Diagnostic methods for Osteomyelitis

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ABSTRACT

Osteomyelitis is a progressive disease caused by a microorganism damaging bone tissue through infectious and inflammatory phases. It is defined as the infection of bone. Although new effective treatment methods have been developed recently, osteomyelitis is challenging to treat, and successful treatment is still far from satisfactory levels. Proper osteomyelitis staging, appropriate microbiological sampling, and antimicrobial and surgical treatment are of importance in successful treatment. Osteomyelitis complications which our study is based on are particularly various. Failure in medical or surgical osteomyelitis treatment results in recurrence of the infection. In severe cases, amputation may be required for infection control. In our study, we explain diagnostic methods used for 24 patients with chronic femur and tibia osteomyelitis whom we treated, as well as effectiveness of such methods in surgical planning and their results. They were followed up for about 3 years. It was found that CRP and leukocyte, X-ray changes, MRI images and microbiological examination were sufficient for diagnosis in our patients; macroscopic imaging corresponds to X-ray and MRI findings during surgery; bacteria isolated from debridement materials during surgery is the same as those taken preop; laboratory and MRI images during follow-up correspond to patient clinics. We found that laboratory, radiological and microbiological methods used are sufficient for surgical planning and patient follow-up.

INTRODUCTION

Osteomyelitis is bone and bone marrow inflammation. Bone infection mainly influences periosteum, cortex and bone marrow [1]. Osteomyelitis is a progressive disease caused by a microorganism damaging bone tissue through infectious and inflammatory phases [2-7]. Osteomyelitis is pathology characterized by inflammatory destruction, necrosis and new bone growing as a result of invasion of microorganisms in several components of bone such as periosteum, medullar cavity and cortex [4,8] [Figure 2-3]. Osteomyelitis is an inflammatory case including destruction in bone tissue caused by osteomyelitis microorganisms. Infection can influence an area limited to only one layer of bone tissue, or a wider area including medullary canal, bone marrow, cortex, periosteum and periphery soft tissue [7,9,10] (Figure 1).

Fig. 1: Bone tissue appearance.

Bacterial agent may be transferred into bone through either blood flow or direct neighboring infection area or penetrant injuries. Although it is commonly seen in children under the age of 2 or those between 8-12 years, the infection can be found at all ages. During childhood, it is found two times more in males than females [1]. In osteomyelitis, necrosis and sequestrum growing is observed in bones. Microorganisms can infuse skeletal system through hematogenous or neighboring [9]. Children with sepsis often develop skeletal system complications. Mostly, metaphysis of long bones is kept, and particularly S. aureus, streptococci, gram

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negative bacillary (such as H. influenza, E. coli and so on) bacteria are active. In adults, osteomyelitis is seen more as vertebra involvement due to bacteremia [1,11]. Many antibiotics with different pharmacodynamic and pharmacokinetic characteristics are used for treatment. Treatment also includes the surgical methods including muscle grafts and ilizarov techniques and the bone cements with antibiotics [5,12]. Despite increased antibiotics variety and effectiveness and improved operating room conditions and operation techniques, bone and joint infections are hard to diagnose and treat, and they may cause severe morbidity, permanent impairment, paralyze and even death [4,8]. With treatment options and developed antibiotics, there has been decrease in death caused by osteomyelitis. Sequel rate seen as a result of disease complication has decreased to 5% [7].

Etiology:

Osteomyelitis is bacteriogenic, which has two types of growing: A) osteomyelitis caused by hematogenous spread and B) osteomyelitis caused by contamination (surgical, traumatic, neighboring infection-focused) [1,7,14]. Acute hematogenous osteomyelitis is mostly seen in children. Caused by microorganisms that spread systemic circulation and reach bones, bacteremia occurs almost every day during childhood. Infection is caused by local reasons in bone tissue (trauma) and low systemic defense (immunodeficiency syndromes, diabetes, malnutrition, chronic diseases, etc.). As abscess grows, bone marrow pressure increases and more bones become segment avascular. Abscess tissue spread more after inoculation [1,7,15]. Intramedullary oxygen pressure decreases, and environment becomes acidic [5]. Finally, purulent material drills cortex, spreads into subperiosteal areas and periphery soft tissues, and fistules into the skin. If the infection is not treated completely during acute period, sequestrum growing and chronic osteomyelitis is inevitable. However, osteomyelitis caused by contamination after compound fractures and surgery is infections mostly seen by orthopedists [1,7,16].

