Sebaceous carcinoma
- Sebaceous lymphadenocarcinoma
- Cystadenocarcinoma
- Low-grade cribriform cystadenocarcinoma
- Mucinous adenocarcinoma
- Oncocytic carcinoma
- Salivary duct carcinoma
- Adenocarcinoma, not otherwise specified
- Myoepithelial carcinoma
- Carcinoma ex-pleomorphic adenoma (CEPA)
- Carcinosarcoma (malignant mixed salivary tumor)
- Metastasizing pleomorphic adenoma
- Squamous cell carcinoma
- Small cell carcinoma (SCC)
- Large cell carcinoma
- Lymphoepithelial carcinoma
- Sialoblastoma

Soft Tissue Tumors
- Hemangioma

Hematolymphoid Tumors
- Hodgkin's lymphoma
- Diffuse large B-cell lymphoma
- Extra-nodal marginal zone B-cell lymphoma

Secondary Tumors

Tumors of the salivary glands are relatively uncommon and represent less than 2 % of all head and neck neoplasms.

3.5.8.2 Benign Tumors (BTs)

Salivary gland BTs occur mostly in the parotid gland, and most of them are pleomorphic adenomas. The BT usually presents as a slowly growing painless mass in front of the tragus of the ear, below the ear lobule, or in upper part of the neck, arising from the superficial lobe of the gland which represents 80 % of the cases. Less commonly, the mass presents as a cheek mass overlying the masseter, arising from the accessory parotid lobe. If the tumor arises from the deep lobe, it presents as a parapharyngeal mass with completely different clinical presentation. In this instance, the patient will complain of difficultly in swallowing and snoring, and physical examination will reveal a soft palate and tonsillar firm, diffuse bulge.

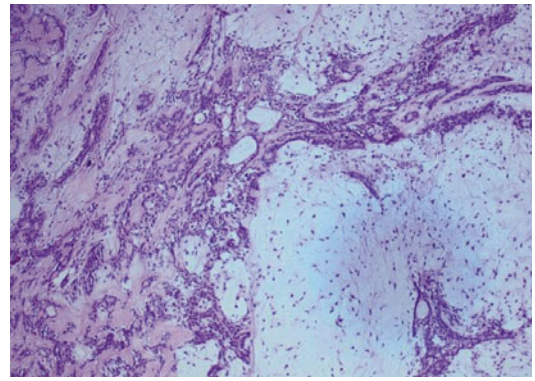

Fig. 3.10 Pleomorphic adenoma: biphasic population of epithelial and mesenchymal cells. Epithelial cells assume tubular profiles, cords, or nests. Stroma is myxoid (H&E, ×100)

Pleomorphic Adenoma (PA)

This *mixed salivary tumor* represents 75–80 % of all benign parotid tumors. It may affect as well the submandibular and minor salivary glands. Its incidence is slightly higher in females and affects most commonly patients between 30 and 50 years of age [80–82]. It is uncommon to be bilateral [78, 83]. It is usually a solitary lesion, although synchronous or metachronous involvement of two or more salivary glands can occur. It may also occur in combination with other tumors, mostly Warthin's tumor.

It is a well-defined tumor, but with small extensions into the adjacent normal tissue through an incomplete capsule, which explains the recurrence after enucleation. It has a pleomorphic matrix, with a non-cystic cut section that may show some islets of cartilage. Microscopically, it is formed of epithelial cells intermingled with a pleomorphic stroma: fibrous, myxomatous, and pseudo-cartilaginous (Fig. 3.10). It is categorized into four types: (1) principally myxoid, (2)

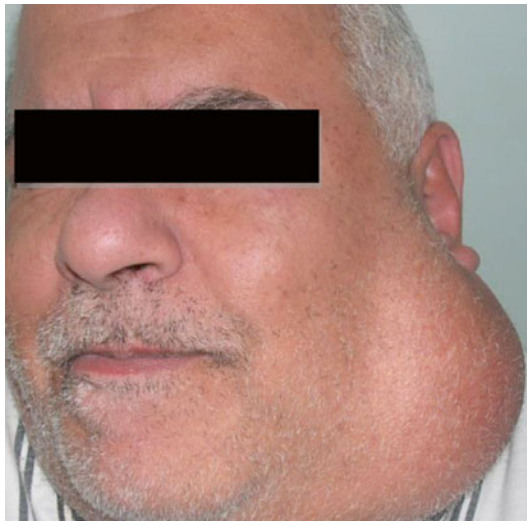

Fig. 3.11 A large left pleomorphic adenoma (PA) of the parotid gland in a 56-year-old male patient

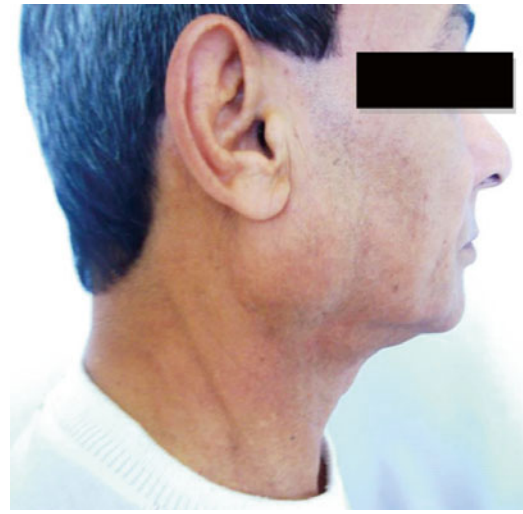

Fig. 3.12 Pleomorphic adenoma in its typical position over the angle of the mandible and below the lobule of the ear

mixed myxoid and cellular components in equal proportions, (3) predominantly cellular, and (4) extremely cellular [84].

It carries a malignant potential of 5–10 %. The presence of hyalinized stroma is the most predictive histological parameter for malignant transformation. The tumor may rarely metastasize without having the histological features of malignancy, but this almost always occurs after inadequate surgical excision, possibly due to altered anatomy secondary to surgery, which gave access to vascular and lymphatic channels.

Roughly 70 % of PAs have cytogenetic alterations that likely play a major role in pathogenesis (tumorigenesis) and can be categorized into 4 groups: those with 8q12 rearrangements, those with 12q13-15 rearrangements, those with miscellaneous clonal changes, and those that are karyotypically normal [85, 86].

The patient presents with a painless, slowly growing, spherical mass, of variable size ranging from pea-size to a large mass, 20–50 cm across [87–89] (Fig. 3.11). The mass usually lies over the angle of the mandible and below the lobule of the ear (Fig. 3.12). However, a swelling of the lower pole of the parotid gland may present in the lateral side of the neck, below and behind the angle of the mandible, giving rise to clinical diagnostic difficulty (Fig. 3.13). The patient's complaint is usually disfigurement. The mass is of heterogonous consistency and mobile, being neither attached to the skin nor to the deep structures. Bosselation of the tumor is demonstrable if it is bigger than 3 cm.

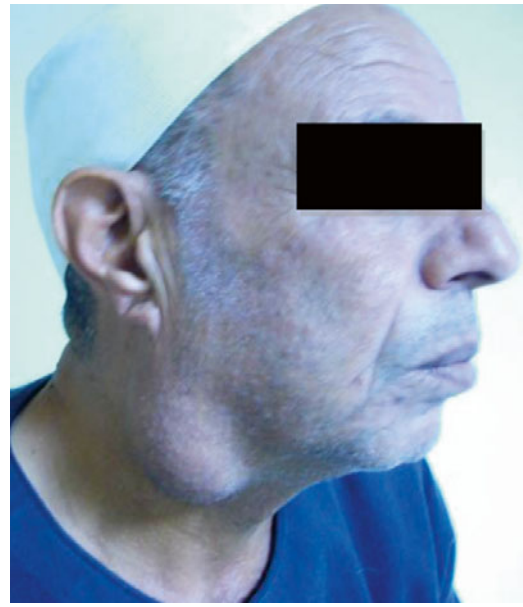

Fig. 3.13 Pleomorphic adenoma arising below and behind the angle of the mandible. Not related to the ear lobule

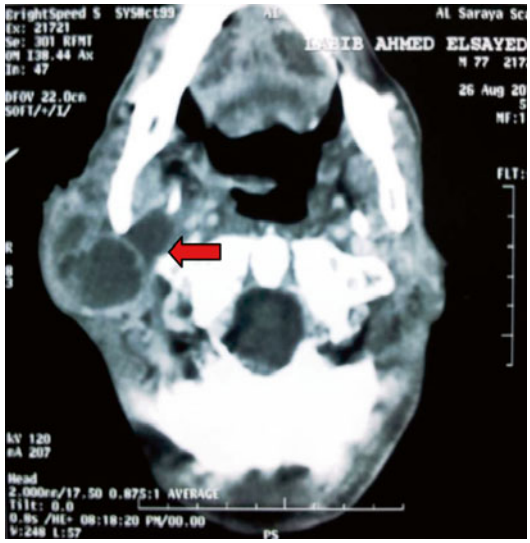

Fig. 3.14 CT scan showing extension of the PA to involve the deep lobe of the parotid gland (*red arrow*)

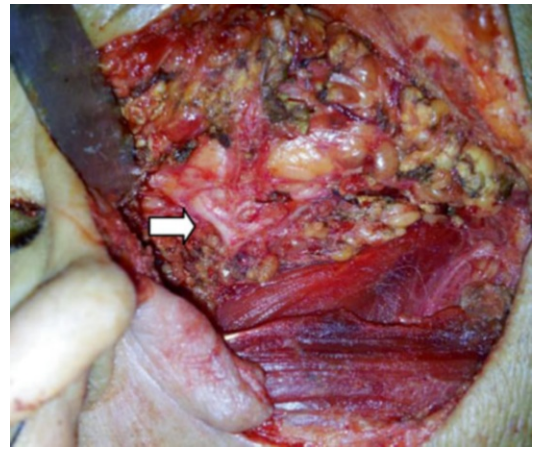

Fig. 3.15 Dissection of the main trunk and only one division, related to the parotid mass (*white arrow*)

While most PAs occur in the superficial lobe of the parotid gland (80 %) [90–92], the deep lobe can be involved (20 %) and is clearly demonstrable by CT scan (Fig. 3.14). Extensions of deep lobe PAs are the most common tumors of the parapharyngeal space constituting 40 % of tumors in this region [83, 92]. The draining LNs are not enlarged and the facial nerve is always intact.

As for any parotid mass, US, CT, and MRI (preferably with diffusion-weighted and perfusion sequences) are the best imaging tools. Fine-needle aspiration cytology (FNAC) is a recognized method for obtaining preoperative diagnosis and is advised to be done after imaging for the fear of hemorrhage. Many studies showed that the use of flow cytometry as a biological parameter for the prediction of recurrence in PAs should be considered. Tumors of a larger size showed a higher percentage of cells in the S-phase fraction and probably a greater tendency for recurrence [93].

Treatment is through surgical excision. Superficial or total conservative parotidectomy with preservation of the facial nerve is done. Partial superficial parotidectomy and extracapsular dissection are other recognized options of resection [94–96]. Partial superficial parotidectomy entails dissection of the main trunk of the facial nerve and only one division with its terminal branches (Fig. 3.15). Enucleation is never done for its high recurrence rate. The skin incision can be the classical lazy-S incision, or recently one can resort to the cosmetically better face-lift incision.

The flaps are raised and the facial nerve trunk is exposed at the stylomastoid foramen, and all its five terminal branches are followed to the muscles to avoid their injury. The incidence of recurrence following surgery varies depending on the surgical technique used, the experience of the surgeon, and the duration of patient's follow-up [97]. Whatever the series and its duration of patient follow-up, a recurrence rate of less than 1 % is considered acceptable. Recurrent PAs have a higher likelihood for second recurrence of about 6–15 % [98]. Uninodular recurrences have a better outcome than multinodular recurrences [99, 100].

Warthin's Tumor (Adenolymphoma)

Warthin's tumor represents about 5 % of all benign parotid tumors and is bilateral in 5–10 % of cases. It occurs almost exclusively in the parotid gland, affecting males more than females. The ratio has decreased drastically during the past 50 years to 2:1 [101, 102]. This gender predilection shift is referred to that it is highly linked to smoking. Smokers have an 8 times higher incidence of developing Warthin's tumors than nonsmokers [103]. The mean age is 62 years. Patients are rarely below 40 years [104, 105].

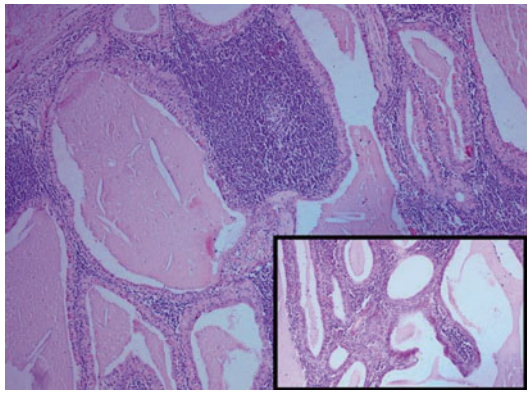

Fig. 3.16 Warthin's tumor: cystic spaces lined by double layer of epithelial cells resting on dense lymphoid stroma. *Inset* depicts intracystic polypoid projections with lymphoid stroma (H&E, ×100)

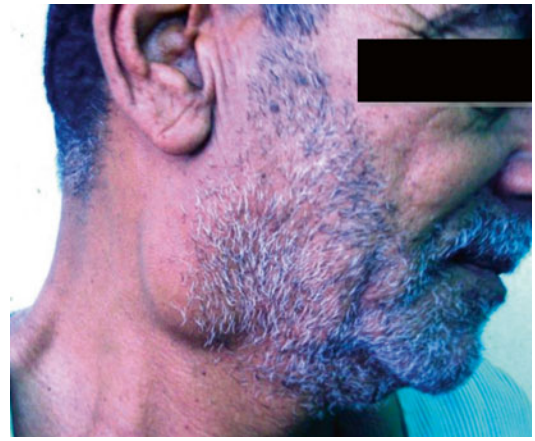

Fig. 3.17 Right adenolymphoma presenting as a small (3-cm), smooth, mass in a 61-year-old gentleman

Macroscopically, it is a reddish-brown mass with a true capsule. Its cut section has many cystic spaces, and the fluid content is characteristically granular brown resembling "motor oil". Under the microscope, it is comprised of a papillary proliferation lined by a double layer composed of surface columnar oncocytic epithelium and a smaller basal layer of small cuboidal cells with myoepithelial characteristics. The surrounding stroma contains a highly ordered lymphoid architecture similar to an actual LN (Fig. 3.16). When Warthin's tumor arises in a cervical LN, it may be mistaken for metastatic carcinoma, particularly from a papillary thyroid carcinoma. Malignant transformation is extremely rare where MEC is the most common histology. The lymphoid component may lead to lymphoma.

