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Erdheim-Chester disease

Erdheim-Chester hastalığı

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Abstract

Erdheim Chester is a rare histiocytic infiltrative disease characterized with bilateral symmetrical sclerotic involvement of the metaphyses and diaphyses of long bones.
Fifty-one years old male patient presented with dull knee and leg pain which was present for two years and did not respond to non-steroidal anti-inflammatory medication was evaluated. His physical examination was normal. His X-rays revealed areas of symmetrical heterogeneous sclerosis in bilateral proximal tibial and distal femoral metaphysodiaphyseal regions. Laboratory findings revealed a mild increase in blood phosphorus levels and a significant increase in urine calcium level. Bone scintigraphy revealed an increased uptake in bilateral proximal tibias, distal femurs and distal end of the left tibia. Abdominal, chest and cranial radiological evaluations were all normal. There were no abnormal findings in bone marrow biopsy. His open bone biopsy obtained from the left proximal tibia revealed foamy lipid-loaded histiocytes, incipient local inflammatory reaction, rare giant cells and osteosclerosis with medullar fibrosis. The patient was given bisphosphonate treatment (Alendronate 70mg/week). There was a decrease in his leg pain in postoperative 1 year follow-up.

Although Erdheim-Chester's is a rare disease, orthopedic surgeons should keep this disease in mind, in the differential diagnosis of patients who present with bone pain and sclerosis.

Key words: Erdheim-Chester disease, sclerosis, histiocytosis, lipoidosis, lipogranulomatosis

Özet

Erdheim Chester uzun kemiklerin metafiz ve diyafizlerinde iki taraflı simetrik skelrotik infiltrasyonla karakterize nadir görülen histositik infiltratif bir hastalıktır.
Ellibir yaşında erkek hasta künt diz ve bacak ağrısıyla başvurdu. Şikayetleri iki yıldır sürüyordu ve steroid olmayan antiinflamatuvar ilaçlara yanıt vermiyordu. Fizik muayenesi normal olarak değerlendirildi. Radyolojik incelemede her iki tibiya üst ucunda ve femur metafizyodiyafizial bölgede simetrik heterojen skleroz saptandı. Laboratuvar tetkiklerinde kan fosfor düzeyinde hafif artış gösterdi. İdrarda kalsiyum düzeyi belirgin olarak artmıştı. Kemik sintigrafisinde her iki tibiya üst ucunda, femur distalinde ve sol tibiyanın distalinde alım artmıştı. Batın, göğüs ve kraniyal radyografiler normal olarak değerlendirildi. Kemik iliği biyopsisi normaldi. Sol tibiya üst ucunda gerçekleştirilen biyopside köpüksü yağ yüklü histiyositler, yerel inflamasyon, nadir dev hücreler ve medüller fibrozla birlikte osteoskleroz saptandı. Hastaya bifosfonat tedavisi (70mg/hafta Alendronat) verildi. Bir yıllık takipte cerrahi sonrası bacak ağrısında azalma saptandı.

Erdheim Chester hastalığı nadir görülmekle birlikte ağrı ve sklerozla seyreden hastalıkların ayırıcı tanısında akılda bulundurulmalıdır.

Anahtar sözcükler: Erdheim Chester hastalığı, skleroz, histiyositoz, lipuidoz, lipogramülomatoz

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Erdheim Chester disease (ECD) was first described in 1930 by the Viennese pathologist Chester and is regarded as a form of Langerhans cell histiocytosis (LHC).[1-5] It is a rare lipoidosis affecting predominantly the metaphysis and diaphyses of the long bones but rarely the axial skeleton. The affected bones show atypical endosteal and periosteal sclerosis. Aside from the skeletal system, inner organs (heart, lungs and kidneys) may be affected.[1] Clinical manifestations are variable and non-specific. The disease can range from a focal asymptomatic process to a multi-systemic fatal condition.[6] The diagnosis of ECD is based on distinctive radiologic findings, with symmetric osteoblastic lesions in long bones and also characteristic pathological lesions of the bones with demonstration of foamy, cholesterol-laden histiocytes in the bone marrow, surrounded by sclerotic bones.[7]

