Surgical pathology of the mouth and jaws

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13. Tumours and tumour-like lesions of mesenchymal tissues

Fibromas and fibrous nodules

The current view is that true fibromas of the mouth are exceedingly rare and in any case cannot necessarily be distinguished with certainty from non-neoplastic fibrous hyperplastic lesions. Rarely, fibromas may be confused with neurofibromas or, more important, with well-differentiated fibrosarcomas. From the practical viewpoint, however, the vast majority of fibrous swellings in the mouth are benign.

Fibrous epulis, denture-induced hyperplasia and other fibrous nodules

These hyperplastic fibrous nodules are the most common tumour-like swellings in the mouth. They are traditionally regarded as resulting from low-grade trauma, but in practice a source of irritation is by no means always found or may be no more severe than in other parts of the mouth.

Clinically, these lesions all form pinkish nodules unless the surface has been injured and has ulcerated. Fibrous epulides form on the gingival margin, typically, in relation to anterior teeth, denture-induced hyperplasias form under the flanges of dentures or sometimes in the vault of the palate, while fibrous ('fibroepithelial') polyps form on the buccal mucosa, edges of the tongue or other sites.

Microscopically, these nodules consist of irregularly interlacing bundles of collagenous fibrous tissue in continuity with the corium and without any capsule or pseudo-capsule. The epithelium is usually mildly acanthotic. The area of an epulis in contact with gingival plaque is usually inflamed. Nodules related to dentures, however, may show no inflammation unless ulcerated or superficially infected by *C. albicans.* Bilatera, symmetrical fibrous overgrowths of the maxillary tuberositis are structurally similar.

Dystrophic calcification, osteoid or bone formation is common in fibrous epulides.

Management

The growth potential of these lesions is not known for certain, as few are left untreated. However, patients' histories often suggest that some of these lumps can remain stationary for several years. Excision is necessary to confirm the diagnosis and is usually curative, but recurrence can follow, particularly if any irritant such as a badly fitting denture, rough restoration or calculus has not been removed.

Small denture-induced lesions may sometimes regress if the denture is trimmed adequately, but excision is required to confirm the diagnosis.

Giant cell fibroma

The giant cell fibroma is a common minor histological variant with distinctive microscopic and clinical characteristics.

Clinically, nearly 60% develop in the first three decades and nearly 60% are in women with an average of 26 years. The single most common site (50%) is on the lower gingiva; other sites together account almost equally for most of the remainder.

Unlike the more common fibrous lesions the giant cell fibroma is typically pedunculated. About 60% have a warty or nodular surface and may be mistaken clinically for a papilloma.

Microscopically, the giant cell fibroma has a distinctive pattern of arcuate or sinuous bundles of collagenous connective tissue which surround but are clearly separated from stellate, rather than multinucleate, giant cells. The nuclei of the giant cells are large and vesicular while the cytoplasm may have prominent dendritic processes and contain melanin granules. Blood vessels, particularly capillaries, are prominent. These features are therefore quite different from the typical giant cell epulis (see below).

Management

The giant cell fibroma is benign and excision is usually curative.

Pyogenic granuloma and pregnancy epulis

Oral pyogenic granulomas usually develop on the gingival margins and less frequently at other sites. They are considerably less common than fibrous overgrowths and there is no evidence to suggest that they are a stage in the development of the latter or are merely inflamed fibrous nodules but, rather, vascular overgrowths. Clinically they form red, soft nodules.

Microscopically, pyogenic granulomas consist of a loose, oedematous and mucinous stroma containing larger, thin-walled blood vessels and are typically infiltrated throughout by leucocytes. The blood vessels are so numerous that the alternative term for cutaneous pyogenic granulomas is 'granuloma telangiectaticum' and Enziger and Weiss (1955) categorize them as polypoid capillary haemangiomas. Their thin epithelial covering is frequently ulcerated and there is then a more intense inflammatory infiltrate and fibrinous exudate on the surface.

Management

Excision is typically curative.

Pregnancy epulis

There is an enhanced tendency to develop a proliferative gingivitis and gingival pyogenic granulomas during pregnancy, particularly in the last two trimesters. Like pyogenic

granulomas in non-pregnant persons, inflammation may be minimal or absent but vascular proliferation is occasionally so active as to suggest a neoplasm. Nevertheless the behaviour is benign.

Management

Gingival hyperplasia of pregnancy should be treated by meticulous oral hygiene. A pregnancy epulis persisting after parturition should be exiced. As these lesions are often a cause of anxiety to the pregnant patient, it may be necessary to excise them during pregnancy if reassurance fails.

Giant cell epulis

This lesion (at one time given the inept and ponderous title of 'peripheral reparative giant cell granuloma') is of unknown etiology, but since it often develops in relation to teeth which have deciduous precessors, it may result from proliferation of the giant cells responsible for their resorption.

Clinically, giant cell epulides are more common in relation to the upper teeth, particularly in the second and third decades, and are rare after 25 years of age. It is equally common in males and females. It is smooth surfaced and sessile: it may be purplish red and soft, but may be indistinguishably clinically from a fibrous epulis.

Microscopically, a giant cell epulis is attached to and appears to arise from the periodontal ligament; it consists of closely set multinucleate giant cells in a vascular stroma of plump spindle cells separated from its epithelial covering by a connective tissue corium. Some specimens contain no more than a small focus of giant cells within a fibrous mass, and are probably regressing.

The giant cell component of giant cell epulis is not histologically distinguishable either from a giant cell granuloma of the jaw or a bone lesion of hyperparathyroidism (Chapter 6) when either of these have eroded through the bone and extended under the mucosa. However, both of these conditions are associated with an underlying area of radiolucency and appear as broad-based mucosal swellings.

Management

Thorough excision, including curettage of the base, is necessary to avoid recurrence, which is relatively common. Occasionally it is necessary to extract adjacent teeth. However, these lesions are completely benign and do not metastasize.

Neoplastic epulides

Epulis is a useful clinical term defining the site of a lesion but it has no specific histological connotation. Most epulides are fibrous and benign, but occasionally malignant tumours, particularly metastatic tumours, can produce lesions clinically mimicking a simple (non-neoplastic) epulis. Rare though this may be, it makes it mandatory to biopsy all such lesions including denture 'granulomas'.

Nasopharyngeal (juvenile) angiofibroma

This uncommon tumour occasionally involves the oral cavity. With rare exceptions it affects males, usually during adolescence, and is exceptionally rare before the age of 10 years. This age and sex distribution suggests a hormonal influence as reviewed by Weprin and Siemers (1991). Nasopharyngeal angiofibroma typically forms a soft polypoid mass in the nasal cavity or sinuses. It grows both expansively and by infiltration peripherally. Typical early signs are nasal obstruction, infection and bleeding (epistaxes) which can rarely be life-threatening. Erosion of the palate can produce and intra-oral swelling or there may be bulging of the face, with loss of the nasolabial fold, which brings the patient to seek attention.

Radiographically, typical features are a soft tissue mass in the nasopharynx, causing a bulging of the posterior wall of the antrum. The bony margins are usually clearly defined, but may occasionally be eroded.

Microscopically, angiofibromas typically consist mainly of cellular fibrous tissue containing cleft-like or wider vascular spaces. The latter are lined by a single layer or endothelium with a thin or incomplete muscle layer; an elastic lamina is typically lacking.

The microscopic appearances often do not adequately indicate this tumour's potential for torrential bleeding. CT scanning and angiography are, therefore, essential investigations to show the extent and vascularity of the tumour.

Management

If an angiofibroma is suspected clinically, biopsy should only be carried out after admission to hospital and in anticipation of severe bleeding. However, the decision is difficult in that the clinical or radiographic features may simulate a malignant tumour, but the risk of dangerous haemorrhage makes the surgeon reluctant to confirm this by biopsy.

