The case:

A 51-year-old woman with diabetes mellitus presents with increasing left knee pain and swelling, an elevated white blood cell count of $18.84 \times 10^3$ mm$^3$, and an elevated erythrocyte sedimentation rate of 118 mm/h. The patient reports gunshot wounds to both legs 30 years ago, with subsequent surgery of her left thigh.

Figure: Anteroposterior (A) and lateral (B) radiographs of the left knee.

Your diagnosis?

For answer see page 650
Osteomyelitis is an inflammation of bone resulting from an infection, most commonly caused by bacteria. The location of the infection can be contained to one area of bone or may involve multiple areas. In acute osteomyelitis, the infection evolves over several days or weeks and can progress to chronic osteomyelitis, which is defined by the development of sequestrum, a separated necrotic segment of bone. Involucra, sinus tracts, and osteosclerosis are also commonly associated with chronic osteomyelitis.

Osteomyelitis can result from the spread of infection through direct inoculation, contiguous spread from adjacent structures, and hematogenous seeding. Direct inoculation and contiguous spread often result from a polymicrobial infection, whereas hematogenous seeding is of a monomicrobial origin. Although osteomyelitis can develop at any age, it is more common in children and those older than 50 years. The long bones are most commonly affected in children, whereas the vertebrae and pelvis are most commonly affected in adults.

The rate of sequestrum development differs based on which bones and devices are infected. Development of sequestrum in vertebral osteomyelitis is relatively slow, whereas sequestrum develops rapidly in the setting of peri-prosthetic infection or compound fractures. The direct medical cost per incident of osteomyelitis is estimated to be approximately $35,000, which includes hospital facility charges, professional fees, and postdischarge costs.

**ETIOLOGY**

Normally, bone is highly resistant to infection; however, the spread of infection may occur through direct inoculation, contiguous spread from adjacent structures, and hematogenous seeding of pathogens. After an open fracture, the incidence of osteomyelitis has been reported to be between 2% and 16%. Once the infection ensues, leukocytes enter and engulf the offending microorganisms and release bone-lyzing enzymes. Pus develops and impairs blood flow, leading to the development of sequestrum. The sequestrum that develops creates an environment for chronic infection. Staphylococcus aureus causes up to 80% of human osteomyelitis. Less common organisms are coagulase negative staphylococci, gram-negative, fungi, and parasites. Staphylococcus aureus is an excellent agent to infect bone and evade eradication because it expresses adhesion receptor proteins for bone matrix components, produces biofilms, and gains antibiotic resistance by persisting intracellularly in osteoblasts.

**CLINICAL FINDINGS**

Chronic osteomyelitis typically presents with pain, tenderness, warmth, fever, swelling, and redness over the area of infection. A draining sinus tract may exist, which is pathognomonic for chronic osteomyelitis. Poor circulation, recent injury, orthopedic surgery, intravenous drug use, kidney dialysis, and catheter use are risks factors for chronic osteomyelitis.

**DIAGNOSIS**

A combination of clinical, laboratory, and diagnostic imaging findings are used to make the diagnosis of chronic
osteomyelitis. The gold standard for diagnosing chronic osteomyelitis is bone biopsy with histological evaluation and culture of the microorganisms. Bacteria isolated from the bone biopsy sample and osteonecrosis shown on histopathology are needed to confirm the diagnosis. Sinus tract cultures are reliable for confirming S. aureus but are unreliable in determining the presence or absence of gram-negative organisms.6

LABORATORY RESULTS

In general, laboratory results are nonspecific. Some patients with chronic osteomyelitis may have leukocytosis. The erythrocyte sedimentation rate and C-reactive protein levels may be elevated in patients with osteomyelitis, but this is nonspecific. Blood cultures may be helpful; however, only a bone biopsy with an isolated microorganism and histopathology displaying osteonecrosis can diagnose chronic osteomyelitis.3

DIAGNOSTIC IMAGING

Radiographs, magnetic resonance imaging (MRI), computed tomography (CT), and nuclear studies can be useful for diagnosing chronic osteomyelitis. The benefits, limitations, and key findings of each modality are described.

Radiographs

Radiographs should be considered the first step in imaging because of their availability and inexpensive cost. Radiographic imaging features suggestive of chronic osteomyelitis include cortical erosion, periosteal reaction, mixed lucency and sclerosis, sequestra, and soft tissue swelling (Figure 1). Studies have reported that the only reliable plain film finding of active bone infection is sequestrum after previous surgery or fracture.3 However, sequestrum is not unique to chronic osteomyelitis and may be observed less commonly in Langerhans cell histiocytosis, malignant fibrous histiocytoma, lymphoma, metastasis, and osteoblastoma.

Magnetic Resonance Imaging

Magnetic resonance imaging is the modality of choice for imaging chronic osteomyelitis, with a high sensitivity and negative predictive value. In chronic osteomyelitis, the infected bone marrow will display bone marrow edema–like signal changes, with low signal intensity on T1-weighted imaging (Figures 2A, B) and a hyperintense signal intensity on T2-weighted imaging (Figures 2C, D). Reduced bone marrow cavity and bone sclerosis with cortical thickening are also common imaging characteristics. Intravenous contrast administration can increase diagnostic confidence; Gadolinium-enhanced T1-weighted images are useful to better identify sequestra, sinus tracts, fistulas, and abscesses (Figure 2E).7