CASE REPORT

A fifty one years old male patient presented with dull knee and leg pain which was present for two years was evaluated. His pain had increased in the last 2 months. His medical and family histories were insignificant regarding systemic illnesses. There was tenderness to palpation in his left proximal tibia with accompanying slight atrophy of the left quadriceps muscle. There were symmetrical medullary scleroses in bilateral distal femora, proximal tibiae and bilateral proximal humeri (Figure 1). Three phase Tc 99m MDP bone scan revealed increased uptake in both distal femora, both proximal tibiae and left distal tibia and uptake was more marked on the left side (Figure 2). There were no pathological findings in abdominal USG and MRI, IVP, lung X-ray and cranial MRI. Findings of MR imaging of the lower limbs showed replacement of the normal fatty bone marrow of the diaphyseal and metaphyseal bone segments by a markedly low signal intensity (hypointense compared with muscle and heterogeneous signal intensity on T1-weighted (T1-W) spin echo images) and by a heterogeneous intermediate signal intensity on T2- weighted (T2-W) and fat-suppressed T2-W images (Figure 3).

His bone mineral densities were as follows: AP spine T score -2.9, left femur T score -1.6. His abnormal laboratory findings were: blood phosphorus: 2.64 mg/dl (N: 2.7-4.5 mg/dl), urine calcium 36.3 mg/dl (8.1-10.4 mg/dl). The blood calcium, BUN, creatinine, alkaline phosphatase, Parathyroid hormone, osteocalcin levels were normal. His C reactive protein (CRP) was: 3.75 mg/d (0-5 mg/dl) and erythrocyte sedimentation rate (ESR): 14 mm/h (ref: 1-15 mm/h). There was a mild mitral and tricuspid insufficiency in his echocardiography.

Bone marrow biopsies which were obtained from the iliac wing were normal. His open bone biopsy taken from the left tibia and the histologic sections of tibia specimens revealed foamy lipid-loaded histiocytes, incipient local inflammatory reaction, rare giant cells, and osteosclerosis with medullary fibrosis (Figure 4). The foamy histiocytes were immunohistochemically positive for CD68 and negative for the S-100 protein, and CD1a. The patient was given biphosphonate (Alendronate, 70 mg/wk) treatment. His leg pain had diminished from a constant pain to a mild occasional pain at 1 year follow-up. There were no detectable X-ray changes. His bone mineral densities at 1 year follow up were: left femur T score -1.3, AP spine T score -2.9. His blood phosphorus was 2.08 mg/dl (N: 2.7-4.5 mg/dl).

