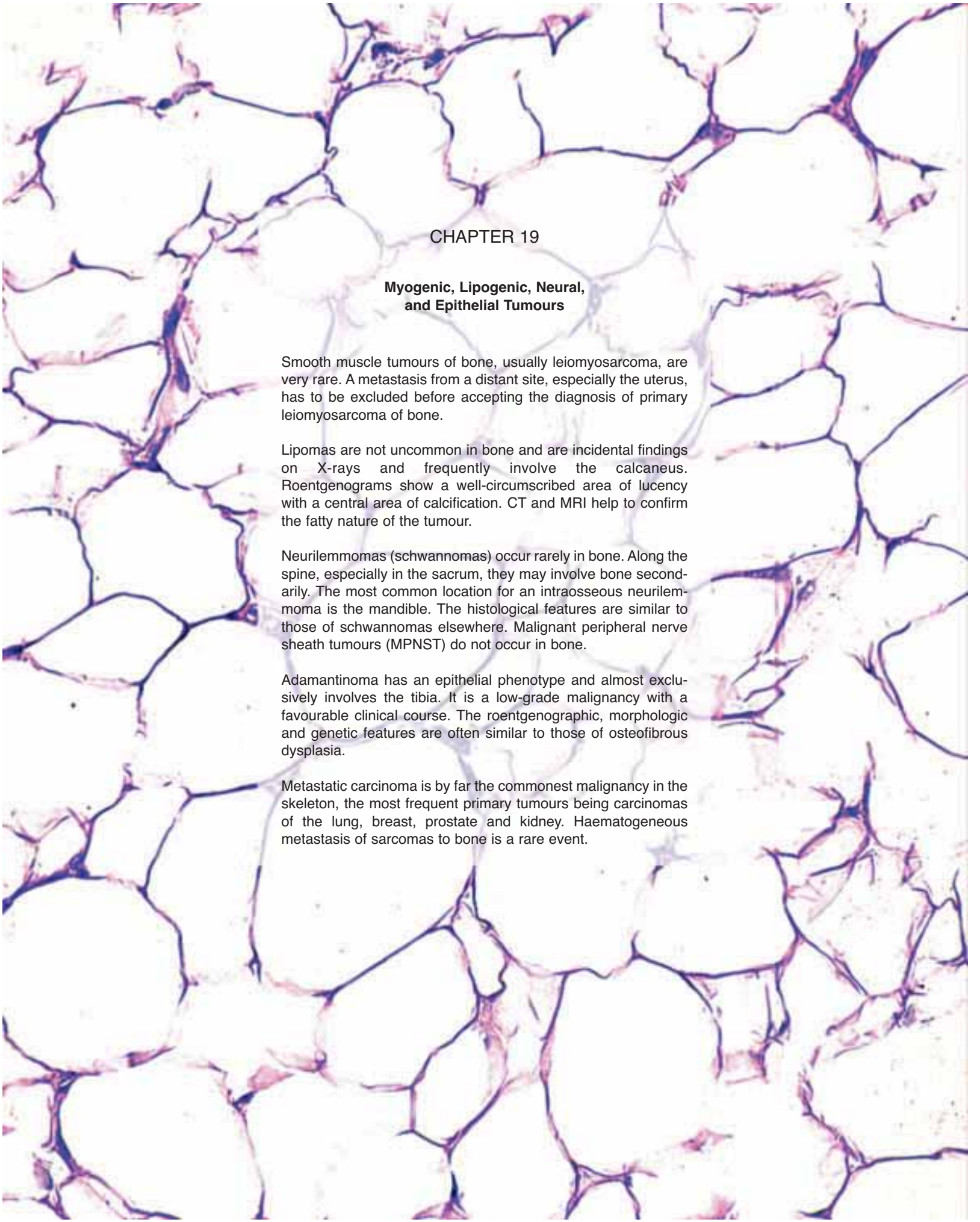

CHAPTER 19

Myogenic, Lipogenic, Neural, and Epithelial Tumours

Smooth muscle tumours of bone, usually leiomyosarcoma, are very rare. A metastasis from a distant site, especially the uterus, has to be excluded before accepting the diagnosis of primary leiomyosarcoma of bone.

Lipomas are not uncommon in bone and are incidental findings on X-rays and frequently involve the calcaneus. Roentgenograms show a well-circumscribed area of lucency with a central area of calcification. CT and MRI help to confirm the fatty nature of the tumour.

Neurilemmomas (schwannomas) occur rarely in bone. Along the spine, especially in the sacrum, they may involve bone secondarily. The most common location for an intraosseous neurilemmoma is the mandible. The histological features are similar to those of schwannomas elsewhere. Malignant peripheral nerve sheath tumours (MPNST) do not occur in bone.

Adamantinoma has an epithelial phenotype and almost exclusively involves the tibia. It is a low-grade malignancy with a favourable clinical course. The roentgenographic, morphologic and genetic features are often similar to those of osteofibrous dysplasia.

Metastatic carcinoma is by far the commonest malignancy in the skeleton, the most frequent primary tumours being carcinomas of the lung, breast, prostate and kidney. Haematogeneous metastasis of sarcomas to bone is a rare event.

Leiomyoma of bone

E. McCarthy

Definition
A benign spindle cell tumour of bone with smooth muscle differentiation.

Epidemiology
Leiomyomas of bone are very rare. Most patients are adults over age 30, although a child age 3 years has been reported. Males and females are equally affected {2166}.

Sites of involvement
The facial bones are most commonly affected by primary leiomyoma. The most common site is the mandible. In the extragnathic skeleton, the tibia is the most common site {2166}.

Clinical features
Patients present with pain. Radiologically, lesions are radiolytic, often multilocular. A sclerotic rim may be present. Occasionally there may be cortical expansion.

Macroscopy
Primary leiomyomas of bone are firm gray tan tumours. Most lesions are 3 cm or smaller in maximum dimension.

Histopathology
Histologically, leiomyomas of bone are identical to leiomyomas in other locations. Uniform spindle cells are present in interlacing bundles. Mitotic figures are extremely rare. The cells are positive with immunohistochemical stains for smooth muscle actin and desmin. Occasionally, thick-walled blood vessels are present in a pattern identical to angioleiomyoma {2166}.

Prognostic factors
Local excision results in a complete cure.

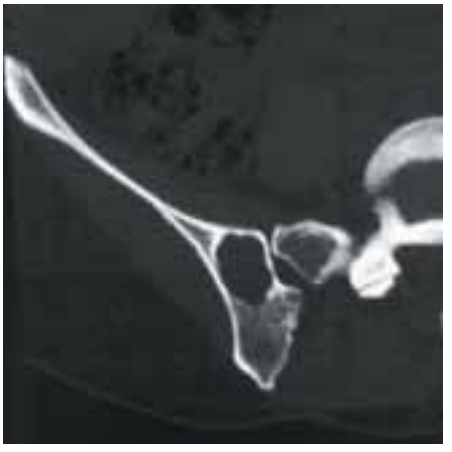

Fig. 19.01 Leiomyoma. CT scan showing a well defined lytic lesion with a sclerotic rim in the ilium.

