LETTER TO THE EDITOR / EDİTÖRE MEKTUP

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Hodgkin's Lymphoma Mimicking Chronic Osteomyelitis

Kronik Osteomiyeliti Taklit Eden Hodgkin Lenfoma

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Dear Editor,

Osteomyelitis is an infection with progressive destruction by involving various components of the bone (periosteum, medullary cavity, cortex). Osteomyelitis is classified as hematogenous or non-hematogenous, and acute or chronic. Symptoms in acute osteomyelitis last for a few days or weeks, while in chronic osteomyelitis it can last for months or years[1]. Bone destruction, which is common in chronic osteomyelitis, may also develop due to non-infective pathologies such as avascular necrosis of bone, bone tumors, charcoat arthropathy and lymphoma[2]. Patients with Hodgkin's lymphoma (HL), which is one of the non-infectious causes, with symptomatic bone involvement may present with findings similar to chronic osteomyelitis[3]. In this article, it was aimed to present a patient who was referred to our clinic with a pre-diagnosis of chronic osteomyelitis, did not respond to appropriate antibiotic therapy, and diagnosed as having HL as a result of further investigations.

A 24-year-old male patient with no known chronic disease or history of trauma was admitted to an orthopedic clinic in another center with complaints of right shoulder pain and a wound drainage on the right scapula continuing for nine months. Because his complaints did not regress despite using various oral and parenteral antibiotics, he was referred to our orthopedic clinic. A bone tissue sample was obtained by applying wound debridement to the patient whose discharge continued. No imaging was done before debridement. *Streptococcus salivarius* (with VITEK® MS, France automated system) was grown in bacteriological culture, The European Committee on Antimicrobial Susceptibility Test[4] was used for antimicrobial susceptibility. Penicillin, cefotaxime, vancomycin and teicoplanin were detected as sensitive. Direct mycobacteriological examination did not reveal acid-fast bacilli and tuberculosis polymerase chain reaction test was negative. Histopathological examination revealed lymphoid cells showing intense compression artifact between the bone trabeculae, and mild fibrosis, and the findings were evaluated in the direction of a nonspecific inflammatory reaction. The patient was referred to our clinic with a pre-diagnosis of chronic osteomyelitis and ampicillin/sulbactam was started with a dose of 8 g/day, intravenously (IV). In laboratory tests, leukocyte count was 12,880/m^3 (70% PNL), hemoglobin 12 g/dl, platelet count 300,000/mm^3, C-reactive protein (CRP) 8 mg/dl (n<0.05 mg/dl), erythrocyte sedimentation rate (ESR) 70 mm/hour, and liver and renal function tests were normal. There was no fever in the follow-up, and there was no growth in the two sets of blood cultures sent in the absence of fever. Human immunodeficiency virus, syphilis and brucella serologies were negative. A dental consultation was requested in terms of possible dental pathologies that could cause osteomyelitis, and no pathological finding was found. Echocardiography performed with the pre-diagnosis of infective endocarditis was evaluated as normal. Since clinical and laboratory response could not be obtained with ampicillin/sulbactam treatment given for 15 days, the

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antibiotherapy was arranged as ertapenem with a dose of 1 g/day IV. Ertapenem treatment was also administered for eight days, but clinical and laboratory response was not achieved. Right axillary superficial tissue ultrasonography (USG) showed multiple lymphadenomegaly with spherical appearance, the largest of which was 30x20 mm in size, some with preserved fatty hilus and some with erased fat hilus. Since USG was performed with a pre-diagnosis of osteomyelitis in the right scapula, it was thought that lymphadenomegaly might belong to the infection, but it was stated that distinction between infection and infiltration could not be made radiologically, and further investigations were recommended. Whole body computed tomography (CT) was performed in terms of differential diagnoses due to USG findings and osteomyelitis with atypical localization. An extrapleural soft tissue lesion with a thickness of 1 cm located near the sternum and a lesion causing destruction and periost reaction in the scapula were reported and it was recommended to investigate lymphoproliferative diseases (Figure 1). Peripheral smear showed no pathology and excisional lymph node biopsy was made from the axillary region, and histopathological examination was reported as "nodular sclerosis HL, grade 1". The patient was consulted with the hematologist, and with the diagnosis of nodular sclerosis HL accompanied by extranodal bone involvement, chemotherapy and autologous bone marrow transplantation (ABMT) were planned. The patient was transferred to the hematology clinic. During his two-year follow-up, complete remission was achieved with chemotherapy. The follow-up of the patient, who underwent ABMT, continued.

