Surgical pathology of the mouth and jaws

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12. Tumours of salivary glands

A great variety of neoplasms can form in the salivary gland tissues. The classification of Thackray and Sobin (1972) (Table 12.1) is still widely used, but inevitably has been overtaken by the recognition of new types of tumours. A modified classification broadly based on changes proposed by the WHO Collaborating Center for Salivary Gland Tumors is therefore shown in Table 12.2, but even so it is not always easy to fit a particular tumour into one of these many categories. Non-neoplastic diseases have been discussed in the previous chapter, but in the parotid gland particularly it is not always possible to distinguish them from neoplasms preoperatively.

Table 12.1 Classification of salivary gland tumours (After Thackray and Sobin, 1972)

Epithelial
A. Adenomas
1. Pleomorphic adenoma (mixed tumour)
2. Monomorphic adenoma
    (a) Adenolymphoma (Warthin's tumour)
    (b) Oxyphilic adenoma (oncocytoma)
    (c) Other monomorphic adenomas

B. Mucoepidermoid tumour
C. Acinic cell tumour
D. Carcinomas
1. Adenoid cystic carcinoma
2. Adenocarcinoma
3. Squamous cell carcinoma
4. Undifferentiated carcinomas
5. Carcinoma in pleomorphic adenoma

Non-Epithelial
Haemangioma
Lymphangioma
Neurofibroma
Lipoma
Others including malignant varieties of the above
Lymphoma.

Age, site and sex distribution in relatin to tumour type

In the British Salivary Gland Tumour Panel series of more than 3500 unselected tumours, there is a wide age distribution, but the peak incidence for benign tumours is in the sixth decade and, for malignant tumours, the seventh. Thus in the third decade, nearly 95% of tumours are benign, but by the seventh decade and after, 30% of tumours are malignant. Overall, women are only slightly more frequently affected, until the eighth and ninth decades, when women are almost twice as frequently affected as men. This, however, must be related

to a female predominance of 2 to 1 at these ages in the general population. For certain tumour types there is also a female predominance, as discussed later.

Table 12.2 Modified histopathological classification of salivary gland tumours

I. Adenomas
- Pleomorphic adenoma
- Myoepithelioma
- Warthin's tumour (adenolymphoma)
- Oncocytoma
- Duct adenomas
  - Basal cell adenoma and membranous variant
  - Canalicular adenoma
- Sebaceous adenoma and sebaceous lymphadenoma
- Duct papillomas
  - Inverted duct papilloma
  - Intraduct papilloma
  - Sialadenoma papilliferum
- Papillary cystadenoma

II. Carcinomas
- Mucoepidermoid carcinoma
- Acinic cell carcinoma
- Adenoid cystic carcinoma
  - Cribriform cystic carcinoma
  - Cribriform/tubular
  - Solid
- Adenocarcinoma (not otherwise specified)
- Papillary cystadenocarcinoma
- Carcinoma in pleomorphic adenoma
  - Intracapsular (non-invasive)
  - Invasive
  - Carcinosarcoma
  - Metastasizing pleomorphic adenoma
- Polymorphous low-grade (termina duct) adenocarcinoma
- Epithelial-myoepithelial carcinoma
- Salivary duct carcinoma
- Basal cell (basaloid) carcinoma
- Sebaceous carcinoma
  - Sebaceous carcinoma with lymphoid stroma
- Oncocytic carcinoma
- Squamous cell carcinoma
- Adenosquamous carcinoma
- Undifferentiated carcinoma
  - Small cell and neuroendocrine carcinomas
- Undifferentiated carcinoma with lymphoid stroma
- Other carcinomas

III. Mesenchymal Tumours
- Angiomas
- Lipomas
- Neural tumours
- Other benign mesenchymal tumours and hamartomas
- Sarcomas

IV. Malignant Lymphomas

V. Secondary Tumours

VI. Unclassified Tumours

VII. Tumour-Like Disorders
- Sialosis (sialadenosis)
- Oncocytosis
- Necrotizing sialometaplasia (salivary gland infarction)
- Benign lymphoepithelial lesion
- Salivary gland cysts
- HIV-related cysts and other disorders
- Küttner tumour (chronic submandibualr sialadenitis).

Over 70% of salivary gland tumours are in the parotid, 11% are in the submandibular glands, and the remainder are distributed as shown in Table 12.3. However, in relative terms, malignant tumours are more frequent in the minor salivary glands; thus only 16% of parotid tumours but 78% of sublingual gland and 46% of minor gland tumours are malignant.

As to minor glands (approximately 14% of all salivary gland tumours), 54% are in the palate, 20% in the lips and 10% in the buccal mucosa.

General clinical features

Though usually painless, a painful salivary gland swelling is strongly suggestive of malignancy. However, non-malignant parotid swellings such as infection, some Warthin's tumours and a few cases of Sjögren's syndrome can also be painful, and there are no reliable clinical indicators of malignancy. However, rapid growth, pain, lymphadenopathy and, in the case of the parotid gland, facial palsy are strongly suggestive and are likely to indicate a poor prognosis.

Within the mout, salivary gland tumours may be firm or rubbery, and may feel lobulated. If benign, they are mobile on deeper tissues, the overlying mucosa is normal, unless traumatized, but sometimes appears bluishj. Growth of some adenomas can be exceedingly slow.

Imaging techniques

Despite the advances in imaging techniques, they will not as yet distinguish neoplastic from inflammatory disease, nor benign from malignant tumours in all cases.

Sialography. This is useful only for chronic inflammatory disease and is of little value in tumour diagnosis.

Computerized tomography. CT scanning distinguishes well between glandular and adjacent soft tissue. It also allows examination in the transverse plane. The density of a gland varies considerably; it is ailways greater than that of fat but less than that of muscle. Most benign tumours have well-defined borders, while those with irregulra or indistinct margins suggest malignancy. The latter may be confirmed by extension into the infratemporal fossa or base of skull, or metastatic deposits. Multiple lesions suggest malignant lymphoma, Warthin's tumour or metastasis.

CT may help to predict the relationship of a mass to the facial nerve. Such information is of preoperative value, as removal of a lesion which distorts the anatomy at the foramen, or has a significant component deep to the nerve, is likely to be demanding. Deep-lobe tumours are as easy to visualize as superficial tumours, and their extent is precisely shown.

CT scanning is also valuable for distinguishing intrinsic from extrinsic parotid disease and may help to distinguish deep-lobe parotid from lateral pharyngeal (minor gland) tumours. Parapharyngeal tumours are usually separated from the gland by a layer of normal fat. If this layer is absent, the mass is probably a deep-lobe parotid tumour. However, large deep-lobe tumours obliterate this plane and make diagnosis difficult.

Intravenous contrast medium may help to demonstrate the relationship of tumours to major vessels and vascular malformations. Jugulotympanic paragangliomas, being highly vascular, are enhanced dramatically by contrast medium. Rarely, a paraganglioma may mimic deep-lobe salivary gland tumours of the parotid clinically.

Unfortunately, extensive dental restorations cause disruptive artefacts which can significantly detract from the quality of CT scans.

Magnetic resonance imaging. MRI is as sensitive as CT for detection of salivary gland tumours. Both T_1 and T_2 images show the margins of the lesion withequal clarity, but T_2 sequences may define tumour composition better. Paramagnetic contrast materials may improve this aspect of MR imaging even further. Unlike CT, MR images are not distorted by dental restorations.