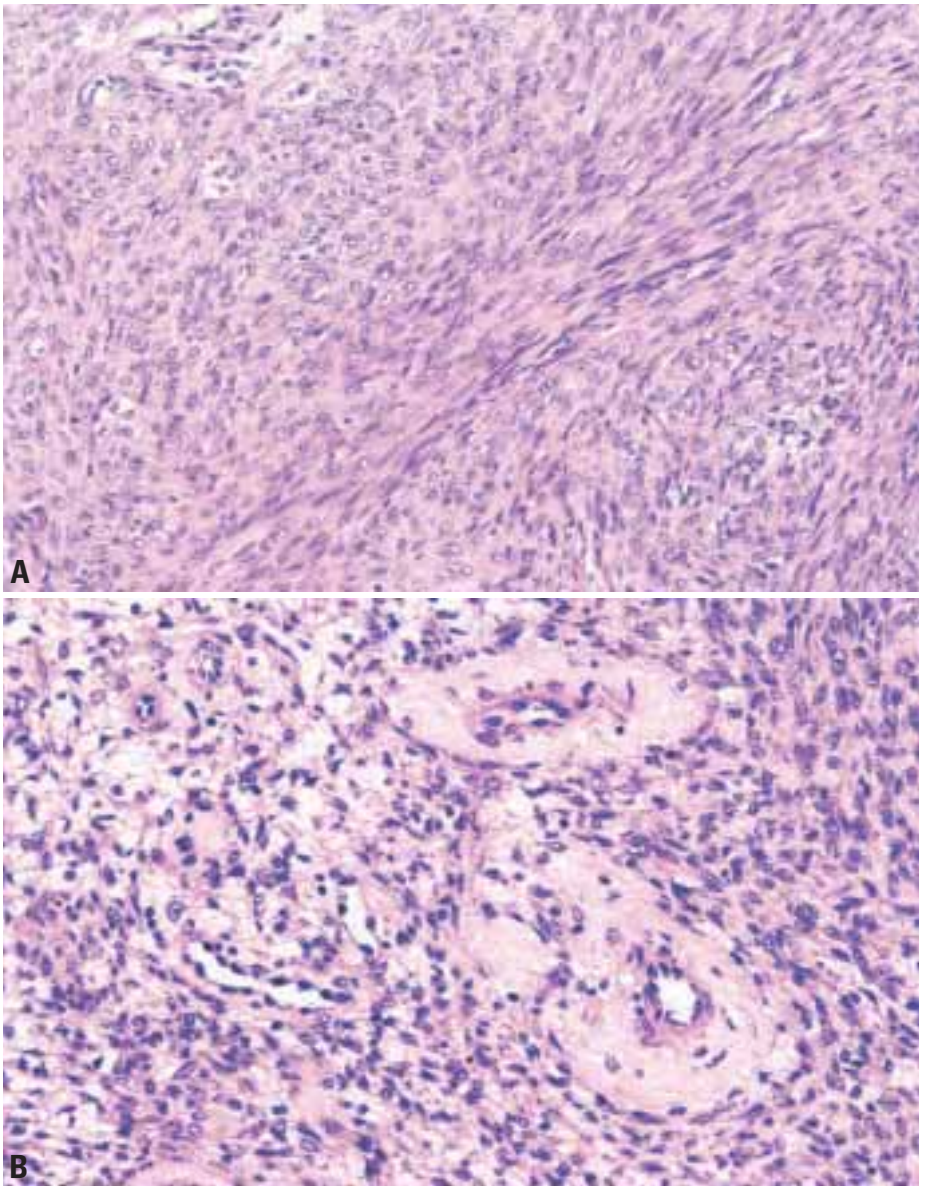

Fig. 19.02 Leiomyoma. **A** Low power view showing bundles of uniform spindle cells. **B** Thick walled blood vessels admixed with spindle cells in a pattern of angiomyoleiomyoma.

Leiomyosarcoma of bone

E. McCarthy

Definition
A very rare malignant spindle cell sarcoma of bone which shows smooth muscle differentiation with immunohistochemical or electron microscopic studies.

Epidemiology
Although the reported age range is from 9 to 87 years, the mean age is 44 years {165,1049,1932}. There is a slight male predominance.

Sites of involvement
Most lesions occur in the lower extremity around the knee, either in the distal femoral metaphysis or proximal tibial metaphysis. The craniofacial skeleton is the next most common area to be involved {68}.

Clinical features
Pain, present from 2 weeks to 1 year prior to diagnosis, is the most common symptom. Approximately 15% of patients present with pathological fracture.
Radiographically, it is an aggressive radiolytic lesion, with poorly defined margins, a permeative growth pattern, and cortical destruction. MRI shows a hypointense lesion on T1 and an iso-or hypointense lesion on T2 weighted studies {2056}.

Macroscopy
Lesions are grey to tan, firm or creamy masses, often with areas of necrosis or cystic degeneration. Despite a broad range in size, lesions average 6 cm in greatest dimension {68}. Cortical penetration is common.

Histopathology
Histologically, lesions are identical to leiomyosarcomas in other locations. Plump and pleomorphic spindle cells are arranged in bundles or fascicles. Mitotic figures are common. Often areas of necrosis are present. Smooth muscle differentiation is demonstrable by positive immunohistochemical staining for smooth muscle actin and desmin. Electron microscopic studies demonstrate fine filamentous actin fibrils in the cytoplasm.

Prognostic factors
Approximately 50% of patients develop metastases to the lungs within 5 years {68}. Ultimately, 50% of patients die from leiomyosarcoma of bone {1099}.

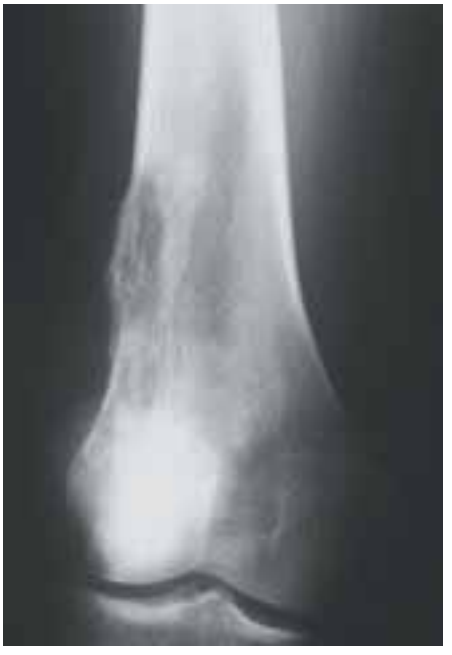

Fig. 19.03 Leiomyosarcoma. X-ray of a tumour in distal femur showing an aggressive, permeative lytic lesion with cortical destruction.

