

Bone scintigraphy in acute myeloid leukemia patient with fungal vertebral osteomyelitis

Fungal vertebral osteomyelitli akut myeloid lösemi hastasında kemik sintigrafisi

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Abstract

The result of the magnetic resonance imaging (MRI) study was reported as “metastasis of primary disease on L2-L3 vertebrae” in a 63-year-old male patient, who developed a back pain after receiving four courses of treatment for AML. The patient, who did not respond to pain medication, was sent to nuclear medicine department for a bone scintigraphy. Diffuse increased osteoblastic activity was reported on L2-L3 vertebrae with a suspicion about infection or fracture, together with a focal osteoblastic activity involvement in the right sacroiliac joint in the bone scintigraphy which was made with Tc99m-MDP. In the mean time, the patient complained about progressive loss of strength on bilateral lower extremities and numbness in legs. Repeated MRI was reported as “irregularities in L2-L3 vertebral disc region concordant with infection, prominent thecal pressure, loss of height in L2-L3 vertebrae associated with osteomyelitis and a mass concordant with paravertebral abscess and granulation tissue”. The patient was operated and necrotic tissue was removed by curettage, relieving the compression on L2-L3 and on the disc distance. In culture examination of the sample “candida albicans” was isolated. Antifungal treatment with Amphotericin B was started. Patient's pain was reduced and MRI findings showed some regression in abscess following the treatment. There was improvement in neurological examination. However, relapse in AML was observed in bone marrow aspiration, performed during follow-up and chemotherapy was started again. On the second day of chemotherapy high fever started and cellulitis developed on the right leg. The patient received hemodialysis treatment due to increase in BUN and creatinine levels. Pulmonary edema and associated respiratory insufficiency was developed and the patient died. Fungal infections are one of the most important clinical problems in leukemia patients. However, vertebral osteomyelitis secondary to fungal infection is relatively a rare condition and delay in diagnosis and treatment may led to serious neurological problems. Suspicion of a probable fungal infection by clinicians seems vital in such cases. Bone scintigraphy has no place in routine evaluation of leukemia patients. However, we consider that bone scintigraphy should be kept in mind in the first stage of evaluation of such cases, together with other radiological examination, we think that evaluation with consideration of three-phase bone scintigraphy would be beneficial.

Keywords: Candida, acute myeloid leukemia, bone scintigraphy, vertebrae osteomyelitis

Özet

Akut miyeloid lösemi (AML) nedeni ile 4 kür tedavi aldıktan sonra, bel ağrısı gelişen 63 yaşındaki erkek hastada yapılan MR incelemesi raporu “L2-L3 vertebrada primer hastalığın metastazı” idi. Ağrı medikasyonlarına yanıt alınamayan hasta, nükleer tıp bölümüne kemik sintigrafisi için gönderildi. Tc-99m MDP ile yapılan kemik sintigrafisinde, enfeksiyon veya kırık şüphesi uyandıran, L2-L3 vertebralarda diffüz osteoblastik aktivite artışları bununla birlikte, sağ sakroiliak ekleminde fokal, osteoblastik aktivite tutulumu izlendi. Bu sırada hastada bilateral progresif alt ekstremelerde güç kaybı ve bacaklarda uyuşma şikayetleri gelişti. Tekrarlanan MR “L2-L3 vertebra disk mesafesinde enfeksiyon ile uyumlu görünüm, belirgin tekal bası, L2-L3 vertebralarda osteomyelite bağlı yükseklik kaybı, paravertebral abse ve granülasyon dokusu ile uyumlu kitle görünümü” olarak rapor edildi. Hasta operasyona alındı ve L2-L3 dekompresyon ve disk mesafesinde küretaj yapılarak nekrotik doku temizlendi. Gönderilen numunenin kültür incelemesinde “Candida albicans” üredi. Amphotericin B ile antifungal tedavi başlandı. Tedaviyi takiben hastanın ağrılarında azalma oldu ve MRI bulguları abscede gerileme gösterdi. Nörolojik

muayenede düzelme vardı. Ancak takipleri sırasında yapılan kemik iliği aspirasyonunda, AML'nin nüks ettiği saptandı ve yeniden kemoterapiye başlandı. Kemoterapinin 2.gününde yüksek ateş, sağ bacakta selülit gelişti. BUN ve kreatinin düzeylerinin yükselmesi nedeniyle hasta diyalize alındı. Akciğer ödemeine bağlı solunum yetmezliği gelişti ve hasta kaybedildi. Fungal enfeksiyonlar, lösemili hastalarda en önemli klinik sorundur. Bununla birlikte fungal enfeksiyonlara sekonder gelişen vertebral osteomyelit nadir bir durumdur ve tanı ve tedavideki gecikme ciddi nörolojik sorunlara neden olabilir. Bu tür vakalarda klinisyenler tarafından fungal enfeksiyondan şüphelenmesi hayati önem taşır. Lösemilerde kemik sintigrafisinin rutinde yeri yoktur. Bununla birlikte, bu tür vakaların değerlendirilmesinde, kemik sintigrafisi diğer radyolojik tetkikler ile birlikte ilk aşamada akılda tutulmalıdır ki biz üç fazlı kemik sintigrafisi ile değerlendirme yapılmasının yararlı olacağını düşünmekteyiz.