Angiofibromas usually behave aggressively and invade surrounding tissues. The Le Fort I down-fracture and other access osteotomies are useful in gaining access, but because of the risk of otherwise uncontrollable haemorrhage, bilateral control of the external carotid arteries before formal excision is essential. Preoperative embolization has been recommended by Siniluoto et al (1993) who found that it reduced blood loss to a third of that in their previous cases. There were also fewer recurrences, presumably because the control of bleeding allowed more complete excision. Cryosurgery and/or radiotherapy are other options but unless excision or destruction of the tumour is complete, the risk of recurrence is high. The hazards of irradiation in the young must be borne in mind and there is a possibility of inducing sarcomatous change. In addition, it is not universally accepted that irradiation will cause the fibrous component to regress, but in over 75% of cases it is likely to control symptoms and cause the tumour to shrink after a single course of 35-50 Gy.

The level of risk from surgery is probably similar to that from irradiation, but if surgery is chosen, it should only be undertaken with a clear appreciation of the hazards.

In contrast to the dangers of treatment, Weprin and Siemers (1991) reported spontaneous regression of an untreated juvenile angiofibroma over a 12-year period, in a boy

whose parents refused consent to surgery. Weprin and Siemers (1991) also reviewed earlier reports of spontaneous regression of these tumours after incomplete excision. Whenever possible, therefore, an expectant approach to the management of these tumours should be considered.

Spindle cell and pseudomesenchymal tumours of salivary glands

Occasionally pleomorphic adenomas consist predominantly of spindle (myoepithelial) cells (Chapter 12). Rarely, also, malignant myoepithelial tumours (malignant myoepithelioma, myoepithelial carcinoma) can have a sarcomatous appearance. Differential diagnosis from true mesenchymal tumours of salivary glands may depend on finding recognizable epithelial elements but, if this fails, the myoepithelial cells should be identifiable by immunostaining for keratin, actin and vimentin.

Fibromatoses

Fibromatoses are proliferative lesions of connective tissue which infiltrate surrounding tissues, have a strong tendency to recur, but are non-neoplastic and do not metastasize. Their aetiology is uncertain and they do not appear to be reactive in nature.

The more common superficial fibromatoses such as Dupuytren's contracture or Peyronie's disease have specific site distributions, while the deep fibromatoses (desmoids) affect the abdomen, particularly after childbirth. The extra-abdominal fibromatoses far more frequently involve the limbs or chest wall and an analysis by Enzinger and Weiss (1995) of 376 extra-abdominal fibromatoses (seen over a period of 20 years at the Armed Forces Institute of Pathology) found only 35 cases affecting the head and neck region. Of these, only 7 cases involved the head.

Fibromatoses mainly affect adults, and infantile fibromatosis is rare. In younger patients, fibroblastic proliferation may be more active; fibromatoses may, therefore, appear even more alarming microscopically than in adults, and be interpreted as sarcomas. Nevertheless, infantile fibromatoses in many sites have, overall, less tendency to recur or may rarely regress spontaneously.

Vally and Altini (1990) were able to find reports of 28 cases in the oral or periotal tissues and to add three new examples. They were also able to add 9 new cases of the intraosseous counterpart, desmoplastic fibroma of the jaws, and found 51 earlier reports.

Of 27 oral or perioral fibromatoses, Vally and Altini (1990) found that the great majority (16) developed within the first 9 years of life, 8 appeared between the ages of 10 and 19 years and only 3 between 20 and 29: the mean age at diagnosis was 8.3 years. The most common site was in the paramandibular region and radiographically there was superficial erosion of the underlying bone of the jaw in 16 cases. All showed similar histological features and these workers considered that there was no valid distinction between the so-called adult and infantile aggressive types of fibromatoses.

Clinical features

Fibromatoses typically form relatively slwoly growing, usually painless, poorly circumscribed, tumour-like masses. Later, if the growth has involved nerve fibres, it can cause pain. Rarely fibromatoses can be multifocal.

In addition to those few arising in the mouth, fibromatoses originating in the neck can spread to the jaw or floor of the mouth.

Microscopy

Fibromatoses consist of proliferating fibrous tissue which ranges in appearance from mature fibrous tissue with abundant collagen to highly cellular lesions consisting of tumour-like fibroblasts alone. The collagen fibres in the more fibrous specimens tend to form short bundles which lack the streaming patterns, and are less well defined than those of fibrosarcomas. These appearances can vary from one specimen to another and also within a single specimen.

The nuclei of the fibroblasts may contain two or three nucleoli, but tend to be small and uniform in size. Mitoses may be seen in the more cellular areas, but are never atypical. Within the fibrous tissue, the blood vessels often form slit or cleft-like spaces. Inflammation is typically slight or absent but, when present due to superimposed infection, can alter the microscopic appearances.

Particularly characteristic of these lesions is their tumour-like infiltration of surrounding tissues including nerve and muscle fibers and occasionally bone. Despite this property and the cellular appearances, fibromatoses do not metastasize. The current belief is that previously reported metastases were of fibrosarcomas rather than fibromatoses. Evidence for the value of microscopy for predicting behaviour is conflicting.

Management

Surgical control of fibromatoses in the oral or perioral area is difficult because of the close proximity of vital structures, their infiltrative nature and the consequent limited room for manoeuvre.

The current consensus is that the treatment should be as wide an excision as possible, but since fibromatoses are not truly magnificent, mutilating operations should be avoided. Nevertheless, recurrence rates range from 25% to 65%, depending on the aggressiveness of the lesion and the completeness of excision. At the other extreme, such lesions have occasionally regressed spontaneously, particularly in infants.

In view of the limited opportunities for total excision of oral or perioral fibromatoses, the likelihood of recurrence must be accepted. Unfortunately, little alternative to such treatment has been offered. The value of megavoltage irradiation has not been widely confirmed and, as always with such treatment, the possibility of inducing malignant change cannot be dismissed. Vally and Altini (1990), in their review of oral and para-oral

fibromatoses, found a recurrence rate of 22%. None of these lesions metastasized or, unlike fibromatoses in other sites, had a fatal outcome despite their proximity to vital structures.

In all cases, prolonged follow-up is necessary. Rarely, recurrences have appeared as long as 10 years after initial treatment. It therefore may be unwise to interpret treatment as being curative unless there is a disease-free period of at least 3 years after excision.

Myofibromatosis

This rare lesion was termed *infantile myofibromatosis* by Chung and Enzinger (1981), but can occasionally affect adults. Speight et al (1991) have described 3 cases (one in an adult) and reviewed earlier reports of oral and perioral cases.

Clinically, myofibromatosis has considerably more varied appearances than fibromatosis but like the latter has no clear margin and infiltrates muscle. There are two cell types. The configurations include spindle cells with eosinophilic cytoplasm and long, blunt-ended nuclei, in diffuse sheets or in streaming, fascicular patterns, sometimes interlacing or in whorls. Small cells are rounded or polygonal and have large nuclei relative to the amount of cytoplasm which is weakly eosinophilic. The small cells form foci in areas of spindle cells, but elsewhere can be close-packed and surround slit-like or dilated blood vessels to give a haemangiopericytoma-like appearance. There are occasional normal mitoses. Speight et al (1991) noted myofibromatous cells within the lumen of veins, and degenerating or reactive musle fibres within the lesion, as a result of infiltration of adjacent tissue. They also noted that manyof the cells were PTAH positive and some showed conspicuous longitudinal striations. Immunocytochemistry showed all the cells to be strongly positive for vimentin and smooth muscle actin. The ultrastructural features were also typical of myofibroblasts.

These varied appearances have led to misdiagnoses of myofibromatosis as neural tumours, leiomyomas, leiomyosarcomas or haemaniopericytomas in the past.

Management

Excision appears to be the treatment of choice, but may have to be repeated. Enzinger and Weiss (1988) consider myofibromatosis to be a hamartoma of myofibroblasts and, if so, this should discourage mutilating surgery.

Gingival fibromatosis

Enzinger and Weiss used to include gingival fibromatosis among the fibroproliferative diseases. However, gingival fibromatosis is obviously not a fibromatosis of the type described earlier. It can be familial or acquired, usually as a result of treatment with phenytoin, or less often with cyclosporin, nifedipine or other calcium channel blockers.