There is little to choose between CT and MRI for the diagnosis of salivary gland disease and the ultimate choice is mainly influenced by the type of scanners available, cost and personel preference. The indications for CT or MRI can be summarized as follows:

Parotid glands

- masses confined to the deep lobe
- tumours with involvement of both the deep and superficial lobes (dumb-bell tumours)
- tumours causing facial weakness, other neural deficit or signs of malignancy
- congenital masses.

Submandibular glands

- tumours with neural deficit or fixation to the mandible.

Minor glands

- tumours of the palate with suspected involvement of the nose or maixillary antra
- any tumours with clinically ill-defined margins.

Neither CT nor MRI should be expected to be completely reliable and the main purpose of imaging is for detecting masses within the salivary glands and providing surgically useful images of the extent of disease. Sensitivity rates approaching 100% are claimed for both modalities, but image quality is influenced mainly by the generation of scanner or protocol adopted.

Ultrasound. The value of ultrasound in parotid disease is limited. The superficial portion of the gland is readily accessible to ultrasound examination, but the deep part is obscured by the ramus of the mandible.

The normal gland is homogenetous and gives fine, medium-range echoes. Its borders, although not sharply delineated, are easily visualized. Useful landmarks are the mandible (linear and strongly echogenic), and the masseter and sternomastoid muscles which are echo-poor compared with the parotid gland.

Ultrasound cannot characterize a focal lesion, but various ultrasonic characteristics may suggest the nature of the mass. It has the advantages of being non-invasive, inexpensive and relatively quick, and is useful if CT or MRI are not available.

Surgical management of parotid gland tumours

Pleomorphic adenomas are the most common tumours and readily recur but cannot be identified clinically. In view of the major risk of tumour cells disseminating during incisional biopsy of parotid gland tumours, fine-needle aspiration biopsy (Chapter 1) should therefore be used wherever possible.

Superficial parotidectomy should be carried out all clinically benign superficial lobe tumours. Total parotidectomy is required for deep lobe and dumb-bell tumours. Deep lobe tumours should never be approached from the pharyngeal aspect as the risk of recurrence is high. The facial nerve should be preserved wherever possible.

The prognosis for many malignant parotid tumours is poor. Radical parotidectomy with sacrifice of the facial nerve may not improve survival significantly, but it greatly worsens morbidity. If not macroscopically invaded by tumour, the facial nerve should therefore be preserved during parotidectomy. This should be followed by radiotherapy.

Anatomical considerations. The superficial lobe of the parotid gland rests on the masseter muscle. The deep part extends behind the mandible posterior to the pterygoid muscles. Medially lie the lateral pharyngeal space, internal carotid artery and internal jugular

vein. The facial nerve leaves the skull at the stylomastoid foramen and enters the posterior surface of the gland between the digastric and sternocleidomastoid muscles. It lies lateral to the retromandibular vein before dividing into its major branches over the ramus of the mandible. The gland is divided into superficial and deep lobes joined by an isthmus. The facial nerve lies in a connective tissue plane between these two lobes.

Successful parotid surgery depends upon taking into account two major anatomical features, namely:

1. The two lobes united by an isthmus.

2. The facial nerve and its branches, is surrounded by these lobes, but invested in loose connective tissue. The facial nerve, except when invaded by tumour, is separable from the substance of the parotid parenchyma.

Despite competent surgery, permanent facial nerve weakness may be expected after approximately 1-2% of parotidectomies. Disturbances of facial nerve function can follow 30% of parotidectomies but are usually of short duration.

Frey's syndrome may develop in a high proportion of patients undergoing parotidectomy, but its onset is usually delayed for about 2 years. Rare complications after parotid surgery include sialocele or salivary fistula.

Surgical management of submandibular gland tumours

All submandibular salivary tumours should be treated by total gland excision. For obviously malignant tumours, this forms part of a radical neck dissection and postoperative radiotherapy is also advocated.

Surgical management of minor salivary gland tumours

Biopsy is usually carried out before surgery. Treatment is by wide local excision, including palatal fenestration for tumours in this site if there is evidence of bony involvement.

Radiotherapy. Salivary tumours are often considered to be radioresistent. This is not necessarily true; regression after radiotherapy is usually slow, but this reflects the slow cell turnover time of the majority of these tumours, rather than the inability of radiation to effect a cure, and there are many reports of long-term local control of large inoperable tumours by radiotherapy. Nevertheless, the cure rate for radiotherapy. Nevertheless, the cure rate for radiotherapy seems to be lower than for squamous cell carcinoma of the oral mucosa, and therefore the primary treatment should be surgical wherever possible.

Radiotherapy may be given postoperatively wherever there is doubt about complete excision, but should only be given for malignant tumours. It should be given prophylactically after excision of any malignant salivary tumour. However, reliable information on the response of particular types of salivary gland tumour to radiation is scanty.

A wide margin around the tumour should be irradiated. This is frequently recommended, particularly for adenoid cystic carcinomas, though there is little evidence that it improves survival. A dose close to the limits of normal tissue tolerance is necessary.

Chemotherapy. There appears to be little place for chemotherapy in the treatment of salivary gland carcinomas, and as yet it seems to be no more than a treatment of last resort. Lymphomas, by contrast, respond well to radiotherapy or chemotherapy, or both.

Benign epithelial tumours

Pleomorphic adenoma

Pleomorphic adenomas account for 63% of parotid, 60% of submandibular and 43% of minor gland tumours. By contrast, they are rarely seen in the sublingual gland. Almost any age can be affected, but the peak incidence is in the fourth and fifth decades. There is a slight female predominance.

Microscopy

The main components are duct cells, often producing a multiplicity of duct-like structures, and sheets of epithelial or myoepithelial cells. The latter are not reliably identifiable by light microscopy as they may be small, darn and nondescript, spindle shaped or resemble plasma cells. Squamous metaplasia of epithelial cells is common. The result is a mixed and variable picture of epithelial and myoepithelial cells together with mucoid or myxomatous tissue, which may form the bulk of the tumour. Cartilage or, less frequently, true bone formation may be seen. This stroma forms 80% of the mass in approximately 50% of tumours. There is no proved correlation between these varied appearances and clinical behaviour, but recurrence may be more common with stroma-rich (mucoid) variants and carcinomatous change is most frequent in highly cellular tumours.

The mixed microscopic pictures are well known, but widespread misapprehensions persist about the capsule and have led to attempts to enucleate parotid gland tumours. Encapsulation may appear complete in the plane of section but the tumour, despite being benign, can bulge through or invade the capsule. Focal infiltration of the capsule is common and subcapsular clefts can provide false planes of cleavage. Whole organ sectioning of excised parotid pleomorphic adenomas by Lam et al (1990) showed that in all cases the capsule was infiltrated by tumour and that in a third of the cases the capsule was incomplete, with tumour in direct contact with salivary tissue. Apparently isolated islands of tumour can also occasionally form outgrowths of the main mass and be joined to it by only a thin neck.

Dysplasia in pleomorphic adenoma

The appearance, within the tumour, of areas of epithelial atypia despite absence of evidence of invasion (also sometimes termed intracapsular carcinoma or 'carcinoma-in-situ') inevitably causes concern. If it is possible to be confident that this change is confined within the substance of the tumour, then it can be treated like other pleomorphic adenomas by parotidectomy or wide excision of other glands. However, follow-up must be rigorous.

