Asian journal of Pharmaceutical and biological research 2231-2218
http://www.ajpbr.org/
Volume 10 Issue 2
MAY-AUG 2021
10.5281/zenodo.5109414

Analysis of morphological changes in the bones after osteomyelitis and features of treatment methods

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Abstract The treatment was based on keeping the wound open for the elimination of purulent discharge and the local application of ointments and other substances. The advent of anesthesia and the expansion of surgical procedures, aswell as the discovery of antibiotics, resulted in significant changes in the clinical and surgical treatments of osteomyelitis

Keywords morphological, osteomyelitis, treatment

Introduction. The infection of bone that contains bone marrow,called osteomyelitis, is as old as humankind and continues to be an important problem for modern medicine owing to its high morbidity and sequelae. [1,2] As a medical term, osteomyelitis has been present in the specialized literature since its description by Nelaton, in 1844, as an inflammatory process of infectious origin in the bones. However, the clinical manifestation as a secretory wound after injury has been mentioned throughout history since carved plates in Sumer. The treatment was based on keeping the wound open for the elimination of purulent discharge and the local application of ointments and other substances. The advent of anesthesia and the expansion of surgical procedures, aswell as the discovery of antibiotics, resulted in significant changes in the clinical and surgical treatments of osteomyelitis. [1] Acute osteomyelitis evolves over the course of days to a few weeks and can be cured with antibiotic therapy alone. Chronic osteomyelitis (COM), on the other hand, is a relapsing and persistent infection that evolves over months to years and is characterized by low-grade inflammation, presence of dead bone (sequestrum), new bone apposition, and fistulous tracts. [3,4] The most important point in relation to chronic bone infections is the difficulty to correctly establish the etiologic agent and the proper treatment to cure the patient. [4] Nowadays, to arrest COM, most experts consider it essential to provide adequate drainage, thorough debridement, obliteration of dead space and soft tissue, wound protection, and intravenous antibiotic treatment for at least 4 to 6 weeks. [2-4] Proper selection of therapy should always be made on the basis of correct identification of the causative organism(s) and knowledge of the pattern of susceptibility. [2,3,5] The choice of bone as the ideal specimen for microbiologic diagnosis of osteomyelitis is based on common sense and a classic retrospective study of 40 patients published by Mackowiak et al6 27 years ago. More recent studies came to a similar conclusion, but data collection was retrospective, included a small number of patients, or had different objectives. [7,10] The difficulties inherent in the process of obtaining bone specimens led to new

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approaches during the last decade, with 3 studies concluding that specimens from sinus tracts and other soft tissue were as accurate as bone to identify the etiologic agents of osteomyelitis. [11,13] Together, these 3 studies evaluated 155 patients, but some experts disagree with these findings and insist that bone specimens must be the gold standard for etiologic diagnosis of COM. [11,16] In fact, it is difficult to draw definitive conclusions from these articles because they have diverse methodologic flaws, thoroughly exposed elsewhere. [7] The lack of agreement on the best sample to use for microbiologic diagno-sis of COM demands new research on the topic because mistakes in the identification of the pathogen will lead to wrong treatment, contributing further to the "no cure" stigma of this expensive illness. [5]

The French surgeon Edouard Chassaignac was the first to introduce the term osteomyelitis in 1852, when extensive debridement and early amputation were the mainstays of treatment. Lister in 1867 applied Pasteur's discoveries using carbolic acid as a disinfectant in open fracture management. Later on, Esmarch in 1873 advised removal of sequestrum and described the Esmarch rubber tourniquet as a means to avoid massive haemorrhage while performing debridement for chronic osteomyelitis. During World War I, Carrel and Dakin used continuous irrigation to chemically sterilize open fractures with good results, reportedly due to the chlorine solution used although it was stated that similar results would be obtained with an inert solution and that the value of the treatment laid in the debridement technique itself. Winnet Orr in 1927 described his technique of extensive surgical debridement followed by Vaseline gauze packing and encasing the limb in plaster cast to allow the infection to 'burn out' inside the cast. As quoted from Orr, 'leave the wound alone. Each time you touch it, you stir up troubles'. Nevertheless, it had the drawbacks of prolonged immobilization producing joint stiffness, disuse atrophy and osteoporosis. The discovery of penicillin by Fleming in 1929 marked the era of antibiotic treatment and some prophesized the eradication of osteomyelitis. Unfortunately, this has yet to be achieved and with increasing antibiotic resistance trials were eventually commenced using combined antibiotic therapy to overcome multiresistant organisms. Early concepts of leaving wounds open and discharging changed to favour early closure with obliteration of dead space. Cancellous bone chips to fill the void of debridement were first described by Hassab and Eid1 then by Papineau et al.2

A real contribution to dead space management was the development of bone transport, as described by Ilizarov. Good results were reported by many authors and the technique was later complemented by advances in soft tissue coverage. These advances have led to increased success in the management of

chronic osteomyelitis and eradication of persistent infection compared to surgical debridement and antibiotic therapy alone.