Familial gingival fibromatosis (typically an autosomal dominant trait) is generalized, and may completely bury the teeth (pseudo-anodontia) and can affect the deciduous dentition. Unlike drug-induced gingival hyperplasia, the fibrous overgrowth extends uniformly along the alveolar ridge. Thickening of the facial features until they may resemble acromegaly, hypertrichosis and sometimes epilepsy, or, rarely, mental defect may be associated. Despite

the deep false pocketing, there may be little gingival inflammation. Drug-induced gingival fibromatosis tends to be associated with poor oral hygiene, and particularly affects the interdental papillae, which become bulbous and separated from each other by pseudo-clefts. Typically, the gingival stippling is enhanced, giving the tissue an orange-peel texture.

Microscopically, fibrous gingival hyperplasia is characterized by dense collagenous fibrous tissue, often with elongation of the rete ridges of the overlying epithelium. The appearances of the drug-induced and familial types are similar.

Meticulous oral hygiene may control this hyperplasia to some extent, but is unlikely to cause it to resolve. Gingivectomy may be justifiable, particularly for cosmetic reasons, but in the familial type should preferable be delayed until after puberty, when regrowth of the fibrous tissue is likely to be slower. Gingivectomy may then be necessary and may ahve to be repeated at intervals.

In all such cases, the fibrous nature of these lesions should be distinguished from the gingival swelling of acute leukaemia.

Diffuse fibrous hyperplasias

Systemic sclerosis (scleroderma) and oral submucous fibrosis have been discussed in Chapter 7.

Fasciites

Fasciites are benign proliferative lesions of fibroblasts. Their aetiology is unknown, but they are thought to be reactive rather than neoplastic, even though any stimulus is unlikely to be identifiable. Despite their name, fasciites are not inflammatory and do not necessarily arise from fascial tissue.

In the body as a whole, fasiites are said by Enzinger and Weiss (1995) to be more common than any other tumour or tumour-like lesion of fibrous tissue. However, such statements, probably take no account of the innumerable fibrous epulides and other fibrous nodules in the mouth.

Fasciites tend to affect the limbs and are rare in the region of the mouth. Barnes (1985) found that among 225 reported cases of nodular fasciitis, 11 were in the mouth and a further 4 had been described as being in the 'jaw and cheek'.

Fasciitis presents the paradox of rapid tumour-like growth and, often also, microscopic appearances which have frequently been mistaken for sarcomas ('pseudosarcomatous fasciitis'), but are considerably less aggressive than the fibromatoses and have little or no tendency to recur after limited excision.

The two chief types of fasciitis most relevant to the mouth are nodular and proliferative fasciitis.

Nodular fasciitis

In keeping with the tumour-like microscopic features, nodular fasciitis produces a rapidly growing localized mass, typically reaching a few centimetres in diameter in 1-3 weeks.

Young adults between the ages of 20 and 35 years are predominantly affected and, in this group, the upper extremity is the most frequent site. Though nodular fasciitis is uncommon in children, the head and neck region is said to be relatively more commonly affected in them.

Microscopy

Fasciites are poorly circumscribed and consist essentially of short irregular interlacing bundles of fibrous tissue characteristically forming feathery patterns as a result of abundant mucopolysaccharide ground substance, but small amounts of mature collagen. The fibroblast nuclei are plump, vesiculated and with large nucleoli. Mitoses are common, but usually normal. Lymphocytes and erythrocytes are often scattered in the fibrous tissue.

Parosteal fasciitis

This rare variant originates from periosteum and may result in destruction of cortical bone and reactive subperiosteal new bone formation. Microscopically, the appearances are those of nodular fasciitis and therefore distinguishable from sclerosing periostitis.

Proliferative fasciitis

Proliferative fasciitis differs from nodular fasciitis in that a slightly older age group (40-70 years) tends to be affected and about 60% of cases are in the arm or leg. Head or neck lesions are certainly no more common and may even be more rare than those of nodular fasciitis.

The usual history is of a firm subcutaneous or submucosal lesion thathas developed within a few weeks and is painless. In the mouth, it may ulcerate.

Microscopy

The mass is poorly circumscribed, and may extend into underlying muscle. The connective tissue forming the mass has no discernible pattern, and consists of immature fibroblasts, including bizarre hyperchromatic giant forms with a highly malignant appearance. There are fine reticulin fibres, but little or no mature collagen apparent, and the stroma is predominantly mucoid. As the lesion matures, it becomes less abundantly cellular, giant nuclei are fewer or absent and there is more collagen. Maturation can be rapid and may develop between the time of an initial biopsy and definitive excision.

Differential diagnosis

The rarity of fasciites in the oral or perioral regions makes diagnosis difficult and the main source of confusion is with poorly differentiated sarcomas. The pathologist, therefore, needs to have the possibility in mind and, under such circumstances, the clinicopathological features described above should make the diagnosis possible.

Management

The essential consideration is that fasciites are benign. They have limited growth potential, less tendency to recur and extend than fibromatoses, and may even resolve spontaneously.

The treatment of choice is limited excision. This should also provide the pathologist with the junction between the lesion and surrounding tissue. Since the rapid growth of fasciites is likely to lead to early treatment (especially in the mouth where even minute lumps cause symptoms), fasciites will usually be small and readily excised.

It is particularly important that the surgeon should not be misled by the rapid growth of these lesions into over-hasty, mutilating operations.

Fibrosarcoma

Fibrosarcoma is particularly rare in the mouth, but can occasionally be a consequence of irradiation of the region. In a series of 29 fibrosarcomas of the head and neck region, seen over a period of 32 years, Mark et al (1991) noted only one each in the tongue and cheek, respectively. Four involved the mandible, one of which also involved the mastoid, tongue and hard palate. Eversole et al (1973) were able to find 20 cases of fibrosarcomas of the oral soft tissues reported between 1921 and 1951.

Clinically, the peak age incidence of oral fibrosarcomas is probably between 35 and 55 years. They form initially smooth, sometimes lobulated, firm swellings, the surface of which may later ulcerate.

Microscopically, the malignant fibroblasts can be well differentiated, and form close-packed, spindle-shaped cells with large but uniform nuclei, in long interlacing bundles streaming through the mass and producing small amounts of collagen. At the other extreme, the fibroblast nuclei can be pleomorphic, vary in size and show frequent mitoses, and little intercellular matrix is produced.

Management

Only a minority even of poorly differentiated fibrosarcomas metastasize, but radical excision at the earliest possible stage is essential. This may be very difficult in the head and neck region and may explain the poorer prognosis for tumours in this site. Well-differentiated tumours appear to have a far better prognosis than poorly differentiated ones, but no clinical feature such as age of onset or duration of symptoms appears to affect the issue. Mark et al (1991) suggest that radiotherapy should be used for patients with positive surgical margins

and may be helpful in controlling high-grade tumours. There is, as yet, no firm evidence for the value of chemotherapy as ancillary treatment to radical excision, though it has frequently been used.

Because of the rarity of these tumours, reported 5-year survival rates vary widely and range from 83% for well-differentiated and 36% to zero for poorly-differentiated fibrosarcomas from all parts of the body. Of the 20 cases reviewed by Eversole et al (1973), 12 were known to be alive and well for periods between 8 months and 18 years. Death is mainly from local recurrence and spread.

Fibrohistiocytic tumours and fibrous histocytoma

The term fibrohistiocytic tumour is used by Enzinger and Weiss (1995) for a variety of tumours and tumour-like lesions which can be benign, malignant or intermediate in behaviour. Within this broad category are the xanthomas and xanthogranulomas which can eb difficult to distinguish fropm sarcomas but are benign or even self-limiting. These tumours predominantly affect the skin or skeletal muscles and are rare in the mouth, where fewer than a dozen cases have probably been reported. The single most characteristic microscopic feature of these tumours is a storiform (knotted or tangled) pattern to the spindle cells, but the appearances are very variable with xanthomatous or myxoid areas, or many giant cells. Ultrastructural and tissue culture studies have largely supported the belief that these tumours arise from a tissue histiocyte which has fibroblastic properties and gives rise to both histiocyte-like and fibroblastic cells histologically.