S. aureus, Streptococcus (S.) agalactiae and E. colikan are microorganisms produced mostly as bone culture in hematogenous osteomyelitis. In children, these are S. aureus, S. pyogenes and Haemophilus influenza. Salmonella and Pseudomonas Aeruginosa is also seen [4,17,18].

In adults, Neisseria gonorrhoeae (N. Gonorrhoeae), S. aureus [4,19] and S.epidermidis are found more. While patients with anemic are susceptible to Salmonella spp and S. aureus, those who use intravenous substance are susceptible to Pseudomonas aeruginosa and S. aureus. Haemophilus influenza causes infection in infants and children [4,20]. S. aureus is the most frequent factor in vertebral osteomyelitis.

Aerobic Gram negative bacillary causes 30% of infectious especially related to hematogenous spread caused by urinary system infection. Coagulase Negative staphilococcus, S. Aureus and Gram Negative bacillary are the common agents of vertebral osteomyelitis followed by medulla spinalis surgery, regardless of a spinal device installation [5,21,22].

Whether osteomyelitis occurs in the hospital may also be a clue for the agent. It is known that in this case, gram negative bacillary and resistant enterococusses are more likely to be agents. It is found that if fungal osteomyelitis occurs after prosthesis in chronic patients who receive intravenous treatment for a long time, the agent can be S.epidermidis, Propionibacterium acne and diphtheroids [4].

Pathology:

In microscopic examination of acute osteomyelitis, acute suppurative inflammation caused by invasion of bacteria or other microorganisms is found [10]. Acute hematogenous osteomyelitis occurs as a result of infusion of the agent into bone metaphysis through vessels. Various inflammatory factors and leucocytes cause damage in tissue, bone trabecula and bone matrix. Due to vascular structures that become squeezed and obliterated through inflammatory processes, ischemia increases and contributes to bone necrosis. If bone segments deprive of blood flow, effectiveness of antibiotic treatment on bacteria decreases. Reactive hyperemia develops with increased osteoclastic activity in infarct area. This activity leads into bone loss and localized osteoporosis. However, new bone growing may be also seen [9,10]. Due to characteristics of veining in children, agent bacteria are localized in metaphysisis sinusoids. Abscess caused by protective role of epithysal plaque tears thin periosteum, and subperiosteal abscess occurs. It is hardly influenced by diaphysis infection, and endosteal circulation of bone is not at risk, so excessive sequestration does not occur and the process does not result in chronic infection. On the other hand, osteomyelitis in children causes extremity deformity, due to damage in epiphysis and epiphysial plaque [1,23]. In children over the age of 2, while epiphysial plaque is still able to prevent the spread of infection from epiphysis to metaphysis, metaphysical cortex has become thicker. Abscess is most likely to spread diaphysis and endosteal circulation [1,23]. As a result of periosteum diverging from bone sue to abscess, periosteal blood flow becomes under risk, which results in excessive sequestration and chronic osteomyelitis. After epiphysis is closed, acute hematogenous osteomyelitis is rarely seen. However, exogenous osteomyelitis is seen more often. Infection may come out from any part of the bone, abscess growing is slow, and wide sequestrum occurs rarely. This phase may result in pathological fracture. With granulation tissue that occurs as the disease becomes chronic, osteoclastic and osteoblastic activity increases. As a result of such increase, necrotic bone is absorbed and replaced with newly grown bone tissue. Dead cortex is absorbed beginning from the surface, and it forms sequestrum, diverging from live bone.
Proteolitic enzymes and osteoclasias begin damaging activity in sequestrum. Therefore, there is a bone whose surface is nibbled in an irregular form. In long-term chronic osteomyelitis, there is a wide space and sequestrum in the bone. Diaphysis becomes thicker and more irregular. Infection in the bone influences periosteum, cortex and bone marrow [1,24].

