Chapter 3: Developmental anomalies, cysts and infiltrations

The main developmental anomalies of the salivary glands are aplasia of glands, atresia of ducts, accessory or ectopic glands, and a variety of cysts. Other types of cysts are acquired but both developmental and acquired cysts are described here.

Congenital tumours such as haemangiomas and embryomas are described in Chapter 8.

Developmental Anomalies

Aplasia and duct atresia of salivary glands

Aplasia of one or more glands has been reported but is exceptionally rare. Even more rarely, it is complete and then results in total failure of secretion of saliva and its complications. Though salivary gland aplasia may be a feature of some congenital syndromes, it is not usually a significant feature of anhydrotic ectodermal dysplasia.

Duct atresia is less uncommon and may affect the submandibular duct. A cyst may develop as a consequence.

Accessory salivary glands

Accessory parotid tissue is so common as almost to be within the limits of normal. It has been found in 20% of persons by Polayes and Rankow (1979). This tissue which forms one or more lobules, lies along the line of, and is closely related to, the parotid duct, into which its ducts open. It has the same histological structure as the parotid gland and suffers from the same tumours and other diseases, though considerably less frequently. A small tumour of accessory parotid tissue may be made more apparent when the mouth is opened and the forward movement of the mandibular condyle or coronoid process displaces the mass outwards.

Ectopic and aberrant salivary tissue

Ectopic salivary tissue can form within the developmental areas of the first and second branchial arches, in the lateral part of the neck, pharynx or middle ear. Salivary tissue is frequently present in lymph nodes or extranodal lymphoid tissue particularly in the parotid and adjacent regions and this is more important from the practical viewpoint as the appearances may be mistaken for nodal metastases.

More rarely, ectopic salivary tissue may be found in a variety of sites within the head and neck region, ranging from the gingivae to the brain.
An uncommon anomaly known as a Stafne bone cyst (Fig. 3.1) as a result of its radiological appearance, is formed by invagination into the bone of the lingual aspect of the angle of the mandible, by a lobe of the submandibular gland. More rarely, normal salivary tissue may be found within the anterior mandible and Buchner et al (1991) were able to find 20 reports and presented four more of the abnormalities. They are seen radiographically as round, sharply defined cyst-like areas of radiolucency.

Intraosseous salivary gland tumours of the jaw are a recognized but rare entity (Chapter 8) and presumably arise from these foci of ectopic tissue. Even more rarely, tumours may develop in any other sites of ectopic salivary gland tissue.

Ectopic salivary tissue lacking an excretory duct can rarely give rise to salivary fistulas.

**Polycystic Disease of the Parotid Glands**

This rare anomaly described by Seifert *et al* (1981) may be unilateral or bilatera. Seifert *et al* (1986) found 2 cases among 8000 salivary gland lesions in the Göttingen Registry and there has been 1 case among 3500 salivary gland tumours in the BSGTP material. This last case was reported and illustrated in detail by Dobson and Ellis (1987).

 Clinically, salivary gland enlargement is typically present in childhood and the swelling may increase in size at meal times. Sialography shows a snowstorm appearance resembling punctate sialectasis. Operation and diagnosis may however be delayed until adult life and the second case reported by Seifert *et al* (1981) did not present until the age of 56 years.

**Microscopy**

Though the normal architecture of the parotid may be preserved, almost the whole of the gland may be occupied by cysts of varying size, which distend the lobules. Between the cysts, there are residual serous acini and normal interlobular septa and excretory ducts (Fig. 3.2).

The cysts are lined by a single layer of flattened, cuboidal or columnar cells (Fig. 3.3). In the case reported by Dobson and Ellis (1987), the columnar cells had more abundant eosinophilic cytoplasm than intercalated duct lining cells and had rounded luminal cell borders. Large amounts of stainable lipid may be present in the epithelial cells.

In places, the cyst-lining cells may be heaped up to give a pseudopapillary appearance. Occasionally, both distended acini and striated ducts can be seen opening into the cysts, while in remaining intact acini the ducts may be dilated (Fig. 3.4). Inflammatory changes are absent unless there has been secondary infection.