Spread, response to treatment and recurrence

Pleomorphic adenomas expand and grow in localized areas of proliferation to form irregular nodular masses. Major difficulties in the management of pleomorphic adenomas include the following:

- removal of tumours from the parotid gland without damage to the facial nerve is technically demanding

- biopsy of parotid gland tumours is not feasible because of their ability to seed in the line of incision to produce multiple recurrences

- the capsule is often incomplete and its integrity cannot be assumed if there is an unwise attempt at enucleation

- mucinous tumours can readily burst to produce multiple seedlings if enucleation is attempted

- removal of recurrences, which are typically multifocal, becomes more difficult with each attempt and the end result can be innumerable nodules of tumour, spreading in the neck far beyond the original site; treatment of recurrences increases the risk of having to resect the facial nerve or they may prove to be unmanageable

- the chances of malignant change are greater in recurrences, increase with each subsequent recurrence and may be increased further if radiotherapy is used.

In short, the ability of seeded tumour cells to proliferate outside the original margins and particularly in the incision scar, after incisional biopsy or incomplete excision, is well established. Malignant change is also more frequent in scarred areas. Recurrences may not become apparent for 10 or even 20 years and this can give a false sense of the completeness of excision and encourage dangerously conservative treatment policy. High reported cure rates after enucleation are based on inadequate duration of follow-up.

These considerations make it clear that incisional biopsy and so-called enucleation are contraindicated and that it is essential to remove pleomorphic adenomas completely by total or subtotal parotidectomy at the first operation.

Irradiation as a supplement to surgery may increase the chances of or accelerate malignant change. If reoperation is necessary, post-irradiation scarring and ischaemia greatly increase the difficulties. Nevertheless, radiotherapy is widely used if the tumour ruptures during surgery.

Myoepithelioma

Myoepithelial tumours are rare and, in effect, a variant of pleomorphic adenoma. The term *myoepithelioma* is frequently used for tumours where myoepithelial cells are predominant but some elements of a pleomorphic adenoma are present.

Microscopy

Spindle cell myoepitheliomas, the most common type, are highly cellular and consist of elongated, slender spindle cells forming interlacing streams with little stroma. They, therefore, resemble mesenchymal tumours such as neurofibroma. Occasionally, immunocytchemistry is required to detect the typical double staining of myoepithelial cells with epithelial (keratin) markers as well as mesenchymal markers, particularly S-100 protein, vimentin and smooth muscle actin.

Aggressive behaviour may not be entirely predictable from the microscopic appearances but mitotic activity and cellular pleomorphism are highly suspicious.

Plasmacytoid myoepitheliomas consist of elliptical or rounded cells, with hyaline, basophilic cytoplasm and eccentrically placed nuclei, in an abundant, loose and myxoid stroma. This variant does not appear to have any potential for aggressive behaviour. It is also unlikely for the resemblance to plasma cells to be so close as to be mistaken for solitary extramedullary plasmacytomas (Chapter 5).

Warthin's tumour (adenolymphoma, cystadenolymphoma)

These tumorus are completely benign, and carcinomatous or lymphomatous change is extraordinarly rare. Strangely, there has been in the past a heavy predominance of males with this tumour, but a male to female ratio of 10 to 1 has fallen to only 1.6 to 1 in the most recent series. The age affected is between 50 and 70 years. In the parotid glands, Warthin's tumour forms 14% of neoplasms, while other types of monomorphic adenoma - mainly the canalicular variant in the upper lip - form 11% of tumours of the minor glands.

Clinically, Warthin's tumour only affects the parotid glands and the authenticity of some of those reported in other glands is questionable. They usually produce soft painless swellings but sometimes there can be pain or rapid expansion, probably as a result of the partly cystic nature of most of them. Occasionally the tumour is bilateral or multifocal in a single gland.

Microscopy

Warthin's tumours have a thin capsule and consist of tall, columnar, finely granular, eosinophilic epithelial cells surrounding lymphoid tissue which frequently forms germinal follicles. The epithelium typically forms papillary projections into cystic spaces. The amount of epithelium and lymphoid stroma is highly variable and either may predominate.

Occasionally, part of the tumour can undergo apparently spontaneous necrosis (infarction) and epithelioid granulomas resembling those of tuberculosis may form. Taxy (1992) has also described squamous and mucinouos metaplasia in foci of necrosis, giving rise to appearances resembling squamous or mucoepidermoid carcinoma. However, Warthin's tumour can also occasionally be concurrent with other salivary gland tumours.

Treatment

Excision is curative but incomplete excision can lead to recurrence. Alternatively, recurrence may result from the tumour being multifocal.

Oncocytoma (oxyphilic adenoma)

Oncocytomas form less than 0.5% of epithelial salivary gland tumours. They particularly affect those in the seventh or eighth decades and are more frequent in women. The parotid glands are the usual site.

Microscopically, oncocytomas consist of distinctive, uniform, plump cells with abundant, granular eosinophilic cytoplasm, separated by fine fibrous septa. Occasionally, transition of oncocytes to clear cells can be seen. Oncocytomas consisting only of clear cells are a recognized entity but exceedingly rare.

Oncocytomas are benign and excision is curative. Reports of recurrences may be due to incomplete removal or failure to recognize either an oncocytic adenocarcinoma or oncocytic change in a carcinoma

Multifocal nodular oncocytic hyperplasia

Foci with a structure resembling that of oncocytomas may be seen, but they are small (up to 1 cm across), multiple and interspersed by normal salivary tissue. It is possible that oncocytomas arise by cofluence of these foci. Clear cells are most frequently seen in these foci, which may thus mimic a clear cell tumour infiltrating the gland.

Oncocytosis

Oncocytic change, which is occasionally extensive, can be seen as an age change in normal duct tissue and in other tumours such as pleomorphic adenomas or, more important, in adenocarcinomas. Since oncocytomas are benign, it is important to differentiate them from oncocytic change in other tumours which are far more difficult to manage. Palmer et al (1990) have shown that the majority of oncocytomas had been incorrectly categorized. Many were the result of oncocytic change in other tumours or oncocytosis.

Duct adenomas

Seventy-five per cent of this group are found in the parotid glands, 22% in the minor glands, where the lip is a site of predilection, but very few in other glands. Duct adenomas constitute about 20% of all adenomas. Duct adenomas comprise basal cell (tubular, trabecular and membranous types) and canalicular types which form slow-growing, well-circumscribed swellings.

Tubular adenomas consist of tubules, containing eosinophilic secretions. The tubules have a lining of small, dark epithelial cells and an outer layer of myoepithelial cells which may also form strands extending between the tubules; alternatively they may be few and

inconspicuous. The stroma is usually scanty and unremarkable, but a rare variant shows myoepithelial stromal proliferation.

Trabecular adenomas consist of a monotonous pattern of cords, uniform in width, of darkly staining cells in a sparse, featureless stroma. Rarely, a trabecular adenomas shows oncocytic change and may mimic an oncocytoma.

Membranous basal cell adenomas are rare. They have a thick, eosinophilic, PAS-positive hyaline layer surrounding the epithelium which may contain lumens and hyaline material. They are usually multilobular and may be incompletely encapsulated. They can also contain foci of normal salivary tissue to add to the impression of invasiveness and enhance their similarities to an adenoid cystic carcinoma.

Membranous basal cell adenomas most frequently affect the parotid glands and then may be associated with multiple similar (turban) tumours of the scalp. They are sometimes, therefore, termed dermal analogue tumours of the parotid. They may rarely undergo malignant change.