The mass is painless, slowly growing, soft, freely mobile, and usually 1–3 cm in diameter. It does not attain a huge size (Fig. 3.17). It has a smooth surface and homogenous consistency and is sometimes cystic. It is often multifocal and may be fixed to the overlying skin [106]. Rarely, infarcted Warthin's tumors may cause pain [102]. Adenolymphoma is the only parotid tumor that can give a hot spot in Tc^{99} scan. If the preoperative diagnosis is certain, then enucleation can be added to the operative options of the surgeon as the tumor is well capsulated and does not recur.

Basal Cell Adenoma (BCA)

Basal cell adenoma tends to occur over the age of 50 years with a female-to-male ratio of 2:1 [107]. It usually occurs in the parotid gland (75 %), much less commonly in the submandibular gland (5 %) [108], and rarely in the minor salivary glands with the exclusion of canalicular adenomas, which were previously categorized with BCA [109, 110]. It typically presents as a slowly growing solitary painless mass [64]. A special variant of BCA, the membranous type (dermal analog tumor) has a propensity for multifocality and can be associated with multiple trichoepitheliomas and cylindromas (*Brooke-Spiegler syndrome*) [111]. Prognosis of BCA is generally excellent. Recurrence rate is low, except for the membranous subtype, which may recur in about 25 % of cases. Malignant transformation is rare, again favoring the membranous subtype [101, 112, 113].

Canalicular Adenoma

Canalicular adenoma, previously categorized with BCA, is a rare tumor comprising <1 % of all salivary tumors [101, 112, 113]. The mean age is 65 years with a female-to-male ratio of 1.8:1 [101, 114]. It rarely affects the parotid glands [101]. The minor salivary glands of the upper lip are the ones most commonly involved (80 %) followed by the buccal mucosa [113] and palate [115]. It typically presents as painless, slowly growing submucosal nodule. Rarely, multiple/

multifocal canalicular adenomas may occur and present clinically with multiple discrete masses, typically occurring in the upper lip and buccal mucosa [64]. The prognosis is excellent and recurrences are extremely rare. Some of these recurrences may be considered as separate tumors [101, 116].

Myoepithelioma

Myoepitheliomas account for about 1.5 % of all salivary tumors. This tumor primarily affects adults with a peak incidence in the third to fourth decades (range 8–82 years) [117, 118]. The parotid gland is the most common site affected (40–50 %), followed by the minor salivary glands in the palate [64]. It usually presents as a slow-growing painless mass. Prognosis is generally favorable; recurrences are relatively rare and are usually the result of incomplete excision [119]. Malignant transformation is uncommon [120].

Cystadenoma

Cystadenoma is a rare benign cystic salivary tumor that resembles Warthin's tumor, though with different clinicopathologic features. Unlike Warthin's tumor, there is a slight female predilection, there is no association with smoking [101, 121], and it is not exclusive for the parotid gland, though it is affected in nearly half of the cases. Other sites include the lip and buccal mucosa [122] and rarely the supraglottic larynx [123]. It affects adults with a mean age of 57 years [124]. Prognosis of cystadenoma is excellent; complete excision is curative.

3.5.8.3 Malignant Tumors

Parotid cancer represents <1 % of all body cancer and about 20 % of all parotid tumors. It is either de novo or on top of PA. There is no sex predilection or males are slightly more affected. Age of developing this cancer is usually above 50 years.

Signs of malignant transformation in a preexisting BT include rapid rate of growth, harder consistency, or fixation to the underlying muscles or the overlying skin, which may be severe enough to show fungation (Fig. 3.18). The patient may develop pain and tenderness which are usually due infiltration of the auriculotemporal nerve with the pain being referred to the ipsilateral ear. Trismus due to invasion of the masseter or pterygoid muscles or due to restricted movements of the temporomandibular joint (TMJ) is another finding.

In 10–15 % of the cases, the facial nerve will be paralyzed. Unequal pulsations of superficial temporal artery may as well be noticed. Manifestations of metastases to regional LNs or distant organs such as the lungs or the liver may ensue. On the first suspicion of any change in the behavior of the preexisting tumor, FNAC should be done immediately after MRI preferably with a diffusion-weighted and perfusion sequences.

Spread of parotid malignancy occurs through the well-established routes of metastases, where the first echelon LN is the intra- and peri-glandular nodes. The next echelon is level II LNs. Local spread can affect any of the critical nearby organs. Hematogenous spread occurs very late and is mainly to the lungs and bones particularly the vertebral column. However, adenoid cystic carcinoma (ACC) tends to grow through perineural lymphatics with increased risk of nerve affection and intracranial extension, as well as increased rate of recurrence.

Mucoepidermoid Carcinoma (MEC)

This is the most common malignancy of the salivary glands [125] and that of the parotid gland (80 % of cases) seems to be less aggressive than that of the submandibular gland (8–13 % of cases) and of better prognosis [126]. It mostly occurs around an age of 50 years, but still, it is the most common salivary malignancy of the pediatric age group [126, 127].

Low-grade and high-grade variants are recognized, where the low-grade one very rarely metastasizes [128–130]. It usually presents as a slowly growing painless mass; however, rapid growth, pain, and tenderness may be seen with the high-grade variant [131, 132] (Fig. 3.19). Metastases occur to LNs, lungs, and bones [126]. Treatment is surgical resection. Neck dissection is needed in high-grade variants [128].

Prognosis is influenced by the grade and stage of the tumor and patient's age and gender. Overall 5-year survival rates range from 92 to 100 % for low-grade tumors and 0 to 43 % for high-grade tumors [133].

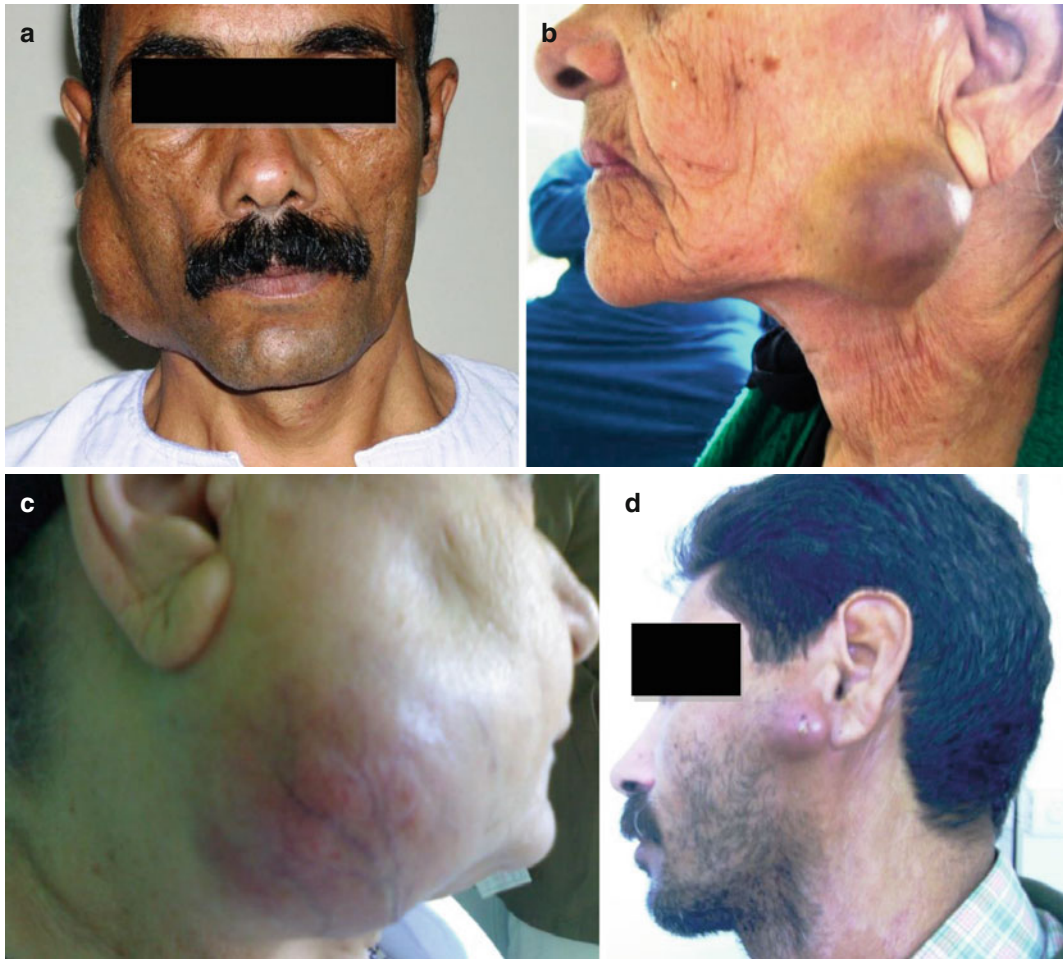

Fig. 3.18 Malignant tumors of the parotid gland present with a hard, rapidly growing mass (**a**) that may become fixed to the overlying skin (**b**) and with erythema and increased vascularity (**c**) miming an abscess and may be severe enough to show fungation (**d**)

Adenoid Cystic Carcinoma (ACC)

This tumor has been given many names since it was first described by *Robin and colleagues* in 1853. From these names, "cylindroma" was particularly discouraged to avoid confusion with the benign cutaneous appendage tumor carrying the same name. This tumor arises not only from major and minor salivary glands but also from seromucous glands throughout the body [134, 135]. It is the second most common salivary malignancy and affects patients between 40 and 60 years of age. It is a slowly growing tumor frequently presenting as a painless mass giving a false sense of security. Lymph node metastases are uncommon, but distant metastases occur in up to 60 % of the cases, mainly to the liver, lung, bones, and brain [135, 136]. It has a high affinity to perineural invasion, which results in paresthesia or paralysis of the nerve affected.

Histologically, low-grade (Fig. 3.20) and high-grade (Fig. 3.21) variants are recognized. Best results of treatment are obtained through radical surgery and postoperative radiotherapy. The tumor is radiosensitive but not radiocurable. Although controversial, neck dissection may be reserved for patients with clinically positive LNs [136–138]. Some studies showed that age over 45 years, advanced clinical stage, paresthesia, as

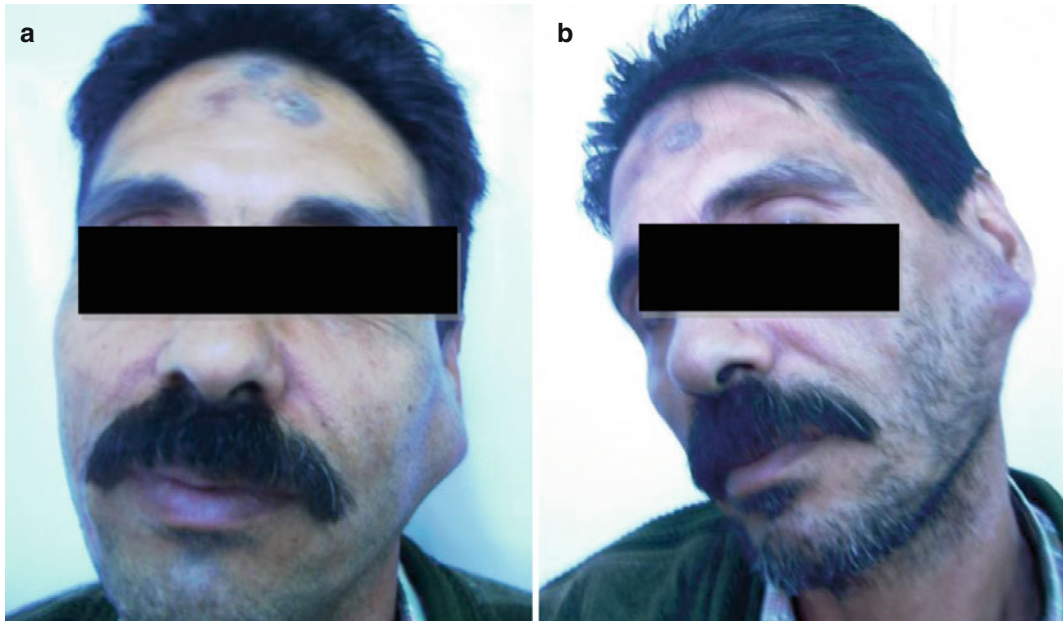

Fig. 3.19 A rapidly growing (high-grade) mucoepidermoid carcinoma (MEC) in a 51-year-old gentleman (**a**) that became fixed to the overlying skin (**b**) within 2 weeks of presentation

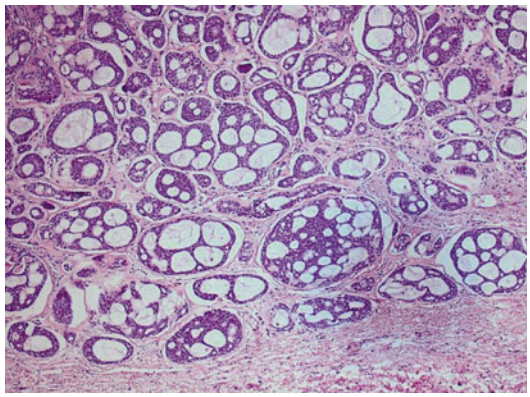

Fig. 3.20 Low-grade adenoid cystic carcinoma (ACC) with a notable cribriform pattern (H&E, ×100)

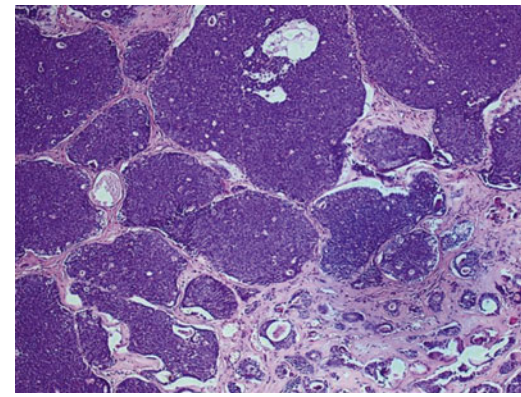

Fig. 3.21 High-grade adenoid cystic carcinoma (ACC) with a predominant (>70 %) solid pattern. The lower right corner still depicts tubular structures (H&E, ×100)

well as increased expression of p53 are associated with poor prognosis [135, 136].

