CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1845521

Available online at: http://www.iajps.com *Review Article*

CAUSES AND MANAGEMENT OF OSTEOMYELITIS

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Abstract:

Introduction: *The term 'Osteomyelitis' refers to the presence of an infectious disease within the bone tissue. Multiple important syndromes are usually seen with osteomyelitis. Following the introduction of penicillins in the 1940s, mortality caused by staphylococcal osteomyelitis significantly decreased from about thirty percent to ten percent, with increasing literature evolving on the discussions of the relative benefits of surgical decompression and antimicrobials treatment in the algorithm for osteomyelitis treatment.*

Aim of work: *In this review, we will discuss the most recent evidence regarding the Causes and management of osteomyelitis.*

Methodology: *We did a systematic search for Causes and management of osteomyelitis in the emergency department using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.*

Conclusions: *Hematogenous osteomyelitis is one of the most common presentations in the pediatrics population and is usually treated medically, although methicillin-resistant Staphylococcus aureus infections might require surgery in some cases. Appropriate management and treatment of infections of diabetic foot include evaluation of the blood supply as a part of the decision-making process regarding surgical debridement. Established infections in patients with open fractures may present as nonunion and require a combination of medical and surgical treatments.*

Key words: *osteomyelitis, Causes, diagnosis, and management.*

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Please cite this article in press Nibras Khaled Aljabri et al., ***Causes and Management of Osteomyelitis.,*** *Indo Am. J. P. Sci, 2018; 05(12).*

INTRODUCTION:

The term 'Osteomyelitis' refers to the presence of an infectious disease within the bone tissue. Multiple important syndromes are usually seen with osteomyelitis. These include hematogenous osteomyelitis, osteomyelitis in the vertebrae, traumatic osteomyelitis, and infection of diabetic foot. Osteomyelitis is known to be an ancient disease, with the presence of documented fossilized evidence of infections in animals more than hundreds of millions of years ago. The discussions present of osteomyelitis in humans goes back to the era of Hippocrates (about 460–370 BC) [1].

Previously, the condition of Acute hematogenous osteomyelitis was termed "abscessus in medulla" by Broomfield in the year 1773 [2]. The term "osteomyelitis" was introduced by Nelaton in the year 1844. Prior to the discovery of antibiotics, the management of osteomyelitis was dependent mainly on surgery, with the standard-care including debridement of the bone, saucerization, and packing the wound with secondary healing? Following the introduction of penicillins in the 1940s, mortality caused by staphylococcal osteomyelitis significantly decreased from about thirty percent to ten percent, with increasing literature evolving on the discussions of the relative benefits of surgical decompression and antimicrobials treatment in the algorithm for osteomyelitis treatment.

In this review, we will discuss the most recent evidence regarding the Causes and management of osteomyelitis.

METHODOLOGY:

We did a systematic search for Causes and management of osteomyelitis in the emergency department using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: osteomyelitis, Causes, diagnosis, and management.

EPIDEMIOLOGY AND CLASSIFICATION:

In the pediatrics population, hematogenous osteomyelitis is most likely to be present in the long bones of the body. On the other hand, osteomyelitis among adolescents and young adults is often associated with traumas or surgeries. Older adults with osteomyelitis will most clinical present with contiguous osteomyelitis that is related to joints arthroplasty, osteomyelitis of the lower extremity that is related to diabetes mellitus type 2 and vascular disease, and osteomyelitis that is caused by decubitus ulceration.

There are two main categorization systems that are used for osteomyelitis. The first system, which was proposed by Lew and Waldvogel,[3] depends on the etiology of the disease. In this system, osteomyelitis is grouped into three categories according to the pathophysiological mechanisms: hematogenous osteomyelitis; contiguous focus osteomyelitis from trauma, surgical operations, prosthetic material, or soft tissue spread; and vascular insufficiency osteomyelitis that is usually found in diabetes mellitus type 2 patients.

On the other hand, the second categorization system, which was proposed by Cierny and Mader,[4] helps by providing some guidance for management of the disease. In this system, osteomyelitis is grouped according to the anatomical stages, and placed in the setting of host health status. The term 'Host health status' is defined by local factors and systemic factors. Local factors include the presence of edema, the circulatory status, smoking status, and the presence of neuropathy, while systemic host factors include the presence of immunocompromising conditions like malignances, organ system failure and diabetes mellitus type 2, age of the patient, and the presence of malnutrition status. Stage I0 disease is classically managed using antibiotics. However, more advanced stages may require a combination of both medical treatment and surgical procedures.