Eosinophilic amorphous material is present in many of the cyst cavities and also there are typically, rounded concretions with a concentric laminated or radial pattern or conglomerates of smaller bodies. They are strongly eosinophilic and PAS-positive. They also stain with Congo red and show the apple-green birefringence characteristic of amyloid.
Electron microscopy shows only the cuboidal cyst lining cells to have features of intercalated duct epithelium. It also confirms the fibrillary structure of amyloid in the spheroliths.

**Behaviour and prognosis**

Polycystic disease of the parotids appears to be completely benign but removal of the glands may be necessary for cosmetic reasons or for confirmation of the diagnosis. As Dobson and Ellis also note, there was similar polycystic disease in ectopic salivary tissue in the cervical lymph nodes and this could have given rise to the mistaken diagnosis of metastatic adenocarcinoma.

**Congenital Sialectasis of the Parotid Glands**

This rare anomaly described by Becker et al (1960) is characterized by ectasia of ducts which, however, open into an otherwise intact duct system. The dilated ducts are lined by a thin layer of flattened epithelium but are distinguishable from acquired duct dilatation only by the absence of any inflammatory infiltrate.

**Congenital and Acquired Cysts of Salivary Glands**

**Ranulae**

The superficial mucous retention cysts of the floor of the mouth may be congenital or acquired and may therefore be found, rarely in the newborn, or more frequently in adults.

Clinically, a ranula forms a superficial translucent swelling in the floor of the mouth with a frog's belly appearance and usually just to one side of the midline. One characteristic effect is to cause loud snoring and it can, if large enough, displace the tongue and interfere with swallowing.

Occasionally, these cysts rupture spontaneously or as a result of unnoticed trauma, to release thick viscid mucus. Recurrence is then common.

**Microscopy**

Ranulae are usually lined by a flattened layer of modified duct epithelium which may be cuboidal or columnar or there may be squamous metaplasia (Fig. 3.5). There is frequently an inflammatory infiltrate in the walls and the cyst may be multilocular.

Treatment should be by dissecting out the cyst together with the sublingual gland if recurrence is to be avoided. Alternatively marsupialization may be successful.

**Plunging ranula**

This is something of a misnomer in that it may not have the frog-belly appearance of a simple ranula, nor is it of the same nature. Plunging ranula is considerably more uncommon than the simple variety.
Clinically, a plunging ranula forms a painless swelling in the submandibular or submental triangle and may be associated with a swelling in the floor of the mouth. Microscopically, a plunging ranula is a mucous extravasation cyst, the wall of which consists of loose cellular connective tissue and which is infiltrated by inflammatory cells. There may be adjacent pools of mucus also surrounded by inflamed connective tissue.

**Treatment**

Removal of the cyst together with its parent salivary tissue should be carried out as, until recently, there has been no diagnostic measure which reliably differentiates a plunging ranula from clinically similar swellings such as thyroglossal cysts, cystic hygromas or dermoid cysts. However, computerized tomography scanning appears capable of making this distinction.

Nevertheless, dissecting out a plunging ranula is surgically difficult, particularly if there have been earlier attempts, and as a result other methods such as insertion of a grommet or even irradiation have been suggested in the past. The value of inserting a grommet has not been tested on any scale but radiation is clearly inadvisable for this benign condition.

**Mucocoeles (mucous extravasation and retention cysts)**

**Mucous extravasation cysts**

These are by far the most common type of mucocoeles of minor salivary glands. The most frequent identifiable immediate cause is trauma, frequently unnoticed or forgotten, causing tearing of a duct and extravasation of mucous into the surrounding tissues.

Clinically, the most common site is the lower lip, but can be the buccal mucosa, floor of the mouth or almost any other site within the mouth. The swelling is dome-shaped, bluish, with a thin, readily ruptured roof and typically a little over a centimetre in diameter (Fig. 3.6). In their earlier stages however the swellings appear solid.

The peak age incidence is in the second and third decades.

