Osteomyelitis

72

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72.1 Definition

- Inflammation of bone and bone marrow, usually secondary to an infectious agent.

72.2 Synonyms

- Pyogenic bone infection.
- Brodie's abscess.

72.3 Etiology

- Though inflammation of any bodily site can be secondary to physical or chemical trauma, most cases of osteomyelitis are secondary to an infectious agent. The most common infectious agents are bacterial, but mycobacteria, fungi, and even viruses have been implicated.
- The establishment of an infection in the bone requires not only an infectious agent but also a route for this agent to enter the bone. Because the bones are isolated from the external environment, infectious agents must be directly introduced into the bone, such as by direct open trauma or from overlying infections of soft tissues that extend into the underlying bone, or from an infection elsewhere in the body that gains hematogenous access to the bone.

72.4 Epidemiology

- There is no preferred gender, race, or ethnic group.
- No particular age group is more susceptible, but the site of involvement and the type of infectious agent are often age-related.
- Patients with diseases affecting the microcirculation or immune system are more prone to develop osteomyelitis. These include patients with diabetes mellitus, chronic renal failure, or sickle cell disease, as well as patients on steroid therapy and the elderly.
- Intravenous drug users are more prone to develop osteomyelitis because of exposure to contaminated needles.

72.5 Sites of Involvement

- In very young children, the mode of infection is usually hematogenous, and because of the vascular supply of the bone, the metaphysis is affected. In addition, the vascular anatomy prior to the development of secondary ossification centers is often associated with spread to the bone ends with accompanying joint infections.
- In children with secondary ossification centers and in adolescents, hematogenous infections usually begin in the metaphysis, probably because the metaphyseal arteries end in arteriovenous loops with momentary stagnation of blood flow near the growth plate.
- In adults with hematogenous osteomyelitis, the infection may gain ingress at the metaphysis, diaphysis, or epiphysis. Infections near the bone end often spread to involve adjacent joints.
- Trauma, especially contaminated open fractures, may happen at any age, allowing direct access to osseous structures for external bacteria or fungi.
- Superinfection of skin ulcers associated with peripheral vascular disease is a common source of osteomyelitis in the elderly and in diabetic patients.
- Children have a higher incidence of infection in the long bones; adults have a higher incidence of involvement of the axial skeleton, particularly the vertebrae.
- Certain patient populations are affected by particular infectious agents. The most common organism to infect bones hematogenously is *Staphylococcus aureus*. In adult intravenous drug users, *Pseudomonas* species are

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particularly common. *Salmonella* species have a predilection for patients with sickle cell disease.

72.6 Clinical Symptoms and Signs

- Pain, erythema, swelling, warmth, and loss of function in the area affected.
- Fever, chills, malaise, and nausea.
- Draining exudate through the skin.

72.7 Imaging Features

72.7.1 Radiographic Features

- There is usually a lag time of 1–2 weeks between the development of symptoms and the presence of radiographic findings, because the secondary effects of infection in bone develop over time. If there is significant soft-tissue edema, there may be a loss of intermuscular fat planes (Fig. 72.1a).
- Later in the course of disease, there is usually radiolucency associated with bone resorption. This may take the form of localized radiolucency, generalized radiolucency, or sometimes a focal radiolucency associated with the formation of a sinus tract (Fig. 72.1b).
- Osteosclerosis may be seen, especially if an infection becomes chronic. This may be within the bone, or it may be a result of periosteal new bone formation.
- Periarticular osteoporosis secondary to disuse or inflammation is unusual because the joints are not symptomatic when the disease is quiescent.
- The joint space is usually preserved; narrowing is unusual until very late in the disease.

72.7.2 Bone Scan

- There is usually increased uptake at the periphery of the affected area, even when nothing is visible on conventional radiography.
- Specificity is low and anatomic localization is suboptimal, but if the scan is negative, infection is almost certainly not present.

72.7.3 CT Features

- Because CT is more sensitive than conventional radiographs, subtle early bone resorption, dead bone fragments, and sinus tracts are more evident than in routine radiography.
- CT detects cortical destruction better than other imaging modalities.
- CT detects fluid earlier than conventional radiography.

72.7.4 MRI Features

- MRI is the procedure of choice after a baseline radiograph, because of early detectional abilities, contrast, and demonstration of anatomy (Fig. 72.1a).
- MRI is very sensitive to fluid and demonstrates abnormal areas, but if increased tissue blood flow persists after treatment, it may give a false impression of treatment failure. If fluid persists, MRI also may be insensitive in detecting recurrence of infection.

72.8 Imaging Differential Diagnosis

72.8.1 Fractures

- Undisplaced (greenstick) fractures may have similar localizing symptoms.
- Fracture line is best demonstrated as a cortical break with edema on MRI.
- A fracture line not visible on initial radiographs may become visible on subsequent radiographs.

72.8.2 Tumors

- Tumors may produce metaphyseal destruction and periosteal reactions, but the periosteal reactions tend to be continuous or solid in infections but discontinuous in tumors.
- MRI demonstrates a soft-tissue mass when tumors are present.
- Soft-tissue masses may contain mineralized matrix if the tumor is an osteosarcoma.
- Bone abscesses (Fig. 72.2) can be distinguished from osteoid osteoma because the center of osteoid osteoma (especially if it is poorly mineralized) gives an increased signal on MRI in fluid-sensitive sequences, whereas necrotic bone in an abscess gives a low signal and may demonstrate associated sinus tracts (Fig. 72.3). A CT scan may also show mineral within an osteoid osteoma and perilesional sclerosis.
- Rarely, tuberculosis of the bone may masquerade as a tumorous process. If a patient is skeletally mature and the process affects the bone end, the radiographic appearance may mimic a primary giant cell tumor of the bone.