Anahtar sözcükler: Candida, Akut myeloid lösemi, kemik sintigrafisi, vertebra osteomyelit

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Introduction

Candidal vertebral osteomyelitis is a rare disease. For diagnosis, the clinician must consider osteomyelitis in patients who are in the risk group in terms of fungal infections. If not treated, this disease shows progression causing vertebral destruction and spinal cord pressure. Acute myeloid leukemia (AML) is a clonal disease, which, in hematopoietic progenitor cells, develops as a result of an acquired somatic mutation, prevailing these cells in proliferation. In these patients the most important problem are infections and hemorrhages. In bone scintigraphy of leukemia patients (both children and adults), especially in images taken at an early stage, abnormal activity involvements in areas where hematopoietic activity increases can be monitored [1]. In acute myeloid leukemia, scintigraphic findings in adults' skeletal system are not typical and focal lesions can be seen. Whereas in children, diffusely increased activity in metaphyseal areas, and loss of epiphyseal- metaphyseal junction and its irregularity attract notice [2]. In AML, occurrence of lytic lesion and metastatic lesion in skeletal system is a rare condition. Although incidence of fungal infection is frequent in immunocompromised patients, fungal osteomyelitis is a highly rare condition.

In this incidence bone scintigraphic findings of an AML case are comparatively given in the light of other findings.

Case report

The result of the magnetic resonance imaging (MRI) study was reported as "metastasis of primary disease on L2-L3 vertebrae" in a 63-year-old male patient, who developed a back pain after receiving four courses of treatment for AML. The patient, who did not respond to pain medication, was sent to nuclear medicine department for a bone scintigraphy. A standard whole body bone scan and static regional images were obtained following three hours later of intravenous administration of 740MBq Tc-99m MDP with a gamma camera, equipped with double head and low-energy&high-resolution collimator (E-CAM, Toshiba, Japan). Diffuse increased osteoblastic activity was reported on L2-L3 vertebrae with a suspicion about infection or fracture, together with a focal osteoblastic activity involvement in the right sacroiliac joint (Figure 1). In the mean time, the patient complained about progressive loss of strength on bilateral lower extremities and

numbness in legs. In bone marrow aspiration performed during that time that blast was lower than 5%, cell density was normal, erythrocytic series activity was normal and bone marrow iron stores were normal. According to these results the patients was considered in remission. Repeated MRI was reported as “irregularities in L2-L3 vertebral disc region concordant with infection, prominent thecal pressure, loss of height in L2-L3 vertebrae associated with osteomyelitis and a mass concordant with paravertebral abscess and granulation tissue” (Figure 2). In neurological examination muscle strength of 0/5 was present. Bilateral lower extremities were sensation deficit from L1-L2 vertebrae, deep tendon reflexes reduced at lower extremities and bilateral babinski response was ambiguous. At this stage, except elevated erythrocyte sedimentation rate (ESR) and elevated C-reactive protein (CRP) level, there was no other abnormal laboratory finding. The patient was operated and necrotic tissue was removed by curettage, relieving the compression on L2-L3 and on the disc distance. Pathology report revealed an acute necrotizing inflammation. In culture examination of the sample “candida albicans” was isolated. Antifungal treatment with Amphotericin B was started by recommendation of the department of infectious diseases. Patient's pain was reduced following the treatment. MRI findings showed some regression in abscess and there was improvement in muscle strength in his legs. In final neurological examination of muscle strength, which was 0/5 before surgical intervention, evaluated as 4/5. The patient became able to walk with the aid of a thoracolumbar corset. However, relapse in AML was observed in bone marrow aspiration, performed during follow-up and chemotherapy was started again. On the second day of chemotherapy high fever started and cellulitis developed on the right leg. The patient received hemodialysis treatment due to increase in BUN and creatinine levels. Pulmonary edema and associated respiratory insufficiency was developed and the patient died.

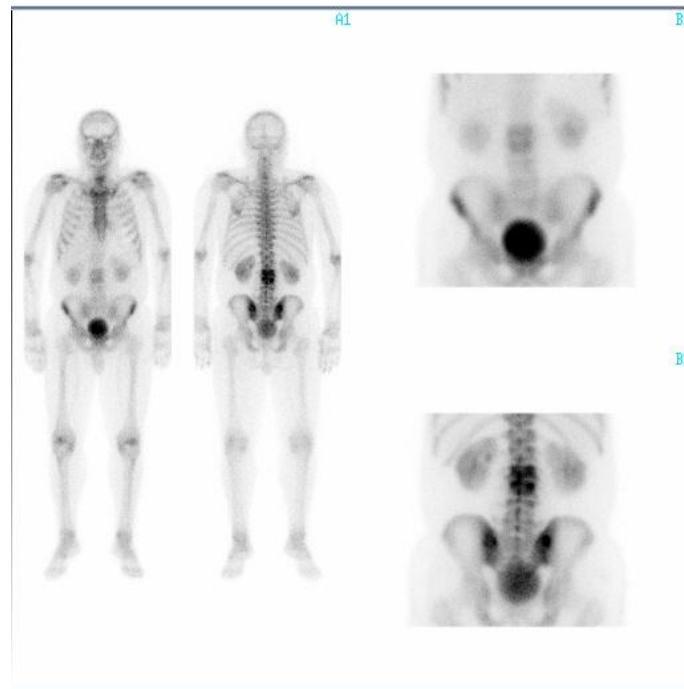


Figure 1. Tc-99m MDP bone scintigraphy. Increase in diffuse osteoblastic activity in L2-L3 vertebrae.