Fibrous histiocytoma

From the few reports of fibrous histocytomas arising in oral or perioral tissues, it is impossible to make generalizations about the clinical features.

Adults are affected and in the case of the most common type (in the lower extremity), the peak age is in the seventh decade. The tumour can develop in the soft tissues or bone where it produces a nondescript swelling or an area of radiolucency.

Grossly the tumour typically forms a multilobulated fleshy mass.

Microscopically, the most common features are short bundles of spindle-shaped cells forming storiform, matted or cartwheel patterns. However, fibrosarcoma-like patterns may also be seen as well as giant cells and pleomorphic areas with plumper histiocyte-like cells and variable numbers of mitoses.

Giant cell variant of malignant fibrous histiocytoma

This tumour which has also been termed *malignant giant cell tumour of soft tissues,* consists of histiocytes, fibroblasts and osteoclast-like cells. As a consequence it may closely resemble a giant cell tumour of bone, apart from the lack of osteoid or osseous tissue. As this variant is considerably less common than the storiform type of malignant fibrous histocytoma, little is known about its behaviour but there is nothing to suggest that it is any more benign.

Malignant fibrous histiocytoma is actively invasive and spreads particularly along tissue planes and unlike other sarcomas has a tendency to involve lymph nodes.

Management

Treatment of fibrous histiocytoma is by radical excision, including the regional lymph nodes, as the malignant variants metastasize in over 40% of cases and may do so even if microscopic features indicative of malignancy are minimal. There is some evidence that postoperative radiotherapy improves the prognosis.

Tumours of neural tissue

Traumatic neuroma

Traumatic neruomas are rare in the mouth and usually result from accidental operative damage. They are often asymptomatic and found only as small nodules in the tissues. Occasionally, they give rise to neuralgic pain, particularly if irritated, for example by a denture.

Microscopically, traumatic neuromas consist of tangled bundles of nerve fascicles separated by fibrous tissue.

Surgical excision with cryosurgery of the nerve stump is curative. When there is neuralgic pain, carbamazepine may be helpful.

Neurilemmomas (schwannomas)

Schwann cells are neuroectodermal cells which ensheath the axons. Individual peripheral nerves, which consist of a group of axons, are surrounded by a sheath of concentric layers of perineural (Schwann) cells and also collagen fibres. The epineurium ensheathes a group of nerve fascicles in a larger peripheral nerve and consists only of fibrous connective tissue.

In the mouth, neurilemmomas form small painless nodules, particularly in the tongue.

Microscopically, neurilemmomas consist of two types of tissue. Antoni A tissue, which usually predominates, forms a closely interwoven pattern of elongated spindle-shaped cells, the nuclei of which are often palisaded or regimented to produce a distinctive picture. Reticulin fibres are also abundant. Type B tissue is loose with relatively scanty, scattered and pleomorphic nuclei. Some of these may be so large and hyperchromatic as to suggest malignancy. Positive reactivity for S-100 protein tends to be considerably stronger in neurilemmomas than in neurofibromas.

Neurilemmomas should be completely excised and should not then recur.

Neurofibroma

Solitary neurofibromas are uncommon and, when they are found, the patient should be investigated for neurofibromatosis. Clinically, neurofibromas form painless smooth nodules.

Microscopically, neurofibromas consist of elongated, bent or sinuous nuclei separated by abundant, fine and equally sinuous collagen fibres. Reticulin fibres by contrast are scanty. Mast cells and lymphocytes are considerably more frequently found among the fibres than in neurilemmomas (Johnson et al, 1989), but reactivity for S-100 protein is patchy and variable. Occasionally, a neurofibroma develops in the inferior dental nerve and is seen radiographically as a fusiform expansion of the inferior dental canal.

Complete excision should be curative.

Plexiform neurofibroma

Plexiform neuromas are exceedingly rare in the mouth. They consist of poorly organized mixtures of nerve fibrils usually unmyelinated and tangled, but sometimes also normal or hypertrophied nerve fibres. There is diffuse proliferation of spindle cells of neural origin, myxoid areas and, often, fat. Mast cells, as in many other fibro-proliferative disorders, are conspicuous and appear to contribute to the overgrowth of neural fibrous tissue. Compact bundles of cells apparently originating from the peri- or epineurium proliferate into the surrounding tissues. Excision should be curative, but plexiform neurofibromas are frequently a sign of von Recklinghausen's disease or multiple endocrine neoplasia syndrome.

Neurofibromatosis (von Recklinghausen's disease)

Neurofibromatosis is one of the phacomatoses ('neurodermatoses') which are genetically determined hamartomatous or neoplastic diseases of the skin and nervous system. There are two genetically and phenotypically distinct forms of neurofibromatosis, namely peripheral and central. The peripheral type (NF I) accounts for over 90% of cases; the central type (NF II), characterized by bilateral acoustic neuromas, accounts for the remainder. Neurofibromatosis (type I) is one of the most common autosomal dominant disorders, and the prevalence of the disease may approach 1 in 3000 of the population.

Clinically, the characteristic features of peripheral neurofibromatosis are multiple coffee-coloured (café-au-lait) macules which typically start to appear within the first year of life, cutaneous and sometimes skeletal neurofibromatosis and Lisch nodules (brownish, dome-shaped hamartomas of the iris). The severity of the disease ranges from inconspicuous to grossly disfiguring tumorous deformities. The skin tumours start to develop at or near puberty, frequently cause itching while actively growing and in severe cases can form in hundreds or even thousands.

The café-au-lait spots resemble freckles but appear in sites shielded from sunlight, such as the axillae. In the absence of obvious neurofibromas, the diagnosis of the disease depends on finding multiple café-au-lait spots and Lisch nodules.

Neurofibromas affect the head and neck region in over 25% of cases, but involve the mouth or jaws in only approximately 5% of cases.

Microscopically, the tumours are typically plexiform neurofibromas which are strongly suggestive, if not diagnostic, of von Recklinghausen's disease or multiple endocrine neoplasia syndrome which may be associated.

Neurofibromas are even more common than plexiform neuromas, but are not distinguishable from those unassociated with von Recklinghausen's disease. Neurilemmomas may sometimes also be found.

Bones can be involved as a result of tumours growing from nerve fibres and forming subperiosteal or more central, cyst-like areas of radiolucency. Localized expansion of the inferior dental canal may, therefore, be seen. Bone destruction may also result from formation of fibroma-like masses containing giant cells.

The café-au-lait spots show melanin hyperpigmentation of both keratinocytes and melanocytes, usually with scattered abnormally large melanin granules (giant melanosomes).

Management

Isolated tumours can be excised for functional or cosmetic reasons and recurrence is unusual. However, sarcomatous change develops in up to 10% of these neurofibromas. Other serious complications include disfigurement, mental handicap or other neurological disease such as epilepsy or paraplegia due to spinal neurofibromas. Skeletal abnormalities and central nervous system tumours, particularly gliomas of the optic nerves or chiasma, may also develop. Acoustic neuromas, contrary to earlier descriptions, are rarely associated.

Mucosal neuromas in endocrine adenoma syndromes

Oral mucosal neuromas, particularly along the lateral borders of the tongue, are a feature of multiple endocrine adenoma syndrome type III (Williams and Pollock syndrome) in which they are associated with medullary carcinoma of the thyroid and phaeochromocytoma.

Neuromas in this syndrome resemble the plexiform or traumatic types, but may be more fibrotic if traumatized.

The recognition of one of these unusual tumours in the mouth is an indication for investigation for endocrine adenoma syndrome, which they may antecede.

Malignant schwannomas and neurofibrosarcomas

Malignant tumours of nerve sheath origin may be malignant schwannmoas or neurofibrosarcomas. However, there is no universally agreed terminology and it is probably justifiable to include them both in the single category of neurogenic sarcoma as there is no clear evidence that histological minutiae affect the prognosis.