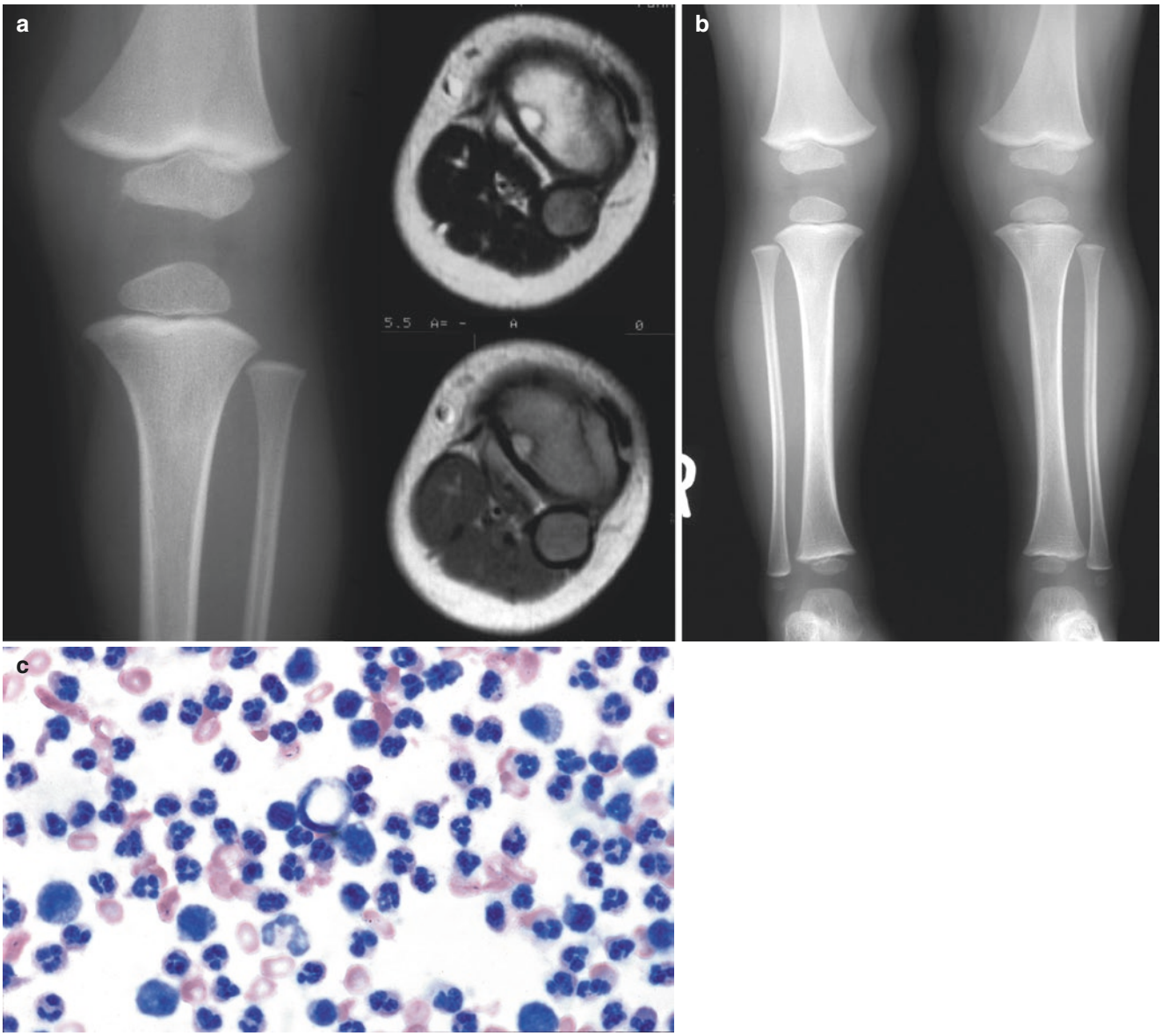


Fig. 72.1 (**a**) Acute osteomyelitis. In the earliest phase, there is no change in the bone (*left*); the MRI panels demonstrating fluid in the marrow (*right*) demonstrate a circumscribed lesion in the posteromedial tibia. (**b**) Ten days later, there is enough osseous resorption in the proximal tibia to have produced an osseous defect in the left tibial metaphysis. (**c**) Almost all the cells are neutrophils in fluid from the defect in the metaphysis

72.8.3 Langerhans Cell Histiocytosis

- Distinction from infection is difficult radiographically; many of the findings are similar, but there is usually no sinus tract in Langerhans cell histiocytosis.
- Periosteal reactions tend to be lamellated, but the layers are usually continuous.
- Radiographs tend to demonstrate that radiolucent lesions, though well circumscribed, have an edge of gradually decreasing radiolucency as the periphery is approached ("beveled edge").

72.9 Pathology

72.9.1 Pathophysiology

- An infection in the bone causes pathological changes that differ markedly from those in viscera or in soft tissues because of the combination of skeletal rigidity and vascularity. The marrow compartment receives its vascular supply from nutrient vessels derived either from periarticular arteries supplying the bone ends, metaphyseal nutrient arteries, or diaphyseal nutrient arteries. The compact bone