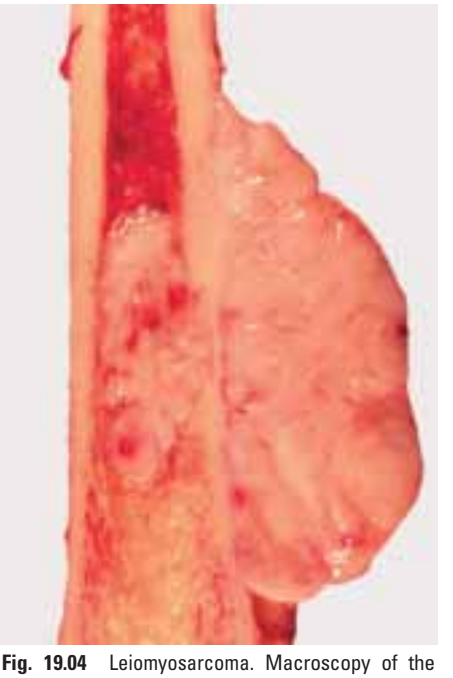

Fig. 19.04 Leiomyosarcoma. Macroscopy of the femoral lesion. Note both an intraosseous and an extraosseous component of the white fleshy tumour.

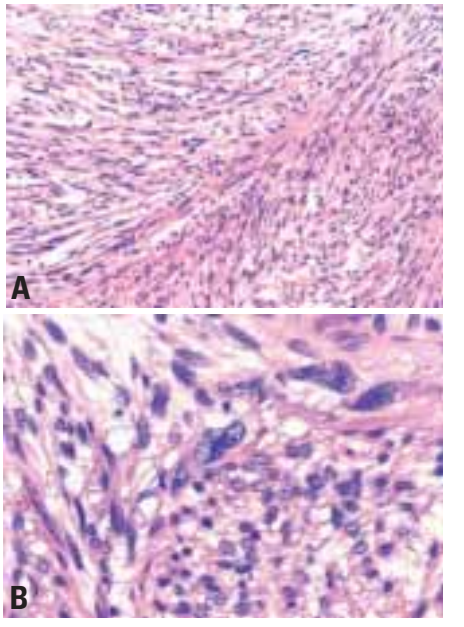

Fig. 19.05 Leiomyosarcoma. **A** Low power photomicrograph showing bundles of spindle cells.
B On high power magnification, note the cellular pleomorphism of the tumour cells.

Lipoma of bone

A.E. Rosenberg
J.A. Bridge

Definition
Lipoma of bone is a benign neoplasm of adipocytes that arises within the medullary cavity, cortex, or on the surface of bone.

Synonyms
Intramedullary lipoma, intracortical lipoma, ossifying lipoma, parosteal lipoma.

Fig. 19.06 Lipoma. Radiograph of intramedullary lipoma of humerus demonstrating an oval lytic lesion with a sclerotic rim.

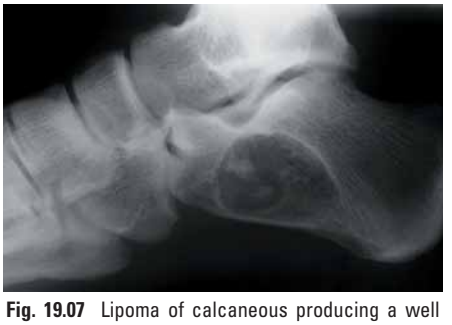

Fig. 19.07 Lipoma of calcaneous producing a well defined lytic lesion with central mineralization. Axial CT confirms the fatty nature of the lesion.

Epidemiology
Lipoma of bone is rare and accounts for less than 0.1% of primary bone tumours; their incidence is not known.
Intramedullary lipoma has a wide age range (2nd-8th decades) but most patients are approximately 40 years old at the time of diagnosis {1458}. Males are affected more frequently than females at a ratio of approximately 1.6:1 {1458}.
Parosteal lipoma usually develops during adulthood and most patients are in their 5th-6th decade of life at the time of diagnosis {1462}. There is a slight male predominance (9:7) {1462}.

Sites of Involvement
The vast majority of intraosseous lipomas arise within the medullary cavity and rarely develop in the cortex {2317}. They most commonly affect the metaphyseal regions of the long tubular bones, especially the femur, tibia and fibula and the calcaneus. However, they have also been described in many bones including the pelvis, vertebrae, sacrum, skull, mandible, maxilla, and ribs.
Parosteal lipomas generally develop on the diaphyseal surface of long tubular bones, especially the femur, humerus, and tibia {1462}.

Clinical features / Imaging
Intramedullary lipoma may be asymptomatic or produce achy pain. Rarely, it presents as a pathological fracture {822, 951, 1458}. Radiographically, intramedullary lipoma usually produces a well defined lytic mass that is surrounded by a thin rim of sclerosis. The lesion may also contain trabeculations or central calcifications. Bony expansion may occur in small caliber bones {822,951, 1458,1732}. CT shows that the fatty component has a low attenuation value similar to that of subcutaneus fat and on MRI the fat has high signal intensity on both T1 and T2 weighted images {1732}.
Parosteal lipoma is frequently asymptomatic and may present as a visible or palpable mass. Radiographs may reveal a radiolucent mass adjacent to the cortical surface that may show thickening or a periosteal reaction. Similar to intraosseous lipoma, the CT and MRI findings have the same features as subcutaneous fat except if there is calcification, cartilage or ossification within the lesion {1079,1752}.

Macroscopy
Intramedullary lipoma is usually 3-5 cm in size, is well defined, soft, and yellow. The surrounding bone is often sclerotic.
Parosteal lipoma is usually 4-10 cm in greatest dimension, is well defined, soft and yellow. Some cases contain gritty spicules of bone or firm nodules of cartilage in the base or scattered throughout the mass.

Histopathology
Intramedullary lipoma is well defined and consists of lobules of mature-appearing adipocytes that may replace the marrow and encase preexisting bony trabeculae. The adipocytes have a single large clear cytoplasmic vacuole that displaces the crescent shaped nucleus to the periphery. Some tumours may demonstrate fat necrosis with foamy macrophages and fibrosis. In ossifying lipomas delicate trabeculae of woven and lamellar bone may be present throughout the tumour {121, 346}.

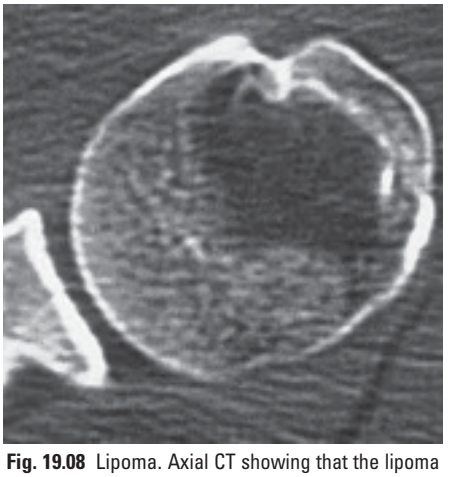

Fig. 19.08 Lipoma. Axial CT showing that the lipoma has the tissue density of fat.