Microscopically, mucous extravasation cysts in their early stages consist of poorly circumscribed pools of extravasated mucus surrounded by granulation tissue or loose vascular connective tissue infiltrated by inflammatory cells and macrophages (Fig. 3.7). If the deposits of mucus are inconspicuous, the true nature of these lesions may be missed and they may be interpreted as purely inflammatory. However, the diagnosis can readily be made if muciphages are identified and occasionally mucus can be seen escaping from a damaged duct (Fig. 3.8). The minor salivary gland of origin can also frequently be seen adjacent to the lesion.

Later, the pools of mucus coalesce until there is typically no more than a single cyst with a wall of compressed connective tissue with a patchy chronic inflammatory cellular infiltrate (Fig. 3.9).

The cyst should be excised complete with its underlying salivary gland.
Mucous retention cysts

These have a lining of compressed ductal epithelium and are comparatively uncommon (Fig. 3.10). They are not distinguishable clinically from mucous extravasation cysts and are treated in the same way.

Subepithelial mucocoeles

Rarely, mucocoeles are so superficial as to be immediately subepithelial (Fig. 3.11). If their origin from salivary tissue is not apparent, these lesions can mimic microscopically and clinically, the bullae of such diseases as mucous membrane pemphigoid.

Limited resection of the cyst and underlying gland is curative.

Salivary duct cysts

Though microscopically similar to mucous retention cysts of minor glands, salivary duct cysts differ in that they mainly form in the parotid glands, usually in elderly men. These cysts are usually unilocular and rarely exceed 2-3 cm in diameter.

Microscopy

The modified duct epithelium lining the cysts may be flat and multilayered (Fig. 3.12). Occasionally it may show oncocytic change or rarely, squamous metaplasia. There may be spherolith formation in mucoid cyst contents.

There is typically only sparse inflammatory infiltration of the cyst walls but small granulomas may form as a result of extravasation of mucus. Increase in size of the cyst can lead to obstructive sialadenitis.

Complete removal of the cyst, with care to preserve the facial nerve, is indicated.

Lymphoepithelial cysts

Lymphoepithelial cysts are uncommon and are unusual in that they mainly affect the parotid glands but can also form in the floor of the mouth.

The essential microscopical features are those of an epithelium-lined cyst in the centre of a dense aggregate of lymphoid tissue of similar cellular composition to a lymph node and which usually contains follicles (Fig. 3.13).

The epithelial lining of these cysts is variable in character though usually flattened but multilayered. It sometimes contains goblet cells or rarely, sebaceous cells. The cyst contents are serous and typically contain desquamated epithelial cells, foam cells and lymphocytes in varying numbers. Cholesterol clefts and granuloma formation may be seen in the stroma.

Lymphoepithelial cysts should be excised completely. However, these cysts should be distinguished from the lymphoepithelial cysts seen in patients with HIV infection. These are
discussed below and in more detail in Chapter 4.

**Branchial cleft cysts**

These congenital cysts lie along the line of the anterior border of the sternomastoid muscle and controversy persists as to whether or not they are different entities from lymphoepithelial parotid cysts, as discussed by Verbin and Barnes (1985). Microscopically, these two types of cyst cannot be distinguished but it seems likely that lymphoepithelial cysts in the parotid gland result from cyst formation in intranodal epithelial inclusions.

Branchial cleft cysts present frequently in children as a consequence of recurrent infection. Incision and drainage in the acute stage should be avoided, because of the risk of damage to the facial nerve. The cyst should therefore be aspirated and appropriate antibiotic treatment given. Elective superficial parotidectomy can be carried out when the inflammation has completely subsided. This may be exceedingly difficult because of local fibrosis and the small size of the child's facial nerve.

Branchial cleft cyst carcinoma is a rarity and discussed by Foss et al (1991), it is also controversial whether it arises as a result of malignant change in the lining or is a metastasis from a tonsillar carcinoma or other occult primary.

