Osteomyelitis and osteonecrosis

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Abstract

We discuss two of the most common conditions of bone seen in general pathology practice. We review the causes and pathophysiology of osteomyelitis and osteonecrosis. We discuss their imaging characteristics and histological features as well as some of the problems in diagnosis faced by a pathologist.

Keywords avascular necrosis; bacterial infections; bone infection; fungal infections; osteochondritis juvenilis; osteomyelitis; osteonecrosis; parasitic infection; tuberculosis

Osteomyelitis

The term osteomyelitis is defined as inflammation of the bone and medullary contents. Infection of the skeleton, the largest organ system of the body, is important, because it is a major site of microbial infestation that is often morbid and sometimes fatal. All types of organisms, including bacteria, mycobacteria, fungi, viruses, and parasites can cause osteomyelitis, but, infections associated with certain pyogenic bacteria and mycobacteria are the most common. The interplay between the microbes and the host produces a wide spectrum of clinical manifestations that are further influenced by the causative event, the bone involved, the specific pathogen and its virulence, the medical condition of the host, the type of therapy, and the clinical course of the disease.[1] Many of the molecular mechanisms underlying these biological interactions have been elucidated and this knowledge has facilitated advances in the stalwarts of therapy, namely, surgery and antibiotics. Regardless, the complexities and problems in diagnosing and treating osteomyelitis have become ever more challenging because of the increase in the numbers of the elderly, joint replacements, prevalence of diabetes, frequency of antibiotic resistant pathogens, and population of immunocompromised patients and their exotic opportunistic infections.

Epidemiology

Clinically, osteomyelitis is seen quite frequently in medicine, however, there are only a few good epidemiological population based studies (as opposed to hospital or institution based studies) that estimate its prevalence and incidence in the community. A Medline search for osteomyelitis and epidemiology revealed 153 papers, but after excluding hospital based studies and specific organisms or specific situations such as patients with endocarditis or kidney disease there were only two papers that fit the criteria.[2,3] One study investigated the epidemiology of osteomyelitis in Olmsted County, Minnesota of the United States and found the overall age and sex adjusted incidence to be 21.8 cases per 100,000 person-years. A French paediatric study that included osteomyelitis (41%) and septic arthritis (52%) found the incidence to be 7.1/100,000. A different type of study from Uganda studying five different hospitals found 10% of outpatient visits and 3.5% of all surgeries were related to osteomyelitis.[4] Globally, osteomyelitis is thought to disproportionately involve children. Unfortunately, most studies do not elaborate on how the diagnosis of osteomyeltis was made — clinically, radiologically or with histological correlation.

Pathophysiology

The fundamental biological processes active in bone infection are independent of pathogen-type. Entry of the organism into bone is the first step in osteomyelitis and occurs by three main mechanisms: (1) carried by the bloodstream (hematogenous seeding), (2) extension from a contiguous site such as a cutaneous ulcer or deep soft tissue abscess, and (3) direct inoculation from penetrating injuries, complication of surgery or compound fracture.

Hematogenous osteomyelitis is usually caused by bacteria and most commonly affects rapidly growing long bones. In children it often presents a presents as a primary solitary focus of infection that likely results from occult bacteremia associated with seeding of a site susceptible to bacterial invasion. In contrast, in adults it is often a complication of any localized or systemic infection. Within a long bone, the anatomic site of infection depends on whether the patient is an infant, child or adult, and the relationship between age and localization is based on the vascular anatomy of the bone.

Briefly, the nutrient artery supplies the majority of blood flow to bone and during growth and development after the first year of life its terminal branches end as capillaries at the base of the growth plate (Figure 1). As the capillaries approach the epiphyseal plate they reverse direction by forming a loop and then merge into a network of sinusoidal venous blood lakes which in turn empty into the venous drainage system of the medullary cavity. The blood flow in the capillary-sinusoid loop region is sluggish and turbulent and phagocyte function is suboptimal, and together, these features facilitate deposition of the organism into the metaphyseal tissue and likely creates local hypoxia — an environment that is conducive to infection. In infants less than 1 year old, some of the terminal branches of the nutrient artery penetrate the growth plate and as they end near the base of the articular cartilage their diameter expands forming large venous lakes resembling metaphyseal sinusoids.[5,6] Thus, in neonates microbes may settle in the epiphysis or quickly spread into this region from a metaphyseal focus of disease.[7] In neonates and children, transphyseal blood vessels facilitate direct extension into the adjacent joint as the metaphysis is intra-articular in this age group. In adults, after closure of the growth plate, the metaphyseal and epiphyseal vessels establish reconnections so bacteria entering the nutrient artery are directed to the vascular loops beneath the articular cartilage. Accordingly, acute hematogenous osteomyelitis in infants and adults often affects the epiphysis, whereas, in children the growth plate acts as an