Malignant schwannomas

These consist of plump spindle-shaped cells arranged in bundles which may be whorled or be interlacing. A matrix of looser fibroblastic cells or of a more mucinous nature may be apparent. In well-differentiated tumours, Antoni type A tissue may be recognizable, but in all types excessive cellularity, nuclear hyperchromatism and mitoses are typical features. One characteristic appearance is that of an area of necrosis surrounded by elongated cells with a palisaded arrangement. Care must be taken not to confuse so-called ancient neurilemmoma which can show foci of atypia. Staining for S-100 protein is frequently positive.

Neurofibrosarcomas

These tumours tend to resemble other fibrosarcomas so closely that their neural origin may not be recognizable unless they can be seen to be in continuity with neural tissue or a typical area of neurofibroma. They are usually composed of interlacing bundles of spindle-shaped cells (but looser and shorter than those of fibrosarcomas and with bent nuclei), either densely aggregated or more loosely arranged in a mucinous or myxoid matrix. The malignant nature of the tumour may be obvious from the cellularity and nuclear changes, but in other cases mitoses may be scanty and the cells lack any significant nuclear abnormalities. However, at the periphery particularly, invasion or tissue destruction may be seen.

Management

Radical excision is the treatment of choice. However the recurrence rate is high as the tumour may infiltrate along the nerve sheath or spread via the bloodstream, and the value of radiotherapy is controversial. Spread to lymph nodes, by contrast, is uncommon. Neville et al (1991) reported 3 patients with oral neurofibrosarcomas: all died from their disease. DiCerbo et al (1992) reported a case of malignant schwannoma of the palate in a patient who survived 7 years after excision before being lost to follow-up.

Cervical paraganglionomas (chemodectomas, 'glomus tumours')

Paraganglionomas arise from neuroendcrine cells associated with autonomic ganglia. Paraganglionomas in the head and neck include (in order of frequency) carotid body (chemodectoma), jugulotympanic (glomus jugulare and glomus tympanicum), intravagal (glomus vagale), laryngeal, nasal and orbital tumours. True glomus tumours (glomangiomas) are described later among the blood vessel tumours.

Ten per cent are multiple and, in 8%, other neural crest tumours are associated. Normally these tumours are benign, but up to 6% may be frankly malignant and capable of metastasizing.

Overall, these tumours comprise only 0.01% of head and neck tumours. However, they are important in the differential diagnosis of masses in the head and neck. Glomus jugulare tumours may masquerade as deep or, rarely, as superficial lobe parotid tumours. Carotid body tumours may mimic deep lobe parotid tumours, branchial cysts or cervical lymphadenopathy,

while Lustman and Ulmansky (1990) have reported a paraganglionoma causing a rubbery exophytic lump on the tongue.

Microscopically, paraganglionomas are characterized by the grouping of the cells in clusters or nests which are often sharply demarcated. The tumour cells typically have rounded nuclei and prominent cytoplasm which ranges from conspicuously granular to clear, sometimes with well-defined cell membranes. Neurosecretory granules, which are argyrophilic, can usually be identified by Grimelius staining, but if this fails electron microscopy may be necessary.

The correlation between the histological features and malignancy is poor. Central necrosis of the cell nests, mitotic activity and invasion of vascular spaces are features or malignancy, but can also sometimes be seen in benign paraganglionomas. However, only about 5% of carotid paraganglionomas are malignant, while malignancy in jugulotympanic paraganglionomas is virtually unknown.

Management

CT and angiography are the investigations of choice. These tumours are vascular and angiograms show their location, pattern, vascular supply and extent. Carotid body tumours lie between the internal and external carotid arteries, and spread them apart, whereas glomus jugulare tumours usually displace them forwards. As pressure on these tumours causes turbulence in the carotid blood flow, the non-invasive Doppler ultrasound (MAVIS - Mobile Arterio-Venous Imaging System) imaging technique can be used to aid diagnosis.

Treatment is by surgical excision; nevertheless, as these are slow-growing tumours and only a minority are malignant, some authors have advocated avoidance of active intervention. However, many such tumours can be peeled off the carotid adventitia with judicious tying off of feeder vessels; others require resection and recostruction of the carotid vessels using a Javid shunt to maintain cerebral circulation. In some tumours, the vascular component is so abundant as to cause troublesome bleeding at operation. Incomplete excision is followed by recurrence. Radiotherapy has also been advocated, but the majority of these tumours appear to be relatively radioresistant.

Tumours of fatty tissue

Lipoma

Lipomas occasionally form within the mouth, particularly from the buccal fat pad or, rarely, within major salivary glands. They form soft fluctuant swellings with a distinctive creamy colour when submucosal. In approximately 5% of patients, lipomas are multiple. The tendency to develop multiple lesions is sometimes inherited as a simple autosomal dominant trait.

Microscopically, lipomas consist of mature fat cells enclosed within fine areolar tissue and surrounded by a fibrous capsule. Many of these tumours contain fibroblasts intermingled with the fat cells and are known as fibrolipomas.

Excision is curative.

Liposarcoma

Liposarcomas are rare tumours, particularly in the mouth. They show a wide variety of appearances, but well-differentiated liposarcomas can be recognized microscopically by obvious fat formation, foamy fat containing lipoblasts and signet-rign cells (vacuolated lipoblasts). Characteristic, irregularly shaped giant cells within foamy cytoplasm may also be present.

Liposarcomas are considerably more cellular than lipomas and may be so cellular as to make their lipoblastic origin less obvious. When fat is present, it usually resembles embryonal adipose tissue and consists of fat cells in myxoid tissue. Liposarcomas which consist entirely of embryonal adipose tissue resemble myxomas.

Management

Radical excision is the treatment of choice, but the margins are frequently difficult to define at operation. Radiotherapy may be useful post-operatively or for palliation, particularly of the myxoid variant if surgery fails. Recurrence is common and is largely related to the degree of differention.

Diseases of muscle

Muscle pathology is a specialized field and few muscle diseases significantly affect the oral tissues. The recognition of muscle diseases in oral specimens is also made more difficult by the normal variations in size of muscle bundles in this part of the body. Artefacts resulting from surgical damage, or preparation of the specimen, further complicate the problems of diagnosis.

Muscle degeneration and regeneration

Muscle degeneration and regeneration are most likely to be seen as a result of trauma or involvement of muscle in infections or malignant tumours.

Muscle degeneration is characterized by hyaline change with loss of cross-striations, vacuolation and, ultimately, necrosis. Infiltration by inflammatory cells and phagocytosis are early consequences.

Regeneration frequently follows muscle damage and is characterized by basophilia of the fibres, indistinct striations, increased number and size of nuclei sometimes with prominent nucleoli (sarcolemmal giant cells), and formation of variably sized but often small fibres.

Inflammatory myopathies: polymyositis and dermatomyositis

These types of myositis are traditionally grouped with the connective tissue diseases and may be immunologically mediated. Adults are mainly affected: women twice as often as men. Muscle pain and weakness, particularly of the proximal limb muscles, are the main

features. Involvement of the flexors and dysphagia may be prominent but the facial and eye muscles are typically spared. Various types of rashes and, sometimes, Sjögren's syndrome, may be associated.

Microscopically, the chief finding is concurrent muscle degeneration and regeneration, associated with infiltration by mononuclear cells and phagocytosis of damaged muscle by histiocytes. Though autoantibodies to extractable nuclear antigen and rheumatoid factor may be associated, there is no specific immunological diagnostic test. Diagnosis, therefore, depends on the clinical, electromyographic and biopsy findings, and raised plasma creatinine phosphokinase (CPK) levels.

Proliferative myositis

This uncommon pseudo-sarcomatous disorder, which may be related to proliferative fasciitis, occasionally affects the masticatory muscles to produce a firm, rapidly growing tumour-like swelling. The head and neck region overall is the site of 33% of cases, but Fujiwara et al (1987), in describing the immunohistochemical findings in an oral specimen, could find only one other earlier case. Adults over 45 are chiefly affected.