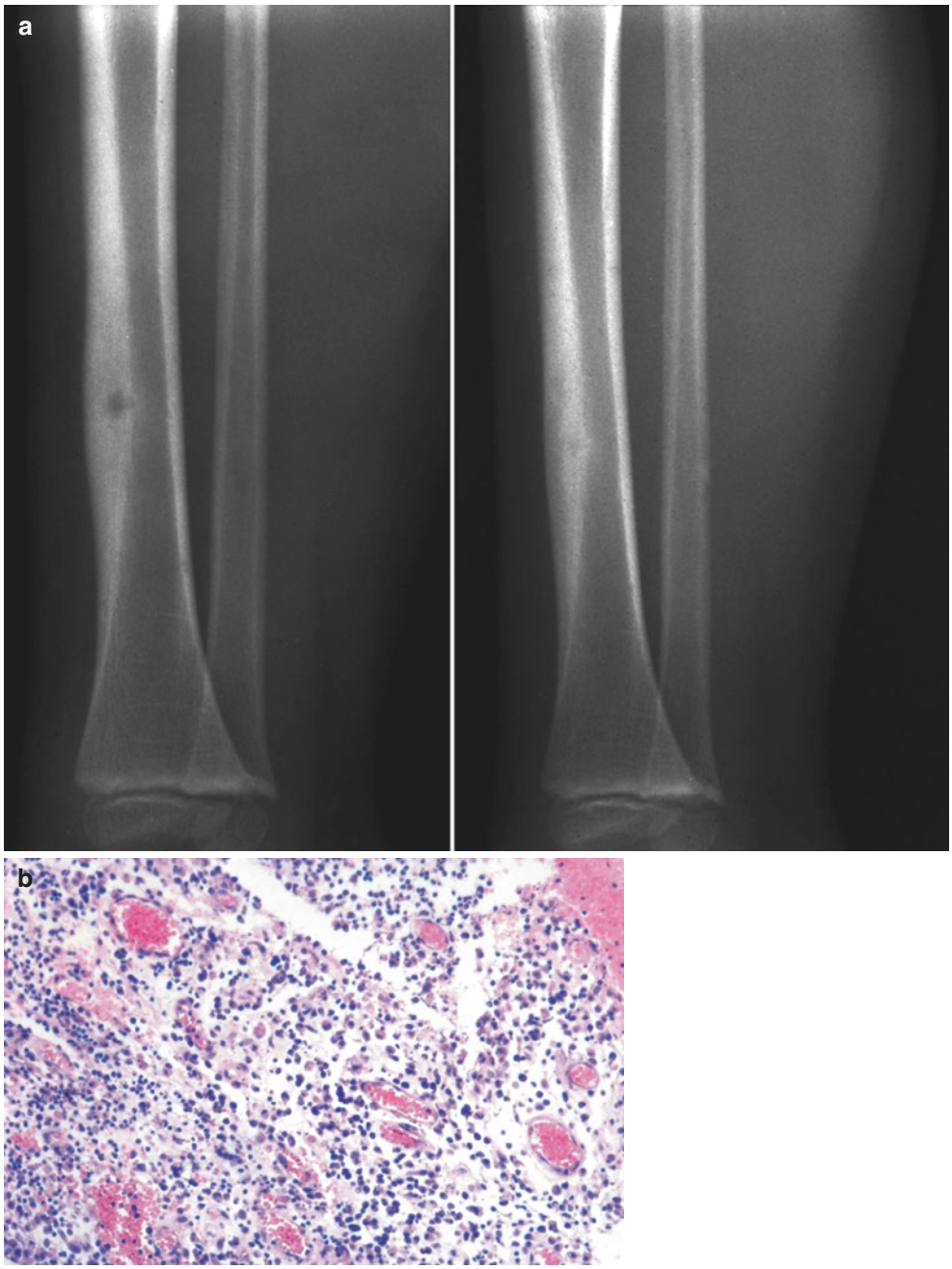


Fig. 72.2 (**a**) Subacute osteomyelitis. The so-called Brodie's abscess here in the cortex of the tibia is well circumscribed and lucent and has stimulated an organized sclerotic periosteal cortical reaction. The clinical picture mimics osteoid osteoma. (**b**) The content of the bone abscess may be inflammatory or even fibrous. In this case, the main constituent was neutrophil, which helps in the pathologic differentiation (200×)

is supplied by segmental periosteal perforating vessels that supply the outer third of the cortex and anastomose with side branches of penetrating nutrient arteries supplying the middle two thirds of the cortex and branches derived from the medullary nutrient vessels supplying the medullary cavity.

- A bone infection causes increased pressure in an essentially rigid medullary compartment. Because there is limited space to house the purulent exudate, it compresses nonrigid structures, including the vasculature of the infected segment. If the vasculature is end-arterial (such as that in the medullary cavity), the result is medullary septic infarction of the bone.
- The cortex, having duality of circulation, is spared from necrosis unless its blood supply is also interrupted; if the exudate is under enough pressure, it is forced out of the marrow compartment, dissecting away the periosteum and compressing perforating vessels. This combination of circumstances may cause devitalization of the compact bone, resulting in the formation of a sequestrum.

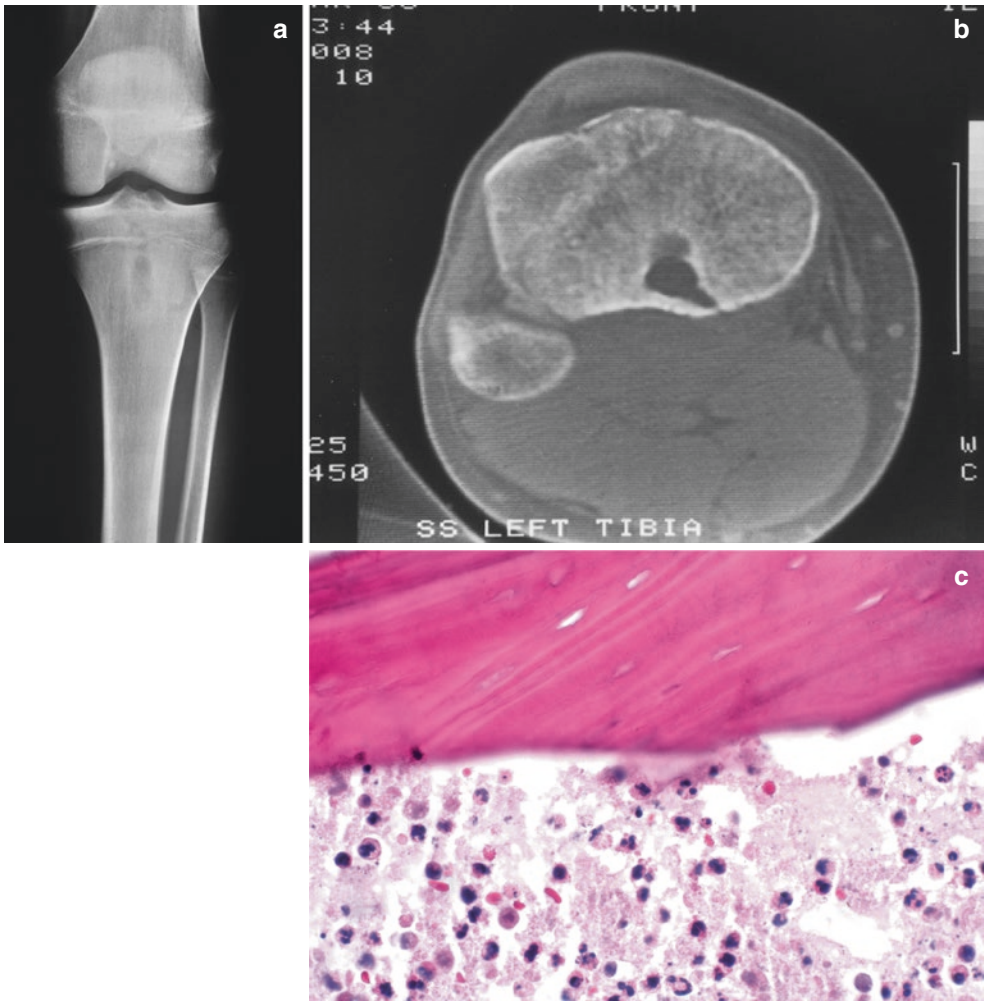


Fig. 72.3 (**a**) On radiography, this bone abscess was thought to be infected because it was too large and ovoid to be an osteoid osteoma, and it crossed the closing growth plate to involve the epiphysis. (**b**) The CT scan helped in differentiating this lesion from infection because it plainly demonstrated that the lesional contents have a sinus track that extends to the posterior cortex. (**c**) The lesion was explored, and the histology demonstrates acute inflammatory infiltrate associated with sequestered (dead) mature bone