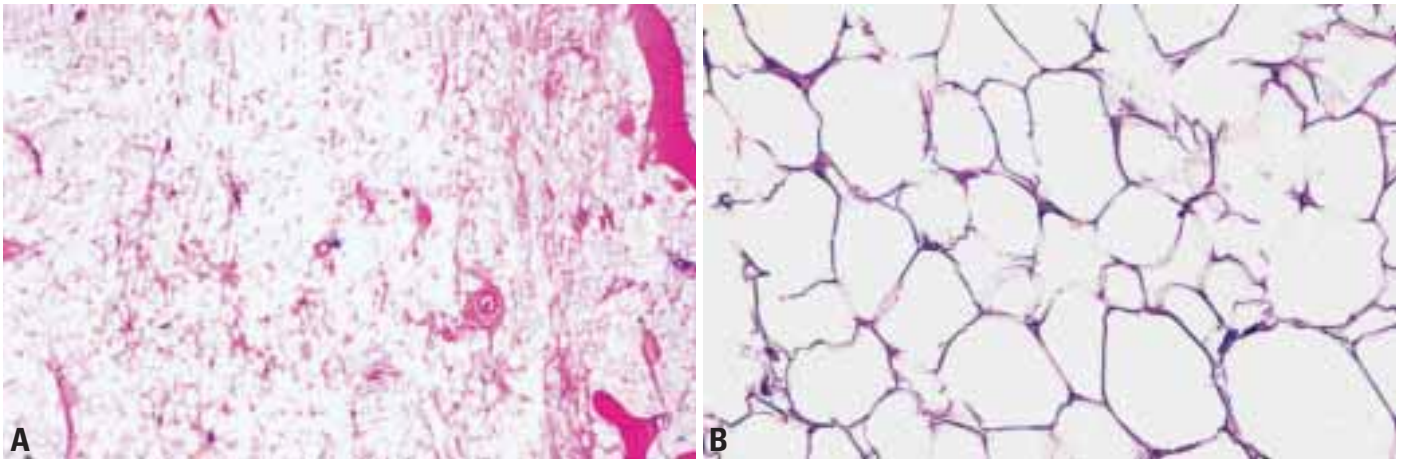

Fig. 19.09 **A** Well defined intramedullary lipoma composed of sheets of white adipocytes. **B** Parosteal lipoma composed of lobules of white fat cells.

Parosteal lipoma is also well defined and consists of lobules of mature appearing white adipocytes. The adipocytes have a single large clear cytoplasmic vacuole that displaces the crescent shaped nucleus to the periphery. Some cases may have bone with or without a hyaline cartilage in the base of the lesion or scattered throughout the mass in small islands {1462}.

Immunophenotype

The neoplastic fat expresses vimentin and S100 protein.

Genetics

The translocation t(3;12)(q28;q14) and its associated fusion transcript *HMGIC/LPP* characteristic of subcutaneous lipoma has been detected in a case of parosteal lipoma {255,1698}.

Prognostic factors

Lipoma of bone has an excellent prognosis and rarely recurs.

Liposarcoma of bone

A.E. Rosenberg

Definition
Liposarcoma of bone is a malignant neoplasm whose phenotype recapitulates fat.

Epidemiology
Liposarcoma of bone is an extraordinarily rare neoplasm. Most cases are described in the form of single case reports in older literature and the validity of the diagnosis in some cases has been questioned {457}. Liposarcoma of bone occurs in all age groups although the majority of patients are adults {15,457, 1090,2121}. Men are affected slightly more frequently than women.

Sites of involvement
Liposarcoma of bone usually develops in the long tubular bones especially the tibia and femur and has been reported to arise in the diaphysis, metaphysis, and epiphysis {15,457,1090,2121}.

Clinical features / Imaging
Liposarcoma of bone presents as a painful mass. Radiographically, the tumour manifests as a well defined or poorly defined mass {15,457,1090, 2121}.

Macroscopy
Most liposarcomas are large, lobulated, soft to firm and are yellow to tan-white in colour. Myxoid tumours may be glistening, slimy and mucinous.

Histopathology
The histological variants of liposarcoma reported in bone include well differentiated lipoma-like, myxoid and pleomorphic types {15,457,1090,2121}. Well differentiated lipoma-like liposarcoma consists of sheets of mature appearing adipocytes with scattered tumour cells having enlarged hyperchromatic nuclei. Some of these atypical cells are lipoblasts and are distinguished by cytoplasmic vacuoles that are round, clear, and scallop the nucleus. Myxoid liposarcoma consists of mildly atypical stellate and spindle cells enmeshed in a myxoid stroma that contains a finely arborizing vascular tree that has a plexiform pattern. Also scattered throughout the tumour are lipoblasts. Sheets of large pleomorphic cells in which the cytoplasm is either eosinophilic or filled with round clear vacuoles characterize pleomorphic liposarcoma. Mitoses are usually numerous.

Immunophenotype
There are no data regarding the immunophenotype of liposarcoma of bone.

Ultrastructure
The cytoplasm of the neoplastic cells contains membrane bound lipid droplets of varying size. Dilated rough endoplasmic reticulum and scattered mitochondria are also present {1650}.

Prognostic factors
Prognostic information regarding liposarcoma of bone is scant. Generally, the behaviour of the tumour should correlate with its histological grade.

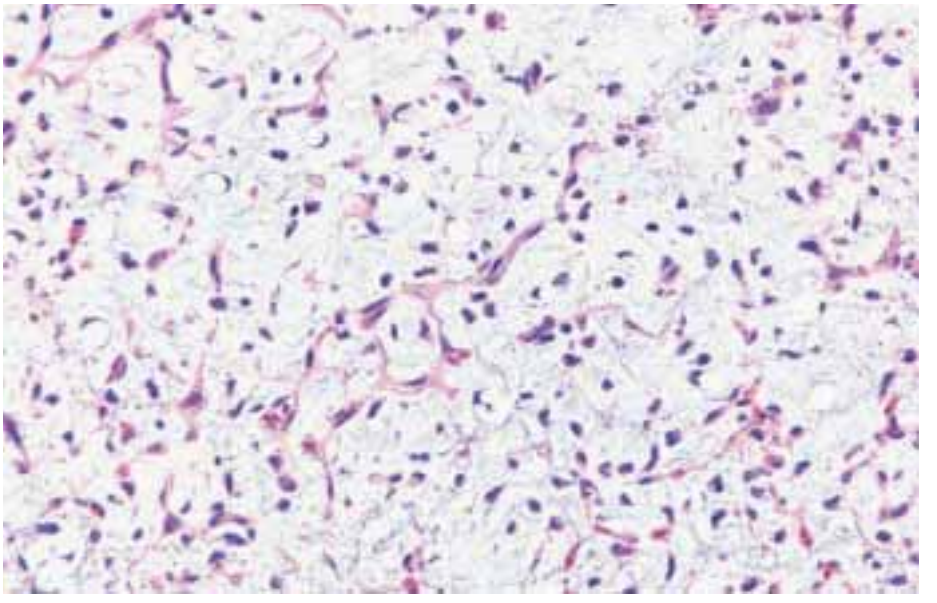

Fig. 19.10 Myxoid liposarcoma consisting of scattered spindle and stellate cells and occasional lipoblasts enmeshed in a frothy myxoid stroma that contains branching small caliber capillaries.