Carcinoma Ex-pleomorphic Adenoma (CEPA)

This is by definition the malignant transformation of a long-standing PA, which occurs in about 25 % of such cases [138–140]. Clinical features predictive of malignant transformation are age, tumor size, long history, and submandibular location. Histologically, the presence of hyalinized stroma is the most predictive parameter for malignant transformation [64, 108]. The carcinoma is usually a high-grade adenocarcinoma or an undifferentiated carcinoma although numerous other types including SCC, MEC, ACC, myoepithelial carcinoma, clear-cell carcinoma, papillary carcinoma, and terminal duct carcinoma

have been reported. Carcinoma ex-pleomorphic adenoma (CEPA) occurs in the major salivary glands in 80 % of the cases, from which again 80 % occurs in the parotid gland. The average age at diagnosis is 50–60 years, which is approximately 10 years older than most individuals with PA. It is extremely uncommon in individuals below the age of 20 years [138, 141]. In 12–55 % of cases, rapid enlargement will be painful and often associated with facial nerve palsy and fixation to the surrounding soft tissues [142].

This carcinoma metastasizes in up to 70 % of the cases to distant sites rather than regionally, with special affinity to the lungs and the vertebral column. Treatment is surgical resection usually with neck dissection. In situ variant is that tumor which did not invade the capsule of a PA and thence was diagnosed postoperatively. In this case, the performed standard resection of a PA is considered curative.

True Malignant Mixed Tumor (TMMT)

True malignant mixed tumor is a very rare neoplasm that may be regarded as carcinosarcoma since both epithelial and stromal components are histologically malignant and both can metastasize. Such metastases are more commonly via a hematogenous rather than lymphatic route, with the lungs and bones being the most frequent sites [143, 144]. There is a wide range of age affection (14–87 years) and there is no sex predilection [144, 145]. Clinical presentation is similar to that of CEPA. Treatment is surgical resection, combined with radiation and chemotherapy. Even with such radical treatment, most patients die within 5 years [141].

Acinic Cell Carcinoma

It is a rare tumor, which is indistinguishable clinically from benign parotid neoplasms being of low-grade malignancy [146, 147]. Yet, it can rarely dedifferentiate into an aggressive high-grade tumor. The parotid gland is the most common site (80 %) followed by the minor salivary glands (16 %) and the submandibular gland (4 %). It is second to Warthin's tumor in bilateral incidence [148], and second to MEC in pediatric age group involvement [149]. Patients typically present with a slowly enlarging painless mass that is not fixed to the surrounding soft tissue or skin. Pain occurs in approximately 22 % of patients and facial nerve palsy in nearly 3–8 % [146, 150].

Treatment is complete surgical resection. Neck dissection is usually not recommended because of the relatively low incidence of metastases to regional LNs [146]. It is usually radioresistant; however, radiotherapy is resorted to when complete resection is not achieved, in case of perineural invasion and if LNs are affected [151, 152]. The recurrence rate averages 10–35 % and the distant metastatic rate 13–16 % [146, 148]. The 5-year survival rate ranges from 78 to 90 % [153, 154].

Basal Cell Adenocarcinoma

Basal cell adenocarcinoma is the malignant counterpart of basal cell adenoma (BCA). It is an uncommon low-grade malignancy that accounts for approximately 1.5 % of all salivary gland tumors and 3 % of all salivary gland malignancies [155]. There is no sex predilection [156], and most patients are in their sixth or seventh decade, although cases have been reported in individuals as young as 2 months and as old as 92 years [155–160]. Most of these tumors arise de novo, as origin in a preexisting BCA is uncommon and usually involves the membranous subtype [156, 157, 160]. Approximately 90 % of the tumors arise in the major salivary glands with the vast majority involving the parotid gland [161]. Patients usually present with a slowly growing asymptomatic mass. Pain and tenderness are uncommon [162]. In 10–15 % of cases, it occurs in conjunction with dermal cylindromas and trichoepitheliomas. This association is lower than the 40 % association of BCA with these dermal tumors [163]. Treatment is complete surgical excision, with neck dissection being reserved for patients with clinically positive LNs [119, 164, 165].

Myoepithelial Carcinoma (Malignant Myoepithelioma)

Myoepithelial carcinoma is the malignant counterpart of myoepithelioma. By definition it is composed of myoepithelial cells with an infiltrative growth pattern. It is a rare tumor accounting for

only 0.2 % of all epithelial salivary gland tumors [119] and involving the parotid glands in 75 % of cases [119, 163, 164]. Approximately 50 % of cases arise in a preexisting BT, usually a PA or a myoepithelioma. Myoepithelial carcinoma is most common in the sixth and seventh decades and occurs with no sex predilection [119]. A painless mass is usually the only clinical complaint. Treatment is complete surgical excision. The clinical behavior of this tumor is unpredictable and unrelated to histological features [165].

Cystadenocarcinoma

Cystadenocarcinomas of the salivary glands are low-grade cystic neoplasms, which are twice as common in the major salivary glands as in the minor salivary glands, and most frequently occur in the parotid [166]. The majority of patients (75 %) are over the age of 50 years [166]. Recognizing these tumors as carcinomas is predicated by finding areas of infiltrative growth. Perineural invasion is not a feature of this neoplasm. Complete surgical excision is usually curative as these tumors are of low-grade malignancy [167].

3.5.9 Parotidectomy

3.5.9.1 Superficial Parotidectomy

The operation is performed under *general anesthesia* with endotracheal intubation with the patient lying supine with the neck hyperextended and the neck turned to the opposite side. If facial nerve monitoring is to be used intraoperatively, nerve electrodes are placed in the ipsilateral facial muscles and tested for electrical integrity.

A modified *Blair (lazy-S) incision* is planned in the preauricular skin crease just in front of the external auditory meatus (EAM), coursing around the ear lobule to the base of the mastoid process and then into an upper neck crease. An alternative incision is a *modified face-lift incision*, which starts behind the tragus down to the lobule of the ear and then behind the ear in the crease and then curved in the hairline for a short distance as indicated.

The skin incision is carried down through the subcutaneous (SC) tissues and platysma muscle. Care is taken to avoid division of the greater auricular nerve. An anterior thick flap is elevated superficial to the greater auricular nerve (which is preserved whenever possible) and the parotid fascia. A posterior, inferior flap is also elevated to expose the tail of the parotid gland. The flaps are retracted with silk sutures or self-retaining hooks.

The tail of the parotid gland is dissected off of the sternocleidomastoid (SCM) muscle and is then elevated to expose the posterior belly of the digastric muscle, which serves as a landmark for the facial nerve. The preauricular space is opened by division of the attachments of the parotid gland to the cartilaginous external auditory canal to expose the tragal cartilage *pointer*, which serves as another landmark for the facial nerve. Thus, identification of the facial nerve is guided by certain anatomic landmarks that include the posterior belly of the digastric muscle, the mastoid tip, the tragal cartilage pointer, and the tympanomastoid suture. If the proximal segment of the facial nerve is obscured, retrograde dissection of one or more of the peripheral facial nerve branches may be necessary to identify the main trunk.

Once the facial nerve is identified, the parotid gland superficial to the facial nerve is divided carefully, preserving the integrity of the nerve. Any bleeding that occurs related to division of the gland is carefully controlled under vision. The facial nerve is followed peripherally, the desired portion of the gland is dissected from successive facial nerve branches and the specimen removed (Fig. 3.22). The facial nerve is preserved except in cases when confirmed malignancy is found invading the nerve. Immediate nerve reconstruction by a nerve interposition graft is usually indicated if resection of the nerve is performed.

A neck dissection is performed for clinically positive LNs. For the clinically negative neck, the first echelon nodes are inspected. Enlarged or suspicious LNs are examined, and a neck dissection is performed if metastatic disease is confirmed by frozen section.

The wound is irrigated with normal saline solution and closed in layers over a closed suction drain, which is usually removed on the first

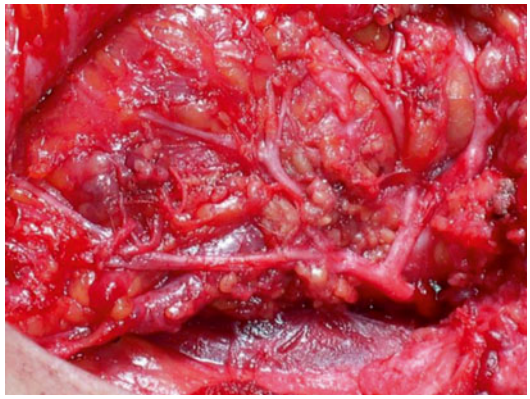

Fig. 3.22 The facial trunk is dissected and followed peripherally to expose and preserve the two divisions and terminal branches before removing the specimen

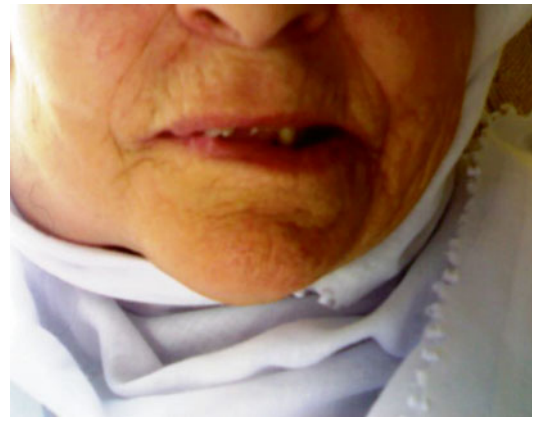

Fig. 3.23 Deviation of the angle of the mouth toward the sound side

Table 3.2 Complications following parotidectomy

Early complications	Late complications
Facial nerve palsy	Frey's syndrome
Bleeding/hematoma	Hypertrophic scar/ keloid
Surgical site infection (SSI)	Recurrence
Skin flap necrosis	Unsightly scar
Salivary fistula/sialocele	Soft tissue defect
Seroma	
External otitis	
Trismus	

postoperative day and the skin sutures are removed within 1 week.

Adjuvant radiation therapy is recommended for selected malignancies including metastatic cutaneous SCC and high-grade and advanced parotid malignancies.

Complications

Early and late complications of superficial parotidectomy are summarized in Table 3.2.

Temporary facial nerve paralysis involving all or any of the branches of the nerve occurs in 10–30 % of superficial parotidectomies [168–172], while *permanent paralysis* occurs in <1 % [171, 172]. The nerve at most risk for injury is the marginal mandibular branch resulting in deviation of the angle of the mouth toward the normal (sound) side (Fig. 3.23) [170–172]. Temporary paresis usually resolves from weeks to months postoperatively. Nerve transection requires immediate microsurgical repair.

Hemorrhage or hematoma is uncommon after superficial parotidectomy and is usually related to incomplete hemostasis during the procedure. Treatment consists of evacuation of the hematoma and surgical control of any identified bleeding vessels under general anesthesia.

Infection is also an uncommon complication after superficial parotidectomy due to the rich vascular supply to the parotid region. It is avoided by the use of aseptic techniques and careful handling of tissues. Perioperative antibiotics are generally not used. Treatment of infection consists of appropriate antibiotics. Abscess formation is rare and requires surgical incision and drainage together with the appropriate antibiotics. *External otitis* can occur postoperatively and can be related to intraoperative blood collection in the external auditory canal. Treatment consists of cleaning the auditory canal and instillation of antibiotic eardrops.

Skin flap necrosis is an uncommon complication. The distal tip of the postauricular skin flap is the most common location of flap necrosis. Smoking, prior radiation therapy, and DM may contribute to this complication by impairing the blood supply to the flap. Treatment entails conservative debridement of necrotic tissue and local wound care.

Salivary fistula or sialocele can occur after superficial parotidectomy in nearly10 % of cases [173] and results from leakage of saliva from

remaining salivary gland tissue. It is usually mild and self-limited. A sialocele is usually treated with repeated needle aspirations. A salivary fistula is managed with local wound care. A chronic salivary fistula is rare following superficial parotidectomy.

Mild trismus may occur following superficial parotidectomy and may be related to inflammation and fibrosis of the masseter muscle. This complication usually resolves with range of motion exercises of the jaw.

