Surgical pathology of the mouth and jaws

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5. Non-odontogenic tumours of the jaws

It is not always possible to be certain whether some tumours of the jaws have arisen from osseous or dental connective tissues, but such a distinction is usually of little surgical significance. Many of these tumours are particularly rare in the jaws and considerably more common in other parts of the skeleton.

Ossifying (cemento-ossifying) fibroma

No distinction is drawn between osssifying and cementifying fibroma, as discussed in the previous chapter.

'Juvenile active (aggressive)' ossifying fibroma

This designation has been given to some rarely reported ossifying fibromas, mainly found in the maxilla of younger patients. They have been locally aggressive and showed a tendency to recur. A more cellular ('active') variant of ossifying fibroma may be difficult to distinguish from an osteoblastoma and should probably be categorized as such.

However, there are no reliable criteria for distinguishing these lesions from more typical cemento-ossifying fibromas.

Osteoma and other bony overgrowths

Neoplasms of either compact or cancellous bone are less common than localized overgrowths (exostoses). Exostoses consist of lamellae of compact bone, but exceptionally large specimens may have a core of cancellous bone. Small exostoses may form irregularly on the surface of the alveolar processes and specific variants develop on the palate (torus palatinus) or mandible (torus mandibularis). They differ from other exostoses only in their characteristic sites of development and symmetricallity.

Torus palatinus may start to develop in early adult life, but is not usually noticed until middle age.

The common site is towards the posterior of the midline of the hard palate and the swelling is rounded and symmetrical, sometimes with a midline groove. If the swelling is large enough to interfere with the fitting of a denture or is otherwise obtrusive, it should be removed.

Tori mandibularis form on the lingual aspect of the mandible opposite the mental foramen. They are typically bilateral, forming hard, rounded swellings. Their behaviour and management is the same as that of torus palatinus.

Compact and cancellous osteoma

The compact osteoma consists of lamellae of bone sometimes arranged like the layers of an onion but not in Haversian systems (osteones). This neoplasm therefore consists of dense bone containing occasional vascular spaces, and is very slow growing.

The cancellous osteoma consists of trabeculae of bone, between which are marrow spaces, surrounded by a lamellated cortex.

Osteomas should be excised only if they become large enough to cause symptoms or make the fitting of a denture difficult.

Gardner's syndrome

Gardner's syndrome comprises multiple osteomas of the jaws, polyposis coli with a high malignant potential, and often other abnormalities such as dental defects and epidermal cysts. It is inherited as an autosomal dominant trait.

The osteomas of the jaws are typically multiple and may be ranged along the alveolar ridge, along the borders of the mandible or form endosteal radiopacities. However, the importance of this syndrome is that most of those affected die of bowel cancer by the age of 50. Though some members of the family do not have polyposis coli, the finding of multiple osteomata of the jaws should prompt examination for bowel disease.

Osteochondroma (cartilage-capped osteoma)

This bony overgrowth grows by ossification beneath a cartilaginous cap. Osteochondromas are rare in the maxillofacial skeleton, but in this area the condyle and coronoid process are most frequently affected. There, it can interfere with joint function and limit opening of the mouth. The bony overgrowth will be evident in radiographs, but the cartilaginous cap may not be obvious. Almost any age can be affected, but the mean age of patients is in the fifth decade.

Microscopy

The appearance is not unlike that of an epiphysis with a cap of hyaline cartilage overlying slowly proliferating bone. The cartilage cells are sometimes regularly aligned but the cartilage is sometimes more irregular and may contain minute foci of ossification. As age advances the cartilaginous cep becomes progressively thinner and the mass consists increasingly of bone which is usually mostly cancellous and contains fatty or haemopoietic marrow. The cortex and medulla of the mass are continuous with those of the underlying bone.

Management

There is doubt as to whether osteochondromas are true neoplasms or developmental anomalies. Those that arise from the condyle cannot readily be distinguished from condylar hyperplasia. Typically, but not invariably, growth of the tumour ceases with skeletal

maturation. Complete excision, together with the overlying periosteum, is curative but in the axial skeleton approximately 3% have undergone sarcomatous change (Henry et al, 1992).

Multiple osteochondromatosis

This rare genetic anomaly is an autosomal dominant trait, but males are somewhat more frequently affected.

Osteochondromas usually appear in early infancy, particularly on the limbs, and may eventually be numbered in hundreds, but the face and jaws are usually spared. Growth of the lesions stops at the end of puberty but chondrosarcomatous change, later in life, may take place in 10-25% of cases.

Soft tissue osteochondromas

The tongue is the most frequently affected site for these rare tumours where they form firm painless swellings. They respond to excision.

Osteoid osteoma and osteoblastoma

These tumours or tumour-like lesions are not histologically distinguishable, but differ clinically and radiographically. They may not therefore be separate entities but variants of the same disorder. They are both rare in the jaws and more common in other bones. Most patients are below the age of 30 years and males are affected twice as often as females.

Osteoid osteoma

The mandible is affected approximately twice as frequently as the maxilla: the typical complaint is of pain which is characteristically worse at night but variable in nature and severity; it is usually troublesome rather than disabling. The pain is characteristically relieved by aspirin, and can occasionally precede radiologically detectable changes. Osteoid osteomas which are less than 2 cm in diameter appear to have limited growth potential.

Radiographically, osteoid osteoma is considerably more frequently cortical than medullary in site and typically shows a nidus of radiolucency surrounded by densely sclerotic bone. In a minority the nidus becomes calcified.

Microscopically, diagnosis depends on finding the nidus, though it may be no more than 1 or 2 mm in diameter. If the whole specimen is available, the nidus may be identifiable grossly as a greyish or reddish core which may be soft or granular. The nidus consists of osteoid and woven bone which is in trabeculae of irregular length and width, and rimmed by osteoblasts. The trabeculae may also show a pagetoid (jigsaw puzzle, 'mosaic') pattern of reversal lines. The connective tissue matrix is highly vascular with many small thin-walled vessels, fibroblasts and multinucleated giant cells.

Management

Excision of the complete nidus, though usually minute, is necessary; otherwise recurrence is likely. The problem of finding the nidus is made easier by smallness of the whole mass, which can be removed entirely. The condition is benign and surgical excision is curative.

Osteoblastoma

Osteoblastomas are even more rare than osteoid osteomas, particularly in the head and neck region, but in this area the mandible is also the most frequent site. As with osteoid osteoma, those aged under 30 years are affected, and males predominate in the ratio of 2 to 1. The chief complaint of dull aching pain is not usually nocturnal, and is said frequently not to respond to aspirin. More important is that osteoblastomas have a potential for progressive growth, can produce swelling of the jaw and may loosen adjacent teeth.

Radiographically, an osteoblastoma appears as a rounded area of radiolucency, usually in the medulla and containing variable amounts of mineralization. Unlike osteoid osteoma, there is no nidus, perilesional sclerosis is usually slight and the mass is larger (2-10 cm diameter). However, the radiographic features are variable and can mimic osteosarcoma or other malignant tumours in up to 25% of cases and show a sun-ray appearance or Codman's triangles.

Microscopically, the appearances of osteoblastoma are the same as those of, and cannot reliably be distinguished from, the nidus of osteoid osteoma.

