sites, and the endocardium. Spread from a contiguous source follows either bone trauma or surgical intervention. Wound infection leading to osteomyelitis typically occurs after cardiovascular intervention involving the sternum, orthopedic repair, or prosthetic joint insertion. Osteomyelitis secondary to vascular insufficiency or peripheral neuropathy most often follows chronic, progressively deep skin and soft tissue infection of the foot. The most common underlying condition is diabetes. In diabetes that is poorly controlled, the *diabetic foot syndrome* is caused by skin, soft tissue, and bone ischemia combined with motor, sensory, and autonomic neuropathy.

Classification of osteomyelitis according to the duration of infection, although ill defined (because there is no clear time limit for the transition from acute to chronic osteomyelitis), is useful because the management of acute and chronic osteomyelitis differs. Whereas acute osteomyelitis can generally be treated with antibiotics alone, antibiotic treatment for chronic osteomyelitis should be combined with debridement surgery. Acute hematogenous or contiguous osteomyelitis evolves over a short period—i.e., a few days or weeks. In contrast, subacute or chronic osteomyelitis lasts for weeks or months before treatment is started. Typical examples of a subacute course are vertebral osteomyelitis due to tuberculosis or brucellosis and delayed implant-associated infections caused mainly by low-virulence microorganisms (coagulase-negative staphylococci, *Propionibacterium acnes*). Chronic osteomyelitis develops when insufficient therapy leads to persistence or recurrence, most often after sternal, mandibular, or foot infection.

Classification by location distinguishes among cases in the long bones, the vertebral column, and the periarticular bones. Long bones are generally involved after hematogenous seeding in children or contiguous spread following trauma or surgery. The risk of vertebral osteomyelitis in adults increases with age. Periarticular osteomyelitis, which complicates septic arthritis that has not been adequately treated, is especially common in periprosthetic joint infection.

Osteomyelitis involving a foreign device requires surgical management for cure. Even acute implant-associated infection calls for prolonged antimicrobial therapy. Therefore, identification of this type of disease is of practical importance.

VERTEBRAL OSTEOMYELITIS

PATHOGENESIS

Vertebral osteomyelitis, also referred to as disk-space infection, septic diskitis, spondylodiskitis, or spinal osteomyelitis, is the most common manifestation of hematogenous bone infection in adults. This designation reflects a pathogenic process leading to involvement of the adjacent vertebrae and the corresponding intervertebral disk. In adults, the disk is avascular. Microorganisms invade via the segmental arterial circulation in adjacent endplates and then spread into the disk. Alternative routes of infection are retrograde seeding through the prevertebral venous plexus and direct inoculation during spinal surgery, epidural infiltration, or trauma. In the setting of implant surgery, microorganisms are inoculated either during the procedure or, if wound healing is impaired, in the early postoperative period.

EPIDEMIOLOGY

Vertebral osteomyelitis occurs more often in male than in female patients (ratio, 1.5:1). The overall incidence is 2.4 cases/100,000 population. There is a clear age-dependent increase from 0.3 cases/100,000 at ages <20 years to 6.5 cases/100,000 at ages >70 years. The observed increase in reported cases during the past two decades may reflect improvements in diagnosis resulting from the broad availability of MRI technology. In addition, the fraction of cases of vertebral osteomyelitis acquired in association with health care is certainly increasing as a consequence of the rising number of spinal interventions and local infiltrations.

MICROBIOLOGY

Vertebral osteomyelitis is typically classified as pyogenic or nonpyogenic. However, this distinction is arbitrary because, in "nonpyogenic" cases (tuberculous, brucellar), macroscopic pus formation (caseous necrosis, abscess) is quite common. A more accurate scheme is to classify cases as acute or subacute/chronic. Whereas the microbiologic spectrum of acute cases is similar in different parts of the world, the spectrum of subacute/chronic cases varies according to the geographic region. The great majority of cases are monomicrobial in etiology. Of episodes of acute vertebral osteomyelitis, 40–50% are caused by *Staphylococcus aureus*, 12% by streptococci, and 20% by gram-negative bacilli—mainly *Escherichia coli* (9%) and *Pseudomonas aeruginosa* (6%). Subacute vertebral osteomyelitis is typically caused by *Mycobacterium tuberculosis* or *Brucella* species in regions where these microorganisms are endemic. Osteomyelitis due to viridans streptococci also has a subacute presentation; these infections most often occur as secondary foci in patients with endocarditis. In vertebral osteomyelitis due to *Candida* species, the diagnosis is often delayed by several weeks; this etiology should be suspected in IV drug users who do not use sterile paraphernalia. In implant-associated spinal osteomyelitis, coagulase-negative staphylococci and *P. acnes*—which, in the absence of an implant, are generally considered contaminants—typically cause low-grade (chronic) infections. As an exception, coagulase-negative staphylococci can cause native spinal osteomyelitis in cases of prolonged bacteremia (e.g., in patients with infected pacemaker electrodes or implanted vascular catheters that are not promptly removed).

CLINICAL MANIFESTATIONS

The signs and symptoms of vertebral osteomyelitis are nonspecific. Only about half of patients develop fever >38°C (100.4°F), perhaps because analgesic drugs are frequently used by these patients. Back pain is the leading initial symptom (>85% of cases). The location of the pain corresponds to the site of infection: the cervical spine in ~10% of cases, the thoracic spine in 30%, and the lumbar spine in 60%. One exception is involvement at the thoracic level in two-thirds of cases of tuberculous osteomyelitis and at the lumbar level in only one-third. This difference is due to direct mycobacterial spread via pleural or mediastinal lymph nodes in pulmonary tuberculosis.

Neurologic deficits, such as radiculopathy, weakness, or sensory loss, are observed in about one-third of cases of vertebral osteomyelitis. In brucellar vertebral osteomyelitis, neurologic impairment is less frequent; in tuberculous osteomyelitis, it is about twice as frequent as in cases of other etiologies. Neurologic signs and symptoms are caused mostly by spinal epidural abscess. This complication starts with severe localized back pain and progresses to radicular pain, reflex changes, sensory abnormalities, motor weakness, bowel and bladder dysfunction, and paralysis.

A primary focus should always be sought but is found in only half of cases. Overall, endocarditis is identified in ~10% of patients. In osteomyelitis caused by viridans streptococci, endocarditis is the source in about half of patients.

Implant-associated spinal osteomyelitis can present as either early- or late-onset infection. Early-onset infection is diagnosed within 30 days after implant placement. *S. aureus* is the most common pathogen. Wound healing impairment and fever are the leading findings. Late-onset infection is diagnosed beyond 30 days after surgery, with low-virulence organisms such as coagulase-negative staphylococci or *P. acnes* as typical infecting agents. Fever is rare. One-quarter of patients have a sinus tract. Because of the delayed course and the lack of classic signs of infection, rapid diagnosis requires a high degree of suspicion.

DIAGNOSIS

Leukocytosis and neutrophilia have low levels of diagnostic sensitivity (only 65% and 40%, respectively). In contrast, an increased erythrocyte sedimentation rate or C-reactive protein (CRP) level has been reported in 98% and 100% of cases, respectively; thus, these tests are helpful in excluding vertebral osteomyelitis. The fraction of blood cultures that yield positive results depends heavily on whether the patient has been pretreated with antibiotics; across studies, the range is from 30% to 78%. In view of this low rate of positive blood culture after antibiotic treatment, such therapy should be withheld until microbial growth is proven unless the patient has sepsis syndrome. In patients with negative blood cultures, CT-guided or open biopsy is needed. Whether a CT-guided biopsy with a negative result is repeated or followed by