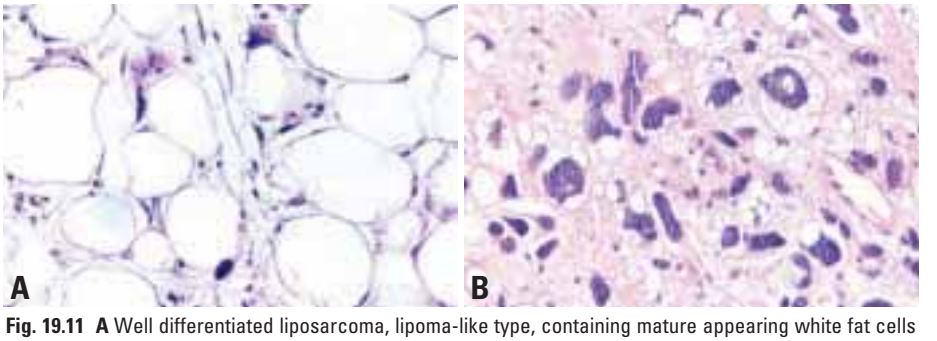

Fig. 19.11 **A** Well differentiated liposarcoma, lipoma-like type, containing mature appearing white fat cells and scattered adipocytes that have enlarged hyperchromatic nuclei. **B** Sheets of pleomorphic cells including lipoblasts characterize pleomorphic liposarcoma.

Schwannoma

K.K. Unni

Definition
Schwannoma is a benign neoplasm of Schwann cell origin arising within bone.

ICD-O code 9560/0

Synonyms
Neurilemmoma, neurinoma.

Epidemiology
Neurogenic tumours of bone are extremely uncommon. Although roentgenographic abnormalities may be found involving the skeleton in patients with neurofibromatosis, there are no well recognized examples of neurofibroma in bone. All benign neurogenic tumours in the skeleton are Schwannomas. They compose less than 1% of all benign tumours in the Mayo Clinic files (unpublished statistics, Unni, K. K.).

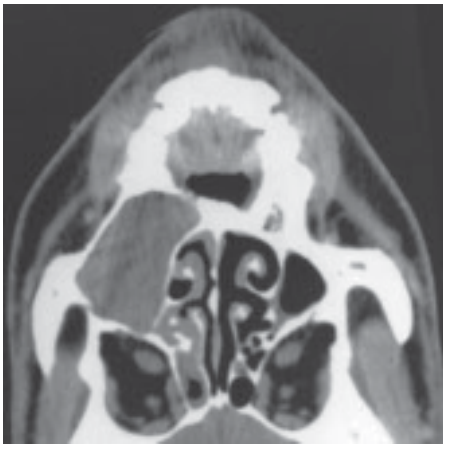

Fig. 19.12 CT of a well-demarcated Schwannoma of the maxilla.

Sites of involvement
The mandible and the sacrum are the most common sites of involvement with neurilemmoma. In the mandible, the lesion almost always involves the mental foramen. When neurilemmoma involves the spine or the sacrum, it is frequently difficult to know whether the tumour is truly of bony origin.

Clinical features / Imaging
Most neurilemmomas are asymptomatic, incidental findings on roentgenograms. Occasionally, they produce pain and/or swelling.

Macroscopy
Schwannomas of bone are extremely well circumscribed and may show a fibrous capsule. They are tan to white and glistening. Foci of yellow discolouration may be seen.

Histopathology
Schwannoma is composed of spindle cells with wavy appearing nuclei. The nuclei frequently are arranged in a palisading fashion. Areas of hypocellularity may alternate with areas of hypercellularity. Focally, the nuclei may be enlarged and pleomorphic appearing. Mitotic activity is rare. Schwannomas are always diffusely and strongly positive with S100 protein.

Prognostic factors
Schwannomas are benign lesions and complete, but conservative surgical removal leads to cure. There are no examples of malignant transformation of neurilemmomas in bone.

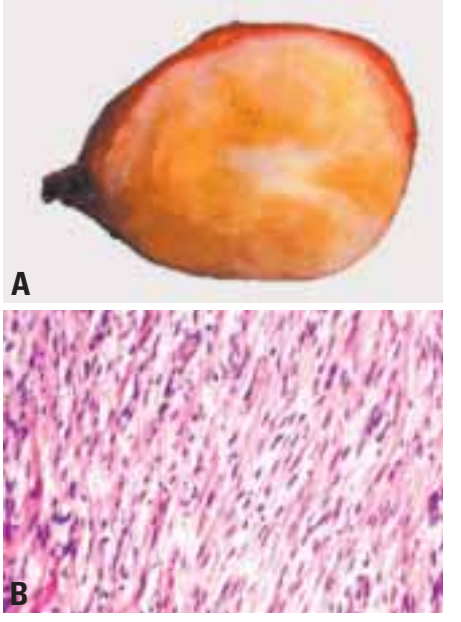

Fig. 19.13 **A** Encapsulated mandibular Schwannoma with tan and white areas. **B** Note the discrete tendency of spindle cell nuclei to palisade. The nuclei do not show cytological atypia.

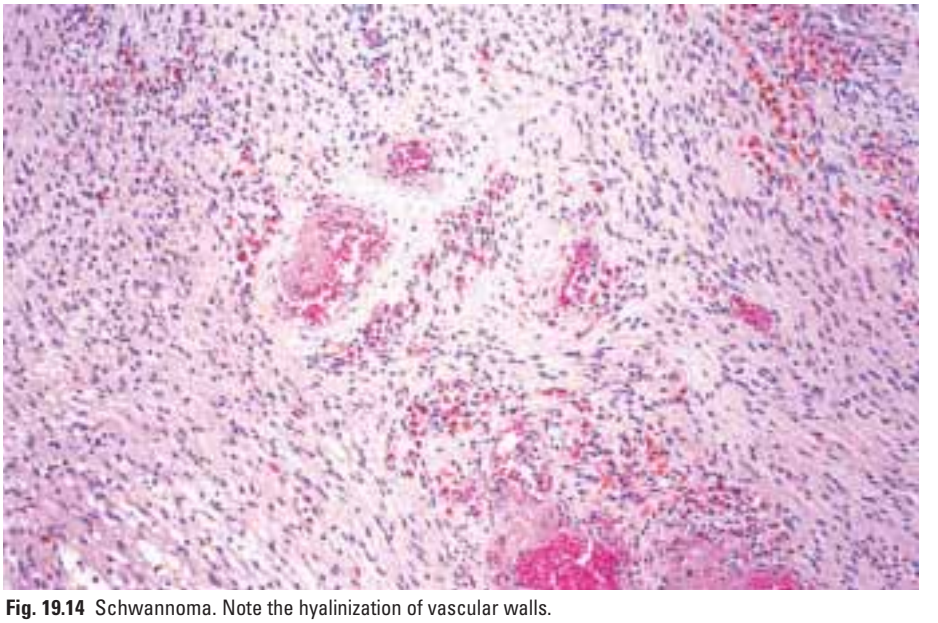

Fig. 19.14 Schwannoma. Note the hyalinization of vascular walls.