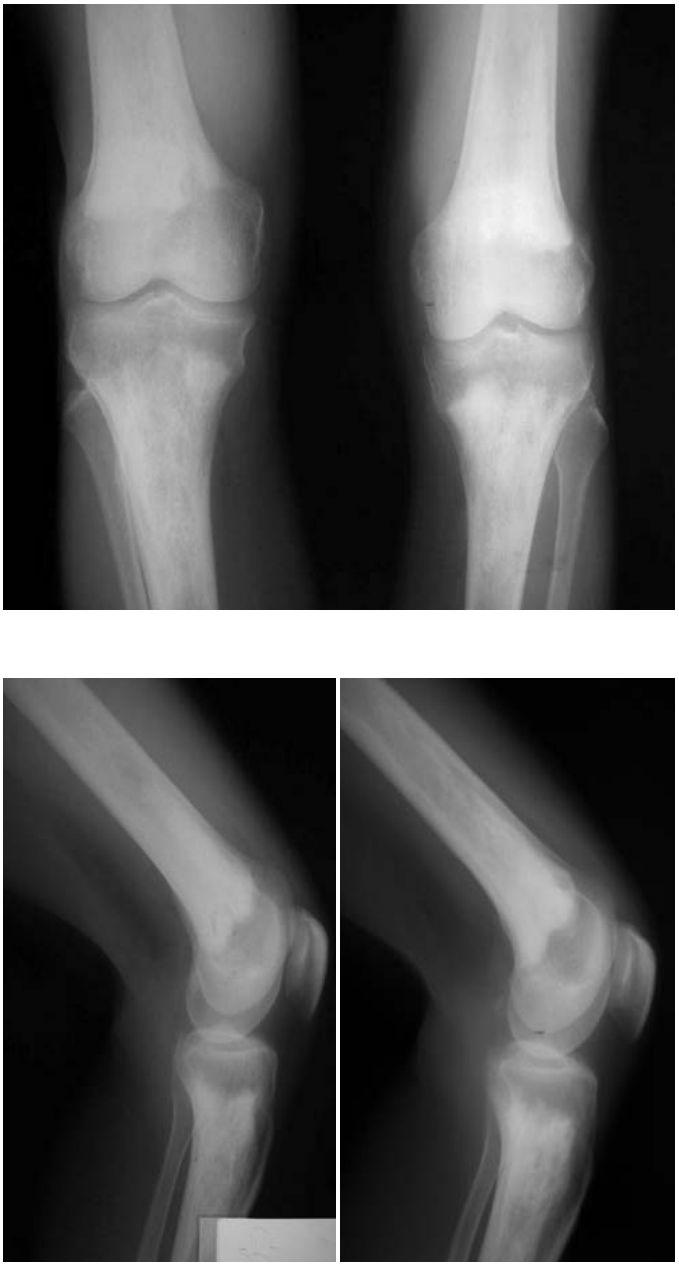

Figure 1. Bone X-rays of both knees in anteroposterior and lateral directions. There is bilateral metaphyseal and diaphyseal symmetrical sclerosis with normal epiphyses.

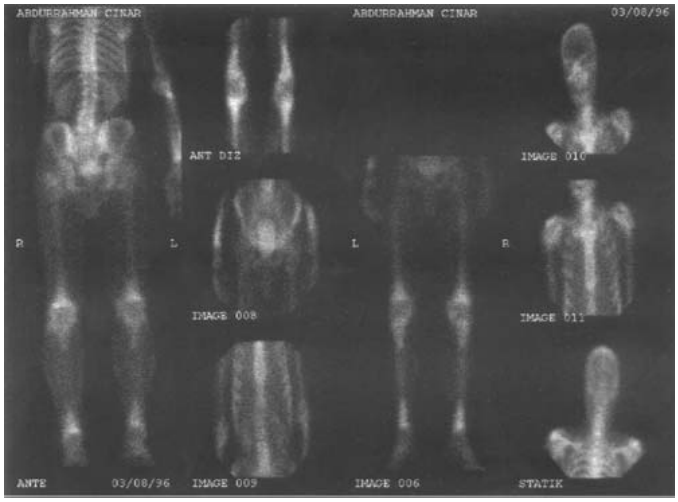

Figure 2. Uptake increase in triphasic bone scintigraphy.

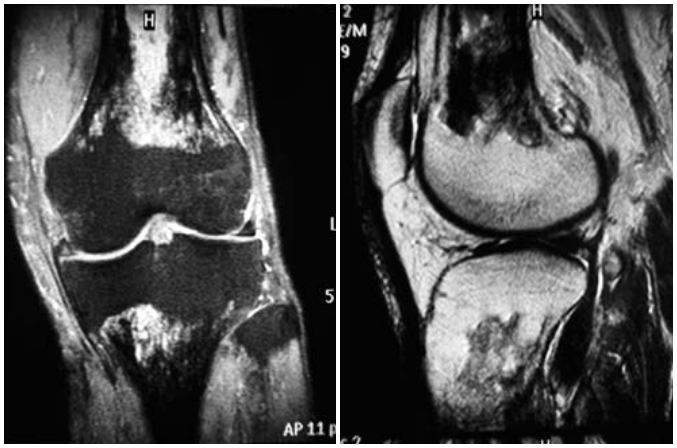

Figure 3. In the left knee MRI scan, the T2-W Fat-sat coronal (A) images demonstrate nonsuppressed, hyperintense areas consistent with cellular infiltration in both femur and tibia metaphysodiaphyseal areas. The same region T1-W sagittal (B) images demonstrate loss of normal bone marrow signals as a result of cellular infiltration resulting in hypointense view. The epiphyses are preserved in both bones.

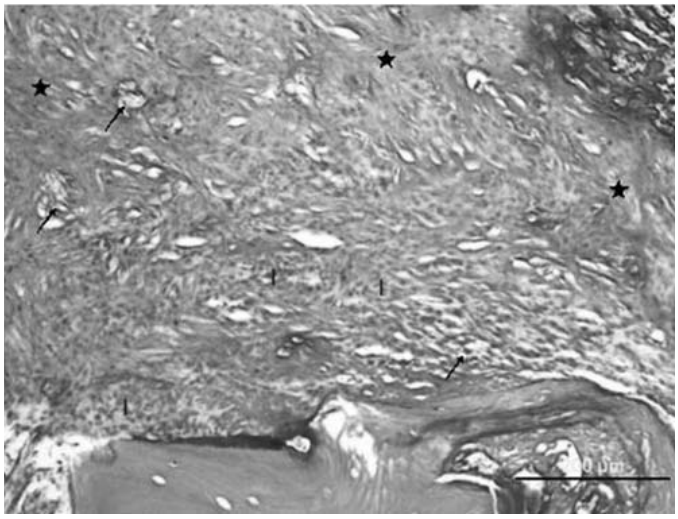

Figure 4. Histologic appearance of biopsy specimens was characterized foamy lipid-loaded histiocytes (Black Arrow), incipient local inflammatory reaction (I), rare giant cells, and osteosclerosis with medullary fibrosis (Black star)(hematoxylin and eosin stain, & 100).