Pathological characteristics of chronic osteomyelitis is dead bone tissue, new bone tissue formation in necrotic bone area, lymphocyte and histiocyte in huge amounts, and mononuclear cell infiltration that sometimes occur in plasma cells [10], it can be summarized as chronic inflammation tissue [1]. New bone growing, which is also known as involucrum [10], is provided by periosteum and endosteme that remains solid within the dead bone tissue [1]. Involucrum has a highly irregular structure. Soft tissue around the infected bone is perforated by purulent material in time, reaching through the surface and may form sinus tract [10]. By this way, purulent material reaches through the surface and takes the form of sinus edge. With ongoing bone tissue formation, thickness and density of involucrum increase in some parts or whole of diaphysis [1]. Involucrum may grow so dense that it can form parts of whole of a new diaphysis [10]. New bone growing continues for weeks or months as long as the infection continues [1,5,10]. Space left after the removal of dead bone tissue through medical or host defense can be filled with new bone tissue particularly in children. It can also be cavitated or filled with fibrosis tissue, or sometimes reached into skin surface through sinus tract [10,25].

Classification Of Osteomyelitis:

There are many types of osteomyelitis: acute osteomyelitis, chronic osteomyelitis, vertebral osteomyelitis, prosthesis-related osteomyelitis, brodie abscess, tuberculosis osteomyelitis, infection of intervertebral disk space (discitis), fungal osteomyelitis [4] and so on.

Osteomyelitis can be divided in different figures. These classifications change according to time period of the disease, age of the patient, presence of an underlying factor, host factors, agent microorganism, forming mechanism of the infection, and reaction of the host to infection [4,17,26,27]. In our study, classification according to time period of the disease is addressed.

Osteomyelitis According to Time Period of the Disease:

Acute:

Presence of systemic findings, but lack of bone change means that story dates back less than 10 days ago [1,24]. Acute osteomyelitis is usually used for the first 6 weeks when there are acute inflammation findings, peristitis is present, and radiological radiolucent view appears [22,29]. In acute osteomyelitis, clinical findings change according to severity of the disease, its location, degree of infection spread, process of the incident, and age and resistance of the patient [5,29].

Exogenous:

Trauma exists in medical story, and it is more often in diaphysis, polymicrobial contamination occurs in culture, and it is seen more often in areas with limited blood build-up [1,24].

Endogenous (Hematogenous):

These are nontraumatic and seen mostly in metaphyseal area with high blood build-up. S. aureus is the most isolated pathological [1,24].

Subacute:

Presence of bone change accompanied by light systemic findings, but lack of previous attack means that story dates back more than 10 days. It is a stealthy and mild form of osteomyelitis that has fewer symptoms. In this type, there are microorganisms with low virulence or patients with high resistance. The agent is mostly S. aureus. There is pain which will not make the patient see a doctor for weeks. Function loss is minimal [1,24]. If the virulence of microorganism is low, and there is balance with body resistance, inflammation reaches a limited level in terms of settlement and subsequent symptoms [5,29].

Chronic:

Notwithstanding the presence of systemic findings, bone change occurs. There is past infection attack(s) in the story. It can be seen due to soft tissue infections in patients with insufficiently-treated acute osteomyelitis, trauma or low immune resistance. COM is mostly seen due to osteomyelitis related to peripheric vessel disease or osteomyelitis spread from neighboring center [4,28]. Prognosis of chronic osteomyelitis is more severe than that of acute osteomyelitis. Treatment failure rate in COM is higher than that of acute osteomyelitis. Moreover, their treatment is different. It is hard to eradicate completely COM. Even if systemic symptoms of osteomyelitis become moderate; purulent material, infected granulation tissue and sequestrum may remain in one or a few centers in bone tissue [4,28] [Figure 2-3-4].
Fig. 2: Xray of the my patient who was operated by me and 24 years old has tibial chronic osteomyelitis.