Frey's Syndrome (Gustatory Sweating)

Frey's syndrome is now considered an inevitable long-term complication following parotidectomy unless preventive measures are taken [174]. It results from aberrant reinnervation of cholinergic sympathetic sweat glands in the skin with postganglionic fibers from the auriculotemporal nerve that have been exposed following parotidectomy. Thus, a stimulus intended for saliva stimulation evokes hyperesthesia and sweating. The patient complains of facial sweating and hotness on smell or taste of food, which might sometimes be associated with pain. Diagnosis can be confirmed with starch-iodine test.

Preventive measures include SCM flap, temporalis fascial flap, and insertion of an artificial membrane between the skin and the parotid bed. Treatment options include auriculotemporal nerve avulsion and/or tympanic neurectomy. Medical treatment of symptomatic Frey's syndrome includes topical application of antiperspirant and topical anticholinergics (1 % glycopyrrolate); however, recently, local intradermal injection of botulinum toxin has yielded good results. Botulinum toxin blocks the release of acetylcholine from presynaptic neurons. It is postulated to provide long-term results due to poor reinnervation of the skin's cholinergic sweat glands. It is performed as an outpatient.

3.5.9.2 Total Parotidectomy

While superficial parotidectomy entails removal of the lateral portion of the parotid gland with preservation of the facial nerve, total parotidectomy is complete removal of the superficial and deep lobes of the parotid. It should be performed for MTs in the following situations: (1) metastasis to a superficial parotid LN from a primary parotid tumor or an extra-parotid malignancy, (2) any parotid malignancy with metastatic involvement of cervical LNs, (3) any high-grade parotid MT with a high risk of metastasis, (4) primary parotid MT originating in the deep lobe, and (5) primary malignancies that extend outside the parotid gland. Total parotidectomy is also performed for multifocal tumors, such as oncocytomas, to ensure complete resection. The operation may involve sparing or sacrificing the facial nerve branches or trunk depending on tumor extent to the nerve.

3.5.9.3 Extended Total Parotidectomy

Excision of the superficial and deep lobes of the parotid gland (total parotidectomy) may also be extended to involve adjacent structures such as the overlying skin, the underlying mandible, the temporal bone and external auditory canal, or the deep musculature of the parapharyngeal space. Such extensions are dictated by tumor growth and behavior. Patients with extensive parotid malignancies should be counseled regarding the possibility of extended resections and the resulting functional and cosmetic morbidity. The head and neck surgeon needs to anticipate the extent of defect and incorporate plans for reconstruction into the overall surgical plan.

3.6 Submandibular Glands

The submandibular gland is the second largest major salivary gland and weighs approximately 10 g. It is classified *as mixed gland* that is predominantly serous with tubular acini. Approximately 90 % of acinar cells are serous and only 10 % are mucinous.

3.6.1 Surgical Anatomy

The submandibular gland is located in the submandibular triangle, which is bounded superiorly by the inferior edge of the mandible and inferiorly by the anterior and posterior bellies of the

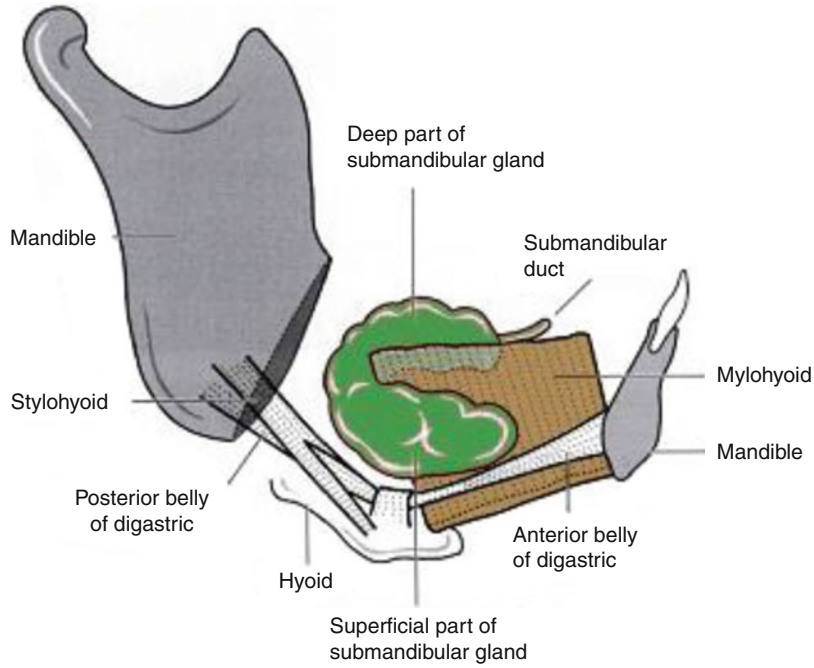

Fig. 3.24 Relationship of the superficial and deep parts of the submandibular gland with the mylohyoid muscle

digastrics muscle. It contains several important neurovascular structures, in addition to the submandibular gland, namely, the marginal mandibular branch of facial nerve, the lingual nerve, the hypoglossal nerve, and the facial artery, as well as lymph nodes (LNs) that can harbor regional metastases from oral and oropharyngeal primary tumors [4, 16, 17].

The submandibular gland lies on the hyoglossus muscle, superficial to the hypoglossal and lingual nerves, and can be arbitrarily divided into superficial and deep parts or lobes according to its relationship with the mylohyoid muscle (Fig. 3.24). The superficial lobe lies superficial to the muscle, reaching upward under cover of the mandible, and is separated posteriorly from the parotid gland by the stylomandibular ligament (Fig. 3.25).

The smaller deep lobe wraps around the posterior aspect of the mylohyoid muscle, and its anterior end reaches as far as the sublingual gland (Fig. 3.26). During submandibular sialoadenectomy or neck dissection, the mylohyoid muscle must be gently retracted anteriorly to expose the lingual nerve and the submandibular ganglion.

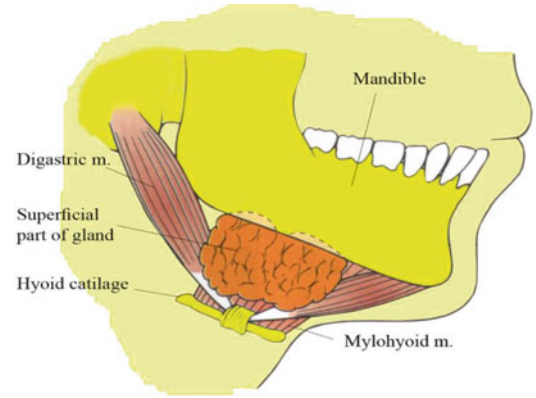

Fig. 3.25 The superficial part of the submandibular gland lying on the mylohyoid muscle and reaching up under cover of the mandible

3.6.1.1 Fascia

The submandibular gland is covered by a capsule derived from the middle layer of the deep cervical fascia. The marginal mandibular branch of the facial nerve lies superficial to this fascia. Thus, division of the submandibular gland fascia, when oncologically appropriate, is a reliable method for preserving the nerve during neck dissection and/or gland resection.

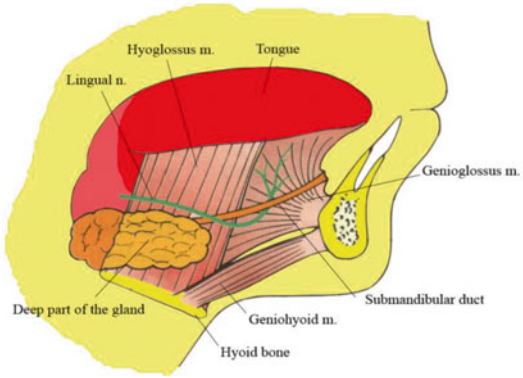

Fig. 3.26 The deep part of the submandibular gland lying on the hyoglossus muscle and the submandibular duct emerges from its anterior end. At the anterior edge of the muscle, the duct is crossed laterally by the lingual nerve

3.6.1.2 Submandibular Duct (Wharton's Duct)

The submandibular gland has both mucous and serous cells that empty into ductules, which in turn empty into the submandibular duct (Wharton's duct) (*Thomas Wharton, 1616–1675, Physician, St. Thomas's Hospital, London, UK*), which is about 4–5 cm long. It emerges from the anterior end of the deep part of the gland, runs anteriorly between the hyoglossus and mylohyoid muscles on the genioglossus muscle, and opens in the oral cavity on the summit of a small papilla, near the frenulum of the tongue behind the lower incisor tooth. On the hyoglossus muscle, it lies between the hypoglossal and lingual nerves, but at the anterior border of the muscle, it is crossed laterally by the lingual nerve (Fig. 3.26), which then ascends medial to the duct. The sublingual veins lie lateral and the sublingual artery medial to the duct, more anteriorly.

3.6.1.3 Lingual Nerve

The lingual nerve, a branch of the marginal mandibular branch of the fifth cranial nerve (CN V), supplies the gland with parasympathetic innervation by means of the chorda tympani nerve (from the seventh cranial nerve, CN VII) and the submandibular ganglion. The lingual nerve passes forward and downward between the duct and the deep part of the gland before passing medially under the duct opposite the first lower molar. While still lateral to the duct, it gives off its sublingual branch, which runs close to the mandible, lateral to the sublingual glands. During submandibular sialoadenectomy, care should be taken to preserve the lingual nerve as it supplies the general sensation and taste to the anterior two-thirds of the tongue.

3.6.1.4 Facial Artery

The submandibular gland is supplied by branches of the facial (main supply) and lingual arteries, branches of the external carotid artery (ECA). The facial artery emerges from under the stylohyoid muscle, runs medial to the posterior belly of the digastric muscle, and then hooks over to pass upward deep to the gland. The artery exits the superior border of the gland at the lower border of the mandible (facial notch), around which it curls to enter the face. During resection of the submandibular gland, the facial artery must be sacrificed twice, first at the inferior border of the mandible and again just superior to the posterior belly of the digastric muscle. The lingual artery runs deep to the digastric muscle along the lateral surface of the middle constrictor muscle and then courses anterior and medial to the hyoglossus muscle and gives off braches to the submandibular gland.

3.6.1.5 Venous Drainage

The submandibular gland is mainly drained by the anterior facial vein (AFV) and to a lesser extent by the venae comitantes of the lingual artery. The anterior facial vein is in close approximation to the facial artery as it runs posteriorly and inferiorly from the face to the lower aspect of the mandible. Since it lies deep to the marginal (mandibular) branch of the facial nerve (CN VII), ligation and superior retraction of the AFV can help preserve this important nerve during surgery of the submandibular gland.

3.6.1.6 Lymphatic Drainage

Lymph nodes draining the submandibular gland are not embedded in the glandular tissue. They are located between the gland and its fascia, in close relation to the facial artery and vein at the superior aspect of the gland, and drain into the deep cervical and jugular chains. These lymph nodes are frequently associated with cancers in

the oral cavity. Thus, care should be taken during ligation of the facial vessels and dissection of the lympho-adipose tissue, to preserve the marginal mandibular branch of the facial nerve, which runs in close proximity to these structures.

3.6.2 Evaluation of the Submandibular Gland

3.6.2.1 Clinical Evaluation

History Taking

Patients with submandibular gland disorders usually complain of swelling and pain during meals followed by reduction in symptoms after meals, which may indicate partial stenosis of Wharton's duct. As with parotid gland disorders, *demographic* data, *medical and nutritional profile* of the patient, as well as history of *medications* and *radiation* can provide helpful clues to the diagnosis of submandibular gland diseases [21, 22].

Physical Examination

Extraoral, intraoral, and bimanual examinations (extraoral with one hand and intraoral with the palmar aspects of the fingertips of the other) should be performed to properly evaluate the submandibular glands clinically.

Extraoral Examination

Extraoral Inspection With the patient facing in front of the examiner, three to four feet away, the examiner should inspect symmetry, color, pulsations, and discharging sinuses on both sides of the patient. Enlargement of the submandibular gland may be unilateral or bilateral. A submandibular swelling presents just medial and inferior to the angle of the mandible. It is often confused with enlargement of LNs, but a submandibular gland swelling is single and generally larger and smoother. Palpation and bimanual examination are necessary to differentiate between both conditions. Significant neurologic deficits should be examined as well. Paralysis of the marginal mandibular branch of the facial nerve with deviation of the angle of the mouth to the sound opposite side should alert the examiner to a malignant submandibular neoplasm.

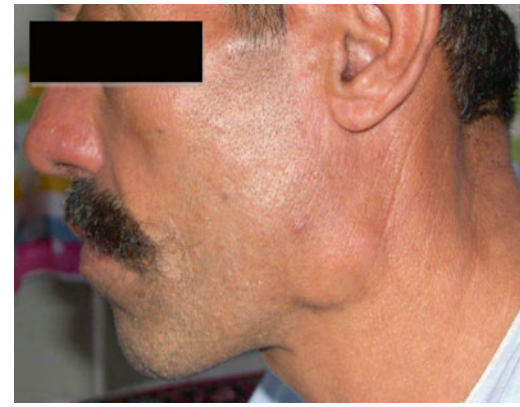

Fig. 3.27 A 43-year-old gentleman with an enlarged left submandibular LN (could be rolled over the mandible contrary to a submandibular gland swelling)

Extraoral Palpation Owing to the superficial anatomical location of the submandibular gland, the size, tenderness, consistency, mobility, and surface of the gland and associated masses can be easily assessed. If the swelling can be rolled over the lower border of the mandible, it is an enlarged LN (Fig. 3.27) and not a submandibular gland swelling since the latter's mobility is restricted by its fascial covering and attachment.