Management

The osteoblastoma is benign and responds to conservative excision, but recurrence is likely if this is inadequate. There have been isolated reports of malignant change in osteoblastoma, but such lesions may have been low-grade osteosarcomas from the start. However, even 'malignant osteoblastomas' appear only to be locally aggressive and, unlike osteosarcomas, appear to have little or no potential for metastasis.

As mentioned earlier, cementoblastoma is also histologically similar to, and can be regarded as a counterpart of, osteoblastoma. If it is related to the root of a tooth and the microscopic findings are appropriate, it seems reasonable to regard it as a cementoblastoma. In addition, a cementoblastoma may be distinguishable microscopically by peripheral radiating columns of cementum surrounded by large cementoblasts. However, the surgeon may justifiably regard such distinctions as of little practical significance.

Giant cell granuloma of the jaw

Most central giant cell lesions of the jaws are hyperplastic and can clearly be distinguished from neoplasms by their behaviour. The name is misleading as there is no granuloma formation in the histological sense; a more appropriate term is *central giant cell lesion of the jaws.* The earlier name 'giant cell reparative granuloma' also derives from an unproven hypothesis (also applied to solitary bone cysts) that it was a reaction to trauma

followed by intramedullary haemorrhage. No evidence supports this idea and giant cell hyperplasia does not follow bleeding into bone after a fracture or enucleation of a cyst. Moreover, these lesions often grow rapidly, and far from being 'reparative' are locally destructive.

Though the giant cell granuloma is the main type of giant cell lesion affecting the jaw, it is uncommon. Its important and distinctive feature is that although it may grow rapidly and simulate a neoplasm clinically, wide excision is unnecessary and regression usually follows mere curettage.

It is probable that this lesion is a developmental disorder and similar collections of giant cells can be seen in fibrous dysplasia and related conditions such as cherubism.

Clinical features

Central giant cell granuloma is usually seen in young people under 20 years old and in females twice as frequently as males. The usual site is the mandible, anterior to the first molars, where the teeth have had deciduous predecessors. There is frequently only a painless swelling, but growth is sometimes rapid, and there may occasionally be pain or paraesthesia of the lower lip. Radiographs show a rounded cyst-like area of radiolucency often with a suggestion of loculation or a soap-bubble appearance. The roots of related teeth can be displaced or, less frequently, resorbed. Occasionally the mass can break through the bone, particularly of the alveolar ridge, to produce a soft tissue swelling. Diagnosis depends on biopsy, but needs to be supplemented by blood chemistry to exclude hyperparathyroidism, as discussed later.

Microscopy

Giant cell granuloma forms a lobulated mass of proliferating connective tissue containing many giant cells. It is frequently highly vascular, so that signs of bleeding and deposits of haemosiderin are often seen. In some cases there is considerable fibroblastic proliferation and in others there is prominent osteoid and bone formation, particularly near the periphery.

There are no changes in blood chemistry, but the histological features are indistinguishable from hyperparathyroidism. These giant cells have been shown by Flanagan et al (1988) by their respone to calcitonin, their activity in tissue culture and by osteoclast-specific monoclonal antibodies to be indistinguishable from osteoclasts. Whitaker and Waldron (1993) have described in detail more aggressive variants which recurred after initial curettage. These patients ranged in age from 30 months to 67 years. In 6 of these cases the microscopy was that of a typical giant cell tumour of bone which generally showed larger, more evenly distributed giant cells with absence of osteoid centrally or peripherally. Nevertheless, of the 4 cases where the outcome after a year or more was known, 2 responded to a second curettage.

Differential diagnosis of central giant cell lesions

- Hyperparathyroidism. The histological appearances are identical. Blood chemistry should be carried out and a raised serum calcium and alkaline phosphatase indicate hyperparathyroidism (Chapter 6).

- Fibrous dysplasia. A limited biopsy may show foci of giant cells, but the radiographic and histological features, and behaviour, are distinctive (Chapter 6).

- Cherubism. The microscopic features may be indistinguishable from giant cell granuloma, but the lesions are symmetrical and young children are affected (Chapter 6).

- Giant cell tumour (osteoclastoma) is an aggressive neoplasm which affects long bones, but may not be distinguishable with certainty by microscopy alone, from a giant cell granuloma. Osteoclastomas occasionally form in such bones as the temporal or sphenoid, but it is questionable how many of the few reported cases of these neoplasms in the jaws can be authenticated, and in their report of a primary malignant giant cell tumour of the jaw, Mintz et al (1981) claimed it to be the first documented case. This tumour metastasized to the lungs and a lymph node.

- Aneurysmal bone cysts may contain many giant cells, but their other histological features (Chapter 3) and, in particular, the multiple blood-filled spaces, should enable the distinction to be readily made.

Management

Curettage of giant cell granulomas is adequate and wide excision is usually unnecessary; small fragments that may be left behind rarely require further treatment and appear to resolve spontaneously. A minority of these tumours are more aggressive, recurrence follows incomplete removal and further surgery becomes necessary. Frequently, further curettage appears to be adequate and wider excision is rarely required.

Osteosarcoma

This highly malignant tumour is the most common primary neoplasm of bone, but is overall rare. Approximately 7% of osteosarcomas may be found in the jaws and according to Garrington et al (1967) their annual incidence in the USA is 1 per 1.5 million persons.

Most cases of osteosarcoma have no identifiable cause apart from the few which have followed irradiation. Osteosarcoma is also a recognized complication of Paget's disease of bone but hardly ever in the jaws.

Clinically, osteosarcoma of the jaws characteristically affects patients considerably later than in the long bones, namely at a mean age of 30-39 years and occasionally in elderly persons. Rarely, it may develop much later as a result of irradiation many years previously. Males are slightly more frequently affected than females. The mandible, and in particular the body, is more frequently affected than the maxilla.

A typical picture is that of a firm swelling which grows in a few months and becomes painful. The teeth may be loosened and there may be paraesthesia or anaesthesia in the mental nerve area. Metastases to the lungs may develop early. However, the fact that some patients have symptoms for many months before diagnosis suggests that some of these tumours may be slow growing.

Radiography

The appearances are varied. In the early stages there may be only subtle changes with only slight variation in the trabecular pattern, but an early feature (Garrington et al, 1967) may be symmetrical widening of the periodontal ligament space around one or several teeth as a result of tumour infiltration. This finding is not specific, but in association with pain, swelling or other radiographic changes is highly suggestive of osteosarcoma.

Later, irregular bone destruction usually predominates over bone formation. Bone formation in a soft tissue mass is highly characteristic of osteosarcoma. A sun-ray appearance at the surface of Codman's triangles at the margins due to elevation of the periosteum and new bone formation may be seen on appropriate radiographs, but are uncommon and not specific to osteosarcoma. The extent of the tumour can be shown by CT scanning.

Microscopy

Osteosarcomas originate from bone cells which have the potentiality to produce a highly pleomorphic picture in which bone formation does not necessarily predominate. The tumour cells are variable in size and shape, many are large and hyperchromatic, and mitotic figures may be prominent, particularly in the more highly cellular areas of the tumour. Cells resembling osteoblasts, fibroblasts and cartilage cells can be recognized; giant cells may be conspicuous, but many cells are of indeterminate appearance.