PATHOPHYSIOLOGY:

Hematogenous osteomyelitis that develops in the long bones often occurs in the metaphysis of the bone.[5] the development of disturbed flow of blood in the vascular loops at the metaphysis and near the epiphyseal plates will lead to the deposition of bacterial organisms and the initiation of an infection. An inflammatory response starts, causing an elevated pressure within the medullary bone. This elevated pressure causes the infection to go through to the cortex and, if not managed early, pass through the periosteum. This can lead to reduced blood supply reaching to the periosteum along with the development of necrosis in the bone. These pieces of necrotic bone tissue, which are usually called a sequestrum, can separate and contain pus. New bone can start to form along the damaged periosteum; this is generally termed as 'involucrum' and may partially circle the sequestrum with continuous drainage.

Osteomyelitis of the vertebrae usually arises from the hematogenous spread of bacterial organisms into the vertebral bodies' metaphysis. The infection will later spread to the intravertebral disc, which is avascular. Classic patterns of the infection are usually explained by the vascular structures, with spread between the intramedullary communicating arteries to the metaphyses of a single vertebra and the involvement of adjacent vertebral bodies which are supplied by splitting arteries from one vertebral artery. Venous drainage through the Batson's plexus is sometimes felt by some professionals to contribute to spondylodiscitis metastasizing from a focus in the urinary tract. Diabetes mellitus can cause compromised macrovascular and/or microvascular blood supply to the lower limbs. In the presence of a sensory neuropathy that is also known to be prevalent among diabetics, patients have a higher risk of developing skin ulceration at the points of trauma or pressure, with later colonization with flora of the skin. Absence of good vasculature can contribute to the decreased local immunity and poor healing of the skin, increasing the risk of infection spread to the underlying bone tissue.

Patients who are confined to wheelchair or bed due to the presence of paralysis or debility are prone to develop pressure-related skin ulceration followed by necrosis, most likely in the sites of the buttocks and sacrum. These ulcerations are usually colonized by polymicrobial flora organisms that emanate from the skin and digestive tracts, with the infection of soft tissues spreading to the pelvic bones and the lower limbs.

In addition, microbial-related factors can play an essential role in the pathophysiology of osteomyelitis. For example, the adhesions of Staphylococcus aureus, occurs with components of the microbial surface that recognizes the molecules of the adhesive matrix.[6] The components of Microbe's surface recognizing adhesive matrix molecules will recognize polysaccharides related to fibronectin, fibrinogen, collagen, and heparin, promoting the adherence to the bone matrix. Staphylococcus aureus that was digested by osteoblasts survive and become more resistant to treatment with antibiotics. Finally, Staphylococcus aureus is likely to block proteolysis inhibition in musculoskeletal structures.

MICROBIOLOGY:

Hematogenous osteomyelitis is frequently due to monomicrobial infection, whereas osteomyelitis cases that result from inoculation or contiguous spread could be monomicrobial or polymicrobial infections .[7] Staphylococcus aureus and coagulase-negative staphylococci in general, are the most common organisms to be isolated from patients with osteomyelitis.

Infections can originate from infected distant foci like skin abscesses or endocarditis, vascular catheters, or injection drug use. Infection with community-acquired methicillin-resistant S aureus has been increasing as a microbe with significant virulence that results from production release of cytotoxins in tissues.[8] Streptococci, aerobic gram-negative bacilli, enterococci, and anaerobes are other commonly encountered organisms in patients with osteomyelitis. Anaerobic gram-negative bacilli including Clostridium species, peptostreptococci, and Bacteroides species can also be isolated in some cases, especially those with polymicrobial infections. Mycobacterium TB can sometimes spread to the thoracic spine originating from a primary infection in the lungs [9].