**Lymphoepithelial cysts associated with HIV infection**

Elliot and Oertel (1990) have reviewed 14 lymphoepithelial cysts from salivary glands. All were in lymph nodes and lined by squamous epithelium. There was a mixed mononuclear cell infiltrate but multinucleate giant cells were present in four cases. All five of the patients tested for HIV infection were positive.

These cysts resemble benign lymphoepithelial lesion in many respects but for the cavity which may form a major part of the mass. In some cases, the lesion is almost entirely cystic with no more than nodules of lymphoplasmacytic tissue, forming mural thickenings. Also unlike benign lymphoepithelial lesion, they predominantly affect young adults males and when seen in such patients are strongly suggestive of HIV infection. These lesions are described in more detail in Chapter 4.

**Infiltrations and Miscellaneous Salivary Gland Diseases**

The following are considered here:

1. Lipomatosis
2. Onocytosis
3. Mikulicz syndrome
4. Amyloidosis
5. Iron deposition
6. Uric acid deposition

7. Familial combined hyperlipidaemia.

**Lipomatosis**

Fat cells are a normal component of the parotid glands and can sometimes be found in the submandibular glands. The fat content of these glands increase with age (Fig. 3.14). Overgrowth of fatty tissue in the salivary glands may result from diabetes mellitus or severe obesity. In such cases, the fat is distributed interstitially, spreads to gland parenchyma apart and can give rise to a swelling. Tissue reduction by conservative surgery may then be required for cosmetic reasons.

Fatty replacement can also follow parenchymal atrophy from any cause. Seifert (1959) has described virtually complete replacement of parotid tissue by fat (lipomatous parotid atrophy) and compares it with a similar phenomenon in the pancreas of infants, a condition thought to result from early viral infection, particularly with coxsackie B viruses which may have a role in some cases of early onset insulin-dependent diabetes mellitus.

**Oncocytosis**

Focal areas of oncocytic change in salivary glands and ducts becomes increasingly common with age (Fig. 3.15). Taked (1993) in a postmortem study of minor salivary glands from 217 cadavers found oncocytic change progressively more frequently with age until after 81 years, 100% were affected. It was more frequent in the duct system, and particularly in the interlobular ducts. Oncocytic hyperplasia (oncocytosis) also became more frequent with age with a peak frequency of 14.7% between the ages of 61 and 70 years. Occasionally, it becomes widespread and can be mistaken for an oncocytoma as discussed in Chapter 6.

**Mikulicz syndrome**

This term is sometimes given to widespread, bilateral enlargement of salivary and sometimes, lacrimal glands as a result of diseases such as infiltration by lymphoma or lymphocytic leukaemia, sarcoidosis, sialosis or other definable diseases. The term 'Mikulicz disease' is sometimes given to the condition more generally known as benign lymphoepithelial lesion as described in Chapter 8. Both of these terms should be avoided as they are a source of confusion.

**Amyloidosis**

Deposits of amyloid can be found in pleomorphic adenomas and possibly other epithelial tumours of salivary glands, but amyloid can also be deposited in otherwise normal salivary glands as a result of systemic amyloid disease. In amyloidosis secondary to immunocyte dyscrasias (characterized by AL-type amyloid - formerly termed 'primary amyloidosis') various parts of the gastrointestinal tract are frequently involved. However, in a series of 229 cases Kyle and Greipp (1983) and in an earlier, detailed review of 236 cases (mainly of AA-type amyloidosis) Kyle and Bayrd (1975) did not not note any salivary gland dysfunction clinically, though these glands were not specifically investigated. In reactive
systemic amyloidosis associated with chronic inflammatory diseases (characterized by AA-type amyloid and formerly termed 'secondary amyloidosis'), the liver, kidney and spleen are most likely to be involved. The apparent absence of salivary gland involvement may also be noted in the clinicopathological investigation of 131 cases of different types of amyloidosis, of which 76 were of AA-type, by Browning *et al* (1985).