Formation of osteoid is the main criterion of diagnosis of osteosarcoma, but it may be small in amount and difficult to distinguish from collagen. Inability to detect osteoid appears to be a factor limiting the evaluation of aspiration cytology. Cartilage and fibrous tissue are usually also present. Predominantly fibroblastic variants appear to have a somewhat better prognosis than the more common osteoblastic type.

The amount of these tissues may vary widely in different parts of the tumour, but in jaw osteosarcomas there is frequently extensive cartilage formation and limited areas of osteoid formation. A small biopsy may, therefore, show malignant cartilage, and can lead to a mistaken diagnosis of chondrosarcoma. Overall, the general picture is one of uncontrolled and irregular cell activity.

A rare variant known as small cell osteosarcoma has a close resemblance to Ewing's sarcoma but for the fact that it forms osteoid. Another uncommon variant appears histologically to be a low-grade tumour and consists largely of spindle-shaped cells and limited osteoid formation. These low-grade intramedullary osteosarcomas are difficult to differentiate histologically from benign lesions such as fibrous dysplasia, desmoplastic fibroma or ossifying fibroma. However, they are infiltrative and pursue a relentless course.

Management

Diagnosis depends on biopsy which may need to be repeated if there is any doubt. Chest radiographs should also be taken, as secondary deposits may be present when the patient is first seen. Fine needle aspiration has been reported by White et al (1988) to give an 80.4% accuracy in the diagnosis of osteosarcoma. Serum alkaline phosphatase levels are raised in about 50% of cases and particularly with those tumours where new bone formation predominates.

Osteosarcomas of the jaws are rapidly invasive, but tend to metastasize to the lungs less frequently or later than those of the long bones. Metastasis to regional nodes may be seen in fewer than 10% of cases. Nevertheless, approximately 50% of osteosarcomas of the jaw recur locally within a year of initial treatment. Only 4 out of 66 patients reported by Clark et al (1983) developed metastases, but most died from uncontrollable local disease. With aggressive surgery, supplemented as necessary by radiotherapy and sometimes chemotherapy, Tran et al (1992) claimed a 49% 10-year survival rate for 15 osteosarcomas mainly of the maxilla or mandible, but deaths continued even after the decade.

Early radical excision of osteosarcoma of the jaws is essential. This involves mandibulectomy or maxillectomy, together with wide excision of any soft tissue extensions of the tumour. However, osteosarcomas often extend within the medulla for some distance beyond the radiographic margins, so that recurrence of the tumour in the excision margins is a major problem. Excision may be combined with pre- or postoperative radiotherapy by such means as high-dose interstitial needling, and adjuvant chemotherapy is increasginly widely used. Immunotherapy has proved to be disappointing.

The prognosis depends mainly on the extent of the tumour at operation and deteriorates with spread to the soft tissues, to the base of the skull, or with recurrence after excision which may happen in over 50% of cases.

Juxtacortical osteosarcoma

Juxtacortical osteosarcoma is a rare variant which, like endosteal osteosarcoma, mainly affects the limbs but can occasionally involve the jaws. Its chief importance is its better prognosis, as reviewed by Millar et al (1990), who reported 4 cases but were able to find only 8 previous reports.

Clinically, juxtacortical osteosarcoma typically affects the mandible, and the average age of patients is about 35 years. It may cause dull aching pain and forms a slow-growing mass on the surface of the jaw or in the adjacent parosteal tissue. The mass is typically rounded with a broad base.

Radiographically, juxtacortical osteosarcoma characteristically has an opaque base and is more lucent superficially. The pattern of and amount of opacity and radiolucency varies widely.

Microscopy

Juxtacortical osteosarcoma characteristically shows a deep zone of benign-looking, parallel trabeculae of bone separated by fibrous tissue: mitotic activity and cellular abnormalities are frequently difficult to find. The more superficial and, particularly, the radiolucent zones are likely to show more obvious neoplastic activity and cellular pleomorphism consistent with osteosarcoma. A minority of specimens show obviously sarcomatous features throughout.

The perms *periosteal* and *parosteal osteosarcoma* result from an attempt to subdivide the variants of this tumour, when affecting the long bones, on the basis of differing radiographic and microscopic features. It is suggested that the periosteal type is a separate entity and tends to be a high-grade tumour with more obviously malignant features. Even so, its prognosis is appreciably better than for endosteal osteosarcoma. However, this subclassification does not appear as yet to be justifiable for jaw tumours.

Management

It is obviously essential to establish the diagnosis firmly as early as possible by adequate biopsy of the superficial radiolucent areas.

Wide excision, including underlying bone, is desirable, though recurrence has even followed hemimandibulectomy. Of the 4 cases reported by Millar et al (1990), all were disease free 1-16 years later and of the 8 earlier cases, 5 were recurrence free for periods of 6-11 years.

Chondroma

The chondroma is a particularly rare tumour of the jaws. Many pathologists, including the present authors, believe that the majority of so-called chondromas of the jaws, ultimately prove to be malignant. In any case, chondrosarcomas in the maxillofacial region are considerably more frequent than chondromas. However, chondromas are described here in deference to those who hold other views.

Chondromas are far more frequently found (though still rare) in the nose or nasal sinuses and hence can occasionally be found in the maxilla rather than the mandible. Clinically, true chondromas are small and likely to be no more than chance findings.

Microscopically, chondromas consist of hyaline cartilage, but the cells are irregular in size and distribution. Calcification or ossification may develop within the cartilage.

Treatment is by wide excision, including an adequate margin of normal tissue all round, because of the difficulty in distinguishing benign from malignant tumours and the probability that a chondroid tumour is malignant.

Chondrosarcoma

Chondrosarcoma of the jaws affect adults at an average age of about 45 years. The maxilla is the site in 60% of cases, most frequently in the anterior alveolar region, but there is no special site of predilection for mandibular tumours.

There is wide variation in the reported relative frequency of chondrosarcomas and osteosarcomas of the jaws. These differences probably result from varying histological criteria for distinguishing chondrosarcomas from chondrogenic osteosarcomas. From a practical viewpoint this distinction may be important, as chondrosarcomas of the jaws appear to have a worse prognosis than osteosarcomas (Garrington and Collett, 1988a, b).

Pain, swelling or loosening of teeth associated with an area of greater or lesser radiolucency are typical feautres. Radiographically, chondrosarcoma of the jaws can be well or poorly circumscribed, or may appear multilocular. Though radiolucency is typical, calcifications are frequently present and may be widespread and dense. Symmetrical widening of the periodontal ligament space around affected teeth may be seen (Hackney et al, 1991).

The radiographic margins are an unreliable guide to the extent of the tumour which can infiltrate between the bone trabeculae without causing their resorption.

Microscopy

The product of the neoplastic chondrocytes ranges from comparatively well-formed cartilage (grade I tumours), which are the most frequent grade in the jaws, to myxoid tissue (grade III). The chondrocytes show the pleomorphism characteristic of these sarcomas; they may be binucleate but show no mitotic activity in grade I tumours. Grade II tumours form myxoid tissue as well as cartilaghe and there are occasional mitoses among the chondrocytes. The amount of calcification in the neoplastic cartilage corresponds with the radiographic appearances and can be punctate or loose and fluffy in appearance.