A number of bacterial organisms are less likely to be isolated in cases of osteomyelitis, but still they should be taken into consideration in areas with higher prevalence or the presence of predisposing factors. For example, nontuberculous mycobacteria are generally found in the presence of trauma or an immunocompromised status. In addition, Bacille Calmette-Guerin infection may follow intra-vesicular therapy used in the treatment of bladder cancer. Candida species can also be a part of chronic infections that occur following surgical procedures or traumatic injuries, in immunocompromised patients, or as following hematogenous deposition with vascular catheters or injection drug abuse. Dimorphic fungi like Blastomyces species and Coccidioides species can infect the bone in endemic areas. Cryptococcus spp and Aspergillus spp can be found especially among immunocompromised individuals.[10] Osteomyelitis due to infection with Actinomyces spp or Sporothrix spp are usually caused by traumatic inoculation. Brucella spp and Salmonella spp are generally found in infections of the spine. Finally, Salmonella spp and S aureus are more common in acute hematogenous osteomyelitis cases that develop in patients with sickle cell disease.

CLINICAL PRESENTATION:

The clinical manifestations that appear on a patient with osteomyelitis depend mainly on the underlying cause. For example, hematogenous osteomyelitis often manifests with a subacute or chronic onset of pain in the areas of bone infection. Fever and chills are, however, less likely to be encountered, but can

still be found in patients infected with virulent organisms like S aureus. Other manifestations like soft tissue erythema, swelling and eventually a draining sinus tract can develop in some cases, and are generally more common in the presence of traumas, fractures, joint arthroplasty, or non-joint orthopedic hardware. Infections that are associated with vascular insufficiency most often manifest with ulcers, swelling, erythema, and drainage that can progress to visible bone in a subacute to chronic pattern. Infections that occur following an open fracture can manifest within weeks or months with poor wound healing or nonunion of the fracture. Fever and chills are less likely to occur in these settings. Osteomyelitis of the vertebrae classically manifests with subacute to chronic pain at the involved bone areas, with fever in some cases. Symptoms and signs of cord compromise and compression can emerge in about one-fourth of cases, with pain that radiates from the roots of compressed nerve and correspond with the level that is involved, followed by limb weakness and impaired bowel functions or urinary bladder functions.

DIAGNOSIS

Clinical manifestations are a crucial part of the diagnosis of osteomyelitis cases. In lower limb osteomyelitis that is due to vascular insufficiency, the presence of probing to bone is usually suggestive of osteomyelitis. Further confirmation of the diagnosis of osteomyelitis often consists of blood investigations, radiological imaging, and microbiology investigations. In most patients, the ESR and C-reactive protein are both abnormal but can be still be normal in cases of infections with specific indolent organisms like Propionibacterium acnes. The WBCs count can either be normal or elevated, and a normocytic; normochromic chronic disease pattern anemia might be found in chronic infection.

Plain radiographs can have a delay of one to two weeks before findings become apparent. Cross-sectional imaging techniques including CT and MRI have higher sensitivity and specificity than X-rays. Nuclear imaging studies are also sensitive but with less specificity than MRI and usually do not show the anatomical definition that is important to assist surgical management of severe cases. Microbiological diagnosis of acute hematogenous osteomyelitis in the pediatrics is usually made with cultures of blood samples. Because blood cultures are less likely to be found positive in adult's patients, biopsy is usually necessary, with guidance with CT imaging or through an open procedure.

MANAGEMENT:

The management and treatment of osteomyelitis usually need a combination of both medical and surgical interventions to achieve a target of a disinfected, painless function. Both coordination and communication between the surgeons and infectious-diseases specialists are crucial in the process of making a unified and effective management plan. Because antimicrobials can poorly penetrate necrotic or damaged bones and infected body fluids, surgical debridement is considered to be the step of treatment when these are found. In addition to making the penetration of antibiotics into affected bone and soft tissue easier, surgical debridement also can have other advantages: First, it gives the opportunity to get data for culture of deep tissues to more accurately direct antimicrobials therapy. Second, because orthopedic instruments create an avascular surface for microbial colonization, their removal improves the likelihood of microbiological cure. Following the removal of infected necrotic tissue and hardware, nonunion of bone can be managed if detected. Local antimicrobials delivery can be started by placing beads or polymethylmethacrylate cement spacers that contain the antibiotic. Eventually, necrotic space can be exposed for flap coverage.