Canalicular adenomas, unlike tubular adenomas, lack myoepithelial cells surrounding the duct-like structures or cords of columnar or cuboidal epithelial cells. Cyst formation may be prominent, while degeneration of the stroma may leave it virtually structureless, and often only ghosts of blood vessels remain.

Treatment

Excision is normally curative. The chief risk with duct adenomas is that of confusing some of them with adenoid cystic carcinomas or basal cell adenocarcinomas. A thorough search of many fields may occasionally be necessary to confirm absence of invasion. If the biopsy is small it may be impossible to make the necessary distinction. Canalicular adenomas in the upper lip, in particular, have been mistaken for adenoid cystic carcinomas.

Clear cell adenoma

In the past, benign clear cell tumours have been described but their existence is doubtful. Most clear cell tumours are malignant, despite a cytologically benign appearance.

Papillary cystadenoma

The papillary cystadenoma is probably also not an entity and such tumours are well-differentiated papillary cystic adenocarcinomas. However, the fact that they may take between 10 and 20 years to recur has led to the belief that they were benign.

Sebaceous lymphadenoma and sebaceous adenoma

Both of these tumours are rare. The sebaceous lymphadenoma resembles Warthin's tumour but with sebaceous cells, forming solid masses and sebaceous cysts in place of the oncocytic cells. The pure sebaceous adenoma is particularly rare and consists of solid masses

of sebaceous tissue in a fibrous stroma. Sebaceous elements can rarely also be seen in pleomorphic adenomas.

Duct papillomas

Sialadenoma papilliferum

Most of these rare tumours have been in the minor glands, usually at the region of the junction of hard and soft palates. Unlike other salivary gland tumours, they form painless exophytic growths that resemble papillomas of the oral mucosa but grow from the orifice of a minor gland. The mean age of incidence is 59, but almost any age can be affected.

Microscopically, the superficial part closely resembles a squamous cell papilloma and consists of stratified squamous epithelium thrown up into papillae with a fibrovascular core. More deeply, this epithelium merges with proliferating, dilated duct-like structures and, frequently, microcysts with papillary projections into their cavities.

Local excision appears to be curative.

Inverted duct papilloma

Inverted duct papillomas of salivary glands are exceedingly rare; Clark et al (1990) found only 5 earlier reports.

Clinically, patients have been adults between the ages of 33 and 66 years, in whom the tumours formed smooth discrete masses 1-1.5 cm in diameter in various sites within the oral cavity, with no features to suggest the diagnosis.

Microscopically, inverted duct papilloma frequently forms just within the orifice of a gland and its epithelium may be continuous with that of the surface mucosa. The tumour consists of thick papillae covered by basal or squamous cells and may contain a few goblet or columnar cells. The papillary overgrowth fills the duct lumen and also bulges into, but does not infiltrate, the lamina propria. Microcysts lined by squamous or columnar epithelium occasionally form.

Excision appears to be curative and there is no evidence of a similar propensity for recurrence to inverted papillomas of the nasal cavity.

Intraduct papilloma

Intraduct papilloma is even more rare than other duct papillomas. It differs from the inverted duct papilloma in its origin more deeply in the salivary gland duct.

Microscopically, it consists of fibrovascular papillae covered by columnar or cuboidal epithelium, forming a mass which distends the duct lumen to form a cyst-like cavity. Unlike inverted duct papillomas, the tumour does not extend into the duct wall but obstruction by the tumour can give rise to secondary duct dilatation proximally. Excision is curative.

Carcinomas of salivary glands

Mucoepidermoid carcinoma

These form 1.5% of parotid tumours, nearly 9% of tumours of the minor glands but are virtually never found in the sublingual glands. Most mucoepidermoid carcinomas are in the parotid (49%) or minor glands (47%). Almost any age can be affected, but the peak incidence is in the fifth decade.

Clinically, most mucoepidermoid carcinomas are usually indistinguishable from benign tumours and rarely cause facial weakness or pain. Intra-oral mucoepidermoid carcinomas may appear more vascular and may grow faster than benign tumours.

Microscopically, mucoepidermoid carcinomas consist mainly of two distinct but contiguous cell types. These are epidermoid (squamous) cells and large, pale, faintly granular mucous cells. Microcyst formation is common and, as with ameloblastomas, mucoepidermoid carcinomas can occasionally consist of a large monolocular cyst with the tumour forming only a mural thickening. Careful assessment of the nature of the lining of salivary gland cysts is, therefore, essential.

In a survey of 143 intra-oral mucoepidermoid carcinomas, Auclair et al (1992) found that a short history, production of symtoms and location in the tongue or floor of the mouth, in association with microscopic criteria for malignancy, were indicative of a poor prognosis. These latter features comprised a small intracystic component, high mitotic activity, neural invasion, necrosis and anaplasia. Six out of 10 of their patients with high scores on these points died from their disease. However, even a benign cytological appearance does not guarantee benign behaviour. Even cytologically benign-looking tumours can sometimes metastasize.

Treatment

Even in the absence of microscopic evidence of invasion, all mucoepidermoid carcinomas should be regarded as potentially malignant and excised completely. Higher grade tumours should probably be treated like squamous cell carcinomas, but their response to radiotherapy is less predictable. Radiotherapy should only be used to supplement excision.

A retrospective analysis of 749 reported cases (Hickman et al, 1984) showed that an estimated 5-year survival rate for mucoepidermoid carcinomas was 70.7% and the 10-year survival rate was 50%. Their prognosis appears, therefore, to confirm that overall they are of relatively low-grade malignancy.

Acinic cell carcinoma

Acinic cell carcinomas usually have a characteristic and benign histological appearance, but nevertheless their behaviour is unpredictable.

Over 85% of acinic cell carcinomas are found in the parotid glands where they comprise about 3% of all tumours. Most of the remainder are found in the minor glands, but

rarely in the sublingual or submandibular glands. Almost any age can be affected, but the peak incidence is in the seventh decade and there is a female preponderance of almost 2 to 1.

Clinically, acinic cell carcinomas are frequently indistinguishable from adenomas, but 17% of poorly differentiated specimens have been reported by Seifert et al (1986) to cause facial palsy.

Microscopically, acinic cell carcinomas usually present an almost uniform picture of large, granular basophilic cells, closely resembling normal serous cells in sheets or in acinar configurations. There are usually many clear round spaces thought to result from entrapped secretion. Sometimes these spaces may be so numerous as to give the tumour a microcystic or lacy pattern. There may also be clear cells which are occasionally numerous or, rarely, predominant.

The tumour usually appears well circumscribed, but even cytologically benign tumours can sometimes be invasive. Occasionally, poorly differentiated acinic cell carcinomas are seen. They are more likely to cause facial nerve paralysis and have a poorer prognosis.

On the basis of only 101 reported cases suitable for analysis, Hickman et al (1984) estimated the 5-year survival rate for acinic cell carcinomas to be 82.2% and the 10-year survival rate 67.6%.

In view of the fact that even cytologically benign acinic cell carcinomas can occasionally metastasize, treatment (as with mucoepidermoid carcinomas) should be by parotidectomy, or wide excision, of other glands. If poorly differentiated, excision should be followed by radiotherapy.

Adenoid cystic carcinoma (cylindroma)

Adenoid cystic carcinomas form 30% of parotid, 30% of submandibular and 40% of minor gland tumours, but only 1% of sublingual gland tumours. Unlike most other salivary gland tumours, 70% of adenoid cystic carcinomas affect the submandibular or minor salivary glands.