Behaviour and management

Chondrosarcomas of the maxillofacial region are aggressive; local recurrence or persistent tumour is the main cause of death. Fewer than 10% of these tumours (usually grade III tumours) metastasize; the lungs or other bones are then the usual sites of distant spread. Metastasis to lymph nodes is very rare.

Chondrosarcomas must be widely excised as early as possible. The first operation is critical, as inadequate excision is likely to lead to recurrences beyond the original area of operation with inevitable problems of management. A major difficulty as mentioned earlier is the ability of the tumour to extend in the cancellous spaces a considerable distance beyond the radiographic margins. Another is the ability of chondroid tumours to seed and grow in the soft tissues of the operation site. Chondrosarcomas only occasionally respond to radiotherapy, and chemotherapy appears to be of little value.

The prognosis of chondrosarcomas of the maxillofacial region is generally worse than for other sites because of the difficulties of adequate excision in this area. The 5-year survival

rate is from 40% to 60% and depends on the tumour stage and grade, and on the extent of the original excision. Maxillary tumours have an even worse prognosis than mandibular, but in the 37 cases reported by Garrington and Collett (1988) there were no survivors from chondrosarcoma of either jaw after 15 years.

Mesenchymal chondrosarcoma

Mesenchymal chondrosarcoma is considerably more uncommon than chondrosarcoma but a relatively high proportion of them (15-35%) are in the craniofacial region. A minority form in the soft tissues.

Clinically, mesenchymal chondrosarcoma has a wide age distribution. It presents no specific signs or symptoms but rapidly developing pain and swelling, sometimes with loosening of teeth, are typical.

Radiographically, there is an area of radiolucency, usually speckled with calcifications. There is only partial circumscription and no peripheral sclerosis.

Microscopy

The overall appearance is that of a highly cellular tumour in which only small foci of tissue are recognizable as poorly formed cartilage; however there are striking variants.

Typically, the bulk of the tumour consists of sheets of irregularly ovoid or sometimes spindle-shaped, darkly staining cells with little cytoplasm, with occasional or numerous mitoses. Scattered about are generally small, poorly circumscribed foci of cartilage in which there may be calcification. These foci may be scanty or occasionally form the bulk of the tumour and some areas of the tumour may be highly vascular.

One variant (haemangiopericytoma-like mesenchymal chondrosarcoma) consists of sheets of small mesenchymal cells surrounding cleft-like vascular spaces. Cartilage can sometimes be very scanty in such tumours. In another variant, the vascular component forms sinusoids within the tumour.

Management

Mesenchymal chondrosarcoma is highly malignant and the frequency of metastases is high. Spread, usually to the lungs but sometimes to lymph nodes, frequently follows local recurrences.

Early radical surgery followed by combined chemotherapy is therefore required. However, its value is as yet uncertain and either local recurrences or metastases can appear 10 or more years after treatment. There are no reliable microscopic guides to prognosis.

Chondromyxoid fibroma (fibromyxoid chondroma)

This rare tumour occasionally forms in the mandible. Lustman et al (1986) found 10 earlier reports and added three more. Twelve of these were in the mandible and Damm et al

(1985) reported another example in the maxilla. Though so few cases have been seen in the jaws, the importance of this tumour is that it is benign but can be mistaken microscopically for a chondrosarcoma.

Clinically. most patients are below the age of 30 and symptoms are frequently slight or absent. However, chondromyxoid fibroma can sometimes simulate a malignant tumour and can cause pain, swelling of the jaw or loosening of teeth.

Radiographically, this tumour is likely to appear as radiolucent areas with irregular but, typically, sclerotic margins and trabeculation or an appearance suggesting loculation. Opacities are rarely seen in the tumour area.

Microscopy

The typical features are lobules of myxoid tissue with more cellular and compact peripheries, and surrounded by fine but highly vascular fibrous tissue septa. In excision specimens the surrounding bone may be seen to be sclerotic.

The cells of the myxoid areas are variable in shape, but many are angular or stellate with long slender processes, or may be within lacunae. The more closely packed peripheral cells tend to be more rounded and may have an epithelioid appearance. Cartilage can occasionally form up to 75% of the tumour but may be present only in minute amount, and calcifications are seen in a minority of cases. Cyst formation and areas of haemorrhage may be seen.

Findings which may add to the impression of malignancy are cells with large hyperchromatic nuclei and osteoclast-like giant cells. Features helping to dinstinguish this tumour from a chondrosarcoma are an earlier age of onset, its sclerotic margins and frequent lack of calcifications or calcifications of a different type from those seen in chondrosarcomas.

Management

Chondromyxoid fibroma can recur if excision is inadequate. Like other chondroid tumours it can grown in the soft tissue as a result of seeding of tumour cells at operation. However, it is doubtful whether sarcomatouc change has been authenticated. The tumous should be excised with as wide as possible a margin of normal tissue.

Chondroblastoma

Chondroblastoma is a benign tumour but involves the maxillofacial region even more rarely than chondromyxoid fibroma. Out of 495 cases reviewed by Kurt et al (1989), only 7 were in the mandible but 23 were in the temporal bone.

Clinically, the median age of presentation of these tumours in the head and neck region is approximately 40 and males have been affected twice as frequently as females. Characteristic radiographic appearances in the long bones are a rounded area of radiolucency with a thin sclerotic border which may sometimes show a scalloped pattern and varying amounts of calcification. These appearances may be less well defined in the jaws.

Microscopy

The chondroblastoma is highly cellular. Rounded cells, with well-defined outlines, eosinophilic or amphophilic cytoplasm and an epithelioid appearance are the main component. Multinucleate giant cells are common and range from those with only two or three nuclei, to large osteoclast-like cells. They are usually associated with areas of haemorrhage or necrosis and secondary aneurysmal bone cyst formation has been seen in up to 25% of cases. The frequency of giant cells in these tumours is indicated by its earlier names of 'calcifying giant cell tumour' or 'epiphyseal chondromatous giant cell tumour'.

Chondroid areas can be shaprly defined or merge imperceptibly into the epithelioid areas. A net-like pattern of calcification extending between the cells or punctate calcifications are characteristic. Calcification in the cartilaginous areas may be seen, but ossification is rare and myxoid areas are absent.

Management

As indicated earlier, information about chondroblastomas of the jaws is scanty. Curettage, followed if necessary by bone grafting, has frequently been successful, but up to 30% of cases may recur. If aneurysmal bone cyst is associated, curettage alone is inadequate and its combination with cryosurgery is probably more effective. There is in either case a good response to radiotherapy for otherwise uncontrollable or surgically inaccessible lesions.

Ewing's sarcoma

Ewing's sarcoma comprises 10-15% of all primary sarcomas of bone, but fewer than 3% are in the jaws. It predominantly affects the legs or pelvis, but of those that affect the head and neck region the mandible is affected twice as frequently as the maxilla.

The histogenesis of Ewing's sarcoma has long been controversial, but immunocytochemistry has shown that the cells stain for neural markers such as neuron-specific enolase. Moreover, the tumour cells may form rosetta-like patterns as seen in neuroblastomas and retinoblastoma. Though Ewing's sarcoma cells may stain for vimenting and have been though to be pluripotential, it is generally accepted that this tumour is of neuroectodermal origin and shares cytogenetic abnormalities with primitive neuroectodermal tumour (Dehner, 1993).