Intraoral Examination

Intraoral Inspection Using a torch or headlight, the orifices of the submandibular ducts are inspected and compared using a light source. They lie on either side of the frenulum of the tongue. A stone (*sialolithiasis*) may be seen exuding from the orifice with edema and redness. Saliva may be seen pouring from the non-affected side only. A *swelling* may be seen in the floor of the mouth, and its characters are recorded. For example, a *ranula* is bluish and transparent, whereas a *dermoid cyst* is yellow and opaque. Dental hygiene and the presence of periodontal disease should also be noted during intraoral inspection.

Intraoral Palpation The gloved index finger is inserted into the mouth, and palpation is started from behind at the end of the alveolus anteriorly. The gland and duct are palpated. A stone may be felt.

Bimanual Examination

With one or two gloved fingers palpating the floor of the mouth and the fingers of the other hand palpating beneath the jaw, a salivary gland swelling is felt to have two components, buccal and cervical. It becomes fixed when the patient contracts the mylohyoid muscle. This is done by asking the patient to open the mouth against resistance by the examiner. If a submandibular gland swelling is felt bimanually, its consistency must be noted. A hard swelling may be a stone or carcinoma, while a firm mass may be due to mixed salivary tumor or chronic sialadenitis. Increased salivation from the duct orifice due to external pressure applied to the gland may indicate inflammation [21, 22].

3.6.2.2 Imaging

Imaging studies can aid in reaching the etiology of the submandibular gland disorders and assist in selection and planning of proper management.

Plain-Film Radiographs

Since the majority (approximately 70 %) of submandibular gland stones (sialolithiasis) is radiopaque, plain X-ray (PXR) using the anteroposterior (AP), lateral, and oblique lateral occlusal views will be valuable in evaluating the presence of such calculi. Conventional plain radiography may also help in detection of infiltration of the mandible by a malignant neoplasm. A plain chest X-ray (CXR) may also be helpful in cases of suspected pulmonary metastases.

Sialography

Sialography can be used to evaluate sialolithiasis (filling defect) and other obstructive disorders (stricture), inflammatory disease (retained secretions), and neoplastic lesions (irregular borders of the submandibular gland). Fistulae and abscesses cavities can also be displayed with this technique. It is, however, contraindicated in cases of acute sialadenitis and presence of iodine allergy.

Computed Tomography (CT)

Imaging with CT can differentiate intrinsic from extrinsic disease, elucidate relationships to adjacent vital structures, assess the draining cervical LNs, and define abscess formation versus phlegmon. However, it is limited in evaluating the ductal system unless combined with simultaneous sialography [23]. Although stones can be identified with CT scanning, submandibular sialadenitis is not generally an indication for CT.

Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging provides better contrast resolution than CT, exposes the patient to less harmful radiation, and yields detailed images on several different planes without patient repositioning. However, it is inferior to CT scanning for the detection of calcification and early bone erosion. Chronic inflammation of the submandibular gland and calculi are not indications for MRI.

3.6.2.3 Endoscopic Examination (Sialendoscopy)

Sialendoscopy, a recent well-tolerated minimally invasive technique, allows direct inspection of the glandular duct and hilum [25]. Through a CO_2-laser papillotomy, sialolithectomy can be easily performed. Pharmacotherapy and laser ablation can also be carried out [26]. This relatively new technique has shown much promise in the diagnosis and treatment of chronic obstructive sialadenitis (COS) and sialolithiasis [27].

3.6.2.4 Biopsy

Fine-needle aspiration cytology (FNAC) should be undertaken if a solid neoplasm masquerading as sialadenitis is suspected. Open biopsy of the lip should be considered when the diagnosis of Sjogren's disease is contemplated.

3.6.3 Submandibular Sialadenitis/ Sialadenosis

3.6.3.1 Acute Submandibular Sialadenitis

Etiology

Acute submandibular sialadenitis is acute inflammation of the submandibular salivary gland. It is usually secondary to obstruction of Wharton's duct and is often recurrent. The most common

organism is *Staphylococcus aureus*. Other *bacterial* organisms include *Streptococcus viridans*, *Haemophilus influenzae*, *Streptococcus pyogenes*, and *Escherichia coli*. Infection is often the result of dehydration with overgrowth of the oral flora. The most common causes are postoperative dehydration, radiation therapy, and immunosuppression. Though rare in the neonate and prepubescent child, infection of the submandibular gland can result from other pathogens such as *Pseudomona aeruginosa* and group B streptococci.

Though less common than bacteria, several *viruses* have been implicated in acute submandibular sialadenitis including mumps virus (typically affects the parotid gland), HIV, Coxsackie virus, parainfluenza types I and II, influenza, and herpes.

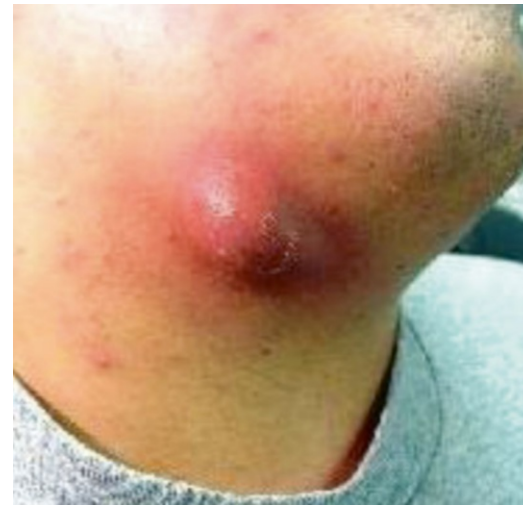

Fig. 3.28 A 33-year-old gentleman with a right submandibular gland abscess with overlying erythema and edema

Clinical Picture

There is no *age* predilection; however, sialadenitis in general tends to occur in older, debilitated or dehydrated patients [175]. No *race or sex* predilection per se exists.

The patient usually *complains* of a painful swelling in the submandibular region and salivary colic, i.e., pain and swelling of the gland with meals. Pain may be referred to teeth or tongue. Infection of the submandibular gland can result in the formation of a submandibular *abscess* (Fig. 3.28). In such cases, the patient may appear toxic with feature similar to acute sialadenitis and, sometimes, spiking fever. The infection may spread to other deep spaces of the neck. *Trismus* may be indicative of parapharyngeal space involvement. Progression to *Ludwig angina*, a life-threatening infection of the submental and sublingual spaces, although rare, may occur.

Physical examination should begin with the gland itself. A tender swelling is felt bimanually. A stone in the duct may also be felt. The orifice of the duct will appear congested and edematous. It may pour drops of purulent saliva on squeezing the duct. Palpation should extend to include the floor of the mouth, tongue, cheek, and neck. All of the major salivary glands should be examined for masses, symmetry, and the presence of discharge. Cervical lymphadenopathy should also be noted. Both eyes should be examined for interstitial keratitis and a cranial nerve examination should be conducted with particular attention to cranial nerves VII and XII.

Investigations (Workup of the Patient)

Laboratory investigations should begin with culture of the offending gland prior to administration of antibiotics, in addition to blood cultures in presence of bacteremia or sepsis. As a rule, needle aspiration of a suspected abscess is not indicated. Electrolytes and complete blood count (CBC) with differential should be obtained to assess for any evidence of dehydration or systemic infection.

Imaging studies should begin with conventional PXR, which is particularly valuable in evaluating the presence of calculi. Sialography is contraindicated in acute sialadenitis. Ultrasonography (US) can differentiate between solid versus cystic lesions of the gland and is helpful in the identification of abscess formation. Computed tomography (CT) scanning is an excellent modality not only in differentiating intrinsic versus extrinsic glandular disease but also in defining abscess formation versus phlegmon. Magnetic resonance imaging (MRI) is of little utility in sialadenitis or sialadenosis.

Treatment

Management of acute submandibular sialadenitis involves a wide range of approaches, from conservative medical treatment to more aggressive surgical intervention.

Medical management focuses on eliminating the causative factor, and the goals of pharmacotherapy are to eradicate the infection, reduce morbidity, and prevent complications. Adequate *hydration* should be ensured and electrolyte imbalances corrected. *Sialogogues* may temporarily increase salivary flow, but this frequently is short lived and better results are obtained by an overall increased fluid intake [176]. Patients are most often treated on an outpatient basis, with the administration of a single dose of parenteral *antibiotics* in an emergency department, followed by oral antibiotics for a period of 7–10 days. Clindamycin (900 mg IV q8h or 300 mg PO q8h) is an excellent choice and provides good coverage against typical organisms. In patients refractory to antibiotics, viral and atypical bacterial causes should be considered. In addition to antibiotics, patients may be treated with *non-steroidal anti-inflammatory* medications, and *narcotics* may be needed in severe cases. When possible, patients are instructed to empty the gland by *external massage*. The submandibular gland is best emptied by a constant compressive motion, starting below the mandible near the angle, with the hand sliding upward toward the chin. A short course of high-dose *steroids* reduces the peri-ductal inflammation and facilitates massage. Patients who are septic, severely dehydrated, or exhibiting significant morbidity should be admitted to hospital, and CT scanning of the affected area should be performed. Small abscesses usually respond to conservative methods; however, if a large abscess is noted, incision and drainage should be considered. Patients with sialolithiasis are initially treated with hydration, warm compresses, and gland massage, as well as antibiotics for the infected gland.

Surgical management includes incision and drainage in case of abscess formation, and excision of the gland, during a period of *quiescence*, in patients with recurrent acute sialadenitis. *Endoscopic management* of sialadenitis frequently obviates the need for gland excision. Results follow a learning curve [177].

Prognosis

The prognosis of acute sialadenitis is very good. Most cases are easily treated with conservative medical measures, and admission is the exception, not the rule. Acute symptoms usually resolve within 5–7 days; however, edema in the area may last several weeks. Patients with sialolithiasis require definitive surgical treatment in most cases, which results in an excellent prognosis.

3.6.3.2 Chronic Submandibular Sialadenitis/Sialolithiasis

Chronic Sialadenitis

Chronic sialadenitis is typically less painful than acute sialadenitis and is associated with recurrent enlargement of the gland (often following meals) typically without erythema (Fig. 3.29). It is associated with conditions linked to decreased salivary flow, rather than dehydration. These conditions include salivary stasis, a change in the fluid and electrolyte composition of the gland, and mechanical obstruction of Wharton's duct. Proximal to the site of chronic obstruction, the duct will be dilated with retention of secretions and chronic infection. Causes of obstruction include calculi, strictures, edema or fibrosis of the

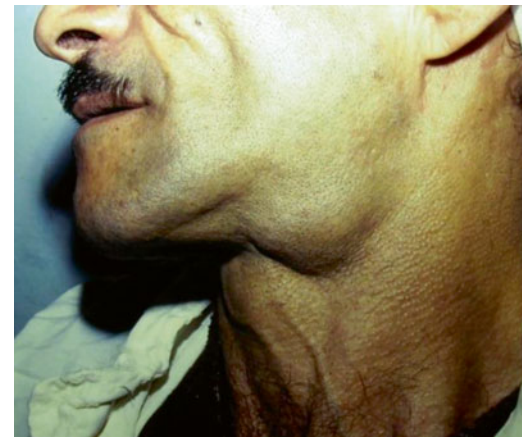

Fig. 3.29 A 56-year-old gentleman with left chronic submandibular sialadenitis. It could not be rolled over the lower edge of the mandible

papilla, pressure on the duct by adjacent masses, or duct invasion by a malignant neoplasm.

Chronic sialadenitis is usually considered a medical disease, with surgical intervention reserved for intractable symptoms of pain and swelling. In patients who present with pain and little demonstrable swelling, sialography may be diagnostic. It may show the evidence of ductal obstruction, the calculus, duct dilatation, sialectasia, or acinar atrophy.

Papillary Stenosis

Ulceration of the papilla of the submandibular duct may follow trauma from a denture. The obstruction and recurrent swelling will subside as the ulcer heals. Repeated trauma results in fibrosis which is only relieved by *papillotomy* with suture of the duct lining to the oral mucosa.

Sialolithiasis

Salivary calculi (sialolithiasis) relate to the formation and deposition of concretions within the ductal system of the gland. Approximately, *85 % of all salivary calculi occur in the submandibular gland* [178], with approximately 70 % of these demonstrable as radiopacities on routine plain radiography. The calculi vary in size and may be single or multiple. The formation of calculi is associated with chronic sialadenitis and, in particular, the recurrent nature of the problem. The exact mechanism of stone formation is unclear, but it appears to be related to the following conditions:

1. Salivary stagnation (stasis): the secretion of the submandibular gland is more viscid than that of the parotid gland, and Wharton's duct is independent (directed forward and upward).
2. Duct obstruction: the end of the duct opens in the floor of the mouth and is more liable to be obstructed by a stone, inflammation, and foreign bodies such as a small piece of a toothbrush or food particles.
3. Epithelial injury along the duct: this results in sialolith formation, which acts as a nidus for further stone formation.
4. Precipitation of calcium salts: the stones themselves are typically composed of calcium phosphate, calcium carbonate, and magnesium phosphate, in association with other salts and organic material such as glycoproteins, desquamated cellular residue, and mucopolysaccharides.