Fig. 3: MRI of the my patient who was operated by me and 28 years old has tibial chronic osteomyelitis.

Fig. 4: MRI of the my patient who was operated by me and 28 years old has tibial chronic osteomyelitis.

The most significant finding in chronic osteomyelitis is fistula. In subacute period before fistula opening, there is local pain, redness, swelling and increased temperature. Pain is released after the fistula edge opens and inflammation is decompressed [29].

a. Active chronic osteomyelitis
b. Inactive chronic osteomyelitis [29].

Effective Factors in Osteomyelitis Development:

Factors that are effective in prevalence and severity of the infection and its treatment reaction can be considered as those related to microorganism, patient and surgeon, and treatment method. Microorganism community usually as stable during one’s life (regular skin and mucosal flora) may help immune system by sticking to harmful pathogeneses, or may be the main reason for the development of disease. Such behaviors of
regular flora are affected by different factors such as pH, temperature, oxygen level and nutrition in the environment [1,7].

One of the effective factors in osteomyelitis development is one’s regular skin and mucosal flora. Microorganism community usually as stable during one’s life (regular skin and mucosal flora) may help immune system by sticking to harmful pathogeneses, or may be the main reason for the development of disease. Hidden areas such as axilla, perineum and interdigital carry more bacteria than such open areas as arms and body. As sweat, temperature and lipid layer over the skin increase, it is more likely to see gram negative bacterial [1,7,30].

Prevalence of wound infection after prosthesis operations is nearly 2%. The most frequent microorganisms in such infections are S. aureus and S. epidermidis. S. epidermidis is the predominant microorganism of regular aerobics skin flora. S. aureus is located more in nasal space and perineum area, and it comprises of 10-40% of the flora. The colonization rate in those with skin disease such as mother of pearl and atopic dermatitis reaches 80%. Other microorganisms in skin flora are propionibacteria, streptococcus and gram negative bacillary [1,7,30].

Clinical Findings:

In acute hematogenous osteomyelitis, the most frequent symptoms and findings in children are acute infection findings and local inflammation such as fever, irritability and lethargy; continuous pain in related joint or bone; shivering; vomiting; stomach ache; swelling, increased temperature, redness, uneasiness, exhaustion and irritability [5,10,31]. If there is involvement in lower extremity, load avoidance and hobbling may be seen. Affected extremity is usually involved in flexion, and spasm occurs usually in periphery muscle tissue [25]. Osteomyelitis in adults generally progresses with ambiguous symptoms in subacute and chronic table. When applied, there is usually an extremity pain continuing intervally for 1-3 months. While systemic findings and symptoms are not observed, non-specific pain may be experienced around the related area. Fever, chills, local swelling and erythema in the related bone proximal are rarely seen. There may be resistance through sinus tract from the related bone area, but this generally develops in months and years [5,10,31] 35% of primary bone infections comprises of subacute osteomyelitis. Mild temperature is rarely seen. Only stable finding supporting the diagnosis is mild-moderate pain. While chronic osteomyelitis results in local bone loss, necrotic tissue areas (sequestrum) and sclerosis development, patients apply mostly due to pain and flix complaint. Local edema and soft tissue abscess may grow in such cases [21]. In patients with vertebral osteomyelitis generally experience severe back ache and fever that do not decrease with resting and may increase to wearing levels [4,8,21]. In vertebral osteomyelitis related to sepsis; there may be overall state disorder, chills, increased temperature with shivering, tachycardia, and predisposing factors such as urinary infection, urinary catheterization, I.V. catheter infection and hemodialysis. However, it is more frequent to progress with mild systemic findings. Main complaints are back ache and neck ache. In cases with brucella spondylodiscitis, there is also arthralgia, fever and night sweating. If osteomyelitis is caused by neighboring, there is flix, pain, vulnerability, swelling and redness in wound or incision area [11].