Microscopically, proliferative myositis consists of a loose arrangement of highly pleomorphic cells and has an infiltrative growth pattern. Giant cells resembling ganglion cells, or rhabdomyoblasts with basophilic or amphophilic cytoplasm, and sometimes two nuclei with conspicuous nucleoli, are prominent. These giant cells are separated by loose, oedematous, proliferating fibroblasts; inflammatory cells are scanty or absent. Remnants of degenerating muscle fibres may be seen, particularly near the periphery. Fujawara et al (1987) found that the ganglion-like cells did not stain for desmin or myoglobin and suggested that they were of myofibroblastic or macrophage origin.

Hardly surprisingly, a diagnosis of malignancy and particularly of rhabdomyosarcoma was initially made in 14 of the 33 cases reviewed by Enzinger and Dulcey (1967). Nevertheless, proliferative myositis is completely benign, as shown by its tendency to spontaneous regression.

Biopsy is essential to establish the diagnosis, but no further surgical intervention may then be necessary. At most, limited local reduction of the masses may be required for cosmetic reasons.

Myositis ossificans

This rare, benign proliferative process can be confused histologically with osteosarcoma. Solitary myositis ossificans (traumatic or ossifying myositis) may follow chronic trauma or an isolated blow to a muscle, but in at least 50% of cases there is no history of injury. Experimentally, trauma to muscle does not reproduce the pathological features of this condition.

Clinically, the masseter or temporalis muscle, usually in a teenager or young adult, can be affected and a localized, painful nodule develops within the affected muscle. A faint,

delicate pattern of ossification typically starts to appear after about 3 weeks and may rarely cause ankylosis (Chapter 7).

Microscopically, there is typically initial reactive fibroblastic proliferation and organization of any haematoma present. In the developed lesion, there is usually characteristic zoning with a border of irregular trabeculae of cellular osteoid and woven bone surrounding a highly vascular central mass of proliferating, immature fibroblasts which are typically pleomorphic and have prominent mitoses. The picture is readily mistaken for sarcomatous change, but the process is benign and self-limiting. Sarcomatous change that has occasionally been reported in ossifying myositis does not seem to have been fully authenticated.

Treatment is by wide surgical excision of the ossifying mass. Recurrences are very common, but systemic bisphosphonates may help to prevent them.

Extraskeletal osteosarcoma and chondrosarcoma

These rare tumours are mentioned only to emphasize the fact that, though pseudo-sarcomatous diseases have been described above, it is also possible for true osteosarcomas or chondrosarcomas to develop in soft tissues. Care must, therefore, be taken not to dismiss osteosarcoma-like or chondrosarcoma-like changes as benign merely because they are within soft tissues. In the case of fibrous histiocytoma also, Enzinger and Weiss (1995) suggest that all gradations may exist from typical soft tissue fibrous histiocytomas to those with small foci of osteoid and typical osteosarcomas.

Granular cell tumour ('myoblastoma')

This oddity, once thought to be a degenerative disease of muscle, appears from its ultrastructural features and, more recently, from reports of positive staining with neuron-specific enolase and for the presence of S-100 ('brain specific') protein, to originate from Schwann cells or their precursor cells. Other ultrastructural reports have suggested an origin from undifferentiated mesenchymal cells and, in any case, S-100 protein is not specific for neural cells. Stewart et al (1988) found that skeletal muscle stained weakly and that 50% of rhabdomyomas also stained positively for S-100 protein. They also found that 70% of granular cell tumours were invested by muscle and only 5% by nerve.

Clinically, the tongue is the most frequent site though overall, granular cell tumours are uncommon. Adults aged between 30 and 60 years are chiefly affected and the tumours often form small circumscribed lumps or firm areas just under the surface. Occasionally, the lesion is large and prominent, or resembles a carcinoma clinically. Rarely, they may develop in the midline of the tongue and then be mistaken for median rhomboid glossitis.

Microscopically, the appearance is difficult to reconcile with a neural origin, as the large granular cells frequently merge with muscle fibres. The granules, which are eosinophilic and PAS positive, may be so coarse as to make the cells conspicuous or so fine as to make them difficult to see. The cell membranes are typically well-defined. Frequently the overlying epithelium undergoes pseudo-epitheliomatous hyperplasia which may be mistaken for a carcinoma and be treated as such (Ogus and Bennett, 1978-79).

Granular cell tumours respond to local excision but can recur if excision is inadequate. Multiple primary lesions have also been reported.

Congenital granular cell epulis

This rare entity is found on the alveolar ridge of the newborn and forms a soft rounded swelling a few millimetres across, or may be so large as to protrude from the mouth. The upper jaw is most often affected and at least 80% of affected infants are female.

Microscopically, the mass consists of closely packed granular cells with prominent cell membranes and among which is a delicate network of capillaries. These cells are S-100 negative, but stain positively for myogenous markers such as myosin and actin and are probably of mesenchymal origin. Rarely, small odontogenic rests may be present. Unlike granular cell myoblastoma, the overlying epithelium is thin and flat and the granular cells are invested by muscle fibres.

Management

Treatment is by excision, but the congenital epulis does not apparently recur, even if excision is incomplete, or may even regress spontaneously. This suggests that it is a hamartoma.

Rhabdomyoma

Cardiac rhabdomyomas, which are usually associated with one of the phacomatoses, are relatively common but the extracardiac rhabdomyoma is one of the rarest of all tumours. Ferlito and Frugona (1975), from a review of the world literature, estimated that there had been only about 50 reports of extracardiac rhabdomyomas. Corio and Lewis (1970) were able to identify 13 more cases from the Armed Forces Institute of Pathology files, but were able to find reports of only 16 cases of oral rhabdomyomas.

Clinically, oral rhabdomyomas affect men at least twice as frequently as women, with a peak age between 50 and 60 years. The tumour typically forms a slow-growing, painless swelling.

Microscopically, rhabdomyomas are well circumscribed or encapsulated and consist of large cells which may contain such large vacuoles as to appear fatty and sometimes cause the granular eosinophilic cytoplasm to have a spidery outline. The cell membranes are sharply defined. In haematoxylin and eosin stained sections, cross-striations can, with careful examination, be found but are more readily demonstrable using PTAH. PAS staining shows glycogen in the cytoplasm and in the peripheral vacuoles.

Diagnosis depends on showing cross-striations and absence of any features of malignancy.

Management

At operation, the tumour may shell out readily and recurrence is uncommon.

Rhabdomyosarcoma

Though overall rare, rhabdomyosarcomas are among the most common sarcomas found in the mouth and second only to AIDS-related Kaposi's sarcoma.

These tumours form rapidly growing, soft swellings which (apart from the botryoid type which is unlikely to be seen in the mouth) are nondescript in character. In the series of 49 oro- and nasopharyngeal rhabdomyosarcomas of Dito and Batsakis (1962) there were 30 in the palate or tongue and 31 in the nasopharynx. Of these patients, 79% were aged under 12 years.

Microscopically, rhabdomyosarcomas are categorized as (a) embryonal, (b) alveolar, and (c) pleomorphic types, depending upon the predominant pattern. The embryonal type is the most common and accounts for about 75% of all cases. It is particularly common in the head and neck area and most examples are seen in children under the age of 12 years. Alveolar rhabdomyosarcoma tends to affect a somewhat older age group and is more frequent in the soft tissues of the extremities. Pleomorphic rhabdomyosarcoma is rare and most often forms in the large muscles of the extremities in adults aged over 45 years, but many authorities believe that many tumours formerly thought to be adult pleomorphic rhabdomyosarcomas should be recategorized as malignant fibrous histiocytomas.

Embryonal rhabdomyosarcoma consists of sheets of ovoid or spindle cells which may be tightly packed or interspersed in a loose myxoid stroma. Some of the round and spindle cells have eosinophilic cytoplasm which may stream out to form racquet- or strap-shaped cells. Cross-striations may be seen, but their presence is not essential for diagnosis. Glycogen is also present in the better differentiated cells, but is usually dissolved out in processing to leave multivacuolate, spider-web cells. Some embryonal rhabdomyosarcomas are highly pleomorphic and contain foci of varying size of larger bizarre cells.

Alveolar rhabdomyosarcoma tends to affect a somewhat older age group; it is considerably less common than the embryonal type and is only occasionally seen in the mouth. It consists of ill-defined nests of ovoid or round cells around central alveolar spaces. The individual alveoli are separated by fibrous septa. Multinucleated tumour giant cells are often also present.