- If regions of a bone have separate compartments and separate blood supplies (such as an actively growing epiphyseal plate separating epiphysis and metaphysis), it is usual for the infection to remain unicompartmental.
- When exudate collects in the subperiosteal space, not only may the underlying cortex become devitalized, but the periosteum may then form a reactive shell of new bone on the outside of the devitalized cortex, or involucrum; continuing accumulations of exudate may cause enough pressure to dissect the periosteum from the involucrum, causing sequestration of the involucrum and additional involucrum.
- The exudate may also dissect entirely through the periosteum, into the soft tissue, and even out through the overlying skin. Such a draining sinus is termed a *cloaca*. Although the sinus tract comes to be lined by granulation tissue, the overlying skin may proliferate and epithelialize the sinus tract, creating a chronic, nonhealing, draining sinus.

72.9.2 Gross Features

- The gross features depend upon the stage of the disease. In general, pathological specimens are seen late in the course of the process, when osseous changes are developed and are not reversible. In the early stages, pus is produced, which may be cultured, but usually it does not come to the dissecting bench.
- Osseous specimens coming to the laboratory that are large enough to have anatomical landmarks demonstrate the interaction of bone with infectious agents. The affected marrow, which should be yellow in appendicular areas and red in axial hematopoietic areas, is often gray from an admixture of fibrous tissue and inflammatory infiltrates. Active areas may show encystification and contain pus.
- Dead bone, or sequestrum, is usually dull rather than shiny when compared with adjacent normal bone. Larger segments of this type of dead bone are often found in the cortex of bones with long-standing chronic disease.

- New reactive bone, or involucrum, is identified grossly as bone that is deposited on the outside of the old cortex. It may be compact, but it often has a more porous character than the underlying cortex. Involucrum that is deposited on the surfaces of bone trabeculae is better identified histologically. The reactive bone may be so exuberant as to effectively form a neocortex and may even noticeably increase the diameter of the bone.
- Sinus tracts, marking the sites of egress of suppurative inflammation, may be observed tracking through the cortex and may even extend to the overlying skin (cloacae).

72.9.3 Histological Features

- The histologic changes are consonant with the stage and type of infection.
  - In the early phases, a bacterial infection results in an acute inflammatory reaction in which the predominant inflammatory cells are neutrophils; the resulting fluid accumulation increases osseous pressure (Fig 72.1c).
  - If intraosseous pressure is increased sufficiently, the medullary circulation is compromised, resulting in the sequestration of some or all of the cancellous bone and marrow necrosis. Histologically, this corresponds to bone devoid of osteocytes and empty osteocyte lacunae. Prior to these histologic changes, the bone marrow will demonstrate fat necrosis and will be devoid of normal marrow.
  - Microbiological cultures are much more sensitive to the presence of bacteria than tissue samples. Gram staining of infected tissues seldom demonstrates organisms if they are not visible in hematoxylin–eosin-stained sections (Fig. 72.4). This is especially true for mycobacterial forms of bone infection (Fig. 72.5).
  - Some types of chronic osteomyelitis are associated with dense sclerosis, bone remodeling, inflammatory infiltrates composed primarily of plasma cells and lymphocytes and seldom demonstrate positivity of microbiological cultures (Fig. 72.6).
  - Osteoclastic resorption, activated by various cytokines, results in resorption of necrotic trabeculae bordering those areas where the circulation remains intact. In addition, if the circulation has been compromised by an increase in pressure that keeps the vascular structures intact, release of that pressure will permit ingress of other cellular elements into the necrotic areas. This can result in appositional osteoblastic activity on the surfaces of dead bone trabeculae (Fig. 72.7).
  - As the infection becomes more chronic, lymphocytes, plasma cells, and fibrosis predominate, but there may still be foci of neutrophilic aggregates (chronic active osteomyelitis) (Fig. 72.8).
  - Later in the course of infection, necrotic bone and fibrous tissue predominate. The amount and type of inflammatory cells vary with the type and number of organisms and whether inflammatory cells can still reach the site.
- Findings in a small biopsy will vary significantly with the area sampled.

72.9.4 Pathologic Differential Diagnosis

- *Osteonecrosis*: Devitalized bone looks the same histologically regardless of its cause. Avascular necrosis of the type that affects the convex surfaces of large joints produces bone trabeculae devoid of osteocytes and acellular marrow. In addition, the healing process, which revascularizes bone at the periphery of a focus of avascular necrosis, is associated with marrow fibrosis and appositional new bone on dead bone trabeculae ("creeping substitution"). These are all findings that can be seen in osteomyelitis. Fortunately, the clinical spectrum and gross findings are usually more than adequate to differentiate these findings from infection. Infections involving the articular ends of bones present as acute events and are associated with septic arthritis. They are not limited to a confined, often triangular segment of subarticular bone, and the overlying articular cartilage—which remains viable and intact in avascular necrosis—is destroyed very early in joint infections.
- *Fracture*: By far the most common reason for osteonecrosis is devitalization of bone at a fracture site. In most cases, the presence of a fracture will be known prior to obtaining tissue, and tissues are usually obtained only in cases of open fracture or pathologic fracture, to rule out a neoplastic process. As with infection, the histological features of fracture vary with the time of sampling and the focus sampled. It is usually during the early phases of fracture that the histological features alone may be mistaken for infection. This happens particularly during the types of microfracture that occur in the subarticular areas of hip and knee joints associated with osteoarthritis. Because inflammation is one of the earliest tissue responses to injury, collections of neutrophils are often associated with acute microfractures, and these sterile microabscesses may be mistaken for infection. It is very important not to make this mistake, because the total joint arthroplasties that yield these specimens are contraindicated in infections.