Diagnosis:

Radiological, microbiological and pathological tests should be examined all together for osteomyelitis diagnosis [32].

- Laboratory findings:

Leukocytosis is seen in acute osteomyelitis attacks [4]. Erythrocyte sedimentation rate (ESR) and C-reactive protein (C-RP) generally increases [10,33]. Sedimentation may increase after risky surgery operations or trauma, so ESR measurement is not a reliable test [5,10]. CRP is an acute phase reactant whose level in blood increases during inflammation or tissue damage. If treatment is successful, CRP decreases faster than ESR. Although CRP is a more reliable test than ESR, it is not enough alone [5,10,34]. The number of leucocytes may increase in acute osteomyelitis and polymorphonuclear leucocyte is dominant in periphery spread, but it is generally normal in chronic osteomyelitis. It is suggested to measure the number of leucocytes, ESR and CRP levels in patient follow-up. The most appropriate approach is once in two weeks during treatment and at the end of treatment [5,10,29].

- Radiological findings:

Imaging methods are of importance in osteomyelitis diagnosis. About 2-3 weeks after the infection; swelling in direct graphillary and soft tissue, intraarticular narrowing or enlargement, bone destruction, and periosteal reaction may be observed [35]. Bone destruction may not be seen in direct film until 10-21 days after the infection [36], [Figure 2]. Ultrasonography is a useful method in early diagnosis of acute osteomyelitis or the diagnosis of purulent material in soft tissue [9]. If conventional radiography is normal, with their high resolution power, Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) methods [Figure 3-
I reveals early bone marrow edema, and therefore it is much more sensitive than CT in soft tissue examination. MRI reveals early bone marrow edema, and therefore it is the most effective radiological application in early diagnosis of the infection [37]. Various radiopharmaceuticals are used for bone scintigraphy. One of the most frequently used ones is metilen diphosphonate, which is bound to areas with bone metabolic activity and is particularly sensitive in early diagnosis of acute osteomyelitis [5]. Leukocyte scintigraphy and combined bone-gallium scintigraphy are other methods used for diagnosis. Specificity and sensitivity is high in demonstration of the infection [14]. Positron emission tomography (PET) applied by using 18-Fluoro-D-deoskiglikoz (FDG) is a high specific and sensitive examination in terms of diagnosis after FDG involvement. It is the best method especially in the diagnosis of chronic osteomyelitis, and it is an examination to be preferred in cases with suspicious diagnosis [38]. Combination of FDG-PET and BT is of high importance in the description of lesions and demonstration of inflammatory activity [39]. Radioactive-marked antibiotics are used with sterile inflammatory lesions to distinguish infection-related osteomyelitis [4,5,10,29].

- **Microbiology:**

  It is significant to know microorganism type and its invito sensitivity for proper medical treatment. For the diagnosis of microorganism; histopathological examination of the tissue obtained through needle aspiration as well as surgery sampling and radiology should be made, and gram coloration, anaerobe and aerobic cultures should be applied. A common application is swab culture taken from drained liquid and wound. $S$. aureus produced from superficial cultures correlates highly with deep tissue cultures. In other microorganisms, correlation with deep tissue cultures is weaker [4,5,10,29,41].

**Implementation:**

For 24 patients (average age is 34.45) with chronic osteomyelitis (16 with tibia and 8 with femur osteomyelitis) who applied to us for different reasons (pain, fistula, walking difficulty, swelling on the diseased part etc); 1) Bilateral direct graphics were taken [Figure2]. 2) MRI [Figure 3–4] was made. 3) Sampling were taken from fistula edge and deep tissue for patients who did not use antibiotics. 4) CRP and leukocyte was observed. 5 of our 24 patients had surgery for their chronic osteomyelitis in the past and they had recurrence of the disease. 8 of the 24 patients had their disease because of the fracture surgery they had in the past.