Clinically, the peak age for adenoid cystic carcinoma is in the sixth decade. The features are similar to those of other salivary gland tumours, but facial palsy is particularly frequent, especially with the solid type.

Microscopically, small darkly staining cells of uniform appearance comprise both duct-lining and myoepithelial-like cells. They are typically arranged in well-circumscribed, rounded groups surrounding more or less circular spaces to give a cribriform (Swiss cheese) pattern. A few of these tumours have a tubular pattern. Hyaline material often forms in the connective tissue surrounding the islands of tumour and in the microcystic spaces. This mucoid material may form in such large quantities as to spread the tumour cells into a lace-like pattern or form coalescing nodules with thin, widely separated strands of tumour cells. At the opposite extreme there may be solid sheets of tumour cells with a solid (basaloid) pattern and,

sometimes, areas of necrosis. Such an appearance is associated with the worst prognosis. However, in all these variants it is often possible to find more typical cribriform areas.

Adenoid cystic carcinoma, though slow growing, has a characteristically infiltrative pattern of growth. Perineural and intraneural invasion is typical of, though not unique to, this tumour. It can, therefore, spread along bony canals and the distance of spread may be far greater than suggested by the radiographic area of bone destruction. Growth tends to be slow but inexorable and metastatic spread is usually late. Metastases are usually in regional lymph nodes and the lungs, but their growth may also be slow and allow survival for many more years. Excision of isolated metastases may be beneficial.

Hickman et al (1984), from reports of 1065 cases of adenoid cystic carcinomas, estimated the 5-year survival rate to be 62.4% and the 10-year survival rate 38.9%. Seifert et al (1986) gives a 5-year recurrence or metastasis rate of 36% for the cribriform type and of 70% for the solid type with areas of necrosis. Their 8-year survival rate was 67% for the cribriform type and 32% for the solid type. Overall, they report 5- and 12-year survival rates of 76% and 33%.

Treatment

There is no definitive protocol of management for adenoid cystic carcinoma. For example, Blanck et al (1967) reported 5- and 12-year survival rates of 73% and 39% for 35 patients, even though only 3 of them underwent parotidectomy. Another reflection of the difficulties in establishing a protocol for treatment is the remarkable degree of spread of reported survival rates which range from 0% at 10 years to 75% at up to 14 years. Even though spread of this tumour is relentlessly infiltrative, the present consensus is that supraradical surgery is not indicated and mutilating surgery cannot be justified. Its value is unproven and Seifert et al (1986) suggest that it may even worsen the prognosis. Since there is even less room for manoeuvre in treating adenoid cystic carcinoma of intra-oral glands, the prognosis may be worse than for the parotid gland. Quite frequently the postoperative history is one of limited local recurrence, each of which responds to local treatment, over the course of years. Adenoid cystic carcinomas should probably, therefore, be treated by radical resection (parotidectomy or its equivalent), with as wide a margin as is anatomically possible, but compatible with reasonable rehabilitation. In the case of the parotid gland, sacrifice of branches of the facial nerve invaded by tumour may be unavoidable. Radiotherapy should also be given. Though Seifert et al (1986) could not confirm that it prolonged survival, the consensus is that the best control is probably achieved by 'simple' radical surgery followed by radiotherapy.

Adenocarcinomas

Adenocarcinomas (not otherwise specified) show neoplastic duct or tubule formation microscopically, but lack any evidence of origin from a pleomorphic adenoma. Two variants, papillary cystic and mucinous adenocarcinomas, are recognized.

Adenocarcinomas probably form less than 5% of salivary gland tumours. Approximately 48% of these are in the parotid, 10% in the submandibular, and 21% in minor

salivary glands; fewer than 1% are in the sublingual glands. Males are usually in the seventh decade and appear to be affected almost twice as frequently as females.

Microscopically, adenocarcinomas consist of duct-like (tubular) structures. The cells may show significant atypia, although the tubules are well formed or the cytology may be relatively bland but tubules are poorly formed. Invasion and destruction of surrounding tissues and, sometimes, perineural invasion may be seen.

Management

The behaviour and prognosis of adenocarcinomas depend mainly on the degree of differentiation. Microscopically, solid (undifferentiated) types tend to have the worst prognosis. However, lymph node metastasis and bloodstream spread is frequent with most types, though the rapidity with which this happens varies widely. Inevitably the prognosis is also strongly affected by the extent of the primary tumour at operation. The overall 5-year survival rate is thought to be approximately 40%.

Papillary cystadenocarcinoma frequently affects the palate and is rare in other glands. Folds of epithelium project as papillary ingrowths into irregular cyst spaces. This epithelium appears cytologically completely bland and such tumours, which may also shell out readily at operation, have been wrongly categorized in the past as papillary cystadenomas. However, despite wide excision and even radiotherapy, these tumours are on record as metastasizing and causing the death of patients 15-30 years later.

Mucinous adenocarcinoma is another rare variant resembling its mucin-producing counterpart in the breast. Mucous cells and microcysts may cause it to simulate, to some degree, a mucoepidermoid carcinoma.

Treatment is by parotidectomy, if necessary with sacrifice of the facial nerve, or wide excision of other glands followed by radiotherapy.

Polymorphous low-grade adenocarcinoma (terminal duct carcinoma)

Patients are usually aged between 50 and 75 years. Minor glands, particularly of the palate, are affected and the tumour typically forms a firm, painless swelling which may later ulcerate.

Microscopically, cytologically uniform, bland-looking cells are in a variety of configurations. The main microscopic patterns are:

- solid lobules surrounded by fibrous tissue
- cribriform areas containing hyaline stromal material
- duct-like structures
- fascicles of cells sometimes in concentric (target-old) arrangement
- papillary or papillary cystic structures.

The stroma is hyaline or mucinous and fibrous or hyaline bands often separate different areas of the tumour. An unusual feature is the survival of relatively large areas of normal gland tissue or fat within the tumour.

Management

These tumours are locally invasive, but appear only rarely to metastasize. Local excision has been followed by recurrences, so that excision should be complete.

Salivary duct carcinoma

This highly malignant tumour consists microscopically of eosinophilic cells in cribriform or papillary configurations, or is solid with central necrosis in the comedo type. It grows and spreads radily. Ruiz et al (1993), for example, reported 9 cases. Five died of the disease, and the outcome was unaffected by the aggressiveness of the surgery or irradiation.

Clear cell tumours

All clear cell tumours (apart from the rare clear cell oncocytoma) should be regarded as at least potentially malignant and treated accordingly. The main types of clear cell tumours are as follows:

- clear cell oncocytoma

- clear cell mucoepidermoid or acinic cell carcinomas

- epithelial-myoepithelial (intercalated duct) carcinoma

- metastatic renal cell carcinoma.

Of these, only the clear cell variant of oncocytoma is benign, while metastatic renal carcinoma inevitably has the worst prognosis. Oncocytoma and mucoepidermoid and acinic cell carcinomas have been described earlier and the behaviour of their clear cell variants does not differ from their more common conventional counterparts. Renal cell carcinoma is discussed later with other clear cell tumours.

Epithelial-myoepithelial carcinoma

Clinically, the mean age of affected patients appears to be about 60 years and the peak incidence is in the seventh and eighth decades. Women have been affected in the ratio of 2 to 1. Over 80% of these tumours have been in the parotid glands and usually caused otherwise asymptomatic swellings. However, a minority have caused pain or facial weakness.