Once surgical debridement of the infected bone has been performed, effective antimicrobial treatment can be initiated. Vancomycin and a third-generation cephalosporin or beta lactam/beta-lactamase inhibitor combination can provide broad coverage against both gram-positive and gram-negative organisms and is the most common and efficient empiric regimen that is used until culture results are available. When methicillin-susceptible staphylococci are detected in cultures, penicillinase-resistant penicillins like nafcillin or oxacillin, or a first-generation cephalosporin like cefazolin are usually used. When detected staphylococci are methicillin resistant, vancomycin is the most commonly used agent. Evidence regarding the administration of more recent agents like daptomycin, ceftaroline, linezolid, dalbavancin, and televancin is emerging [11]. In cases with penicillin-susceptible streptococci or enterococci, penicillin G and ampicillin can be used. in cases with susceptible gram-negative bacilli, ceftriaxone or ertapenem might be administered once daily for prolonged IV treatment. When Pseudomonas aeruginosa is detected, ceftazidime, cefepime, or meropenem are the best choices and are administrated through the IV route.

The use of hyperbaric oxygen as an adjunctive

therapy is controversial for patients with osteomyelitis [12]. Two possible mechanisms have been hypothesized for its actions in osteomyelitis: First, higher oxygen tension can have a direct killing effect on anaerobic bacterial organisms. Second, it is thought that polymorphonuclear leukocyte killing of organisms is improved by higher oxygen tension.

Acute Hematogenous Osteomyelitis in Children:
When dealing with the pediatrics population, they most often get osteomyelitis through the hematogenous route. More than fifty percent of cases occur before the age of five years [13]. Long bones are more likely to be affected, especially the femur, tibia, and humerus. The spine accounts for less than five percent of cases [14].

Neonatal infections are associated with bacteremia in the presence of an indwelling catheter, abnormal urinary tract anatomy, and the presence of infections of the skin or soft tissue. When dealing with children older than three months, the presence of sickle cell disease and immunodeficiency should be suspected and investigated. The most common organism in this age group is S aureus. Streptococcus pneumoniae is common in patients who are in an immunodeficiency states, asplenic individuals, or patients with hypo-splenia. In the neonates' population, Escherichia coli and Streptococcus agalactiae (group B) can also be common.

The pathophysiology of children hematogenous osteomyelitis is usually different from adults in that the infection is not always confined to the metaphyses of bones. Infections usually spread through the growth plate or the cortex into the joint space. In neonates, the presence of a thinner cortex can facilitate the rupture into soft tissues. As the cortex of bones become thicker with age, subperiosteal collection of pus can develop instead of rupture. Diagnosis is made using imaging, and microbiology is often established with blood cultures.

Lower Extremity Osteomyelitis in Patients with Diabetes Mellitus:
Patients who are diagnosed with diabetes mellitus type 2 usually have complications resulting from the presence of both ischemic vascular diseases and peripheral neuropathy. In these settings, these patients are usually not aware of the pressure phenomenon that is associated with footwear fit, along with subsequent callus formation and breakdown of normal cutaneous barriers to infection. Additionally, diabetic patients who have developed neuropathy usually cannot recognize trauma, which further increases their risk of skin breakdown. Once bacterial organisms pass the skin, the spread of infection is enhanced by the hyperglycemic status and the decreased blood supply. Infections usually spread to the underlying bones, which may be visible in the ulcer.

Diagnosis is usually made following a complete physical examination that will show erythema, warmth, tenderness, and swelling. The ability to probe to bone has high specificity for diagnosing osteomyelitis, which can exceed ninety percent [15]. Imaging techniques, like MRI and nuclear studies, can be used to define the anatomy. Due to the difficulty of wounds healing in poorly vascularized extremities, it is important to alter antibiotics therapy according to the findings of swab cultures. However, this practice can have multiple limitations. First, there can usually be a discordance between the wound and the deep soft tissue or the bone cultures. Additionally, swab cultures can be insufficient for anaerobic cultures. Therefore, infections of the diabetic foot are recommended not to use swab cultures, especially in cases of undebrided wounds.

CONCLUSIONS:

Hematogenous osteomyelitis is one of the most common presentations in the pediatrics population and is usually treated medically, although methicillin-resistant Staphylococcus aureus infections might require surgery in some cases. Staging of osteomyelitis can address both the disease extent and the underlying general health status of the host and can aid in planning appropriate management and treatment plans. Probing to bone usually has a significant association with the presence of an infection in patients with diabetic foot ulcers. Cross-sectional techniques like MRI can be used to suggest the diagnosis when clinical presentation is less obvious. Appropriate management and treatment of infections of diabetic foot include evaluation of the blood supply as a part of the decision-making process regarding surgical debridement. Established infections in patients with open fractures may present as nonunion and require a combination of medical and surgical treatments.

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