After patients were determined to have chronic osteomyelitis, with general or epidural anesthesia; fistula tract was excised, enough cortical window was opened in bone tissue with chronic osteomyelitis, a wide debridement was made and bleeding bone tissue was reached, surgical area was continuously washed. We took sample for microbiology and after that gived prophylactic antibiotics to the patient. Muscle interposition was applied to medulla through bone window. All layers were closed with drain. The part of tissues debrided from the patient were sent for microbiological examination. After the surgery, all patients started to use proper antibiotics according to culture antibiogram. We isolated $S$. aureus in 19 of our patients and $.epidermidis$ in 5 of our patients. Patients were followed up in outpatient clinics. Their wounds were healed without any infection. All patients didn’t had any complication and activation of chronic osteomyelitis during follow up. All the patients had good walking gait without any pain and no need to any supporting device. They were followed up for about 3 years. For follow-up, CRP, leukocyte and MRI were requested.

It was found that CRP and leukocyte, X-ray changes, MRI images and microbiological examination were sufficient for diagnosis in our patients; macroscopic imaging corresponds to X-ray and MRI findings during surgery; bacteria isolated from debridement materials during surgery is the same as those taken preop; laboratory and MRI images during follow-up correspond to patient clinics.

**Discussion:**

Chronic osteomyelitis is a disease that usually requires surgery and has a high recurrence rate [10,28]. Pathological characteristics of chronic osteomyelitis is dead bone tissue, new bone tissue formation in necrotic bone area, lymphocyte and hystioocyte in huge amounts, and mononuclear cell infiltration that sometimes occur in plasma cells [10], it can be summarized as chronic inflammation tissue [3]. Prognosis of chronic osteomyelitis is more severe than that of acute osteomyelitis. Treatment failure rate in chronic osteomyelitis is higher than that of acute osteomyelitis. Because of these reasons, chronic osteomyelitis is very important disease and we study on this debilitating disease.

In our study, we used the 24 patients who had long bone (femur and tibia) chronical osteomyelitis so this may be the limitation of study because of number of the patients and not including many kinds of the bones, we need the studies including everykind of the bones and done with more patients ( Figure 2–3–4).

5 of our patients (20.83 %) had a surgery in the past because of chronical osteomyelitis and we followed our patients for 3 years, so rate of these patients had surgical treatment in the past is low in our patients and our follow up of the patients is just 3 years, because of this the good result (all patients did not have recurrence of
A microorganism damaging bone tissue through infectious and inflammatory phases. Treatment in bone and joint infections is challenging and may take longer due to several anatomic and pathological characteristics. Radiological, microbiological, and pathological tests should be examined all together to diagnose osteomyelitis. The number of leukocytes, sedimentation, CRP controls as well as radiological controls can be repeated periodically in patients. Long-term treatment of skeletal system complications in patients with infection requires an enduring approach by patients and physicians.

Our patients applied to us with many problems (pain, fistula, walking difficulty, swelling of diseased part etc) because of chronic osteomyelitis of tibia and femur. We treat all of the patients with the same surgical technique (bone debridman and muscular interposition) and antibiotics treatment according to microbiological results. We got no recurrence with all the patients during 3 years follow up.

We found that all treatment and follow-up phase of the patient can be planned through clinical, laboratory (CRP and sedimentation), microbiological and radiological (MR and X-ray) examination in cases with chronic osteomyelitis. We assume that there is no need for high radiation tests such as scintigraphy and computerized tomography in many patients, and so such examinations should only be made for specific patients. Chronic osteomyelitis is lifelong disease and the patients have to apply doctors and done many radiological examination like direct x rays, computed tomography, sintigraphy including radiation which can harm so we must use the tests we need certainly like we do and show in this study.

REFERENCES