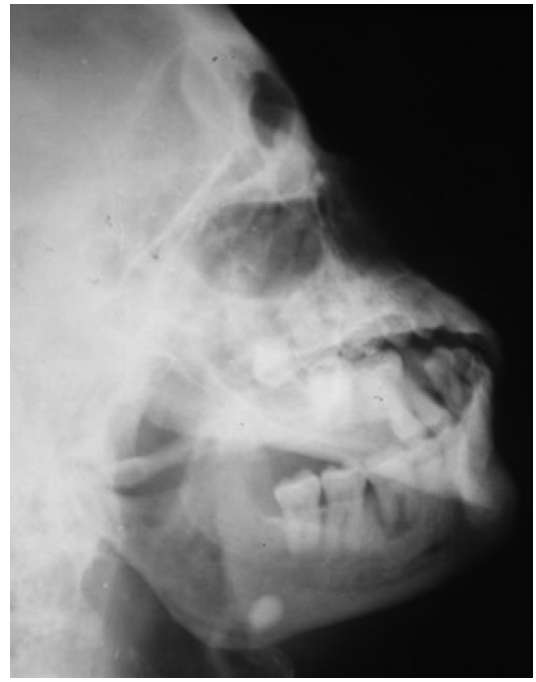

Fig. 3.30 Plain X-ray showing a radiopaque right submandibular calculus

Clinical Picture

The patient presents with a firm or hard submandibular *swelling*, which simulates a tumor and increases in size with meals. *Pain* is associated with meals and this helps to differentiate it from pain of dental origin. Intake of lemon juice (*lemon juice test*) causes aggravation of pain and increase in the size of the swelling.

Oral examination of the orifice of the duct reveals saliva pouring on the unaffected side, with little or no secretion seen ejecting from the swollen (affected) side. With *bimanual examination*, a stone may be felt within the duct or within the gland. The swelling itself may also be felt.

Investigations

Submandibular calculi are relatively easy to demonstrate by *plain radiography* (Fig. 3.30). *Sialography* may show a filling defect, if the stone is translucent (Fig. 3.31). In 2009, Bozzato

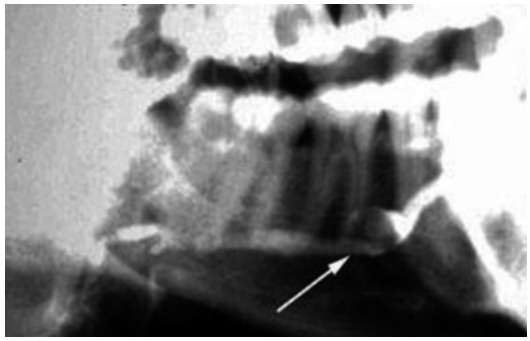

Fig. 3.31 Sialography showing a filling defect in the right submandibular gland indicative of a radiolucent calculus

et al. [179] reported that application of ascorbic acid as a contrast agent can aid in the *ultrasound* assessment of obstructive sialadenitis of the submandibular (and parotid) glands.

Treatment

In patients with *calculi* in proximity of the Wharton's duct opening, the duct can be cannulated and dilated, and the stone removed via a trans-oral approach. For ductal calculi in the floor of the mouth, a stitch is passed under the duct proximal to the stone to stop the stone slipping backward. An incision is made in the mucosa over the duct, which is then mobilized, and a stay suture is passed under the duct to bring it up into the top of the wound and to control it while the wall is incised to release the stone. Patients with deep intraparenchymal stones or multiple stones should have their glands excised on an elective basis. Ultrasonic lithotripsy is rarely effective.

3.6.3.3 Autoimmune Sialadenitis

Sjogren's Syndrome

Autoimmune diseases, in particular *Sjogren's syndrome,* can be associated with sialadenitis, affecting *all* major salivary glands, though preferentially affecting the parotid gland. Minor salivary glands are also affected. In these cases, the salivary and lacrimal glands are infiltrated with lymphocytes, smaller ducts are blocked, and the acini progressively destroyed. Intense infiltration of the gland with lymphocytes can result in diffuse enlargement or the formation of localized nodules, which must be distinguished from neoplasms. *Mucous* gland metaplasia of the duct epithelium leads to the formation of a gelatinous saliva in some patients. Strictures, duct dilatations, and ascending infection complicate the picture. Patients with Sjogren's syndrome are at greater risk than the rest of the population for developing reticulum cell sarcoma, either in the glands or in the related LNs [62].

The disease, which is associated with keratoconjunctivitis sicca, xerostomia, salivary gland enlargement, and lingual papillary atrophy, is confirmed through *biopsy* of the minor salivary glands of the lip. Numerous laboratory tests are also used to confirm the diagnosis, such as autoantibodies Sjogren's syndrome A (SS-A) and Sjogren's syndrome B (SS-B), rheumatoid factor, and antinuclear antibodies. Erythrocyte sedimentation rate (ESR) should also be conducted. Lack of lacrimal secretion can be shown by the *Schirmer test* and keratitis by r*ose bengal and fluorescein* staining.

Good hydration and prevention of complications should be undertaken. The dry eyes can be treated by diathermy obliteration of the lacrimal punctum and the instillation of artificial tears composed of methyl cellulose drops. Dental hygiene should be strictly maintained in order to prevent carries, and dental and rheumatology consults should be sought. Steroids and immunosuppressive agents generally alter the course of the disease but are rarely used in view of their side effects and the increased risk of ascending infection. Gland excision is rarely indicated [63].

Mikulicz's Disease/Syndrome

Mikulicz (*Johann von Mikulicz-Radecki, 1850–1905, a Polish surgeon*) described this disease in 1892 as a triad that includes (1) symmetrical enlargement of all the salivary glands, (2) narrowing of the palpebral fissures due to enlargement of the lacrimal glands, and (3) parchment-like dryness of the mouth.

Mikulicz's disease has been used to describe patients with a benign lymphoepithelial lesion characterized by bilateral lacrimal and salivary gland enlargement. Its meaning is somewhat

vague at present and should best be included as a variant of Sjogren's syndrome with its more specific histopathological changes of lymphoreticular cell proliferation, atrophy of the acinar parenchyma, and duct changes signifying chronic inflammation.

Mikulicz's syndrome, however, is used to describe enlargement of the salivary and lacrimal glands seen with some diseases such as leukemia, lymphoma, tuberculosis, syphilis, and sarcoidosis [176].

3.6.3.4 Sialadenosis

Sialadenosis refers to nonneoplastic noninflammatory swelling in association with acinar hypertrophy and ductal atrophy. *Etiologies* fall into five major categories:

1. Nutritional (e.g., vitamin deficiency, bulimia)
2. Endocrine (e.g., DM, hypothyroidism)
3. Metabolic (e.g., obesity, cirrhosis, malabsorption)
4. Inflammatory/autoimmune (e.g., Sjogren's disease, Heerfordt's syndrome)
5. Drug induced (e.g., thiourea)

Physical examination shows a non-tender swelling that is often bilateral and symmetric but can be unilateral and asymmetric. Treatment should be directed toward managing the underlying problem and achieving homeostasis. Gland excision is *not* indicated.

3.6.4 Tumors of the Submandibular Gland

Tumors of the submandibular gland are the second most frequent major salivary gland neoplasms after tumors in the parotid gland. They account for about 10 % of all salivary neoplasms [180–182], and approximately 50 % are malignant [181, 182].

3.6.4.1 Benign Tumors (BTs)

The most commonly encountered BT of the submandibular gland is the *pleomorphic adenoma* (approximately 50–65 %), the histological features and biological behavior of which are similar

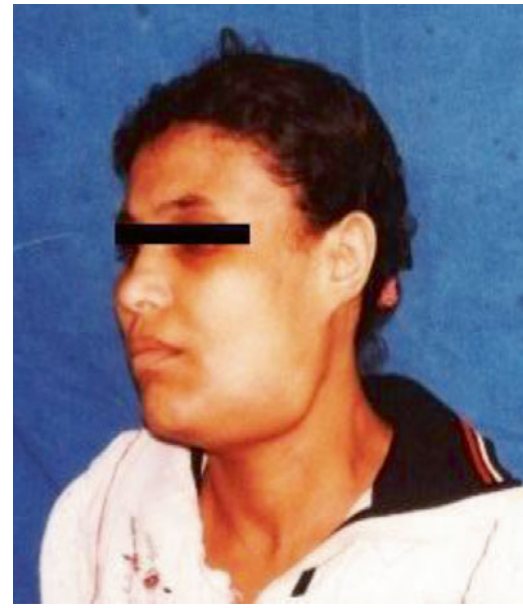

Fig. 3.32 A 27-year-old lady with a slowly growing left submandibular mass (proven histologically to be a pleomorphic adenoma)

to those of the parotid gland, but with an incidence of 1:10, respectively [64, 183, 184]. Typical presentation is that of a slowly growing painless mass (Fig. 3.32). Larger tumors have a multinodular appearance. The high recurrence rate associated is believed to be due to pseudopod formations at the periphery of the tumor and to inadequate excision (enucleation). Recurrence may occur months to years following inadequate excision, and malignant transformation (approximately 2–6 %) may also occur, particularly in long-standing tumors or in those that have recurred [184].

Other types of adenomas, such as the basal cell adenoma, are much less common, and *other BTs*, such as Warthin's tumor, oncocytomas, and myoepitheliomas, are very rarely encountered in submandibular (and sublingual) glands.

Hemangiomas affect mainly the parotid gland (90 % of cases), but occasionally, the submandibular gland is affected, as a part of massive facial lesions.

3.6.4.2 Malignant Tumors (MTs)

Malignant neoplasms of the submandibular (and sublingual glands) can be classified into three

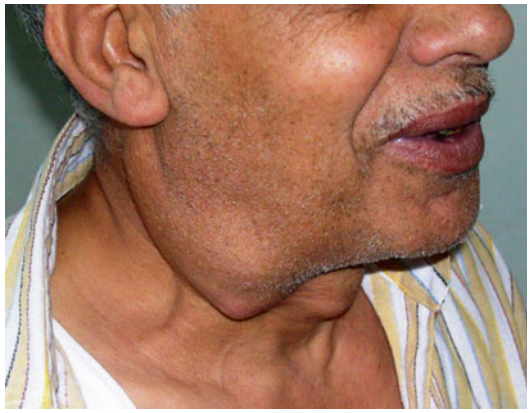

Fig. 3.33 A 62-year-old gentleman with a right submandibular mass of rapid growth, proven by histopathology to be an adenoid cystic carcinoma

major categories: (1) tumors of epithelial origin (MEC, ACC, acinic cell carcinoma, malignant mixed tumor, SCC, salivary duct carcinoma), (2) tumors of non-epithelial origin (sarcomas, lymphomas), and (3) secondary tumors. Among MTs, the most frequent is ACC, accounting for 36–63 % of cases [183–186], followed by MEC (17–22.2 %), SCC (17.3 %), and adenocarcinoma (15.4 %) [185].

Adenoid cystic carcinoma (ACC) usually develops over a short time as a submandibular mass (Fig. 3.33) with rapid growth and is frequently associated with pain and fixation to the mandible. Regional LN metastases may occur in approximately 30 % of patients. This tumor has a propensity to invade nerves, thus posing a risk of perineural spread through the mandibular or cervical branches of the facial nerve and through the lingual and hypoglossal nerves toward the skull base. The risk of distant metastases and the development of late recurrences are similar to those observed in the parotid gland [184].

Mucoepidermoid carcinomas (MEC), the next most common cancer, may be *low, intermediate, or high grade* in their histological appearance, with eventual outcome dependent upon this grading. Low-grade tumors are usually well circumscribed, resemble benign mixed tumors grossly, and recur after excision in approximately 15 % of patients. High-grade tumors, on the other hand, are aggressive and invade locally, causing fixation and extension to the nerve. On presentation, up to 50 % of patients with high-grade tumors have LN metastases [183, 184], and the risk of local failure can be as high as 40 % [184].

Squamous cell carcinoma (SCC) usually presents as a hard mass, often fixed, with a short history of 1 year or less. It is often asymptomatic but may be painful in 20 % of patients, and nodal metastases can occur in nearly 50 % of patients. It is important to ensure that this tumor is a primary tumor of the gland and not a metastatic lesion to the submandibular LNs from other SCC in the head and neck. Differentiating it from MEC must also be confirmed. Locoregional recurrence can occur in approximately 50 % of cases [184].

Adenocarcinoma arises infrequently in the submandibular gland. These are very aggressive tumors that invariably present with LN metastases, local extension to soft tissues, and invasion of the mandible, resulting in poor local control that adversely affects prognosis [184].

3.6.4.3 Clinical Presentation

Benign and malignant tumors of the submandibular gland usually present with a *painless* (72–87 %), firm, lobulated, solitary mass in the submandibular region [183, 186]. The presence of pain suggests malignancy, but sialadenitis must be ruled out first. The discharge of purulent saliva from the salivary duct is usually diagnostic of an inflammatory glandular process. Nevertheless, it must be borne in mind that a salivary gland tumor can coexist with obstructive sialopathy leading to sialadenitis.

Physical examination, including bimanual palpation, is important in order to evaluate the extension to adjacent structures. Sensory (lingual nerve) and motor (hypoglossal and marginal mandibular nerves) nerve deficits denote malignancy [186]. Occasionally, MTs may fungate by direct extension through the skin or in association with dermal lymphatic permeation.

3.6.4.4 Differential Diagnosis

A primary neoplasm of the submandibular gland should mainly be differentiated from *sialadenitis* and *metastatic* SCC to a LN. It should also be

differentiated from other causes of cervical LN enlargement such as atypical mycobacteria infection, cervicofacial actinomycosis, sarcoidosis, acquired or congenital cysts, benign follicular lymphadenopathy, and cat-scratch disease [128].

Episodic pain and mass are the hallmark of inflammatory disease (sialadenitis), although one-third of the lesions may be asymptomatic. Obstructive sialadenitis, due to stricture or calculus in the duct, is a common cause of enlargement of the submandibular gland. In these instances, pain and swelling are associated with eating, receding after several hours. Erythema may occur over the mass, and a stone may be palpated in the duct which can, occasionally, drain purulent saliva when the gland is compressed [187, 188]. A solitary SCC metastatic to a submandibular LN in the absence of an obvious primary lesion in the oral cavity (occult primary) is rather uncommon.