Clinically, the majority of patients are white males, usually aged from 5 to 20 years, and rarely over 30 years.

Typical symptoms are bone swelling and often pain, progressing over a period of months. Teeth may become loosened and the overlying mucosa ulcerated. Fever, leucocytosis, raised ESR and anaemia indicate a poor prognosis.

Radiographically, Ewing's sarcoma appears as an irregular osteolytic lesion with or without cortical expansion. The onion-skin appearance due to the periosteal reaction, sometimes seen in long bones, is rare in the jaws. The clinical and radiographic findings in 105 reported cases have been reviewed by Wood et al (1990).

Microscopically, Ewing's sarcoma cells resemble but are about twice the size of mature lymphocytes, having a darkly staining nucleus, surrounded by a rim of cytoplasm, which is typically vacuolated. The tumour cells are in diffuse sheets or in loose lobules, separated by septa. Grouping of tumour cells round blood vessels, and areas of haemorrhage and necrosis, may be seen.

Important diagnostic features are the presence of intracellular glycogen in approximately 75% of cases, but absence of reticulin from the stroma.

Ewing's sarcoma may be difficult to differentiate from metastatic neuroblastoma or malignant lymphoma unless intracellular glycogen is present. Alcohol fixation is useful for increasing the reliability of staining for glycogen. Small cell osteosarcoma may also appear similar but for small foci of osteoid.

Management

The most common sites for metastases are the lungs and other bones. Since Ewing's sarcoma is so rare as a primary tumour in the jaws, the possibility that such a tumour is a metastasis from another bone may need to be investigated by a skeletal survey. Lymph nodes are involved in 10-20% of cases.

Currently, the initial treatment of choice is probably as wide excision as possible, together with megavoltage irradiation and multi-agent chemotherapy. This combination treatment appears to have improved the 5-year survival rate from about 10% to 60% or more. However, there is a significant increase in second (particularly lymphoreticular) tumours as a consequence of the chemotherapy and there is insufficient information as to the effectiveness of multimodal treatment of Ewing's sarcoma of the jaws.

Extraskeletal osteosarcoma, chondrosarcoma and Ewing's sarcoma

These sarcomas can rarely also develop in the soft tissues where they must be distinguished from a variety of pseudosarcomatous lesions or other sarcomas (Chapter 13).

Desmoplastic fibroma

Desmoplastic fibroma of the jaws is a fibromatosis, a term which describes tumour-like fibrous proliferations which infiltrate the surrounding tissues like a fibrosarcoma, but never metastasize (Chapter 13).

Clinically, the majority (75%) of patients are below the age of 30 and 50% are between the ages of 10 and 20 years. The mandible, usually at the junction between the ramus and body, is the most common site in the head and neck region. Of 49 previously reported lesions affecting the jaws reviewed by Hashimoto et al (1991), only 6 were in the maxilla.

The main manifestation is a gradually enlarging swelling but occasionally there is aching pain. Radiographically, desmoplastic fibroma gives rise to a well-circumscribed area of lucency which has a honeycomb or trabeculated appearance, and usually has a partial or

complete sclerotic rim. Roots of related teeth may be resorbed and, rarely, the margins suggest infiltration of the surrounding bone.

Microscopy

The mass consists of fibroblasts and collagen fibres forming broad bundles. These fibrous bundles interlace to some degree, but do not form the streaming or herring-bone appearances seen in fibrosarcomas. The nuclei of the fibroblasts show no atypia, but may be more plump and vesiculated than normal and contain 2 or 3 minute nucleoli. Mitotic activity is virtually absent. The margins are less well circumscribed than suggested by the radiographic appearances and merge with the surrounding bone.

Management

Desmoplastic fibroma is progressive but, as mentioned earlier, does not metastasize. Because of its infiltrative character, curettage or local excision is followed by recurrence in up to 30% of cases. Excision with an adequate margin of normal bone is therefore required and wider excision still is necessary for lesions which have extended into the soft tissues. However, mutilating surgery is not justified as any recurrences are purely local and can be controlled when they appear. Malignant change has been reported after radiotherapy which is therefore contraindicated.

Fibrosarcoma of bone

Fibrosarcomas of bone account for less than 5% of primary malignant bone tumours. The most common sites are the metaphyseal region of the medulla of a bone of the leg. In approximately 20% of cases, fibrosarcoma is secondary to some other bone lesions such as Paget's disease or a giant cell tumour, or a complication of previous radiotherapy of a soft tissue lesion.

Approximately 15% of fibrosarcomas of bone are in the head and neck region, with a predilection for the skull or jaws. The mandible, particularly the body, is affected more frequently than the maxilla in the ratio of 3-4 to 1. Males are slightly more frequently affected than females; most patients are between 30 and 40 years of age, but there is a wide age distribution.

Clinically, fibrosarcoma of the jaws causes pain, swelling and loosening of teeth. Radiographically it causes an ill-defined lucent area with no distinctive features or, rarely, a relatively well-circumscribed area of radiolucency.

Microscopically, fibrosarcoma of bone appears similar to its soft tissue counterpart (Chapter 13) with long interlacing fascicles of spindle-shaped fibroblasts and some collagen formation. The chief difficulty in differential diagnosis is with desmoblastic fibroma describe earlier.

Management

The treatment is radical surgical excision, possibly supplemented by radiotherapy. The tumour may metastasize to the lungs or other bones, but though data on fibrosarcomas of the jaws is limited, they are thought to have a better prognosis than osteo- or chondrosarcomas. About 30% of fibrosarcomas arise from the periosteum and appear to have a better prognosis than intramedullary fibrosarcomas. Five-year survival rates for fibrosarcomas of the bones of the head and neck range from 27% to 40%. The prognosis is affected by the extent of the tumour at operation and the degree of dedifferentiation. Fibrosarcomas of bone secondary to other diseases generally also have a worse prognosis.

Malignant fibrous histiocytoma

Fibrous histiocytoma range, in behaviour, from benign to malignant and, in many parts of the body, lesions earlier reported as fibrosarcomas or other sarcomas have been found on reassessment to be malignant fibrous histiocytomas. These tumours are predominantly soft tissue tumours (Chapter 13) but a minority are intraosseous. Block et al (1986) were able to find reports of 16 cases affecting the maxilla and added another.

Clinically, malignant fibrous histiocytomas of the jaws do not show any distinctive features to distinguish them from other sarcomas. Pain, swelling and loosening of teeth are typical effects.

The microscopic features are described in Chapter 13.

Management

Fibrous histiocytomas, even if histologically benign, should be widely excised. One patient reported by Besly et al (1993) required exenteration of the orbit. The possibility of lymph node involvement should also be considered and neck dissection carried out if necessary. The prognosis appears to be remarkably poor, and (apart from 1 patient lost to follow-up) of the 16 patients reviewed by Block et al (1986), the longest known period of disease-free survival was only 27 months and 8 quickly died from their tumours or had metastases. Adjuvant radiotherapy or chemotherapy or both have frequently been given but their value is uncertain. Factors which may affect the prognosis are discussed in Chapter 13.