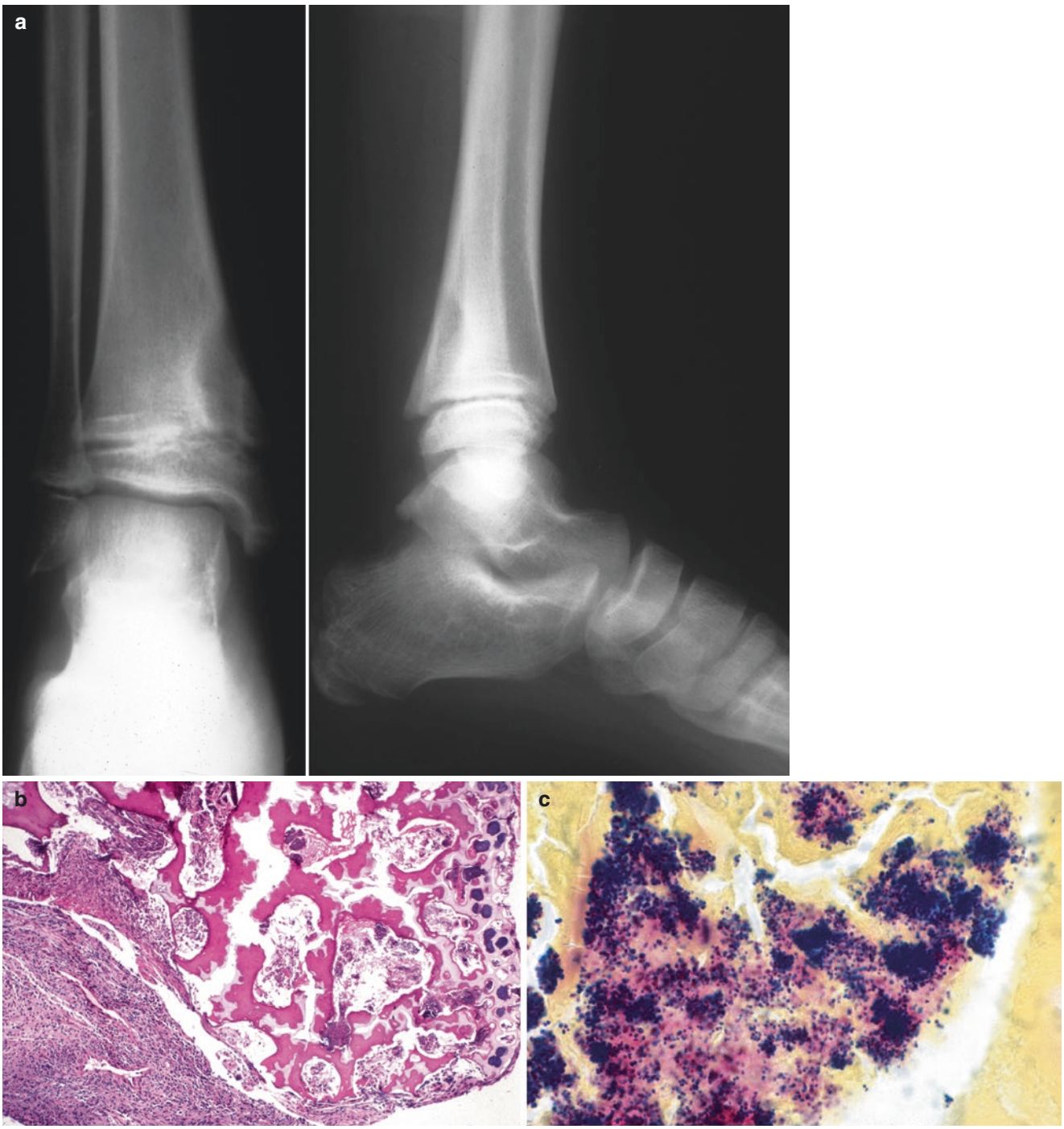


Fig. 72.4 (**a**) Bone abscess in the metaphysis of a 9-year-old boy. The AP and lateral radiographs demonstrate an eccentric radiolucency that was confused with a tumor radiographically, but this patient presented clinically with fever, redness, swelling, and local tenderness. (**b**) A decompression osteotomy was performed along with drainage of the defect, demonstrating dense, acute inflammation (*lower left*) and primary spongiosa (mixed cartilage and bone spicules, *upper right*). The basophilic clumps represent thrombi of the metaphyseal arteriovenous arcades filled with coagulase-positive *Staphylococcus aureus* bacteria (50×). (**c**) Clumps of gram-positive cocci from the primary spongiosa are clearly shown with a gram stain (500×). This degree of bacteria is a very rare histologic finding