There have also been several studies on the oral manifestations of amyloidosis and an extensive autopsy study was carried out by Van der Wal *et al* (1984) who also reviewed previous reports. Macroglossia is the main oral effect of systemic amyloidosis, but even these studies do not appear to have noted any salivary gland involvement in terms of swelling or diminished secretion.

The rarity of substantial deposits of amyloid in salivary glands is emphasized by the fact that the report of a localized primary amyloid tumour-like mass in a parotid gland by Stimson *et al* (1988), was claimed to be the first such case in the English literature. This patient, a man of 65 years, had a painless parotid swelling of one year's duration but was otherwise well and had no detectable systemic abnormalities. The patient remained well at one year later.

In a woman of 58 years with xerostomia and xerophthalmia, reported by Gogel *et al* (1983), no autoantibodies suggestive of Sjögren's syndrome could be detected, but minor salivary gland biopsy showed gross amyloid deposition and acinar atrophy. Biopsy of other organs showed widespread amyloidosis (Adelta VI type), from which she died three months afterwards.

Despite the paucity of reports of significant deposits of amyloid in the major salivary glands of patients with amyloid disease, Delgado and Mosqueda (1989) have reported that in 19 patients with secondary amyloidosis, amyloid deposits were found in the labial salivary glands in all cases.

**Microscopy**

The gland parenchyma is progressively replaced by homogeneous eosinophilic material with the staining properties of amyloid (Fig. 3.16), a patchy inflammation and sporadic giant cells (Fig. 3.17). The amyloid also shows the characteristic birefringence in polarized light (Fig. 3.18). In the cases of secondary amyloidosis reported by Delgado and Mosqueda (1989), the deposits in the labial glands were not immediately obvious in haematoxylin and eosin-stained sections but were made apparent by Congo red and crystal violet staining. The distribution was periductal in all cases, and also periacinar in 84%, perivascular in 68% and interstitial in 37%. The amount of deposit ranged from a thin periductal layer to massive infiltration of the gland.

It seems, therefore, that amyloid deposition is unlikely to cause any significant clinical sign or symptoms of salivary gland dysfunction. However, detection of amyloid in the labial glands, as suggested by Delgado and Mosqueda (1989), may be a highly sensitive method of diagnosis in secondary amyloidosis. If, therefore, amyloid deposition is found by chance in salivary glands and is not associated with a tumour, then the patient should be investigated for possible causes of systemic amyloidosis.
Iron deposition

Iron deposits in the salivary glands can be found in haemochromatosis and a resulting sicca syndrome has been reported by Blandford et al (1979) and also by Vrielinck (1988) in a patient with myelodysplastic syndrome and transfusion-related haemochromatosis.

Iron deposits are likely to be more frequently found in thalassaemia since, worldwide, this is a far more common disease. In thalassaemia, iron deposition in salivary tissue may also be associated with a sicca syndrome. In a 20-year-old male with thalassaemia minor, reported by Borgna-Pignatti et al (1984), the disease had been diagnosed 19 years earlier and heavy deposits of iron were found in the labial salivary glands.

Microscopy

The salivary glands show acinar atrophy, interstitial fibrosis and brownish deposits of iron particularly in the periphery of the acinar and duct cells (Fig. 3.19). The nature of these deposits is readily confirmed by Prussian blue (Perl) staining (Fig. 3.20).

Uric acid deposition

Eilon et al (1982) have reported a patient with hyperuricaemia and a recurrent, mildly painful parotid swelling in a 26-year-old man. Microscopic analysis of the saliva from the swollen gland showed uric acid crystals and the salivary uric acid was the same as that of the serum (9.6%).

Lowering the serum uric acid level with probenecid resulted in improvement in the symptoms and it was suggested that the deposition of uric acid crystals in the salivary ducts had led to recurrent episodes of obstruction and infiltration.

Familial combined hyperlipidaemia

Xerostomia may be a major complaint in patients with type V hyperlipidaemia (raised cholesterol, triglyceride, chylomicron, and very-low-density lipoprotein levels) as reported by Reinertsen et al (1980). Salivary gland scans suggest that focal inflammatory infiltrative lesions and obstructions may be present.