Haemangioma of bone

Solitary haemangiomas form less than 1% of tumours of bone, but a high proportion are in the head and neck region. Of these, about 30% are in the jaws, the mandible being involved twice as often as the maxilla. Women are twice as frequently affected as men, but the tumour can be seen at virtually any age.

Clinically, a haemangioma of the jaw gives rise to progressive painless swelling. When the overlying bone becomes sufficiently thinned, the swelling may become pulsatile, teeth may be loosened and there may be profuse bleeding, particularly from the gingival margins involved by the tumour. Some behave aggressively with rapid erosion of surrounding bone.

Radiographically, a haemangioma appears as a generally rounded or pseudoloculated area of radiolucency with ill-defined margins and often a soap-bubble appearance.

Microscopy

Haemangiomas of bone are essentially similar to their soft tissue counterparts (Chapter 13). They are usually cavernous and rarely capillary or mixed, but arteriovenous tumours are most likely to bleed severely.

Management

Obviously enough, the chief problem is that of haemorrhage at operation, but in view of the overall rarity of such tumours, the possibility of an intraosseous haemangioma is unlikely to be suspected from the clinical or radiographic appearances, if there has been no bleeding or superficial signs of a vascularity. Theoretically, haemangioma should be considered in the differential diagnosis of radiolucent lesions of the jaws, particularly those having the radiographic features described earlier. It is clearly not feasible to carry out angiography on every doubtful case, but it is probably the strongest argument for aspiration of cyst-like lesions of uncertain nature. However, an important warning is the appearance of a bluish swelling when the periosteum is elevated at operation.

Opening a haemangioma or extracting a related tooth can give rise to torrential bleeding. Lamber et al (1979) reported a death and found reports of 10 earlier failures from this cause. Super-selective angiography indicates that haemangiomas can be vernous (cavernous) capillary or arteriovenous. The last (fast-flow angiomas) have one or more large feeder arteries, tend to be the most rapidly expanding and are most likely to bleed severely, when opened. When there are identifiable feeder vessels, selective arterial embolization makes any subsequent resection very much easier and safer. Surgery should follow embolization as soon as possible, and certainly within 3 days as collateral vessels quickly open up. Wide en bloc resection, with the margins in normal bone, is the only practical method of dealing with high-flow haemangiomas, as recommended by bunel and Sinder-Pedersen (1993) who also reviewed the variable clinical manifestations and treatment options. Following selective external carotid angiography, all feeder vessers should be tied off, if necessary including the ipsilateral external carotid artery. In the case of low-flow tumours, mucoperiosteal flaps are raised to expose the affected area, all related teeth are extracted and the haemangioma should be thoroughly curetted. The resulting cavity is then packed tightly with bone mush from the ilium. The mucoperiosteal flaps are then closed over the cavity. Healing can then progress without recurrence.

Should a tooth in the area of an unsuspected haemangioma be extracted, torrential haemorrhage can result. In such circumstances the tooth should be immediately reinserted into its socket and the patient told to bite hard pending transfer for definitive management of the tumour as already described.

Angiosarcoma of bone

Angiosarcoma is a particularly rare tumour, but in reviewing 133 reported cases, Barnes et al (1985) identified 7 examples in the mandible.

Dull pain and swelling are typical symptoms and, as with other malignant tumours, teeth may become loosened. If neglected, the tumour can erode through the bone and spread into the soft tissues. The radiographic appearance is a poorly circumscribed area of radiolucency without any distinguishing features.

Microscopically, angiosarcomas range from those with capillary-like spaces lined by plump endothelial cells showing few mitoses (grade I), to those where vascular formation can only be recognized by reticulin staining to show malignant endothelial cells within its sheath (grade III). These cells are mitotically active, have prominent nucleoli and there are foci of necrosis. Lymphocytes and eosinophils can be so numerous in the stroma as sometimes to lead to misdiagnosis, if the biopsy is inadequate.

The treatment of choice appears to be wide surgical excision with radiotherapy for any inaccessible areas of tumour. The prognosis appears to depend greatly on the degree of differentiation, and well-differentiated examples (grade I; sometimes termed haemangioendotheliomas) are less likely to metastasize. Data on the prognosis of jaw tumours are limited.

Leiomyosarcoma of bone

Leiomyosarcoma is another rare tumour, but 40% of oral cases may arise in the maxilla or mandible where they form locally destructive lesions not clinically or radiographically distinguishable from many other malignant tumours.

The microscopic features are essentially the same as those of the soft tissue counterpart and described in Chapter 13.

The treatment is radical surgical excision, but the prognosis is poor.

Melanotic neuroectodermal tumour of infancy

This rare tumour was thought in the past to be odontogenic and termed *melanotic adamantinoma* because of its development in close proximity to the teeth. However it is widely accepted that its origin is from the neural crest.

Clinically, melanotic neuroectodermal tumours develop in the first year of life. Mosby et al (1992) identified reported of 195 cases, of which 64% were in the maxilla, 11% in the mandible, 5% in the brain and isolated examples in almost any other site. In the maxilla it forms an expansile mass, stretching but not ulcerating through the overlying mucosa, which appears bluish because of the underlying pigmentation. Radiographs show an area of bone destruction with irregular margins and sometimes displacement of teeth.

Microscopy

The tumour consists of slit-like or larger spaces lined by cuboidal, melaning-containing cells in a fibrous stroma. Small round cells, which are non-pigmented, form clusters in the stroma or lie in the alveolar spaces. These round cells resemble those of a neuroblastoma and may be associated with neurofibrillary material resembling glia.

Ultrastructurally the pigmented cells show both epithelial and melanocytic features. The rounded, non-pigmented cells have a slender cell process and cytoplasmic neurofilamentous material that suggest a neuroblastic origin. Slootweg (1992) has reivewed the immunocytochemistry and confirmed that, unlike melanomas, none of the cells is S-100 positive.

Management

The radiographic, CT scans and MRI are not diagnostic in themselves, but the appearance of a destructive maxillary tumour in an infent, together with high levels of vanillylmandelic acid, is distinctive. Melanotic neuroectodermal tumour is widely thought to be benign, but up to 15% of cases may recur and a few have metastasized. Radical excision may be indicated, but where this was not feasible, radiotherapy and/or chemotherapy has been used.

Primary lymphoma of bone

Involvement of the jaws is typical of African Burkitt's lymphoma but, rarely, other primary lymphomas can arise in bone. Pileri et al (1990) have reported 17 cases affecting the mandible in detail. There are no distinctive clinical features and radiographically the tumour forms a poorly demarcated area of bone destruction. The diagnosis depends purely on the microscopic findings.

Microscopy

Most lymphomas of bone appear to be large B cell lymphomas and earlier were frequently categorized as 'reticulum cell sarcomas' as the lymphocytes may resemble histiocytes. However, the nuclei are larger, with fine nuclear chromatin and more abundant cytoplasm. Fine reticulin fibres surround single or small groups of these lymphocytes.

Diagnosis and particularly differentiation from Ewing's sarcoma depend on immunostaining or gene product analysis which will indicate whether these large cells are B or T lymphocytes.

Management

It is necessary first to exclude disseminated lymphoma.