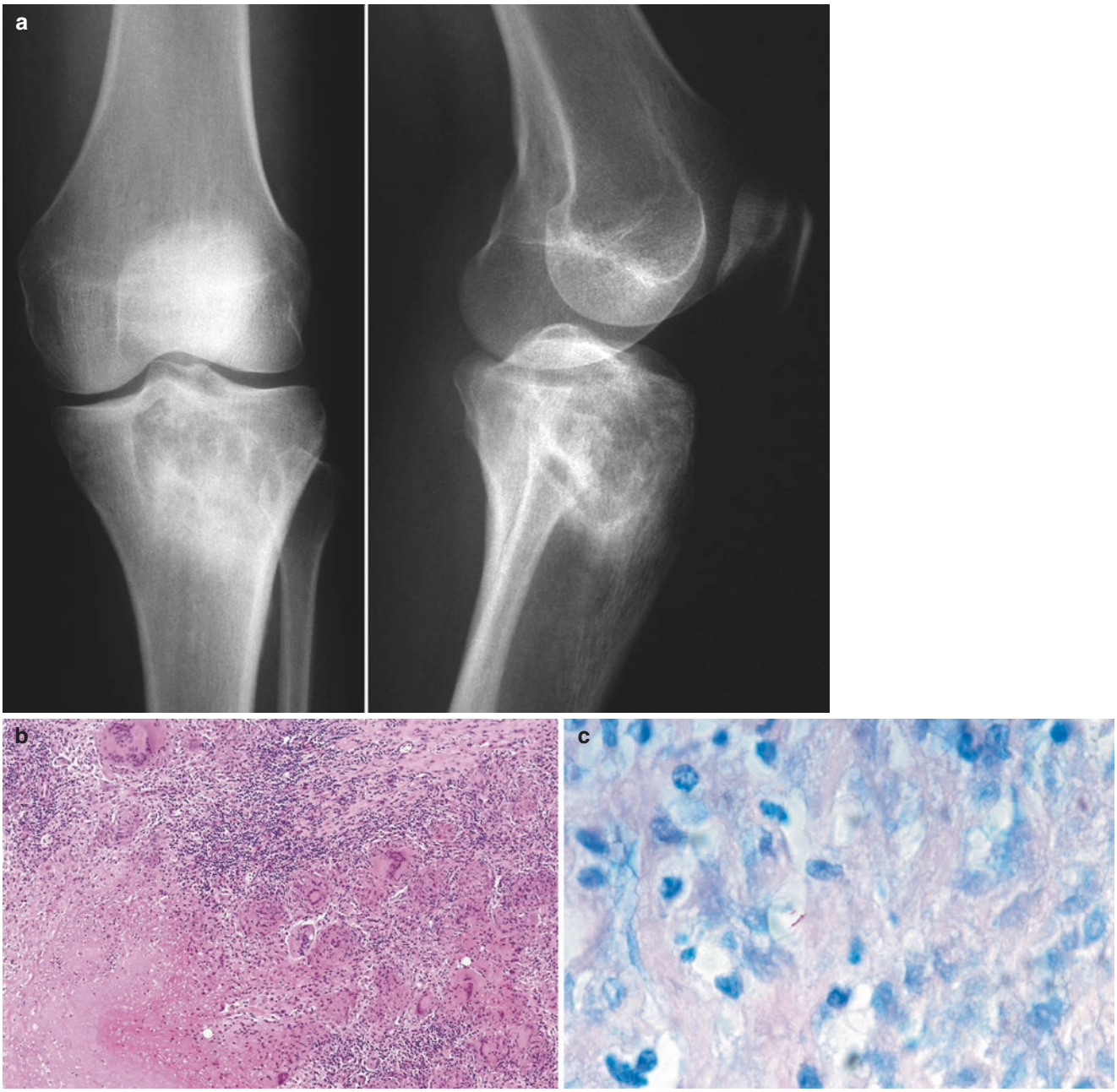


Fig. 72.5 (**a**) This 28-year-old woman complained of arthritis-like joint pain, local tenderness, and decreased range of motion of her knee for several months. A well-circumscribed, destructive lesion of her upper tibia without a periosteal reaction extending to the knee joint was thought likely to represent giant-cell tumor of bone. (**b**) The biopsy demonstrated necrotizing granulomatous inflammation in a lymphocytic background (200×). (**c**) Stain for acid-fast bacilli demonstrated rare beaded acid-fast bacilli (787×), and cultures were positive for *Mycobacterium tuberculosis*. No abnormalities were discerned on chest radiographs

72.10 Prognosis

- Early stages of the disease are more curable than late stages.
- The prognosis of osseous infections depends upon the type of organism, the site of infection, host factors, and the chronicity of the process.
- Before the development of surgical techniques such as limb lengthening procedures and vascular free flaps (largely invented for limb salvage in orthopedic oncologic procedures), at least 30% of cases of osteomyelitis were considered incurable.
- For all cases, the cure rate is now considered above 90%.