Adamantinoma

P.C.W. Hogendoorn
H. Hashimoto

Definition
A low grade, malignant biphasic tumour characterized by a variety of morphological patterns, most commonly epithelial cells, surrounded by a relatively bland spindle-cell osteo-fibrous component.

ICD-O code 9261/3

Synonyms
Adamantinoma of long bones, extragnathic adamantinoma, differentiated adamantinoma, juvenile intracortical adamantinoma.

Epidemiology
Adamantinoma comprises about 0.4% of all primary bone tumours {987,1503, 1518}. Patients present with this tumour from 3 up to 86 years, with a median age of 25-35 years. The youngest age group predominantly includes patients with osteofibrous dysplasia-like adamantinoma, but very young patients with classic adamantinoma (age 3) and older ones with the osteofibrous dysplasia-like subtype (age 38) have been reported {918, 1502,2069}. There is a slight predominance in males.

Sites of involvement
The tibia, in particular the anterior (meta-) diaphysis, is involved in 85-90% of cases. In up to 10% this is combined with one or more lesions in the ipsilateral fibula as well. Rare other sites have been reported, especially the ulna.

Clinical features / Imaging
The main complaint is swelling with or without pain. Adamantinoma often displays a protracted clinical behaviour. Clinical symptoms like swelling or radiographic abnormality may last for more than 30 years prior to diagnosis, whereas local recurrences or metastases may develop years after primary, intralesional or marginal surgical treatment. On X-ray, typically a well circumscribed, cortical, (multi-)lobulated osteolytic lesion with intralesional opacities, septation and peripheral sclerosis is seen {217,987}. Multifocality within the same bone is regularly observed. The lesion commonly seems to remain intracortical and extends longitudinally, but may also destroy the cortex and invade the medullary cavity or surrounding periosteum and soft tissue. This is usually accompanied by lamellar or solid periosteal reaction. Aggressive tumours occasionally present as single large lytic lesions. MRI is useful to document multicentricity, the extension of the lesion, and eventual soft tissue involvement.

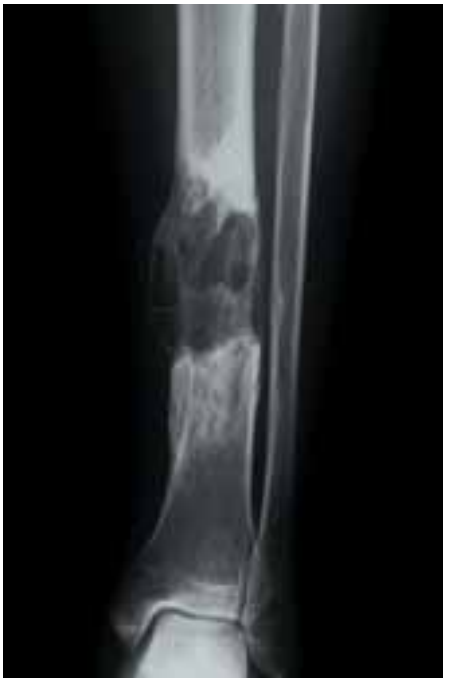

Fig. 19.15 Classic adamantinoma. The radiograph of the distal tibia shows an expansive, lobulated, lytic lesion with a defect of the outer surface of the cortex.

Fig. 19.16 Osteofibrous dysplasia-like adamantinoma. The lateral radiograph of the proximal aspect of the tibia shows a multilocular, lytic lesion with surrounding osteosclerosis of the anterior cortex.

Macroscopy
Classic adamantinoma usually presents as a cortical, well-demarcated, yellowish-grey, lobulated tumour of firm to bony consistency with peripheral sclerosis. It may be a single lesion, but its multifocal appearance with apparently normal cortical bone lying in between is occasionally striking. Small lesions remain intracortical, and are usually white and gritty. Larger tumours show intramedullary extension and cortical breakthrough with soft tissue invasion in a minority of cases. Macroscopically detectable cystic spaces are common, filled with straw-coloured or blood-like fluid.

Histopathology
Classic adamantinomas are characterized by an epithelial and an osteofibrous component, that may be intermingled with each other in various proportions and differentiation patterns. The four main differentiation patterns of classic adamantinoma are basaloid, tubular, spindle cell, and squamous {2235}. The first two patterns are encountered most commonly, but all patterns may be present in one lesion. The spindle cell component is more often observed in recurrences, lining cystic spaces, and in metastases. The osteofibrous compo-

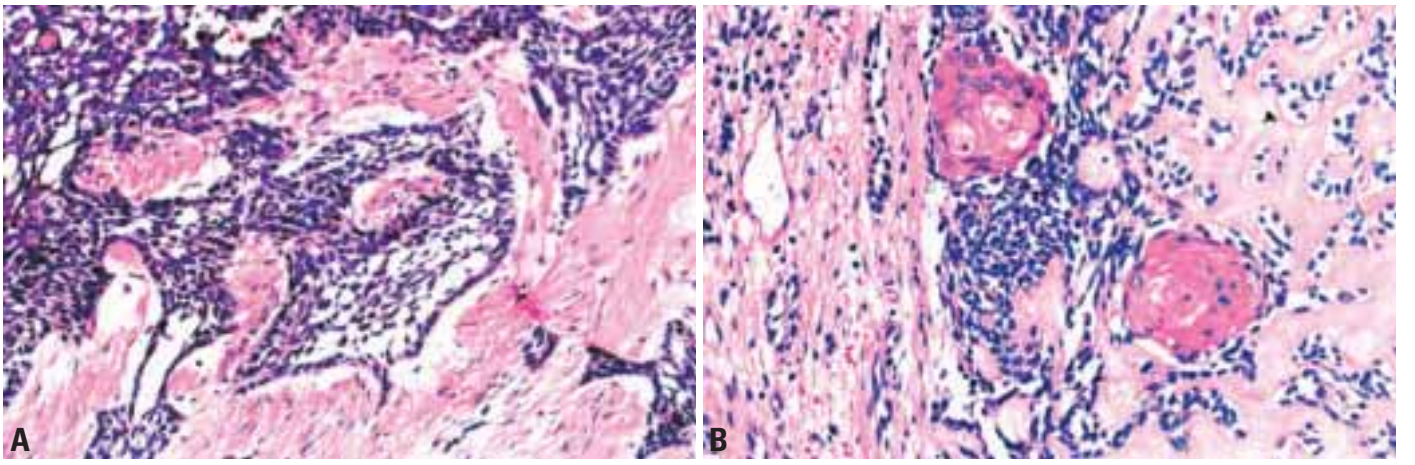

Fig. 19.17 Adamantinoma. **A** Basaloid pattern. Easily distuingishable epithelial fields without clear pallisading. **B** Squamoid pattern.