The diagnosis of chronic osteomyelitis remains a challenge. Recognition of the clinical symptoms, along with imaging and laboratory investigations are mainstays for diagnosis. The clinical features are heterogeneous and usually non-specific depending on the age of the patient, causative pathogen, area of involvement as well

as the presence of co-morbidities. The most commonly reported clinical symptoms include relapsing pain, swelling and bone tenderness with sporadic episodes of low-grade pyrexia, often associated with persistent sinus tracts with purulent discharge. These symptoms are a reflection of the pathogenesis of chronic osteomyelitis, with cyclical pain that increases in severity and subsides when pus breaks out through the sinus. It must be remembered that a Marjolin ulcer, as a result of malignant squamous cell transformation in chronic osteomyelitis, is an easily missed but serious complication with the duration of osteomyelitis being the single most important risk factor. [5,17,21]

A number of laboratory investigations can aid with the diagnosis, although all lack specificity for osteomyelitis. Raised inflammatory markers such as C-reactive protein (CRP) anderythrocyte sedimentation rate (ESR) are an adjunct to diagnosis and are useful for gauging clinical response to treatment. Typically, CRP and ESR are raised although white cell count is usually within normal limits. A normal CRP and ESR does not exclude osteomyelitis. The gold standard for diagnosis is positive microbial cultures from bone biopsies and is the most sensitive diagnostic tool. Several investigators have emphasized the need for multiple culture samples in order to increase sensitivity and to overcome the problem of contamination. Most agree that samples from five or more sites should be obtained to increase the diagnostic yield. A broth enrichment medium is usually used to enrich growth of suspected pathogens in the culture sample. Tissue samples should undergo both microbiological and histopathological analysis. Microscopy showing a significant presence of neutrophils and organisms on special stains indicates the presence of infection, even before culture results, and can show fungal spores. False-negative results can result from inadequate sampling or if samples were acquired after the start of empirical antibiotics. Conventional blood cultures are useful only in cases of haematogenous osteomyelitis. Imaging modalities ranging from conventional radiography up to novel nuclear imaging techniques are invaluable contributors to the diagnosis of osteomyelitis. Plain radiographs are cheap and widely available. Changes include osteopenia, scalloping of the cortex and loss of the trabecular architecture of bone. The appearance of these findings is usually delayed by up to 2 weeks after the onset of infection and not until at least 30%of bone density is lost. Despite poor sensitivity or specificity and delayed diagnosis, it is still helpful in excluding other conditions such as fractures or malignancies. Sinography, which is the opacification of a sinus tract by retrograde injection of contrast material, defines the course and extent of the sinus tract and its communications. Sinography may be performed using plain radiography or combined with CT for better delineation of the sinus tracts. Computed tomography (CT) provides the most detailed imaging of the cortical bone, and excels over other modalities in its ability to identify sequestrum, periosteal reactions and sinus tracts. It is useful both for diagnosis and surgical planning.3 However, it is important to mention that in the presence of metalwork, there is substantial loss of image resolution and artifacts limit its reliability in such cases. Magnetic resonance

imaging (MRI) is more accurate in assessing bone marrow and soft tissue changes that usually precede any bony changes, allowing earlier diagnosis. It provides excellent spatial resolution and so can differentiate between intraan extra-osseous involvement or bone from soft tissue infections. Nevertheless, its value is limited in the presence of implant, fibrous tissue and recent surgery. Intravenous gadolinium contrast MRI better differentiates between necrotic areas and fibrotic areas, such as in cases with previous surgical procedures. Ultrasonography (US) is mainly used in the early stages for detecting purulent collections under elevated periosteum. Some authors suggest that in some cases it can be diagnostic and particularly helpful in directing guided biopsies, but reliable estimates of its specificity and sensitivity are yet to be determined. It is particularly useful in regions that are complicated by metal instrumentation and therefore might not be well visualized with MRI or CT, or in patients where MRI is contraindicated. Bone scintigraphy has limited specificity and false-positive results occur particularly in cases of mechanically unstable non unions or crystal arthropathies, although it is less affected by metal artifact. Several agents have been studied, including technetium-99melabeled methylene diphosphonate (99mTc-MDP), gallium-67 citrate, and indium-111-labelled white blood cells. Technetium-99m three-phase scans show accumulation of isotope in areas of increased blood flow and reactive new bone by adsorption into the hydroxyapatite crystals. On the other hand, gallium attaches to transferrin, which leaks from the blood-stream into areas of inflammation or infection but it does not specifically bind to bone. This indicates that gallium scans are more specific for infection, correlating more closely to it than do technetium scans. [4] It may reveal osteomyelitis even when technetium scans show decreased activity or cold lesions.Leukocytes tagged with indium-111, similarly to gallium-67,do not show bony detail or distinguish osteomyelitis from soft tissue infections but are more specific for infection. The use of radiolabelled antibiotics is a novel technique offering even better differentiation between infection and sterile inflammatory lesions. The compound most extensively studied is 99mTc-ciprofloxacin. [1,2,5] A similar technique uses nuclear monoclonal immunoglobulins to tag leukocytes at areas of infection. The sensitivity for detection of osteomyelitis can reach 100% in lower leg and ankle infections using this modality. [6] Positron emission tomography (PET) using fluorine-18 luorodeoxyglucose (FDG), however, has the highest sensitivity and specificity and its use is only limited by the high costs.7 FDG has an affinity towards inflammatory cells, which usually have increased expression of glucose transporters, and so their differential FDG uptake is abnormally increased.

Acute and chronic osteomyelitis are discussed, with presentation of the general epidemiological concepts and the commonly used classification systems. The main guidelines for the clinical, laboratory and imaging diagnosis of infections are discussed, as well as the guidelines for surgical and antimicrobial treatments, and the role of hyperbaric oxygen as adjuvant therapy. [4, 11,16]. Until now, a unified surgical tactic has not been developed, which leads to many methods of surgical

treatment [2, 5, 6].The urgency of the problem of treating chronic osteomyelitis (CO) is determined by the significant prevalence of the disease due to the steady increase in injuries, as well as the severity and duration of the pathological process, the difficulties of prevention and treatment of this disease [3,7,13,16]. The pathomorphological basis of chronic osteomyelitis is a complex of ischemic, infectious-inflammatory and reparative changes in the bone and surrounding soft tissues. These structural and functional changes are determined by the characteristics of the causative agents of the infectious process, the nature and severity of inflammatory and proliferative processes in the affected area. [8,9,14].

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