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Figure 1 Graphic of vascular supply to long bone in a child. The nutrient artery traverses length of the diaphysis and terminal branches in the region of the growth plate form capillaries that create a loop and empty into venous sinusoids that merge with veins. The vascular anatomy of the bone often influences the focus of infection in hematogenous osteomyelitis.

effective barrier and the infection is usually limited to the metaphysis. In the spine, blood-borne pathogens usually localize to the subchondral regions of the vertebral body. These areas have the richest vascular supply and are fed by branches of the spinal artery and drained by a venous plexus.

Osteomyelitis resulting from contiguous spread may affect any bone adjacent to a cutaneous or mucosal ulcer or soft tissue abscess, and is more commonly seen in the setting of periodontal and sinus disease, cellulitis of diabetic feet, epidural abscess, decubitus ulcer, or septic arthritis. In these situations the inflammatory process must first destroy the periosteum or articular surface before it accesses the bone. Unlike hematogenous osteomyelitis, the cortex instead of the medullary cavity is initially infected, and the site at which this occurs influences the rapidity of spread and extent of disease.[8,9]

Direct implantation of pathogens into bone takes place in a variety of circumstances and the causative event and the degree of associated hemorrhage, tissue fragmentation and necrosis influences the infection. Also, the balance between the biological characteristics of the pathogen and host impacts the extent of the osseous disease and the ability of the host to confine and eradicate the organism. All too frequently, the pathogens remain viable and continue to proliferate in an environment of necrotic tissue inaccessible to the immune response and therapeutic antibiotics. In this fashion a smouldering chronic infection is generated which maintains the potential to cause future havoc when conditions are permitting and successful eradication may require surgical intervention.[10–13]

Microbiological considerations

Bacterial infection:

Hematogenous osteomyelitis – *Staphylococcus aureus* is responsible for 80%–90% of the cases of bacterial hematogenous osteomyelitis in which an organism is recovered.[14] Aspects of the infection may be related to virulence factors elaborated by different clonal types. Group A and B streptococci and gram-negative organisms are important etiologic agents in neonates. Haemophilus influenzae has become less important following the introduction of vaccination to this organism. Salmonella complicates sickle cell disease and *Escherichia coli*, Pseudomonas, and Klebsiella are more frequently isolated from patients with genitourinary tract infections or who are intravenous drug abusers.

Contiguous spread osteomyelitis – the type of organisms is influenced by the nature of the associated disorder. Osteomyelitis of the jaws frequently follows periodontal disease and caries. Many patients also have a history of previous radiation which compromises the gingiva and induces necrosis of the underlying bone. The exposed bone acts as a good medium for bacterial pathogens which frequently becomes infected by multiple organisms including staph aureus, streptococcus species, and actinomyces. Actinomyces also is the pathogen in most jaw infections that occur in patients treated with bisphosphonates.[15] Bone infection in diabetic patients with ulcers of the feet are often caused by *S. aureus* which may be methicillin resistant followed by *Staphylococcus epidermidis, E. coli, Klebsiella pneumonia*, *Proteus* spp. and *Pseudomonas aeruginosa*.[9] Osteomyelitis that complicates a decubitus ulcer is polymicrobial and includes aerobes (*Proteus mirabilis, E. coli, Enterococci*, *Staphylococci*, and *Pseudomonas* spp.) and anaerobes (*Peptostreptococcus* species, *Bacteroides fragilis*, and *Clostridium perfringens*).[8]

Direct implantation osteomyelitis – a host of different bacteria may behave as pathogens including those that normally colonize the skin, the contaminating soil or nosocomial organisms acquired during hospitalization and restorative surgical procedures. The most frequent offenders are Staphylococci and aerobic gram-negative bacilli, however, enterococci are also infrequently implicated.

Mycobacterial infection: currently, within the genus Mycobacterium, greater than 150 different species are recognized. The majority are not pathogenic, and are ubiquitous in the environment with their natural reservoirs being water, soil, aerosols,

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