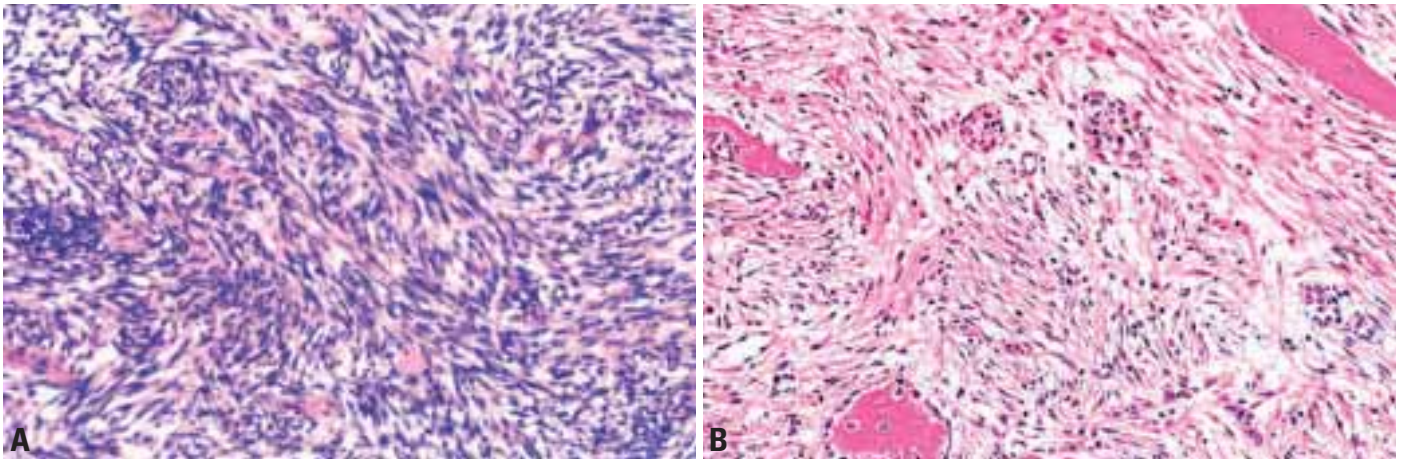

Fig. 19.18 Adamantinoma. **A** Spindle cell pattern. **B** Osteofibrous dysplasia like adamantinoma. Small epithelial clusters in a fibro-osseous stroma.

nent is composed of storiform oriented spindle cells. Woven bone trabeculae are usually present in or next to the centre of the lesion, prominently rimmed by osteoblasts, and with varying amounts of transformation to lamellar bone at the periphery of the tumour. Foam cells or myxoid change may be present, and mast cells or multinucleated giant cells are occasionally detected. Mitotic activity is usually low. A fifth histological pattern, the so-called osteofibrous dysplasia-like variant, is characterized by predominance of osteofibrous tissue, in which small groups of epithelial cells are only encountered by careful search or immunohistochemistry. The majority of classic and osteofibrous dysplasia-like adamantinomas display a "zonal" architecture. In classic adamantinoma, the centre is usually dominated by the epithelial component, and only few, small immature bone trabeculae are present in the fibrous tissue. Towards the periphery, the epithelial islands decrease to inconspicuous elements and the osteofibrous component gradually takes over with increasing amounts of woven bone trabeculae, transforming to lamellar bone. In osteofibrous dysplasia-like adamantinoma, the centre is occupied by fibrous tissue with scanty and thin immature woven bone trabeculae with epithelial elements. Small clusters of epithelial cells are the only feature which differentiate osteofibrous dysplasia-like adamantinoma from osteofibrous dysplasia.

Immunophenotype

The fibrous tissue is vimentin-positive. The epithelial cells show co-expression for keratin, EMA and vimentin. Chain-specific keratin expression {917,1050} revealed a predominantly basal epithelial cell differentiation, regardless of subtype, with widespread presence of basal epithelial cell keratins 5, 14, and 19. Also keratins 1, 13 and 17 are variably present. Keratins 8 and 18 are virtually absent. In classic adamantinomas, the epithelial component is surrounded by a continuous basement membrane, whereas less distinct epithelial islands show multiple interruptions or no surrounding basement membrane at all {919}. EGF/EGFR expression is restricted to the epithelial component. FGF2/FGFR1 is present in both components {242}.

Ultrastructure

Electron microscopic studies have confirmed the epithelial nature of adamantinoma, showing intracytoplasmic hemidesmosomes, tonofilaments, and microfilaments. Irrespective of histological subtype, the epithelial cells are bound by desmosomes and basement membranes have been found to surround the epithelial nests.

Genetics

Adamantinomas, classic as well as osteofibrous dysplasia-like, show recurrent numerical chromosomal abnormalities, mainly gain of chromosomes 7, 8, 12, and 19 {920,1058,1318,2004}. DNA flow cytometric and image cytometric studies showed that in aneuploid tumours, the aneuploid population was always restricted to the epithelial component {916}. *TP53* gene aberrations – as detected immunohistochemically or by loss of heterozygosity analysis - are restricted to the epithelial component of adamantinoma. There have been some cases reported with histological features of adamantinoma as well as Ewing sarcoma, sometimes called 'atypical' or 'Ewing-like' adamantinoma {741,1013, 1273,1400,1891,2178}. Cytogenetic ana-lysis combined with FISH and RT-PCR of two cases formerly described as atypical or Ewing-like adamantinoma revealed an (11;22) translocation, typical for Ewing sarcoma {257}. Because of these findings these tumours were labelled "adamantinoma-like Ewing sarcoma". The t(11;22) translocation is not present in adamantinoma {908,1318}.

Prognostic factors

Risk factors for recurrence are intralesional or marginal surgery and extracompartmental growth {918,1050,1084, 1739}. Recurrence percentages after non-radical surgery may rise up to 90% {918,1050,1084}. Recurrence is associated with an increase in epithelium-to-stroma ratio and more aggressive behaviour {918,1084,1503}. Besides, male sex {1050,1084}, females at young age {1503}, pain at presentation {1084}, short duration of symptoms {918,1084}, young age (<20 years) {918}, and lack of squamous differentiation of the tumour {918, 1084} have been associated with increased rates of recurrence or metastasis. Adamantinomas metastasise in 12-29% of patients with comparable mortality rates {918,1084,1503,1739}. Metastatic tumours are all classic adamantinomas, although rarely osteofibrous dysplasia-like adamantinomas may metastasise after recurrence and subsequent progression to classic adamantinoma {918}. The tumour spreads to regional lymph nodes and the lungs, and infrequently to skeleton, liver, and brain.

Metastases involving bone

N.A. Jambhekar
A. Borges

Definition

A tumour (usually malignant) involving bone, which has originated from another (distant) site.

Synonyms

Metastatic carcinoma, skeletal deposits, osseus metastasis, secondaries in bone, bony implants.

Epidemiology

The skeletal system is the third most common site to be involved by metastatic tumour after the lungs and liver {174}. Metastatic carcinomas are the most common malignant tumour affecting the skeleton {2154}. Over two-thirds of patients with bone metastasis are between 40-60 years of age {504}. Most metastases originate from common cancers namely breast, lung, prostate, kidney and thyroid gland which account for 93% of all deposits {504}. A complete radiographic and clinical search will identify the primary site in up to 85% of cases {1812}.

Although metastases are rare in children, when they occur, they most often include neuroblastoma, rhabdomyosarcoma and clear cell sarcoma of kidney.