Microscopy

The growth is typically multinodular and though the tumour appears circumscribed, encapsulation is incomplete. The tumour consists of duct-like structures or larger spaces which sometimes contain eosinophilic, PAS-positive material. Alternatively, the cells may be

predominantly in an organoid or thecal pattern with a well-defined basal membrane which may be thickened and hyaline.

Small dark cells line the duct-like spaces and are surrounded by large glass-clear cells which usually predominate. The clear cells are considerably larger, of rounded polygonal shape and usually contain glycogen.

The patterns and numbers of clear cells can vary between individual tumours or within a single example. In some areas there may only be solid sheets of clear cells. In others, there are cyst-like spaces into which there are papillary projections of tumour cells. Mitoses are rarely found, but there may be perineural infiltration or intravascular growth.

Electron microscopy and immunocytochemistry have confirmed that the dark cells are epithelial but that the clear cells are myoepithelial. Positive staining for S-100 protein, vimentin, myosin and keratins may, therefore, be useful in confirming the nature of the clear cells. Additionally, Jones et al (1992) have reported that the outer layer of the myoepithelial cells reacts positively for alpha smooth muscle actin.

Behaviour and prognosis

These tumours have recurred in a significant number of the reported cases and some patients have died with metastases to lymph nodes, lung or kidney. Seifert et al (1986) suggest that the 5-year survival rate is 65%.

Management

Despite the relatively bland microscopic picture, the behaviour of epithelial-myoepithelial carcinomas suggests that radical parotidectomy or *en bloc* resection of other glands is indicated.

Metastatic renal cell carcinoma (hypernephroma)

When any feature suggests that a clear cell tumour of a salivary gland is a secondary deposit, the kidney is the only important source. Metastases are frequently the first sign of a renal cell carcinoma. If renal symptoms are absent, microscopic haematuria alone may be found in 60% of patients and about 50% of patients have non-specific systemic symptoms such as fever, fatigue or loss of weight. Gross haematuria, pain in the loin and a renal mass are late in appearance and present in only 10% of patients.

Microscopy

Renal cell carcinoma consists of solid masses of clear cells with small eccentric nuclei in an organoid or trabecular arrangement. The blood vessels are typically dilated, form scattered sinusoids and may leave foci of haemorrhage and deposits of haemosiderin. Granular cells may also be present and, in some cases predominate.

Differentiation from epithelial-myoepithelial carcinomas microscopically can sometimes be very difficult. Ellis and Gnepp (1988) suggest that a helpful distinguishing

feature is that epithelial-myoepithelial carcinoma has small blood vessels running between the groups of tumour cells, but renal cell carcinomas have large sinusoids. In unblocked material, the presence of fat is typical of renal carcinomas but not invariably present.

If doubt remains, intravenous urography and if necessary a CT or ultrasound scan should be carried out. Excision of a primary renal cell carcinoma and a metastasis has occasionally proved curative.

Basal cell adenocarcinoma

These tumours are predominantly found in the parotid or submandibular glands and the mean age affected is approximately 60 years.

Microscopy

Multiple nodules of small dark cells with scanty cytoplasm are frequently surrounded by larger, eosinophilic or amphophilic cells, but the latter are rarely palisaded. A distinct perinodular, hyalinized basal membrane and hyaline intranodular droplets are frequently present.

Basal cell carcinomas closely resemble basal cell adenomas, particularly the membranous variant, and diagnosis depends on finding cellular or nuclear pleomorphism, mitotic activity, foci of necrosis or, particularly, evidence of infiltration which may be perineural or intravascular, even in cytologically benign-looking tumours. Some examples may have cribriform areas simulating an adenoid cystic carcinoma.

Management

From the limited data available, basal cell adenocarcinomas appear to be of low-grade malignancy. Recurrence or metastasis after wide excision is relatively uncommon, but occasionally metastases may appear more than a decade later. Total conservative parotidectomy (and its equivalent for other glands), therefore, seems to be the minimal requirement.

Squamous cell (epidermoid) carcinoma

Despite the frequency of squamous metaplasia in pleomorphic adenomas, squamous cell carcinomas of salivary glands are rare. They account for only 1-3% of salivary gland tumours. They are a disease of the elderly: men are more than twice as frequently affected as women at a mean age of 70 (range 50-90) years. Nearly 70% of these tumours are in the parotid glands.

Clinically, squamous cell carcinomas do not seem to have any distinctive features, though they may be particularly firm on palpation and readily ulcerate. Facial palsy may also develop and metastasis to regional nodes is rapid. In the mouth, squamous cell carcinomas of minor salivary glands may not be distinguishable from those arising from the mucosa.

Microscopy

These tumours do not differ from squamous cell carcinomas from other sites and range from well-differentiated, keratinizing tumours to poorly differentiated examples without keratinization. However, it is essential to determine whether they are primary salivary gland tumours, metastases from elsewhere (when the prognosis is particularly bad) or have spread from a mucosal or skin tumour. It may occasionally be difficult to distinguish them from high-grade mucoepidermoid carcinomas and to be certain that mucous cells are absent.

Management

The reported survival rates of such rare tumours are not very helpful in predicting the response to treatment, but Seifert et al (1986) quote a 5-year survival rate of 40%. Treatment is by radical excision, neck dissection and radiotherapy.

Undifferentiated carcinomas

Undifferentiated carcinomas are rare and of similar frequency to squamous cell carcinomas. Sixty-three per cent of these tumours are in the parotid glands, while 22% are in the submandibular glands.

Microscopy

A variety of appearances can be seen, but typically there are sheets of small cells which may be more or less spheroidal or spindle shaped, have a basaloid appearance or can closely resemble an oat cell carcinoma of the lung. The cells have large nuclei and the cytoplasm is scanty and poorly defined. Nuclear pleomorphism and mitotic activity may be prominent. The centres of cell masses may undergo necrosis. Neuroendocrine differentiation is sometimes detectable by means of such stains as Grimeleus's in the first instance, but appears not to affect the prognosis. Large cell undifferentiated carcinomas may also be seen occasionally.

Management

Metastasis from a distant site must be excluded as the prognosis is likely to be hopeless. Even with primary salivary gland tumours, rapid spread of undifferentiated carcinomas, particularly to regional lymph nodes, is to be expected, while distant metastases are likely to be the chief cause of death.

Radical excision of the gland and neck dissection should be followed by radiotherapy. The 5-year survival rate is approximately 25% (Seifert et al, 1986).

Undifferentiated carcinoma with lymphoid stroma (lymphoepithelial carcinoma; malignant lymphoepithelial lesion)

This neoplasm is common in some Eskimo races and Southern Chinese, but very rare in those of European origin. Men are more frequently affected.

Microscopy

Ill-defined islands of poorly differentiated epithelium, which often appears syncytial, are buried in a dense stroma of lymphocytes. This appearance is identical to that of one type of nasopharyngeal carcinoma which is even more common in these racial groups, so that occasionally a salivary gland tumour is a metastasis from the nasopharynx. Better differentiated, low-grade tumours may also be seen.

Management

The frequency of metastases is so high that, in addition to radical excision, there is some argument for neck dissection even in the absence of palpable nodes, unless the tumour is unusually well differentiated. Radiotherapy must be used if complete excision is not possible, but its value is questionable.

Carcinoma in pleomorphic adenoma

Malignant change in a pleomorphic adenoma is more common in long-standing tumours (more than 10 years) or in multinodular recurrences. Thackray and Lucas (1974) suggest that up to 25% of pleomorphic adenomas may undergo malignant change if left untreated for a decade or more. As a consequence, carcinoma in pleomorphic adenoma is typically a tumour of older persons with a mean age of 63 (range 25-83 years). The incidence is between 5% and 6% of epithelial tumours, but this may be an underestimate because of cases where the carcinomatous component has obliterated the adenoma.