In the case of a true primary bone lymphoma, excision should be followed by multi-agent chemotherapy. Little data on the prognosis after modern treatment of these rare tumours is available, but they possibly have a better prognosis than most soft tissue non-Hodgkin lymphomas.

Multiple myeloma and solitary plasmacytoma

Multiple myeloma is a neoplasm of plasma cells which causes multifocal bone-destructive lesions. These are usually the main cause of symptoms, namely, bone pain and

tenderness. However, a jaw lesion occasionally gives rise to the first symptoms. Alternatively, one of the major complications, in particular amyloidosis, may dominate the clinical picture.

Skeletal radiographs typically show multiple punched-out areas of radiolucency, particularly in the vault of the skull.

As a result of the proliferation of myeloma cells in the marrow, there is frequently anaemia and sometimes thrombocytopenia. Increased susceptibility to infection may result from depressed production of normal immunoglobulins.

The picture just described is that of advanced disease. However, myeloma can be detected early in its asymptomatic phase by the chance finding, in a routine blood examination, of a greatly raised ESR, as a result of the overproduction of immunoglobulin. The diagnosis is confirmed by electrophoresis showing a monoclonal immunoglobulin or fragment spike.

Microscopy

Myeloma appears as sheets of plasma cells which, when well differentiated, have an eccentric nucleus with peripheral clumpling of the chromatin, giving a cartwheel appearance and a perinuclear halo. The area of cytoplasm is relatively large and baso- or amphophilic. With loss of differentiation, the nuclei become larger and lose their characteristic chromatic pattern, while the cytoplasm may form no more than a rim round the nucleus. Multiple nuclei and mitoses may be seen.

Investigation

Bone marrow biopsy is usually diagnostic, but recognition, by microscopy alone, of poorly differentiated myeloma may be difficult. Confirmation depends on the electrophoretic findings as well as the clinical features. Serological findings in multiple myeloma are a greatly raised ESR, rouleaux formation of red cells in a blood smaple and raised plasma protein levels, all of which result from the increased immunoglobulin production. Serum electrophoresis shows a monoclonal spike of IgG in the majority of cases.

Immunocytochemical demonstration of monoclonal production of immunoglobulin or immunoglobulin fragments provides substantiation. Light chain overproduction, demonstrable by serum electrophoresis, is common and leads to Bence-Jones proteinuria.

Management

There is frequently an initial response to treatment with combination chemotherapy, but the median survival for multiple myeloma is about 2 years. Fewer than 20% of patients survive for 5 or more years.

Dental treatment may be complicated by anaemia, haemorrhagic tendencies or abnormal susceptibility to infection.

Solitary, soft tissue (extramedullary) plasmacytoma

These are rare tumours, but approximately 80% of them form in the head and neck, usually in the nasal cavity or nasopharynx rather than the mouth. Involvement of the antrum may, however, give rise to a maxillary tumour. Microscopically, extramedullary plasmacytoma does not differ from multiple myeloma and can be shown to be monoclonal by immunocytochemistry. Solitary extramedullary plasmacytoma is not associated with a monoclonal peak in the serum.

Irradiation is highly effective, but multiple myeloma develops in up to 50% of patients, usually within 2 years.

Solitary plasmacytoma of bone

This equally rare tumour occasionally develops in the jaws but has a significantly better prognosis than soft tissue plasmacytoma.

Clinically, bone pain, tenderness or a swelling and a sharply defined area of radiolucency or, rarely, a soap-bubble appearance are typical features.

Microscopically, the cellular features are the same as those of multiple myeloma, which should be excluded as described earlier. A small rise in serum or urine monoclonal immunoglobulin is detectable in a minority of patients with solitary endosteal plasmacytoma. The monoclonal peak in the serum should disappear with treatment, but persistence indicates that treatment has been inadequate or that the disease has disseminated.

Treatment is by localized radiotherapy. Over 65% of patients survive for 10 or more years, but the majority eventually develop multiple myeloma, occasionally even after several decades.

Amyloidosis

Amyloidosis is the deposition in the tissues of an abnormal protein with characteristic staining properties and electron-microscopic appearances. It can be systemic or localized, and is classified according to the nature of the amyloid fibril and of the related serum protein. A fibrillary protein forms the essential structural element of amyloid, but a non-fibrillary glycoprotein (amyloid P component - AP) is present in virtually all types. In the case of myeloma and monoclonal gammopathies, amyloidosis results from overproduction of immunoglobulin light chains.

Amyloid deposition in the mouth, particularly the tongue, is most commonly a manifestation of a monoclonal gammopathy (non-neoplastic, plasma cell dyscrasias with overproduction of immunoglobulin) or of myeloma. In a survey of 225 patients, Kyle and Greip (1983) found macroglossia in 22% of cases of light chain associated amyloidosis (myeloma or monoclonal gammopathy). Reactionary (secondary) amyloidosis, resulting from rhenumatoid arthritis or chronic infections, is more common overall, but rarely affects the mouth.

Clinically, deposits of amyloid can cause macroglossia or soft tissue tags or swellings, particularly on the gingivae. An enlarged tongue due to amyloid is frequently lobulated, particularly along the margins, and can be so large as to protrude from the mouth. Purpura and anaemia may also be associated and give the tongue a pale or purplish colour, or cause ecchymoses in the surrounding tissues.

Microscopy

Amyloid appears as weakly eosinophilic, hyaline homogeneous material which is often perivascular. It stains positively with Congo red, which also shows a characteristic apple green birefringence under polarized light. There is also positive fluorescence with thioflavine T and a characteristic fibrillary structure by electron microscopy.

If the underlying disease has not alrady been identified, a blood picture and plasma protein electrophoresis should be followed, if positive, by marrow biopsy and skeletal radiographs.

Management

The prognosis of myeloma-associated amyloidosis is poor, either from the tumour itself or from widespread amyloid deposition and, in particular, renal damage. So-called benign monoclonal gammopathy has a poor prognosis ultimately, either as a result of eventual development of myeloma or of widespread amyloid deposition and renal failure. However, progress of the disease may be delayed by chemotherapy with melphalan and prednisolone.

Tongue reduction, though desirable, should be avoided if possible, as the tissue is friable, bleeding can be difficult to control and any benefit is often only temporary.

Langerhans cell histiocytosis (histiocytosis X, eosinophilic granuloma)

In this rare, predominantly osteolytic, tumour-like disease, there is a proliferation of histiocyte-like Langerhans cells. Both the surface markers of Langerhans cells and the characteristic Birbeck granules can be found in the tumour histiocytes. Three main forms, in order of severity, are usually recognized:

1. Solitary eosinophilic granuloma.

2. Multifocal eosinophilic granuloma (including Hand-Schuller-Christian disease).

3. Letterer-Siwe disease.

Letterer-Siwe disease was thought to be a different entity such as a lymphoma, but Birbeck granules have also been demonstrated in the tumour cells and the bone lesions may not be distinguishable microscopically from those of the other variants. In a review of 1120 cases, Hartman (1980) found that there was oral involvement in 114 cases and that the mandible was affected in 73%.