Figure 2. Lombar MR. Irregularities in L2-L3 vertebral disc region concordant with infection, prominent thecal pressure, loss of height in L2-L3 vertebrae associated with osteomyelitis and a mass concordant with paravertebral abscess and granulation tissue.

Discussion

Incidence of fungal infections is remarkably high in patients receiving high dose of chemotherapy during neutropenia period, in patients with central venous catheter, in organ transplantation and in bone marrow transplantation [3]. In such infections early diagnosis is crucial and increases the speed of response to treatment. Candidiasis and Aspergillus are the most frequently observed fungal infections in cancer patients [3, 4]. *Candida albicans* and other strains of *Candida*, which are commensally found in human digestive system, notably the mouth, and genitourinary system, might cause mucosal, subcutaneous or deeply localized infections when normal defense system of the host falls down. They also might cause life threatening systemic infections through multiple organ failures resulting from septic shocks [5, 6]. However, the frequency of bone and joint infection is low and vertebral osteomyelitis is rare [7-10]. Nevertheless, vertebral region is the most frequently affected area [11]. Indeed, the number of case reports is limited in the literature, relating osteomyelitis associated with *Candida* infection in patients with leukemia. Another reason for the rare occurrence of such cases might be that patients probably die before diagnosis. Vertebral osteomyelitis, if not diagnosed timely and treated effectively, might cause neurological deficits. Spreading into the bone is by hematologic route or by direct inoculation [12]. The type of fungal pathogen most frequently seen in vertebral osteomyelitis is “*Candida albicans*”. Less frequently seen strains are *Candida tropicalis*, *Candida glabrata* and *Candida parapsilosis* [8, 13]. In vertebral osteomyelitis most affected bones are lumbar vertebrae. Chronic progressive back pain is the only symptom and fever is absent in most patients [13]. Blood count values are usually normal, however sedimentation rate is high in almost all cases. MRI is highly sensitive in early detection of vertebral osteomyelitis [14]. But, MRI findings of *Candida* spondylitis are similar to other pyogenic spondylitises. CT imaging can be of help in making a distinction between malign lesions and fungal spondylitis [12]. Nevertheless none of the clinical, laboratory and radiological findings are specific in *Candida* osteomyelitis. Ferrá et al. [15] defined vertebral osteomyelitis caused by *Candida tropicalis* in late period after fungemia in 2 out of 532 patients who underwent bone marrow transplantation between 1980 and 1993. Miller et al. [16] also reported only 59 vertebral osteomyelitis cases between 1966 and 2000, caused by *Candida albicans*. In their report, the great majority (95%) of cases was with lower thoracic and lumbosacral vertebrae affection and only three cases were with the cervical vertebral involvement. *Candida* osteomyelitis has no typical laboratory findings. However, in this article primary laboratory disorder of patients was reported as increased ESR (87%), and in only 17% of

the patients an increase in WBC was detected. In our patient, number of white blood cells was normal but ESR was high. Menzin et al. [3] evaluated 2306 AML patients by a cohort study and detected fungal infection in 80 patients. Among those patients, *Candida* was found to be the most frequent factor, as was the case in other studies.

Bone scintigraphy has no place in routine evaluation of leukemia patients. Osteolytic lesions are rarely seen in acute myeloid leukemia [17, 18]. Nonetheless, osteolytic lesions are a sign of poor prognosis in AML [18]. Lima et al. [18] detected views associated with osteolytic lesions in BT and bone scintigraphy of an atypical AML patient, whose primary symptom was back pain, and bone marrow fibrosis and osteolytic lesions were found. After remission they monitored that bone scintigraphy findings were persistent despite there were no findings in bone marrow aspiration and biopsy, and an increase in the intensity of lesions compared to the pattern before radiotherapy. Nevertheless, twelve months later the patient returned with AML relapse and died because of sepsis. They pointed out that in diagnosis of such atypical AML patients, besides histological studies, CT and bone scintigraphy are also important for detecting osteolytic lesions.

Fungal infections are one of the most important clinical problems in leukemia patients. However, vertebral osteomyelitis secondary to fungal infection is relatively a rare condition and delay in diagnosis and treatment may led to serious neurological problems. Suspicion of a probable fungal infection by clinicians seems vital in such cases. Should solely MRI or CT examination is taken as a reference as in the presented case, missed diagnosis as metastatic disease might occur, affecting the comfort or even prognosis of the patient. We consider that three-phase bone scintigraphy should be kept in mind in the first stage of evaluation of such cases, together with other radiological examination, so that a timely diagnosis would be obtained.

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