Hodgkin lymphoma is a characteristically painless, progressive nodal B cell neoplasia with lymphadenopathy, most commonly located in the cervical region and then mediastinum[3]. Its incidence in Europe is 2-3 per 100 thousand people annually. It constitutes 10% of all lymphomas and 0.45% of all cancers in the United States[5,6].

It is divided into two groups as classical type HL and lymphocyte and nodular lymphocyte predominant HL. Nodular sclerosis HL is the most common subtype of classical type HL. It is more common in adolescents and young adults, and is most frequently located in the cervical, supraclavicular, and mediastinal regions[6]. Extranodal involvement is seen in <1% of all patients with HL and the most common areas of involvement are; gastrointestinal system, pulmonary system, central nervous system and bone tissue[7]. Although our patient was young in accordance with the literature, he presented with atypical bone tissue involvement in the right sternal and scapular regions.

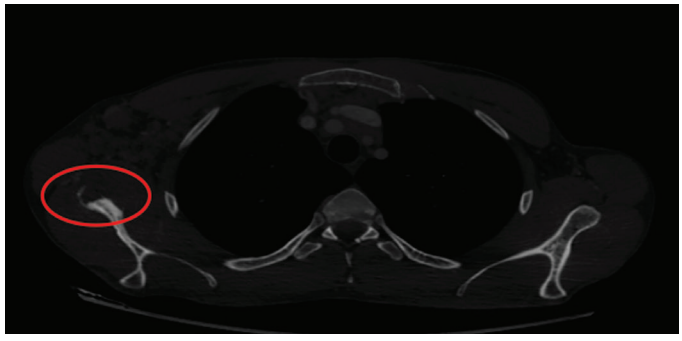

Figure 1. Destruction and periosteal reaction in the bone structure starting from the neck of the scapula on the right and continuing along the lateral edges of the right scapula

Chronic osteomyelitis often involves vertebrae and extremities by hematogenous or non-hematogenous (surgical, trauma, etc.) routes[2]. Gram-positive cocci (especially *Staphylococcus aureus*) are usually detected as causative agents, while pathogens such as Gram-negative bacilli (*Pseudomonas aeruginosa, Serratia marcescens*), *Mycobacterium tuberculosis, Brucella* spp., *Propionobacterium acnes,* and *Bartonella henselae* are found less frequently[2]. In the bacteriological examination of the debridement material of our patient, *S. salivarius* was grown. Culture growth was evaluated in favor of soft tissue infection accompanied by secondary bacterial infection.

Chronic osteomyelitis and malignancies such as HL with bone involvement can often be confused because of the similar initial symptoms and signs. Isolated bone involvement without extraosseous disease is seen very rarely as in our patient[3,8,9]. Generally, patients present with nonspecific complaints such as prolonged bone pain, subfebrile fever, and fatigue in both[8,9]. Erythrocyte sedimentation rate and CRP levels are often found to be high. In our patient, ESR was 70 mm/hour and CRP was 8 mg/dl at admission. Visualization of the bone, regardless of the modality used, is also insufficient to distinguish HL from osteomyelitis[10]. In our patient, further imaging was not performed due to the inability to distinguish infection and infiltration with USG and CT, and excisional lymph node biopsy was applied. He was diagnosed as having HL as a result of biopsy, like other similar patients in the literature[3,8,9].

As a result; in patients with bone destruction, it is not always possible to distinguish osteomyelitis and other non-infectious processes, especially malignancies, by clinical features, elevation of inflammatory markers and imaging methods. Non-infectious etiologies and other causes should be kept in mind especially in patients with atypical localization, recurrence, no pathogen detected, or without clinical and laboratory responses despite appropriate antimicrobial therapy. It should be kept in mind that pathological examination of the bone tissue may not be diagnostic, and other histopathological examinations such as excisional lymph node biopsy are recommended.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.A., H.P., M.I.T., Concept: D.A., M.I.T., D.S., Design: M.I.T., D.S., Data Collection or Processing: H.P., D.S., M.I.T., Analysis or Interpretation: O.R.S., H.P., M.I.T., D.S., Literature Search: D.A., S.M., M.I.T., Writing: D.A., S.M.

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