Sites of Involvement

Metastatic carcinomas involve bones with persistent red marrow such as vertebra, proximal femur ribs, sternum, pelvis, skull and shoulder girdle. Out of 114 histologically evaluated lesions 44.3% involved axial skeleton, 28.8% the appendicular skeleton and 26.9% involved multiple bones {504}. The lumbar spine {757,1872} and proximal femur {757} are favoured sites. Bones of the hands and feet are rarely involved {923, 1252,1433,1507,1925}.

Clinical features

Pain, swelling, fracture and neurological symptoms (spine) are common {278}. Skull base metastasis may cause Collet-Sicard syndrome {1865}; hypercalcaemia may accompany osteolysis {1520}.

Plain radiographs reveal lytic, blastic or

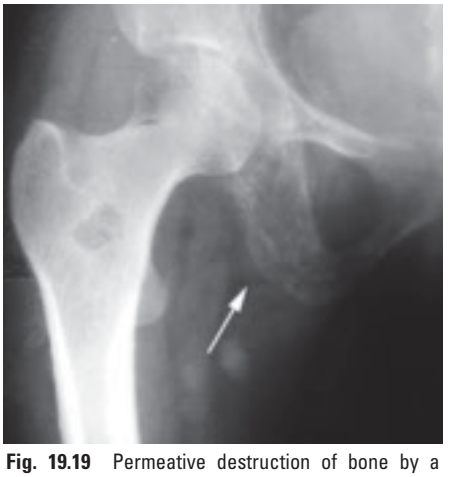

Fig. 19.19 Permeative destruction of bone by a metastasis (primary tumour unknown).

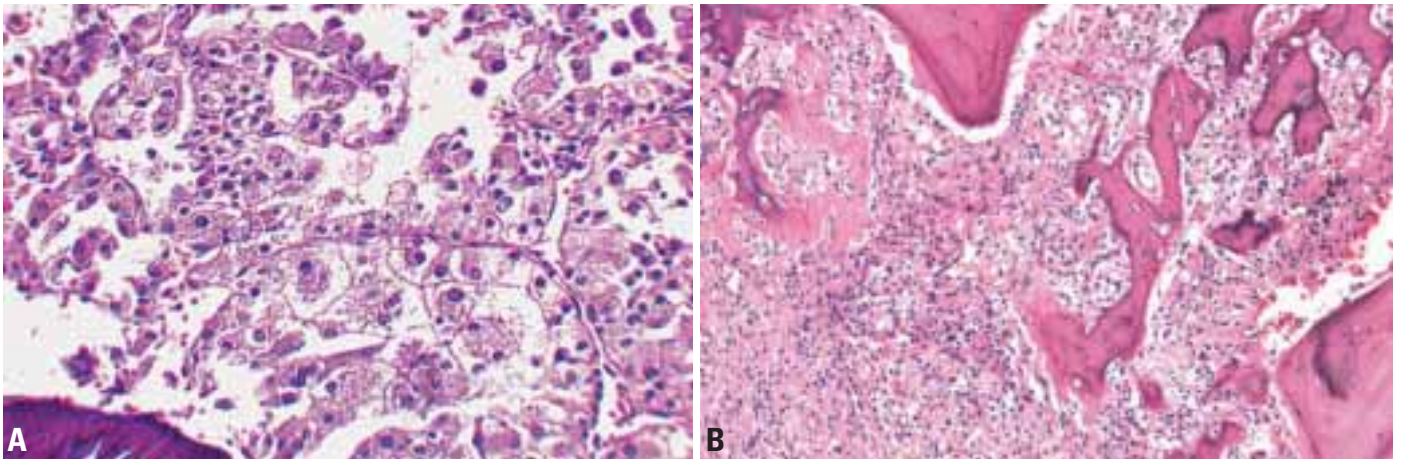

Fig. 19.20 **A** Metastatic renal cell carcinoma showing an alveolar and nesting pattern. **B** Metastatic prostate carcinoma; note monotonous small cells and irregular osteoid deposition.

mixed patterns {756}. Lung and breast deposits cause irregular lytic destruction, but are occasionally osteoblastic {1460, 1514}. Thyroid and kidney deposits are purely lytic; prostatic deposits are osteoblastic. Solitary metastasis {2120}, or an irregular periosteal reaction {1238, 1581} may simulate a primary bone sarcoma.

Plain radiographs are unreliable to detect vertebral deposits {707,1872} and despite gross evidence of spinal deposits in 36% of 832 autopsied patients dying of cancer, 26% had negative plain X-rays {1872}.

Bone scintigraphy is a sensitive method for the detection of skeletal metastases, because it covers the whole skeleton, making it valuable for identifying the extent of the disease. CT scan is useful for guiding needle biopsies. MRI has also been used in some cases to detect and delineate metastases.

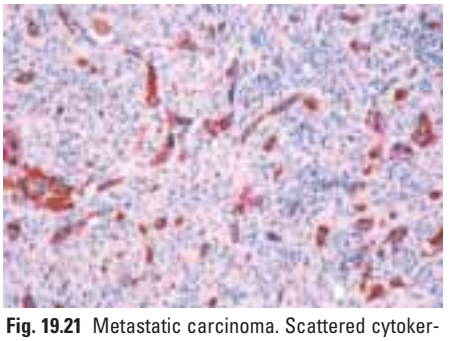

Fig. 19.21 Metastatic carcinoma. Scattered cytokeratin-positive tumour cells confirm the epithelial character of the lesion.

Aetiology

The location of the primary tumour and the local pattern of blood flow determine involvement of skeletal sites. The vertebral venous plexus (Batson's plexus) is a high volume, low pressure, valveless venous system independent of the pulmonary, portal and caval systems; it communicates directly with veins of the pelvis, proximal half of lower extremity, proximal half of upper extremity and head and neck {140}. Any increase in intrabdominal or intrathoracic pressure during exhalation or straining causes a backflow into the vertebral plexus bypassing the heart and lungs. This explains the preferential involvement of the vertebral and the proximal appendicular bones, and the occassional occurrence of extensive skeletal deposits despite lack of visceral involvement {1470}.

Macroscopy

The macroscopic appearance of skeletal metastasis varies depending upon the amount of bone produced in response to the tumour. Thus, osteoblastic metastases from the breast are greyish white firm, whereas renal cell carcinoma produces soft haemorrhagic deposits.

Morphology

Metastatic tumours attempt to recapitulate the original tumour. Squamous carcinomas from most sites look alike, however, many adenocarcinomas such as renal cell, prostate and thyroid retain morphological similarities to the primary tumour. An accompanying fibroblastic, vascular, osteoblastic and osteoclastic response may be present. Sarcomatoid (spindle cell) carcinomas originating in the kidney or the lung may simulate a primary bone sarcoma.

Immunophenotype

Immunohistochemistry is useful when the diagnosis of metastatic carcinoma is straightforward but not distinctive enough to identify the primary site, or, when the differential is broad and includes sarcoma, carcinoma and melanoma {514}.

Prognostic factors

Bone metastasis usually heralds incurability and treatment is palliative. The outcome depends upon the primary site and the extent of disease.