Computed Tomography

Although MRI is superior to CT for diagnosing chronic osteomyelitis, CT can be useful when MRI is not available or if a contraindication exists to MRI. Findings of chronic osteomyelitis on CT are sequestra, sinus tracts, involucra/periosteal reaction, osteosclerosis, medullary low-attenuation areas, focal cortical erosions, and soft tissue swelling (Figure 3). Computed tomography is superior to MRI in displaying cortical destruction and intraosseous or soft tissue gas.8

Nuclear Studies

Nuclear studies are a useful diagnostic alternative to MRI. Three-phase bone scans, gallium, tagged white blood cells, and fluorodeoxyglucose positron emission CT are nuclear modalities that can aid in the diagnosis of chronic osteomyelitis. Positive findings of chronic osteomyelitis in 3-phase bone scans are increased flow activity, blood pool activity, and positive uptake on 3-hour images. When positive in all 3 phases, sensitivity for osteomyelitis is 73% to 100%.3 Compared with the 3-phase bone scan, gallium image quality is poor and requires a longer acquisition time. However, gallium scans can be used in conjunction with the 3-phase bone scan to improve specificity. Studies have shown that fluorodeoxyglucose positron emission CT scans are highly accurate and show promise in the diagnosis of chronic osteomyelitis.9,10

TREATMENT

Chronic osteomyelitis requires both surgical debridement of necrotic material and antimicrobial therapy for infection eradication.

Surgical Treatment

Currently, no definitive evidence-based guidelines exist for the treatment of chronic osteomyelitis. However, the goals of surgical treatment are removal of necrotic devitalized bone and soft tissue, removal of any foreign bodies, restoration of vascular blood flow, management of dead space, and restoration of bone stability. Excision of necrotic devitalized bone and soft tissue should contain...
normal healthy tissue margins to ensure removal of all of the infection to prevent recurrence. All foreign bodies need to be removed due to their ability to be biofilms carriers.\textsuperscript{11}

The dead space created by the debridement of the infected bone must be managed to prevent infection recurrence. The goal of dead space management of bone defects is to fill the space with vascularized tissue, temporary antibiotic-laden polymethylmethacrylate beads, autologous bone graft, vascularized free fibula, or iliac crest bone grafts. Associated soft tissue dead space defects are treated with skin graft, local muscle flaps, or vascularized free flaps. Healing by secondary intention and closed irrigation systems have been shown to have a success rate less than 70%.\textsuperscript{12} Temporary antibiotic-laden polymethylmethacrylate beads are used as a temporary filler for the dead space and are removed 2 to 4 weeks postoperatively and replaced with cancellous or vascularized bone graft. It has been reported that temporary antibiotic-laden polymethylmethacrylate beads have a 92% success rate.\textsuperscript{12} Myoplasty, free muscle flaps, and Ilizarov technology have shown successful results for large osseous defects.

It is important to remember that no set guidelines for surgical treatment exist, and the anatomic aspects of the patient’s infection and comorbid conditions must be taken into account.\textsuperscript{12} Hyperbaric oxygen therapy can be used in cases of refractory osteomyelitis, but its reliability has yet to be proven.\textsuperscript{13}

**Antibiotic Therapy**

Antibiotic therapy should be ordered according to the culture and sensitivity findings. Broad-spectrum empiric therapy should be administered if the results of the cultures are not known. For gram-negative organisms, fluoroquinolones are appropriate. For methicillin-susceptible \textit{S aureus}, rifampin-cotrimoxazole or cloxacillin can be used because they have been shown to have equal efficacy.\textsuperscript{14} Vancomycin is used for methicillin-resistant \textit{S aureus}. Rifampin is commonly used with other antibiotics because of its ability to penetrate bio-

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**Figure 2:** Coronal (A) and axial (B) T1-weighted magnetic resonance images showing the hypointense, linear sequestra (arrows) in the central marrow, surrounded by intermediate signal intensity soft tissue and low signal sclerosis of the surrounding marrow. The intraosseous sinus tract (arrowhead) extends through the medial cortex. Note the anteromedial subcutaneous soft tissue defect from a remote postoperative change after debridement for a gunshot wound. Axial fast spin echo T2-weighted fat-suppressed magnetic resonance image showing the intraosseous sequestra (black arrow) due to surrounding marrow edema–like signal changes and the anterior and medial sinus tracks (arrowheads) (C). A more inferior axial fast spin echo T2-weighted fat-suppressed magnetic resonance image showing the extruded sequestra in the posterior soft tissues (arrows) and enlarged femur from chronic, well-organized periosteal reaction (D). Sagittal T1-weighted enhanced fat-suppressed magnetic resonance image shows sequestra (large arrows) within the central canal and posterior to the distal femur. Note the markedly enhanced marrow in the more distal marrow (small arrows), suggesting reactive changes from active infection (E).

**Figure 3:** Axial computed tomography images taken sequentially through the distal femoral shaft showing the anteromedial sinus tract (arrowhead) (A) and isolated sequestra (arrows) (B). Note the heterogeneous osteosclerosis and diffuse enlargement of the femur. Sagittal 2-dimensional reconstructed computed tomography image showing the isolated sequestra within the canal (arrows) and extruded posteriorly (arrowhead) (C).
films and increase the efficacy of other antibiotics. Although no proven guidelines exist for the appropriate duration of antibiotics, they are typically administered for approximately 6 weeks postoperatively. It is theorized that 6 weeks is necessary because it takes 2 to 4 weeks for the previous area of osseous defect to revascularize after debridement. The key to successful treatment of chronic osteomyelitis is complete debridement of necrotic infected tissue and proper antibiotic therapy.

REFERENCES