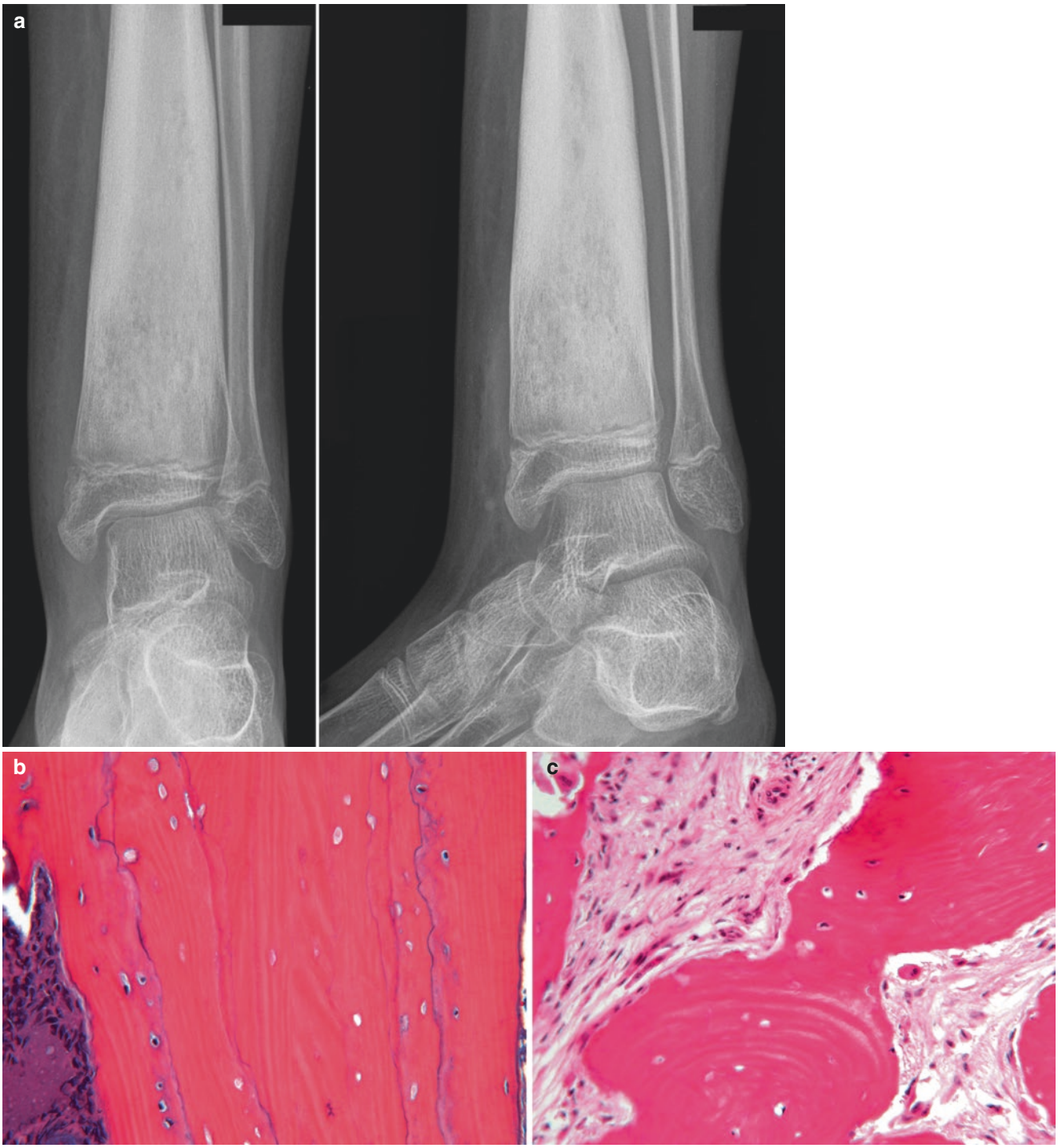


Fig. 72.6 (**a**) This 12-year-old girl had been experiencing lower leg pain for months with occasional episodes of low-grade fever. Her distal leg was tender and had soft-tissue swelling. The radiographs demonstrated diffuse distal sclerosis of the tibia, containing a few irregular radiolucencies. There was a modeling deformity of the distal tibia, with a loss of normal taper and increased anteroposterior diameter and organized periosteal new bone formation. (**b**) A biopsy including tibial cortex demonstrated waves of thickening and remodeling of the compact bone marked by long cement lines separating layers of the lamellar bone. The innermost and outermost lamellae are viable, but the inner layers are necrotic and represent sequestrum ("creeping substitution"). (**c**) Portions of the cancellous bone in the biopsy specimen demonstrate thicker-than-normal osseous trabeculae, which are partially viable and which show evidence of active osteoclast resorption (*upper left*) and old inactive resorption (*middle left*). The intertrabecular spaces are actively replaced by neovascularized fibrous tissue and contain scattered inflammatory cells. The cultures were repeatedly negative

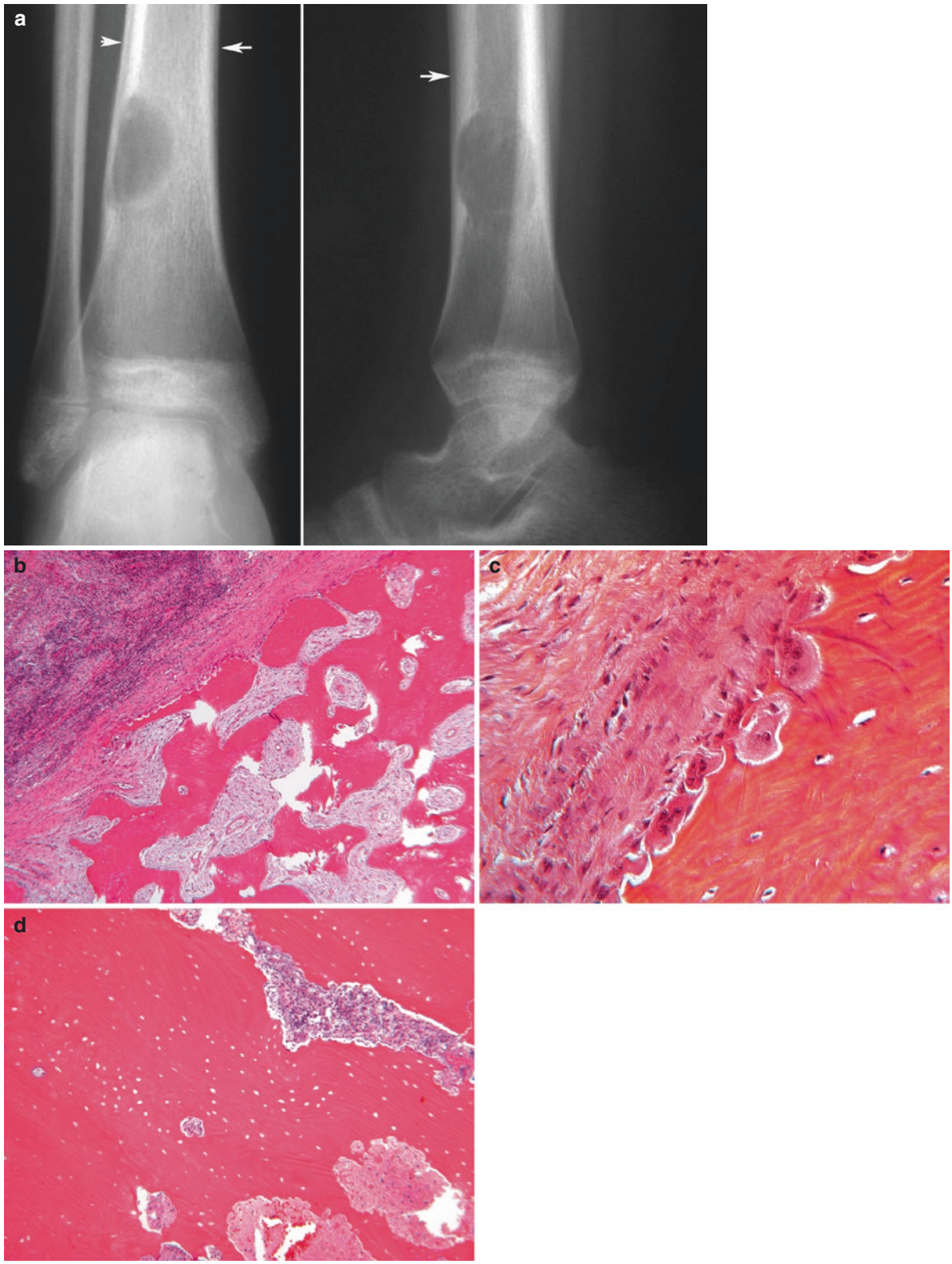
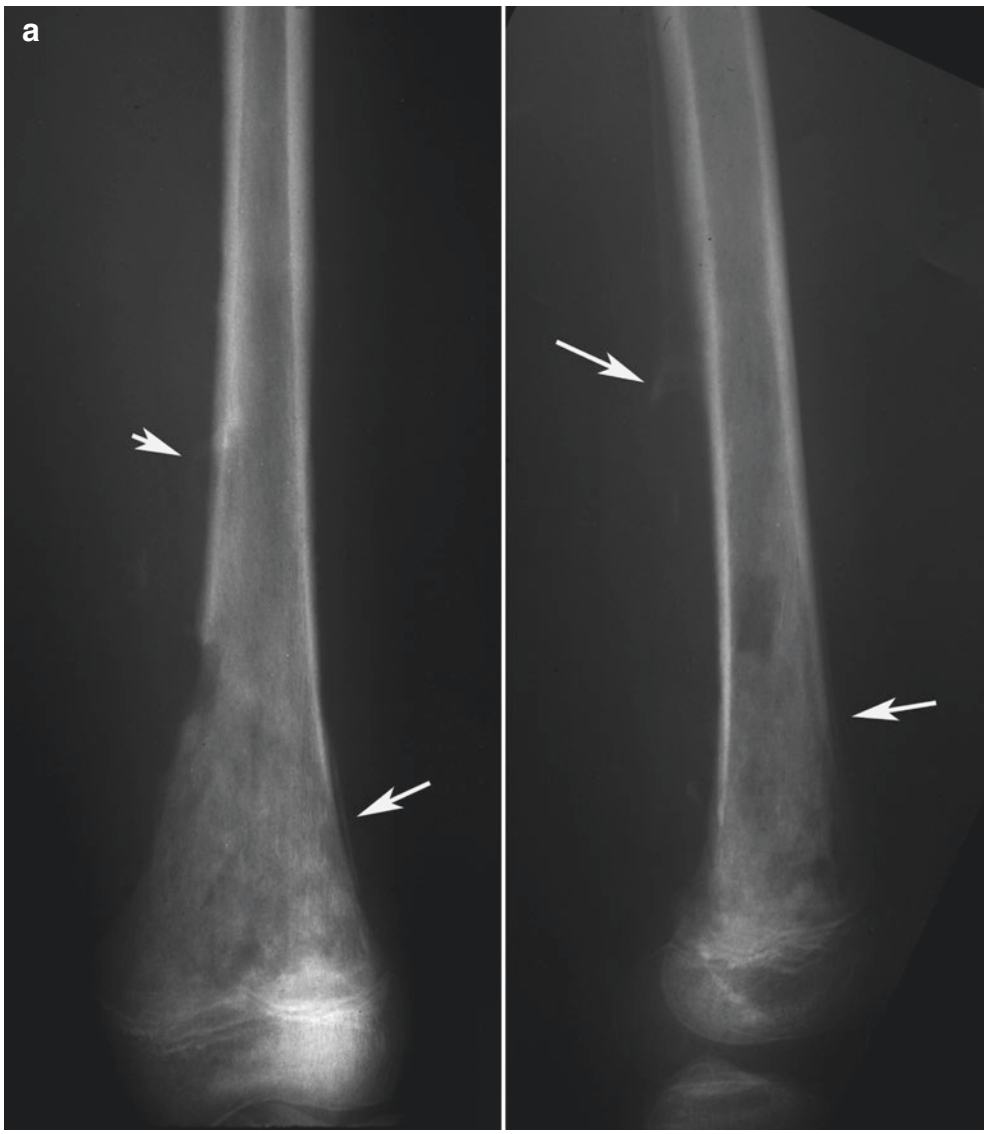