Pleomorphic rhabdomyosarcoma, which most often affects adults over the age of 45 years, consists of round, pleomorphic cells of variable size and with varying amounts of cytoplasm which may be eosinophilic. Some may be racquet- or tadpole-shaped, but rarely show cross-striations. Many tumours previously thought to be adult pleomorphic rhabdomyosarcomas are probably malignant fibrous histiocytomas.

Diagnosis of rhabdomyosarcoma can be difficult and depends primarily on the identification of neoplastic rhabdomyoblasts, though cells with well-marked cross-striations are present in only 20-60% of cases and mainly in the embryonal type. Myoglobulin is the most specific marker, but is usually negative in poorly differentiated tumours. Immunostaining for desmin, vimentin and myosin are widely used and when positive serve to distinguish poorly differentiated rhabdomyosarcomas from other small round cell tumours such as

Ewing's sarcoma. However, Rangdaeng and Truong (1991) found that up to 17% of non-myogenic tumours stained with muscle-specific actin or desmin or both.

Management and prognosis

The prognosis is poor with local recurrence or distant metastases in many cases. Lymph nodes, often at a distance, may be involved in up to 50% of cases, but favoured sites of metastases are the bones or lungs.

It appears that combination therapy has greatly improved the prognosis. For this purpose, radical surgery should be followed by intermittent multi-drug chemotherapy.

Tumours and hamartomas of blood and lymphatic vessels

Leiomyoma and angioleiomyoma

Leiomyomas are rare in the mouth and arise from muscle cells in the walls of blood vessels. They are termed angioleiomyomas or leiomyomas according to whether or not their vascular origin is apparent. The tongue is the most common site and lesions form slowly growing nondescript swellings which are usually painless. Angioleiomyomas may have a bluish colour due to the prominent vascular component.

Microscopically, leiomyomas consist of interlacing bundles of spindle-shaped cells. The nuclei are often blunt-ended and myofibrils can be demonstrated by PTAH staining. Differentiation from other spindle cell tumours such as neurofibromas may be difficult and depend on electron microscopy to demonstrate myofibrils. Immunocytochemistry may be helpful, but neurogenous tumours may also stain positively for desmin, actin and vimentin. Angioleiomyomas consist of thick-walled blood vessels and bundles of smooth muscle so that their nature is more obvious.

Treatment

Leiomyomas and angioleiomyomas are benign and respond to conservative excision.

Leiomyosarcomas

Leiomyosarcomas are exceptionally rare in the mouth. Poon et al could find only 24 documented cases in the preceding 75 years. Clinically, they form initially painless, nondescript smooth swellings.

Microscopically, leiomyosarcomas are spindle cell tumours with elongated, weakly eosinophilic cells with blunt-ended nuclei like leiomyomas, but show cellular pleomorphism and mitotic activity. Differentiation from other malignant spindle cell tumours is frequently difficult unless myofibrils can be demonstrated by electron microscopy or other means. Positive staining for muscle-specific actin and desmin is helpful, but some leiomyosarcomas fail to stain.

Treatment is surgical excision, but there is an exceedingly poor prognosis.

Haemangiomas

Most haemangiomas are hamartomas of blood vessels. They are either congenital, capillary type (vascular naevi) or cavernous and may then increase in size with age.

Haemangiomas form flat or prominent, soft purplish lesions which characteristically blanc under pressure and may bleed profusely if traumatized. Extensive, usually capillary-type, haemangiomas are a cause of macroglossia. Haemangiomas (usually cavernous or mixed type) can also rarely form intraosseous tumours (Chapter 5).

Microscopically, capillary haemangiomas consist of a dense mass of capillaries or imperforate rosettes of endothelium. Cavernous haemangiomas consist of dilated, blood-filled vascular spaces with endothelial linings and are frequently poorly circumscribed.

Intramuscular haemangiomas are a rare variant and, in the perioral region, are most likely to form in the masseter muscles as a slow-growing sometimes painful mass. The overlying skin may become purplish red and warm to the touch. Angiography is necessary to confirm the diagnosis.

Treatment

Superficial haemangiomas should be recognizable clinically and treatment should usually be avoided. Early onset haemangiomas may regress spontaneously, but regression is unlikely in adults. Even prominent cavernous haemangiomas, despite the possibility of being bitten, may cause little or no trouble, but if there has been significant or recurrent bleeding then an attempt should be made to eradicate them using selective embolization. For large tumours, preoperative angiography is essential to determine their extent and if possible to identify feeder vessels.

Small, predominantly capillary lesions respond well either to cryotherapy or injection of sclerosing agents such as sodium tetradecyl sulphate, which gives better cosmetic results than surgical excision in such sites as the lips. Alternatively, laser surgery can be used.

Extensive, mixed capillary/cavernous haemangiomas are more common in the masseteric region of the cheek. Following angiography and control of the feeder vessels, such lesions, which are often diffuse, should be removed surgically as completely as possible. The margins are then infiltrated with sclerosant, and full-thickness compression sutures (tied over cotton rolls externally to protect the skin) are placed for 5 days.

Extensive, especially caverous, lesions can be excised after preoperative angiography and ligation of all feeder vessels. Alternatively, intra-tumoral ligation can be combined with injection of sclerosant solutions (Popescu, 1985). This less radical approach is suitable for diffuse cavernous lesions where surgical ablation would result in gross cosmetic deficit.

It is not usually possible to excise large haemangioomas of the tongue completely as this may require total glossectomy and excision of a large part of the floor of the mouth. Considerable morbidity or disability would thus result. A better alternative is to partially debulk the haemangioma to allow normal tongue function to be retained. Following

angiography, tapes are placed around major feeder vessels and a soft intestinal clamp is fixed across the tongue at the line of resection. The excess tissue can then be excised and the resection margin oversown with non-resorbable sutures. Healing should be uncomplicated and further surgery can be undertaken if the haemangioma enlarges in later years.

Sturge-Weber syndrome and mucocutaneous angiomatosis

Vascular naevi of the skin may be isoltaed abnormalities or part of a syndrome such as the Sturge-Weber syndrome. The latter comprises angiomatosis within the distribution of the trigeminal nerve and of the leptomeninges of the same side, leaping to epilepsy or hemiparesis and, usually, mental defect. A more limited form consists only of a diffuse vascular naevus of the face and of the underlying oral tissues including the gingivae. This type may have sharply defined lower and midline boundaries. When the gingivae are involved, the swollen tissue can cause false pocketing and inflammation or, rarely, local trauma can induce the formation of a rapidly growing, sarcoma-like mass.

These naevi are developmental anomalies and usually consist of grossly dilated vessels. There may be a genetic component in their aetiology, as suggested by several syndromes of which they are a feature. Similar lesions can also be induced by the drug thalidomide given during pregnancy or be a feature of the fetal alcohol syndrome.

Isolated naevi are rarely of clinical significance unless they are visible and disfiguring. Ugly angiomas of the face can be treated by means of skin grafting, liquid nitrogen cryotherapy or laser-induced fibrosis.

Glomus tumours (glomangiomas)

True glomus tumours arise from specialized arteriovenous shunts involved in body temperature regulation. Though glomus tumours may, to some degree, resemble paragangliomas microscopically, glomangioma is a preferable term. They are rare oral tumours, but Geraghty et al (1992) reported a case and reviewed 14 previous examples.

Microscopically, the cell of origin appears to be a modified smooth muscle cell, and the tumours typically consist of small dark cells with punched-out nuclei and little cytoplasm, surrounding dilated vascular channels lined by endothelium.

Treatment

Simple excision is usually effective and recurrence is rare.

Lymphangiomas

Lymphangiomas are more uncommon than haemangiomas but, like them, may be superficial or deep and capillary or cavernous.

Superficial lymphangiomas are pale or pink, translucent and may have a finely nodular surface. They may blacken when traumatized as a consequence of bleeding into the lymphatic

spaces. Deep lymphangiomas particularly affect the tongue and are another rare cause of macroglossia, or can affect the lip causing macrocheilia.