3.6.4.5 Diagnostic Imaging

The main objectives of imaging of major salivary gland lesions in general are:

1. To establish whether the mass is intrinsic or extrinsic.
2. To determine its relationship to the nerves.
3. To evaluate its full extent and possible invasion of surrounding structures. If there is any radiological evidence of malignancy, the study is extended to include the neck.

Plain radiographs, sialography, and nuclear scans add very little to the diagnostic information and are seldom indicated for evaluation of submandibular (and sublingual) gland tumors.

Ultrasonography (US) can differentiate between solid and cystic masses and between intra- and extra-glandular nodules. It can also provide important information regarding the contents of the mass, its size, and limits. Nevertheless, there are no definitive US criteria to differentiate between benign and malignant tumors.

Color Doppler sonography usually shows enhanced vascularization in MTs when compared with the normal parenchyma or with BTs. Low-grade MECs, particularly those <2 cm, however, usually have a homogeneous structure and present with smooth borders and may be erroneously considered as benign. High-grade MECs, in contrast, have irregular borders and typical heterogeneous echo pattern. It is noteworthy, however, that patterns of extra-glandular spread, such as perineural invasion and infiltration of the parapharyngeal space, mandible, and base of the skull, are *not* easily visible at US [189].

Computed tomography (CT) and magnetic resonance imaging (MRI) permit better visualization of masses within the salivary glands. Both are equally satisfactory in differentiating cystic from solid lesions and allow evaluation of the relationship with adjacent structures, including soft tissues and bones. However, CT scans are especially useful in the assessment of bone erosion, while MRI better evaluates soft tissue involvement and may detect tumor extension along cranial nerves.

3.6.4.6 Cytopathologic Diagnosis

Fine-needle aspiration cytology (FNAC) can accurately establish cytological diagnosis in over 90–95 % of patients in experienced hands [190]. Diagnosis of pleomorphic adenoma poses no difficulties in cytopathologic specimens. Aspirates are highly cellular containing both myxocartilaginous stroma and large sheets or small aggregates of epithelial cells. Determining the histopathological type of the primary tumor preoperatively can help in deciding the extent of surgical procedure (with or without neck dissection).

High-grade cancers such as adenocarcinomas and SCCs should be considered for neck dissection based on significant increased rates of occult LN metastases. On the other hand, sarcomas, ACC, and other histological types which are unlikely to involve LNs may not benefit from elective treatment of the neck [191].

3.6.4.7 Patterns of Spread

Malignant tumors of the submandibular gland may extend through the capsule to involve the adjacent mandible, mylohyoid muscle, tongue, as well as the lingual and hypoglossal nerves. Moderate to severe pain is usually associated with advanced tumors, while nerve deficits involving cranial nerves V, VII, and XII may be

found in 14 % of patients [187, 192]. Skin invasion and ulceration and extension to the oral cavity can occur in advanced cases.

3.6.4.8 Management

Benign Tumors

A subfascial dissection is usually performed to remove the submandibular gland without a cuff of surrounding normal tissue in cases of benign diseases such as small BTs and sialolithiasis or sialadenitis refractory to conservative management. This technique is rapid and has a low complication rate. Alternatively, Weber et al. [36] recommend level I neck dissection (submental [level Ia] and submandibular [level Ib] LNs) during the routine resection of submandibular gland tumors as this would provide adequate margins in the treatment of BTs and also serve to sample LNs adjacent to the gland in the treatment of MTs [193].

Malignant Tumors

Comprehensive management of MTs of the submandibular gland includes definitive treatment of the primary tumor and treatment (therapeutic or elective) of the neck; eventually, only neck observation is advised, as many neoplasms have a low propensity for lymphatic spread. Most of the clinical variables required to predict survival can often be obtained before definitive surgery. Based on findings of clinical evaluation, MRI, and FNAC, patients may be counseled as to surgical approach, need for neck dissection, and need for postoperative radiotherapy.

Factors Influencing Selection of Therapy

The *size of the primary tumor and histological grade* are the most important tumor factors affecting choice of initial therapy. Clinical (advanced-stage and submandibular site) and histological (higher cancer grade, presence of perineural invasion, presence of LN metastases) parameters are considered independent predictors of poorer clinical outcome in most series of major salivary gland MTs [183, 185, 186, 192–200]. Vander Poorten et al. [186] found that *age at diagnosis* ($p = .0006$), T stage ($p = .001$), and clinical skin invasion ($p = .005$) were the most significant predictors of poor survival among their patients. Interestingly, Hocwald et al. [200] reported that older patients tend to have a higher incidence of more aggressive tumors as compared to younger patients (79 % versus 56 %, respectively). They also observed that *men* tended to present with higher T stage tumors at diagnosis than did women, 53 % versus 26 % ($p = .02$). Bhattacharyya [185] identified patients with younger age, decreased tumor grade, and the addition of radiation therapy as factors associated with improved survival ($p < .001$, .005, and .015, respectively) in his series. *Factors predicting tumor recurrence* in most series include higher TNM stages, perineural growth, and LN metastases [183–186, 192–194, 200].

Resectable Tumors

Low-grade, low-stage MTs can be treated by excision of the submandibular gland with nodal dissection of level I. *High-grade, high-stage MTs*, however, require supraomohyoid neck dissection (SOND), in conjunction with the excision of the submandibular gland. For *advanced (loco regional) tumors*, more radical local resection and neck dissection are indicated [10, 22, 23, 36, 37]. It is worth mentioning that the morbidity secondary to sacrifice of hypoglossal, lingual, and marginal branch of the facial nerve is better tolerated than that after loss of the entire facial nerve. *Reconstruction* with regional, and sometimes microvascular free flaps, may be necessary. *Adjuvant postoperative radiotherapy* may be indicated, in selected cases, in an attempt at improving local and regional control. High-grade malignancies, recurrent tumors, gross or microscopic residual disease, tumor adjacent to the nerves, regional nodal metastases, and invasion of muscle, bone, skin, or nerve are all strong indications for postoperative radiotherapy [194–199].

Advanced Non-resectable Tumors

These are generally treated by radiotherapy with palliative intent. Treatment with neutron beam therapy is of particular value for adenoid cystic carcinomas.

Management of the Neck

Although the role of neck dissection in clinically proven metastases in salivary gland cancer is

Table 3.3 General guidelines for treatment of submandibular gland cancer [16]

	T1 and T2 (N0)	T1 and T2 (N0 and N1)	T3 and T4 (N0 and N+)
	Low grade	High grade	High grade
Tumor type	MEC (low grade) Acinar cell (low grade) Adenocarcinoma (low grade)	MEC (high grade) Acinar cell (high grade) Adenocarcinoma (high grade) Adenoid cystic Ex-pleomorphic adenoma Salivary duct carcinoma SCC	Any histological type
Treatment	Level I ND	Supraomohyoid ND (N0) Comprehensive ND (N+) PORT	Supraomohyoid ND (N0) Comprehensive ND (N+) PORT

MEC mucoepidermoid carcinoma, *SCC* squamous cell carcinoma, *ND* neck dissection, *PORT* postoperative radiotherapy

straightforward, routine elective treatment of the negative neck remains controversial. Some investigators recommend neck dissection only for patients with clinically evident LNs, whereas others also recommend elective neck dissection for tumors based on various prognostic factors [183–185, 193, 201].

The incidence of LN metastases in submandibular carcinomas at the time of initial presentation varies from 8 to 33 % [192–194, 199], which reduces the 5-year survival rates from 40 to 9 % [192, 194, 202–206].

Several authors have attempted to determine predictive factors for cervical metastases in salivary gland malignancy. Several studies have shown that risk of occult nodal metastases is higher in anaplastic, high-grade MEC, SCC, adenocarcinoma, and salivary duct carcinoma than in low-grade MEC, ACC, acinic cell carcinoma, and sarcoma [183, 184, 191, 193–196, 202–204]. An increased risk of occult metastases is also associated with advanced-stage primary cancer. Medina [207] summarized the indications reported in the literature for elective neck dissection in salivary gland cancers: high-grade tumors, T3–T4 tumors, tumors >3 cm, facial nerve (neural) invasion, age >54 years, extra-glandular extension, and perilymphatic invasion [183, 184, 193, 194, 199–207].

The treatment of *clinically positive node* metastases is surgical. The extent of neck dissection is determined by the grossly involved LNs, and an attempt should be made to preserve vital structures. The most common levels of neck involvement in submandibular (and sublingual) MTs are levels I–III [202, 204]. Since contralateral neck affection is rare, only the ipsilateral neck is treated.

Treatment of the *clinically negative neck* has included observation, elective neck dissection, and primary radiation. Currently, treatment of the N0 neck is only appropriate when the risk for occult metastases is high.

The general guidelines for treatment of submandibular gland cancer are shown in Table 3.3.

Chemotherapy

The role of chemotherapy in the treatment of salivary gland MTs has been confined to metastatic disease and locoregional disease not amenable to either salvage surgery or radiation therapy.

The most studied *single agent* is cisplatin. Licitra et al. [208] analyzed the results obtained from 25 patients treated for advanced carcinoma in a phase II trial (100 mg/m^2 of cisplatin every 3 weeks). They observed a response rate of 7 and 18 % rate in metastatic lesions and locoregional recurrence, respectively. The median response duration was 7 months and the median survival time was 14 months.

For *combination chemotherapy* with cisplatin, the most common agents used include 5-fluorouracil, cyclophosphamide, and doxorubicin. A regimen using all four drugs was tested in

17 patients and a 50 % response rate was observed. The median duration of response was 8 months and medial survival was 18 months [209].

Several *molecular targets* have been identified in salivary gland cancer such as C-kit proto-oncogene, EGFR, HER2 proto-oncogene, androgen receptors, p53 protein, and VEGF. These may ultimately provide useful information into diagnosis, biological behavior, and management of cancer of the salivary glands [210–217].

Take-Home Messages

- There are equal proportions of malignant and benign lesions in the submandibular gland.
- Nerves at risk during operations involving the submandibular gland are the marginal mandibular, lingual, and hypoglossal nerves.
- The smallest operation for benign tumors of submandibular gland is excision of the whole gland.
- Low-grade, low-stage MTs can be treated by excision of the submandibular gland with dissection of level I. High-grade, high-stage tumors, however, require supraomohyoid neck dissection, in conjunction with the excision of the submandibular gland.

3.6.5 Surgical Technique: Submandibular Sialoadenectomy

3.6.5.1 Steps of the Procedure

- The patient is placed on the operating table under general endotracheal anesthesia in a supine position with the neck turned to the opposite side.
- The skin incision is placed in an upper neck skin crease at least two fingerbreadths below the angle of the mandible to protect the mandibular branch of the facial nerve.
- The upper flap consisting of skin, subcutaneous fat, platysma muscle, deep cervical fascia, and the fascial capsule superficial to the gland is elevated up to the level of the lower border of the mandible in order to avoid injury of the nerve.
- The lower border of the gland is grasped and lifted up, the gland is separated from the muscular floor of the submandibular triangle, and the hypoglossal nerve is identified on the hyoglossus muscle. The anterior segment of the gland is released from the mylohyoid muscle. The facial artery is then identified and divided proximal to the gland between strong ligatures. This frees the gland posteriorly.
- The gland is retracted downward in order to divide its superior fascial attachments to the mandible and expose the facial artery and anterior facial vein just below the mandible. These vessels are divided as close to the gland as possible to avoid accidental damage of the mandibular branch of the facial nerve. Division of the facial vessels allows caudal retraction of the submandibular gland, providing full exposure of the underlying mylohyoid muscle.
- The mylohyoid muscle is retracted forward, thus exposing the deep part of the gland. With traction on the gland still maintained in a downward direction, the lingual nerve is dragged down from its position deep to the mandible and its attachment to the gland severed.
- Wharton's duct is isolated and divided as close as possible to the floor of the mouth. During this dissection, the hypoglossal nerve is seen in a deeper plane to Wharton's duct and should be carefully protected.
- After the removal of the surgical specimen, meticulous hemostasis is obtained followed by irrigation with saline solution. A single suction drain is inserted and the wound is closed in layers.

3.6.5.2 Postoperative Complications

The most common complication after submandibular gland excision is *injury to the marginal mandibular branch of the facial nerve* [218]. Temporary injury (temporary paresis) has been reported to range from 1 to 10 % of patients [219–221].

It is highly recommended that the incision should be placed at 3 cm below the angle of the mandible to consistently avoid injury to branches of the facial nerve. Injury to *the lingual nerve* is uncommon unless tumor or chronic inflammation presents difficulty in its separation from the gland. Rarer still is injury to the *hypoglossal nerve* in the course of resection of the contents of the submandibular triangle [220]. *Great auricular causalgia* and/or the development of *neuroma* is uncommon [222].

Injury to other important structures in the neck may also occur during submandibular sialoadenectomy such as the facial artery leading to severe hemorrhage and wall of the pharynx resulting in fistula formation. With careful dissection these complications are rarely encountered in experienced hands.

The *scar* that results from cervical incision may be aesthetically unsatisfactory in many patients, particularly those with a slender neck. Avoiding tension of the surgical wound and the use of intradermal sutures can help in preventing an unsightly scar.

3.7 Sublingual Glands

The paired sublingual salivary glands are the smallest of the three major salivary glands, weighing approximately 2 g each.

3.7.1 Surgical Anatomy

Sublingual salivary glands are almond shaped and lie immediately below the mucous membrane of the floor of the mouth just above the submandibular fossa. According to Batsakis, these are poorly encapsulated glands that do not represent unit organs but, rather, a *mosaic* composed of a large segment (major sublingual gland), which is drained by the sublingual or *Bartholin's* duct, and a group of 8–30 smaller glands (minor sublingual glands), which are drained by several openings (ducts of *Rivinus*) directly into the oral cavity or into the submandibular duct [223].