Solitary eosinophilic granuloma

Solitary eosinophilic granuloma predominantly affects adults and, when involving the jaws, usually affects the mandible to produce a localized area of bone destruction with swelling and often pain. A typical radiographic appearance is a rounded area of radiolucency with margins somewhat less sharply defined than those of a cyst, and frequently extending into the alveolar ridge. Teeth which appear to be floating in air is a typical radiographic appearance. Dagenais et al (1992), in reviewing the radiographic findings in 29 cases, found that they comprised solitary intraosseous lesions, multiple lesions of the alveolar ridge, periosteal new bone formation and root resorption in 10 out of 15 cases. The radiolucent areas were well defined, but only those involving the alveolar ridge showed marginal sclerosis. The mandible alone was involved in 20 out of the 29 cases, and with the maxilla in 8 more. The maxilla was the sole site in only 1 case.

Occasionally, gross periodontal destruction with exposure of the roots of the teeth is a feature.

Microscopy

Histiocytes are associated with eosinophils, sometimes with other types of granulocytes. The histocytes have pale, vesiculated and often lobulated nuclei, and weakly eosinophilic cytoplasm. Mitotic activity is typically absent. Eosinophils may be scattered among histiocytes or in conspicuous clusters. The matrix consists of unremarkable poorly fibrillar or granular material. These appearances may vary with the stage of the disease, with a high proportion of eosinophils at first, then growing numbers of histiocytes, and finally, in resolving cases, increasing fibrosis.

The diagnosis my be confirmed by demonstration by electron microscopy of Birbeck granules but Fartarsch et al (1990) have reported that positive staining of Langerhans cells for S-100 protein and peanut agglutinin is as reliable.

Multifocal eosinophilic granuloma

As well as the mandible, other sites of predilection are the skull, axial skeleton and femora. Almost any of the viscera (hepatosplenomegaly) or the skin (seborrhoeic dermatitis) may be involved in multifocal disease, but rarely without osseous lesions.

Such disease may be termed *Hand-Schuller-Christian disease,* but the classical triad of exophthalmos, diabetes insipidus and lytic skull lesions is present only in a minority.

Letterer-Siwe disease

Letterer-Siwe disease differs from the other types of Langerhans cell histiocytosis in that infants or, less often, young children are affected and the disease may be rapidly fatal. Though some believe that Letterer-Siwe disease is a separate entity, Birbeck granules have been seen and suggest that this disease is also a neoplasm of Langerhans cells. Both soft tissues and bone are commonly involved and rashes may be the earliest manifestation. Other features can include lymphadenopathy and splenomegaly, fever, anaemia and

thrombocytopenia, and infections such as otitis media. Many organs can become involved and become enlarged as a result of histiocytic infiltration.

Radiographically, the bone lesions do not differ from those in other types of Langerhans cell histiocytosis.

Management

The natural history of Langerhans cell histiocytosis ranges from isolated lesions with spontaneous regression, to widespread disease and a rapidly fatal outcome despite treatment. Though the behaviour of this disease is unpredictable, the very young have the worst prognosis, and have a mortality rate of about 50%. In those over 2 years of age, the mortality is reported to be about 15%. In general, the greater the number of organ systems affected, the poorer the prognosis. Monocytosis or thrombocytopenia are also associated with a high mortality.

In addition to biopsy of the oral lesions, physical examination, skeletal survey and blood picture will give an indication of any dissemination and its degree.

For a localized jaw lesions, curettage followed if necessary by corticosteroid or cytotoxic chemotherapy, or irradiation, usually suffices, but, as mentioned earlier, the course of the disease is so unpredictable that prolonged careful follow-up, and sometimes further treatment, is necessary. For multisystem disease, a combination of cytotoxic agents (often vinca alkaloids), corticosteroids and irradiation to active bone lesions is required.

Eosinophilic ulcer (atypical or traumatic eosinophilic granuloma)

Tumour-like, often ulcerated lesions with a microscopic picture resembling that of Langerhans cell histiocytosis may occasionally be seen in the oral soft tissues, particularly the tongue, but also the gingivae and, occasionally, other sites. In some cases there has been a history of trauma and, experimentally, crush injury to tongue muscle can induce a proliferative response with tissue eosinophilia. However, Doyle et al (1989) found trauma to be a possible cause in only 5 out of 15 cases.

Clinically, the ulcerated mass may be mistaken for a carcinoma: almost any age can be affected.

Microscopy

The typical appearance is a dense aggregation of eosinophils and other cells which resemble histiocytes. The latter lack the ultrastructural features and surface markers of Langerhans cells, but there have been a few cases where these histiocytes were pleomorphic, and showed prominent nucleoli and mitotic activity. This cellular infiltrate may extend into the epithelium.

The differential diagnosis is from Langerhans cell histiocytosis, which can be excluded by investigations, as suggested above, and by the use of immunostaining to identify Langerhans cells. In practice, spontaneous resolution, usually within 3 to 8 weeks, is to be

expected, and with an isolated soft tissue mass having these characteristics an expectant policy is usually justified.

Metastatic tumours

Most metastases in the jaws are carcinomas and the primary growth is usually in the bronchus, breast or prostate. These are common tumours and are the most common carcinomas to cause bony metastases. Other important sites of primary growths are the thyroid and kidney, but adenocarcinomas from almost any primary site can metastasize to the jaws.

Symptoms from a malignant deposit in the jaw can rarely provide the first sign of the disease and lead to diagnosis of the primary. In other cases the jaw is the first apparent site of secondary deposits from a growth treated a year or more previously. Though the jaw is much less frequently involved than other bones, secondary carcinoma is an important malignant tumour.

Patients are usually middle-aged or elderly. Typical symptoms are pain, which is often severe, or swelling of the jaw. Paraesthesia of the lip may be caused by involvement of a nerve trunk.

Radiography

Typically, there is an area of radiolucency with a hazy outline. It sometimes simulates an infected cyst or may be quite irregular and simulate osteomyelitis. Sometimes the entire mandible may have a moth-eaten appearance. Sclerotic areas may rarely be the main feature, particularly with metastases from the prostate.

Microscopy

Secondary deposits are usually adenocarcinomas or less frequently squamous cell carcinoma, according to the nature of the primary growth. Bone destruction by osteoclasts near the periphery of the deposit is the most common effect, but bone sclerosis can result particularly from metastases from the prostate. The latter are associated with raised prostate-specific antigen levels.

Management

Biopsy of the mass in the jaw will usually indicate whether it is a metastasis. A detailed history, especially of previous operations, and general examination are necessary. Radiographs of the rest of the skeleton may show other deposits. Blood examination is necessary to exclude anaemia due to replacement of the marrow by metastases.

The primary tumour should be treated if this is still feasible, but bony metastases are a sign of bloodstream spread of the disease and only palliative treatment may be possible. However, in many cases of breast cancer, tamoxifen can dramatically prolong survival, sometimes with complete resolution of bony metastases for several years. In prostatic cancer, anti-androgenic treatment may cause secondary deposits to regress for a time. If all else fails, irradiation may make the patient more comfortable and cause the tumour to regress for a time.

Should the deposit fungate into the oral cavity or face, cryosurgery may help to control pain and haemorrhage, and reduce bulk.

Some sarcomas, particularly Ewing's sarcoma, can metastasize to other bones and exceptionally rarely the jaws are involved.