A rare variant is the lymphangioma of the alveolar ridge of neonates.

Microscopically, lymphangiomas differ little from their haemangiomatous counterparts and consist of capillary or cavernous lymphatic channels but which appear empty or filled with eosinophilic colloidal material. However, capillary lymphangiomas frequently cannot be distinguished from haemangiomas if there has been pre- or perioperative bleeding into the capillary spaces. Cystic hygroma is a term given to cavernous haemangiomas with unusually large, cyst-like lymphatic spaces; it is most common in the neck.

Treatment

Lymphangiomas need only to be treated if frequently traumatized with resulting inflammation and increased swelling. However, lymphangiomatous macroglossia may interfere with swallowing, cause drooling and, when traumatized, enlarge and may become infected. Excision is then necessary. Small lesions can be completely resected. Limited resection, sufficient to restore normal function, can be carried out on large lesions and there is a good chance that the lesion will remain static after growth is complete. Large lymphangiomas in the neck may require such extensive dissection that complete removal may not be possible.

Haemangiopericytoma

Haemangiopericytoma is a rare tumour and its most common site is the skin or subcutaneous tissues. The mouth is only occasionally involved. Lesions usually form solitary, firm nodules.

Microscopically, haemangiopericytomas consist of small closely packed cells with ill-defined cytoplasm and darkly staining nuclei. Interspersed among them are slit-like or sinusoidal vascular spaces. Occasionally, the pericytes may have a palisaded configuration or may show interstitial mucoid degeneration. It may be noted that other tumours such as mesenchymal chondrosarcomas or synovial sarcomas may have extensive haemangiopericytoma-like areas.

Rare, more obviously malignant, haemangiopericytomas are more cellular, show cellular pleomorphism and mitotic activity, and sometimes areas of haemorrhage or necrosis.

Management

The behaviour of haemangiopericytomas is variable; most are entirely benign but some are infiltrative and can metastasize. One of the main problems in dealing with this tumour is, therefore, the difficulty of predicting its behaviour from the histological features.

Adequate excision is the treatment of choice, as these tumours are not radiosensitive. Success has been claimed for chemotherapy of more malignant variants.

Haemangioendothelioma

In infants, there may be proliferation of the endothelial lining of capillary haemangiomas so that the endothelial cells appear rounded and the lesion consists of thin capillary channels and solid cords of cells. Such lesions are sometimes called benign haemangioendotheliomas.

A rare tumour, particularly in the mouth, is termed an epithelioid haemangioma. It may form a bluish swelling which may ulcerate. It is frequently centred on a blood vessel and characterized by rounded vacuolated cells with eosinophilic cytoplasm. These cells may be arranged in cords or small nests and surrounded by reticulin, while their matrix may have a hyaline or cartilage-like appearance. Paradoxically, vascular channels are inconspicuous.

Epithelioid haemangioendotheliomas, despite a bland cellular appearance, are regarded as being of borderline malignancy. Wide excision is the treatment of choice.

Kaposi's sarcoma

Classical (sporadic) Kaposi's sarcoma was described in 1872 in Central Europe among elderly persons of Mediterranean or Jewish origin. It is predominantly cutaneous, mainly affects the lower extremities and visceral lesions are rarely clinically apparent. Head and neck involvement is exceedingly rare. Kaposi's sarcoma with broadly similar characteristics is considerably more common in Africa, particularly in Zaire, where it formed about 12% of all malignant tumours in the pre-AIDS era. This form of Kaposi's sarcoma has both an indolent course and a good response to chemotherapy.

Clinically, AIDS-related Kaposi's sarcoma frequently involves the head and neck. The site may be oropharyngeal, cutaneous or in the cervical lymph nodes. Within the mouth, the palate is the most commonly affected site and the tumour typically produces a flat or nodular purplish lesion. It can have a similar site distribution in immunosuppressed patients, but is a relatively rare complication of such treatment in the West. Clinically, the differential diagnosis is from oral purpura and bacillary angiomatosis from which it can be distinguished by microscopy.

Microscopy

Kaposi's sarcoma originates in endothelial cells, as shown by the presence of the factor VIII marker. It produces florid angiomatoid proliferation with some resemblance to granulation tissue. Recognition of the tumour may, therefore, be difficult, particularly in the early stages.

In the earliest ('presarcomatous') stage of development, there is angiomatous proliferation with formation of irregular slit-like vascular spaces and perivascular cuffing by lymphocytes and plasma cells. In the intermediate stage, the angiomatoid changes are more widespread with irregular vascular spaces, together with perivascular proliferation of spindle-shaped and angular cells. Finally, the picture becomes increasingly dominated by proliferation of the interstitial spindle-shaped and angular cells and mitoses may be prominent. There is

typically also extravasation of erythrocytes and deposition of haemosiderin, and there may be central necrosis.

Management

In 'classical' (sporadic) Kaposi's sarcoma, radiotherapy is the accepted treatment for localized disease, while combined chemotherapy is used for disseminated disease.

In the case of epidemic (AIDS-associated) Kaposi's sarcoma, a great variety of treatment regimens such as single agent, combined chemotherapy or zidovudine with alpha interferon and radiotherapy have been tried. The prognosis of the tumour itself as a result of such treatment is often good in the short term, and death is usually from the associated opportunistic infections secondary to the immunodeficiency. Symptomatic lesions within the mouth are best treated with two or three fractions of radiotherapy, to which they rapidly respond.

Bacillary epithelioid angiomatosis

Bacillary angiomatosis is a rare vasculoproliferative disease which can be seen in AIDS and in other immunodeficient patients. It can be mistaken for Kaposi's sarcoma clinically and sometimes histologicallhy, as described by Glick and Cleveland (1993) who were able to demonstrate the causative bacteria in an oral lesion which had caused alveolar bone loss. The distinction from Kaposi's sarcoma must be made because of the therapeutic and prognostic implications.

Microscopy

The vasoproliferation can somewhat simulate that of Kaposi's sarcoma, but characteristic features of bacillary angiomatosis include the plump, epithelioid appearance of the endothelial cells which line well-formed vascular channels, and an inflammatory infiltrate, largely of neutrophils: factor VIII staining may be negative. When seen, the definitive finding is that of granular amphophilic aggregates of the causative bacilli which show positive Warthin-Starry staining.

The response to antimicrobials such as erythromycin or doxycycline is usually good.

Synovial sarcoma

Synovial sarcoma falls into none of the preceding categories. Paradoxically it affects tissues adjacent to or unrelated to joints, rather than joints themselves. The extremities, particularly the lower extremity, are most commonly involved: about 8% are in the head and neck region.

Clinically, synovial sarcoma frequently forms an insidiously growing, deep soft tissue mass which may eventually become painful and, if related to a joint, limits movement.

Microscopically, synovial sarcoma is characteristically biphasic, with both spindle cell and epithelial elements. The spindle cells are fibroblast-like while the epithelial cells, which stain positively with epithelial cell markers, are typically tall and columnar.

The spindle cells usually form the bulk of the tumour and are usually uniform, with plump nuclei and indistinct cytoplasm. They may form well-orientated streams of cells resembling a well-differentiated fibrosarcoma.

The epithelial cells can form a variety of arrangements such as whorls or solid cords, or they may confer a gland-like appearance to the area. Sometimes they may line clefts or cyst-like spaces and thus may resemble normal synovium. Occasionally, epithelial elements are so scanty and difficult to find that the tumour is termed 'monophasic'.

Varying degrees of calcification or even ossification develop in about 40% of these tumours and is an important radiological feature.

Management

The prognosis of synovial sarcoma is related to the degree of differentiation rather than to the relative amounts of the two cellular components, but despite its slow growth, the tumour has a poor prognosis. The reported 5-year survival rate varies between 25% and 50%. Wide excision is necessary and radiotherapy may be beneficial, but since recurrences after limited resection may be delayed for a decade or more, it is difficult to assess cure rates. Metastases are most frequently to the lungs, but sometimes to lymph nodes or occasionally to the bone marrow.