The sublingual glands are separated by the paired midline genioglossus and geniohyoid muscles. A crest of mucous membrane along the frenulum (*plica sublingualis*) represents the projection of the glands and openings of the sublingual ducts.

The blood supply to the sublingual gland comes from the sublingual and submental arteries, and the nerve supply from the chorda tympani and lingual nerves [1]. Lymphatic drainage goes into the submental and submandibular LNs.

3.7.2 Tumors of the Sublingual Glands

True sublingual gland tumors are rather unusual, and approximately, 75 % are *malignant*; MEC and ACC comprise 80 % of all carcinomas arising in this region [10]. *Benign tumors* of the sublingual gland are very rare, except for ranulas, which are benign cystic lesions.

Tumors of the sublingual gland, which are very rare, usually present as a painless mass under the lateral aspect of the ventral tongue. It may be associated with minimal discomfort, pain, numbness of the tongue, and difficulty with retention of a dental prosthesis. A high degree of suspicion must be employed for lesions in this region of the floor of the mouth. These salivary gland tumors can be differentiated from mucosal lesions of the floor of the mouth by their *submucosal* location. However, it is almost impossible to differentiate primary tumors of the sublingual glands from tumors of minor salivary origin in the floor of the mouth [9, 21].

3.7.2.1 Ranula

Its name derives from the Latin word *rana* (frog), due to the typical bluish appearance, similar to a frog's belly [224].

Pathogenesis There are two different concepts for the pathogenesis of ranula: (1) it is a *true cyst* (with an epithelial lining) resulting from due to ductal obstruction, and (2) it is a *pseudocyst* (without an epithelial lining) resulting from injury of the duct and extravasation of mucus

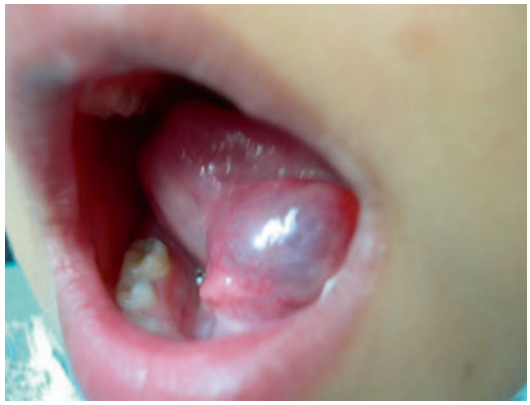

Fig. 3.34 Ranula. A cystic, translucent swelling with a bluish tinge in the floor of the mouth lateral to the midline

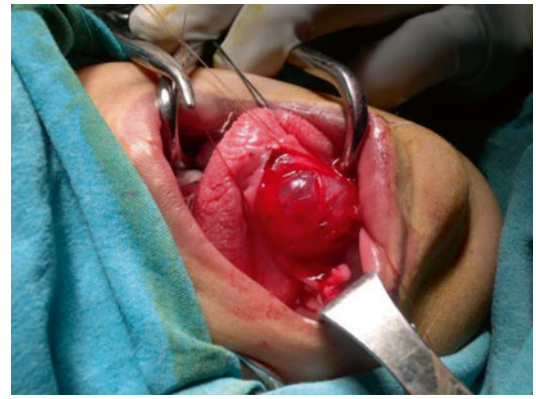

Fig. 3.35 Dissection of ranula

[225–227]. Recently, typical ranulas have been considered as an extravasation phenomenon of the sublingual gland [227, 228].

Types According to its extension, ranulas are sublingual, sublingual-submandibular, or submandibular [229]. The sublingual type is a simple ranula, while the other two extending into the neck are *plunging* ranulas (deep cervical ranulas).

Clinical Picture It usually affects children and young adults with no gender predilection. The clinical presentation is that of a slowly growing submucosal mass in the floor of the mouth, with a cystic appearance. Pathologically, there is a simple or multi-loculated cavity filled with amorphous or mucoid material [224]. The cyst varies in size between 1 and 5 cm in diameter. It is characteristically translucent and has a bluish tinge (Fig. 3.34). It is smooth and covered by tortuous veins, and the submandibular duct is displaced and stretched over it. The edge is difficult to feel and the cyst *cannot* be compressed or reduced.

Treatment Different approaches for treatment of ranulas have been proposed including simple incision, cyst extirpation, marsupialization, and excision of sublingual gland, which is most recommended [225–228]. Yoshimura et al. [230] compared three methods of ranula treatment in 27 patients and reported a recurrence rate of 25 % with excision of ranula only, 36 % with marsupialization, and 0 % with ranula and ipsilateral sublingual excision. Moreover, the comparative study in children by Crysdale et al. [231] showed a recurrence rate of 61 % with marsupialization, and 0 % with either excision of ranula only or with ranula and ipsilateral sublingual gland excision.

With the patient under general anesthesia, nasotracheal intubation and oropharyngeal packing (to prevent aspiration), excision of a ranula can be achieved through the oral cavity, which is opened with a self-retaining mouth retractor. An elliptical incision is then made over the curve of the cystic swelling and the mucosal flap over the cyst is carefully freed from the ranula, by both blunt and sharp dissection (Fig. 3.35).

The cystic swelling is then grasped with serrated forceps and freed from Wharton's duct by blunt dissection and from its connections with the underlying mylohyoid muscle. All small vessels in the field are controlled with bipolar coagulation forceps. After excision of the ranula together with the sublingual gland, the sound lingual nerve can be seen lying on the floor of the mouth next to Wharton's duct. After careful hemostasis, the wound is irrigated with saline solution and the mucosa is closed with 3–0 Vicryl sutures. Frequent oral irrigations with oral antiseptic solutions are recommended for optimal oral hygiene, and oral feeding is started with clear liquids and pureed foods.

3.7.2.2 Treatment of Sublingual Malignant Neoplasms

Since the sublingual gland lies directly beneath the mucosal surface of the anterior floor of the mouth, and close to the inner aspect of the mandible, treatment of a sublingual MT usually entails removal of the gland with a surrounding cuff of normal tissue (floor of the mouth and lateral aspect of the oral tongue). The development of a soft tissue cuff around an MT confined to the sublingual gland without extra-glandular extension can be achieved through excision of the mucosa (floor of the mouth and small segment of the tongue), the mylohyoid muscle, and the periosteum of the mandible.

Most salivary gland cancers arising in the floor of the mouth are done in concert with at least level I neck dissection, thus removing the submandibular gland. Treatment of a moderately advanced sublingual gland cancer includes ipsilateral neck dissection with resection of the sublingual gland and surrounding tissues (floor of the mouth and lateral aspect of the tongue), usually in association with a marginal resection of the mandible. A more advanced or recurrent cancer of the sublingual gland is likely to require resection of the floor of the mouth along with a partial glossectomy, mandibulectomy, supraomohyoid structures, and the lingual and hypoglossal nerves. The neck dissection is completed in the usual fashion except for level I, through which the specimen is attached to the primary tumor.

Removal of the sublingual gland is not without potential morbidity, most notably injury to the lingual nerve with subsequent numbness, injury to Wharton's duct with the possibility of obstructive sialadenitis, and ductal laceration causing salivary leakage [228].

3.8 Minor Salivary Glands

About 600–1,000 minor salivary glands, ranging in size from 1 to 5 mm, are found throughout the oral cavity, with the greatest density in the buccal and labial mucosa, the posterior hard palate, and tongue base. They can also be found along the tonsils, supraglottis, and paranasal sinuses. Any of these sites can be the source of glandular tumors.

3.8.1 Surgical Anatomy

Each gland has a single duct which secretes saliva directly into the oral cavity, which can be serous, mucous, or mixed. The majority of these glands are either mucinous or seromucinous, except for the serous *Ebner's glands* on the posterior aspect of the tongue [228]. Postganglionic parasympathetic innervation arises mainly from the *lingual nerve*. The palatine nerves, however, exit the sphenopalatine ganglion to innervate the superior palatal glands. The oral cavity region itself determines the blood supply and lymphatic drainage of the glands [224].

3.8.2 Tumors of Minor Salivary Glands

Tumors of the minor salivary glands account for 10–15 % of all salivary gland neoplasms [68]. The most common location is by far the palate, followed in decreasing order by the maxillary antrum, tongue, cheek, lips, and nasal cavity. Malignancy rates vary from 30 to 90 % [176, 204, 232].

3.8.2.1 Clinical Presentation

Tumors of the minor salivary glands rarely produce symptoms unless they have reached a relatively large size. The majority of patients are aged 60 years or older [222], with women slightly more affected than men [232]. Most present with a painless non-ulcerative, submucosal mass that is firm or hard, mobile or fixed. The mucosal layer is adherent to the mass and a small ulcer may be present. According to the location of the tumor, patients may also present clinically with nasal obstruction, Eustachian tube obstruction, hoarseness of voice, or dyspnea. Approximately one-quarter of patients present with local pain [222, 225], which warrants investigation by MRI to rule out nerve invasion [233]. At the time of presentation, more than 15 % of patients will have cervical LN metastases [142, 234].

3.8.2.2 Diagnosis

Physical examination and high suspicion of a submucosal swelling in the head and neck to

originate from minor salivary glands and to be more likely of malignant rather than benign origin are the most important clinical information that will help give an accurate diagnosis.

Imaging using CT and/or MRI will aid delineation of the tumor, accurate staging, and correct planning of surgical intervention. The use of FNAC may be helpful in correctly classifying the tumor as benign or malignant; however, the use of incisional or punch biopsy may reveal the correct histological type. Complete excision should be avoided as it is likely that the margins will be close or positive and that orientation of these incomplete margins will not be possible at the time of pathological analysis and will thus interfere with proper subsequent planning of surgical salvage. Searches for distant metastases are worthwhile but should not alter plans for surgical ablation for a symptomatic primary lesion. In many instances, distant metastases, particularly to the lungs, may remain indolent for many years.

3.8.2.3 Benign Tumors

Pleomorphic Adenoma It is the most frequent BT of minor salivary glands, most commonly occurring in the hard palate, followed by the upper lip. It has also been located in areas as diverse as the tongue [187, 220], nasal cavity and septum, larynx, and trachea. Young children may also present with pleomorphic adenoma [90, 91], the majority of which are located in the hard palate region. Some of these pleomorphic adenomas can become massive with malignant degeneration before presentation [223].

Other Benign Neoplasms Other BTs of minor salivary gland origin that have been reported in the oral cavity include basal cell adenoma [142].

3.8.2.4 Malignant Tumors

The most frequently encountered MTs of minor salivary glands are adenoid cystic carcinoma (32–69 %) [190, 235] and mucoepidermoid carcinoma (15–35 %), and the less frequently are acinar cell carcinoma, polymorphous adenocarcinoma, myoepithelial carcinoma, and carcinoma ex-pleomorphic adenoma [190].

Adenoid Cystic Carcinoma (ACC) It is a locally vicious tumor that spreads with perineural invasion with bone and soft tissue destruction. Margin failure at surgical resection is common, and LN metastases occur in approximately 15 % of patients and hematogenous spread, particularly to the lung and bone, in nearly 50 % [235]. These tumors can be graded according to Szanto et al. [236] as cribriform or tubular (grade I), <30 % solid (grade II), or >30 % solid (grade III).

Adenocarcinoma It arises from the mucous glands of the high nasal cavity, the nasopharynx, and the paranasal sinuses. Adenocarcinomas occur as papillary, sessile, and alveolar-mucous types, and most of them behave like the adenoid cystic variety, with a propensity for extensive local growth and rare regional metastases to cervical LNs [235]. Polymorphous low-grade adenocarcinoma (PLGA) needs to be differentiated from other types of adenocarcinoma because of differing biological behaviors, with generally better prognosis [224, 227, 237].

Mucoepidermoid Carcinoma (MEC) When present in the minor salivary glands, MECs tend to be intermediate or high grade, with an increased incidence of LN metastases as compared to other types of carcinomas, particularly when they occur in the oral cavity.

Carcinoma Ex-pleomorphic Adenoma (CEPA) It is much less common in the minor salivary glands than in the major salivary glands.

3.8.2.5 Treatment

The hallmark of treatment of resectable tumors of minor salivary gland origin, whether benign or malignant, is *wide surgical excision* in order to avoid recurrence. A multidisciplinary is essential. Patients requiring maxillectomy are fully evaluated preoperatively by the maxillofacial prosthodontist, and a preliminary prosthesis is fabricated so that it can be placed at the time of definitive surgery. Currently, neck dissection is only indicated when there are demonstrable metastases present (clinical or imaging) or when the neck is being surgically entered as an approach to the primary tumor.

Postoperative radiotherapy is frequently employed in the large primary tumors and those with close margins and has been shown to be effective in nearly all forms of these tumors, particularly adenoid cystic carcinoma [238, 239].

Primary radiotherapy is indicated for patients who refuse surgery or those with an inoperable/unresectable tumor [201]. The role of neutron radiotherapy is indicated, when available, for unresectable or inoperable locoregional cancer [240].

The role of chemotherapy remains controversial and should individualized, such as in a palliative situation for relief of symptoms when the cancer is unresectable or recurrent after treatment, for patients not amenable to radiotherapy, and those with distant metastatic cancer.

3.8.2.6 Prognosis

In general, treatment of all tumors of minor salivary glands has been disappointing, with cure rates of about 30 % of all patients at 10 years [235]. Tumor stage, histology, and grade are the most important predictors for survival [205]. These variables are able to influence treatment outcome, although stage seems to be more important than grading [234, 241].

In ACC, the prognostic factors associated with poor prognosis are perineural invasion, positive margins, and solid histological features. In MEC, reduced survival was associated with male gender, LN metastases, high-grade of malignancy, strong expression of proliferating cell nuclear factor (PCNA), and weak expression of c-erbB-2 gene (a gene with an important role in the development, differentiation, and mitogenic signaling in normal cells) [242].

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