Clinically, malignant change in pleomorphic adenoma is suggested by a sudden acceleration of growth or the onset of pain or facial palsy after years of gradual or episodic growth.

Microscopy

Both pleomorphic adenoma and carcinoma can be seen contiguously. The malignant component may form only a small part of the tumour; alternatively, the original adenoma may be difficult to find. However, ghost-like areas of cartilage tend to resist destruction and can provide a marker of a pre-existent pleomorphic adenoma.

The malignant component is most often an adenocarcinoma or undifferentiated carcinoma or, less frequently, other types of carcinoma.

As noted earlier, carcinoma in pleomorphic adenoma must be distinguished from atypia without invasive activity within the substance of a pleomorphic adenoma.

Management

The importance of recognizing carcinoma in pleomorphic adenoma histologically is that the prognosis appears to be poorer than for similar carcinomas arising *de novo.* Metastasis to lymph nodes was reported in nearly 60% of cases by Seifert et al (1986) and later to

distant sites. Treatment depends on the type of carcinoma and its extent, and is usually by radical excision in the first instance.

On the basis of analysis of 383 reported cases, the 5-year survival rate appears to be 55.7% and the 10-year rate 31% (Hickman et al, 1984).

Carcinosarcoma is a very rare variant in which both the epithelial and mesenchymal elements of a pleomorphic adenoma have undergone malignant transformation. Bleiweiss et al (1992) reviewed earlier reports and described the findings in a submandibular glands carcinosarcoma, which combined an adenocarcinoma with an osteogenic sarcoma. Both carcinomatous and sarcomatous elements can, therefore, be seen adjacently in the same tumour. The prognosis is poor.

Metastasizing mixed tumour

Rarely, a cytologically benign pleomorphic adenoma proves to be invasive or metastasizes, or both. The metastases reproduce the benign cytology of the primary. Such tumours are rare and frequently not distinguished from carcinomas in pleomorphic adenomas in reports. Wenig et al (1992) have reported the findings in 11 cases and reviewed the findings in 34 case reports. Metastases appeared from 6 to 52 years after the primary tumor was first treated. Metastases either coincided with local recurrences or followed them by 5 to 29 years. No histological variable or flow cytometry was successful in identifying criteria for predicting metastasis.

Since the potential for metastasis is unpredictable, initial treatment has to be the same as that for a pleomorphic adenoma.

Other rare carcinomas of salivary glands

These include malignant oncocytomas, sebaceous carcinomas and sebaceous carcinomas with lymphoid stroma.

Non-epithelial tumours and tumour-like lesions of salivary glands

Almost any variety of tumour can develop from mesenchymal components of salivary glands, but in them, lymphomas are the most common non-epithelial tumours. Overall, less than 5% of salivary gland tumours are non-epithelial.

Benign lympho-epithelial lesion

Benign lymphoepithelial lesion (BLL) gives rise, clinically, to a tumour-like mass and is usually treated as a tumour. However, the histological features of BLL are the same as those of Sjögren's syndrome and it is questionable whether they are distinct entities. However, in patients with tumour-like parotid swelling, the possibility of autoimmune disease is rarely considered, especially as remarkably few patients with proven xerostomia complain spontaneously of dry mouth. Nevertheless, Ostberg (1983) has shown by postoperative investigation that over 80% of patients with BLL have symptoms or other abnormalities consistent with Sjögren's syndrome.

Clinical aspects

The diagnosis of BLL is rarely made preoperatively but should be suspected in:

- women of 50 years or over, with firm, smooth, diffuse parotid gland swellings which are not fixed superficially or deeply

- bilateral parotid swellings, though unilateral swelling is more common

- patients with rheumatoid arthritis or any other connective tissue disease

- patients with dry mouth or eyes, though neither may be clinically obvious.

Pain is present in approximately 40% of patients.

Microscopy

Benign lymphoepithelial lesion is characterized by lymphocytic infiltration of the gland with destruction of acini, but preservation of some duct tissue which becomes transformed into so-called epimyoepithelial islands. The final picture is one of sheets of lymphocytes among which are scattered epimyoepithelial islands. The interlobular septa and capsule are preserved. However, careful examination should be made for early lymphomatous change, as discussed below.

Management

Since the diagnosis is rarely made preoperatively, parotidectomy is usually carried out. Once the diagnosis has been made, the patient should be investigated for Sjögren's syndrome and, if it is present, treated appropriately. Prolonged follow-up is essential because of the risks of development of salivary gland or extra-salivary lymphoma later.

Parotidectomy is also appropriate treatment of BLL or of persistently painful, swollen glands in Sjögren's syndrome, as it allows full examination for possible lymphomatous change. Irradiation or cytotoxic/immunosuppressive drug treatment increase the risk of lymphomatous change and are contraindicated.

Lymphoma

Primary lymphomas of salivary glands are uncommon. They most frequently arise in intra- or periglandular lymphoid tissue and are frequently a result of disseminated disease. CT scanning or other staging procedures are, therefore, essential.

Occasionally, destruction of the nodal architecture makes it appear that the tumour has arisen in the gland parenchyma, but even in such cases, the possibility that it is a secondary deposit needs to be excluded.

Clinically, lymphomas of salivary glands most frequently develop in the parotids which have a significant content of lymphoid tissue. The submandibular gland accounts for

15-20% of cases and the remainder are in the minor glands, particularly of the palate. Lymphomas produce firm swellings usually of rapid growth and a history of little more than 6 months' duration. Pain and facial nerve palsy develop early in a minority. Fixation to deep or superficial structures and involvement of regional lymph nodes are also uncommon early, but frequently develop later if the tumour is neglected. Most patients are aged between 50 and 70 years and women are more frequently affected in the ratio of 2 to 1. In younger males especially, the possibility of HIV infection must be excluded. Exceptionally rarely, a lymphoma may develop in the lymphoid tissue of a Warthin's tumour.

Microscopy

Most lymphomas of salivary glands are non-Hodgkin's type. The salivary tissue is replaced to a greater or lesser extent by sheets of lymphocytes either diffusely or in a follicular pattern. The degree of maturation and differentiation is also variable, but are the same as lymphomas in other sites (Chapter 14).

Signs of malignancy, namely, destruction of interlobular septa and capsule, and invasion of surrounding tissues, may be evident. Typing of lymphomas and sometimes even recognition of these tumours is difficult, and wherever possible should be referred for a specialist opinion.

Lymphoma in benign lymphoepithelial lesion and Sjögren's syndrome

The incidence of lymphoma in BLL or Sjögren's syndrome may be 20% or more. Takahashi et al (1992) found that in 32 salivary gland lymphomas the initial diagnosis had been myoepithelial sialadenitis in 9 cases. Lymphoma is typically a complication of long-standing disease and is, therefore, more likely to be seen in the elderly, particularly women. There is also a greater risk of lymphoma in patients with connective tissue diseases, particularly rheumatoid arthritis.

Lymphoma may be difficult to recognize in the lymphoproliferation characteristic of these diseases. It is indicated by cytological features of malignancy, signs of invasion, destruction of adjacent tissues, and evidence of intracytoplasmic monoclonal immunoglobulin production by immunostaining. Most are B cell lymphomas but almost any type of lymphoma may develop. Persistence of epimyoepithelial islands or of germinal centres does not exclude the diagnosis of lymphoma.