Fig. 72.7 Organized chronic osteomyelitis and abscess formation of the lower tibia, thought to be Langerhans cell histiocytosis clinically. (**a**) The AP and lateral radiographs demonstrate a radiolucent, very well-circumscribed lesion of the tibial diametaphysis predominantly in the medullary cavity but also causing scalloping of the cortex. The mass had no sclerotic border, but its edge was described as "beveled" by the radiologist. There is a long periosteal new bone reaction (*arrows*) that is multilayered but continuous, as would be associated with a benign process. (**b**) Interface of lucent lesion (*upper left*) and adjacent bone (*middle* and *lower right*) shows a dense, vascularized polymorphous inflammatory infiltrate at *upper left*, compact bone at *lower right* with inflammatory fibrous tissues in the expanded Haversian systems, and osteoclastic resorption of the inner cortex at the interface of bone and inflammatory infiltrate (100×). (**c**) The interface resorption at higher power (400×). (**d**) Other areas of the cortex are devitalized, and their vascular canals show scalloped resorptive edges and contain residual purulent exudate (200×)



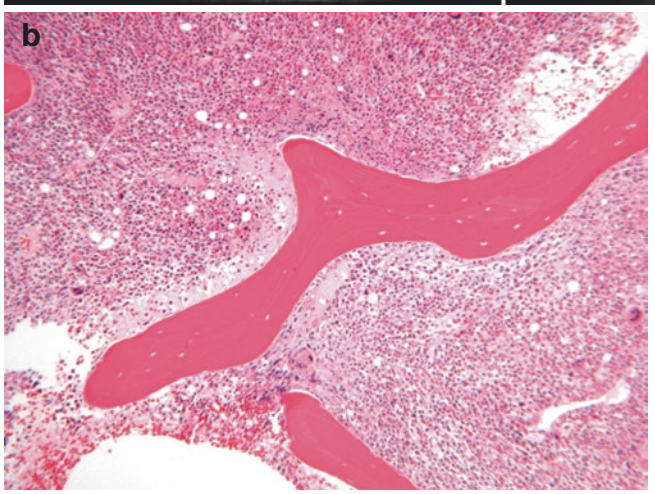


Fig. 72.8 (**a**) Chronic active osteomyelitis in the distal femur of an 11-year-old girl. The radiographs demonstrate permeative destruction with mottling of the bone and no delimitation of the process. There is a diffuse periosteal reaction (*arrows*), which is at least partially interrupted, forming a classic Codman triangle in the lateral view. This appearance is characteristic for highly malignant, fast-growing tumors without matrix, especially Ewing's sarcoma. The rectangular radiolucency seen in both views represents the site of biopsy and is not part of the process. (**b**) Endosteal tissue from the biopsy (250×) demonstrates osteonecrosis (microsequestration) of the large central bone trabecula and an acute inflammatory infiltrate in the hematopoietic marrow, which obliterates most of the marrow fat but does not entirely displace the marrow. (Note a few residual megakaryocytes)

72.11 Treatment

- Acute infections are treated early with systemic antibiotic therapy.
- Antibiotic therapy is supplemented with surgical therapy if clinically indicated.
- Ancillary antibiotic therapy, including antibiotic-laden cement or beads, is used when clinically warranted.
- It is very difficult to treat a chronic and established focus of osteomyelitis, because there is such an admixture of devitalized tissue fragments containing bacteria. More complicated surgical management may be required for late-stage or chronic infections.

Suggested Reading

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