Management

Histological typing and staging must be carried out as for a lymphoma in any other site. From the limited published data it appears that salivary gland lymphomas are usually stage I or II. Treatment is determined by extent of the disease as well as by the histological subtype. Though the prognosis might be expected to be affected by the stage at presentation, this has not been confirmed in all reported series (Gleeson et al, 1986).

Excision is likely to have been carried out in the first instance, but typing and staging will determine the need for radiotherapy or chemotherapy or both.

Among 36 cases from the British tumour panel material, the median survival was only 49 months. Other reports have indicated considerably better survival rates, but overall the numbers are so small, and the variables affecting prognosis so many, that generalizations are not useful.

Hodgkin's disease

Primary Hodgkin's disease of salivary glands is very rare. The figures are sometimes inflated by inclusion of disease of juxtaglandular cervical lymph nodes, but the gland parenchyma is rarely involved. However, the mass may occasionally be mistaken for a salivary gland tumour, particularly of the submandibular gland, but in many cases the disease has already disseminated. Unlike non-Hodgkin's lymphomas, Hodgkin's disease has a peak in the third and fourth decades, and males predominate in the ratio of 4 to 1.

Microscopy

Lymphocyte-predominant, nodular sclerosing and mixed types appear to be virtually equally frequent, but lymphocyte-depleted disease to be rare.

Management

Histological typing and staging investigation should be carried out. The findings should determine whether treatment is by radiotherapy or combination chemotherapy and is by currently accepted protocols.

Salivary gland tumours in infancy and childhood

Only 3.5-5% of salivary gland tumours are in infants or children, but a major problem in their surgical management is the difficulty of avoiding damage to the developing facial nerve.

Haemangioma of the parotid gland

Juvenile haemangioma may be evident at birth, is usually seen before the age of 10 and is exceedingly rare in adults. It gives rise to a soft, sometimes bluish, enlargement of the gland.

Microscopy

Only isolated remnants of glandular tissue, particularly ducts, can be seen in the vascular tissue, which is usually capillary in type.

Management

Progress of these lesions is variable - some may grow or even spread into adjacent tissue for a time, but may regress spontaneously. However, the extent of the vascular proliferation may occasionally be so gross as to produce an arteriovenous shunt which can, rarely, give rise to high output circulatory failure.

If the tumour shows no signs of regressing, treatment should be delayed until the age of at least 5 years to lessen the risk of damaging the delicate, developing facial nerve. Excision, if it cannot be avoided, should be curative. Alternatives, such as injection of sclerosing agents or irradiation as primary treatment or to reduce the bulk of the tumour preoperatively, are likely to cause complications which outweigh any possible benefits.

Epithelial salivary gland tumours in children

Epithelial salivary gland tumours in the young are considerably more frequently malignant than in adults. The parotid glands are most often affected and Callender et al (1992) report that 21 out of 29 epithelial salivary gland tumours in children were malignant. Shikhani and Johns (1988) found that pleomorphic adenomas formed 87% of the benign tumours, but the recurrence rate was between 20% and 40% when enucleation was carried out. Two of the recurrent tumours developed into highly aggressive carcinomas. Of the malignant tumours, mucoepidermoid carcinomas appear to be the most common type. Two of the 29 patients reported by Callender et al (1992) died from their tumours.

In view of the high recurrence rate of pleomorphic adenomas and the high incidence of malignant tumours, radical parotidectomy seems to be necessary for epithelial salivary gland tumours in children. However, the chances of damaging the facial nerve are high, particularly in younger children, and even superficial parotidectomy of pleomorphic adenomas has a high chance of being followed by recurrence.

Embryoma (sialoblastoma)

Embryomas are congenital or neonatal salivary gland tumours and can be benign, but 25% may be malignant. Rarely, they are so large as to cause difficulties in delivery.

Microscopy

Embryomas consist essentially of tissue resembling embryonic salivary gland epithelia in a loose mesenchymal stroma. The appearances are varied, but typically consist of small dark cells with scanty cytoplasm forming duct-like structures, trabeculae or occasionally a cribriform pattern and may, therefore, resemble a basal cell adenoma or adenoid cystic carcinoma. Like other embryonic epithelia, this tissue is able to grow infiltratively even when benign. Malignant embryomas may be recognized by greater atypia, but more objectively by invasion of such structures as nerves or blood vessels, and foci of necrosis.

Treatment is clearly difficult and depends on the histological findings. In the case of malignant embryomas, interstitial irradiation may have to be considered.

Other mesenchymal tumours of salivary glands

As mentioned earlier, mesenchymal tumours other than juvenile haemangiomas are rare in salivary glands. Neural tumours are the most common single type, but any other may occasionally be seen. These tumours do not differ from their counterparts in other sites and are considered in more detail in Chapter 13.

Because of the rarity of mesenchymal tumours in salivary glands, it is not clear whether their behaviour differs from that of histologically similar tumours elsewhere, and no practical comments can be made. However, in the case of sarcomas, despite the fact that unusually small tumours are likely to be recognized in salivary glands, the outcome is worse than that for sarcomas in general. The difficulties of surgery, particularly in the parotid region, may contribute to this poor prognosis.

As mentioned earlier, a myoepithelioma may occasionally be mistaken microscopically for a mesenchymal tumour, but if necessary can be identified by immunohistochemistry.

Metastatic tumours in salivary glands

Metastases to salivary glands are rare. The most frequent metastases are from skin tumours, particularly melanomas and epidermoid carcinomas, but are usually in juxtaglandular nodes as are many other metastases which appear as salivary gland tumours. Frequently, the possibility of a salivary gland tumour being a metastasis may be suspected, but metastatic renal cell carcinoma occasionally presents special problems, as noted earlier.

In the case of melanomas, as with other metastases, the prognosis is poor and the diagnosis is likely to be made only after parotidectomy, but Ball and Thomas (1990) state that parotidectomy and elective neck dissection provide valuable locoregional palliation, though the long-term prognosis remains poor.

Juxtaglandular tumours

Tumours of adjacent tissues occasionally involve or appear to involve salivary glands. An example is lymphomas in juxtaglandular lymph nodes, as discussed earlier.

Skin tumours can extend into the parotid gland especially, but are likely to be recognized as such. Rarely, a jugulotympanic paraganglioma can mimic a parotid gland tumour. A mandibular or masseteric tumour can also involve the parotid region. All of these possibilities are exceedingly rare, but should be borne in mind when a salivary gland tumour has unusual features.

Intraosseous salivary gland tumours

Rarely, salivary gland tumours form within the jaw from foci of ectopic tissue such as the Stafne bone cavity (Chapter 3) and are most frequently near this site in the region of the angle of the mandible. They do not differ microscopically from their soft tissue counterparts and most have been mucoepidermoid carcinomas. Benign tumours are exceptionally rare.

Radiographically, intraosseous salivary gland tumours present a variety of appearances, such as uni- or multilocular cyst-like areas of radiolucency whose nature is only recognizable after biopsy or excision. More malignant tumours are likely to show peripheral bone destruction and be less sharply circumscribed.

Management

If histology shows a malignant tumour, the possibility that it is a metastasis may be considered, but only becase adenocarcinomas of other organs can occasionally resemble salivary gland tumours microscopically.

Treatment of intraosseous mucoepidermoid carcinomas or more malignant tumours should be wide excision and, if necessary, grafting. Rare benign intraosseous tumours have been enucleated satisfactorily.