DISCUSSION

ECD is a rare multisystemical disease characterized by xantogranulomatous infiltration of various tissues. Histological findings are similar to those of Langerhans cell histiocytosis (LCH) with an infiltration by foamy histiocytes, surrounded by fibrosis and irregularly thickened bone trabeculae. They differ, however, from LCH with negative immunostaining for protein S 100. Other than immunohistochemical differences, symmetrical involvement of long bones is specific for ECD and differentiates it from other histiocytoses.[6] The diaphyses and metaphyses typically demonstrate diffuse or patchy increased density, a coarsened trabecular pattern, medullary sclerosis and cortical thickening. This feature has led to differentiate it from LCH in which the bone lesions are usually osteolytic and long bones are rarely involved. In ECD there is usually sparing of the epiphyses and axial skeleton, although exceptions have been described.[8,9] The most commonly affected bones are the femur, tibia and fibula and less frequently the ulna, radius and humerus.[10] Radioactive tracers Technetium 99m MDP and Gallium 67 citrate accumulate in the involved metaphyses and parts of the diaphyses of the long bones.[1] MRI is helpful in evaluating the degree of cancellous bone involvement. The normal fatty bone marrow is replaced by a heterogeneous tissue exhibiting low signal intensity on T1-W images and intermediate to high signal intensity on T2-W images according to the respective amount of fibrous and edematous components. Gadolinium-enhanced MRI, bone marrow areas that exhibited high signal intensity on T2-W images enhanced with a slightly heterogeneous pattern. Such areas of high signal intensity on T2-W and gadolinium-enhanced images suggest active lesion.[2] MRI has been reported to show features of marrow replacement with low signal on TI-weighted sequences, mixed signal on T2 and some enhancement post-gadolinium contrast.[11,12] The bony involvement and the radiological findings of our case were similar to the ones in the literature.

In the literature regarding ECD, ages ranged from 7 to 84 years at the time of diagnosis. There was a slight male predominance. Although the bone changes may be asymptomatic, up to 50% of patients develop symptoms referable to the bone lesions.[3] Bone pain was the most frequent symptom, and was sometimes isolated. It mainly affected the lower limbs, especially the knees and ankles. Other symptoms were fever, loss of weight, exophthalmos, dyspnea, neurological symptoms, and central diabetes insipidus which were caused by multiorgan infiltrations. Multiorgan involvements by order of frequencies are: retroperitoneum, retroorbital space and brain infiltration. The most frequently reported causes of death were respiratory distress,

pulmonary fibrosis and heart failure with or without pericardial effusion.[3, 4] Similar to the literature, in our case, the patient was a male and had pain as the major symptom. We did not detect any other symptoms or other organ involvements.

Laboratory values are nonspecific in ECD.[5] CRP and ESR levels were elevated in some cases. A mild increase in alkaline phosphatase activity was found in 7 patients. Consistent with the relevant literature, the blood calcium, BUN, creatinine, alkaline phosphatase, parathyroid hormone, osteocalcin levels were normal in our case but the blood phosphorus level was at the lower limit and there was an increased calcium excretion in the urine. Brain and retroperitoneum are the second and third most commonly involved organs after the bone.[3] As there was excessive calcium excretion, we inspected the retroperitoneal space but could not find any radiologic abnormality. As there was low bone mineral density, the excess of calcium excretion was attributed to osteolysis.

Differential diagnoses include mastocytosis, Gaucher`s disease, fluoride intoxication, myeloid metaplasia, lymphoma, metastatic disease, toxic osteoarthropathy, and adult progressive diaphyseal dysplasia (Engelmann disease).[4, 13] However, 5%-8% of patients with ECD also have lytic lesions, either on the flat bones, like the ribs and skull, or on the long bones.[3] Apart from myeloma, metastatic disease, and squeal from previous fracture or osteomyelitis, the main diagnostic problem with these lytic lesions is that they can resemble those in another form of histiocytosis. They must prompt the clinician to ask for long bone radiographs in order to ensure the radiological diagnosis of ECD and to guide a bone biopsy.[3, 10, 14]

Steroids, chemotherapy, radiation, immunotherapy (IFN-α) and biphosphonates were all tried for the treatment.[15, 16] None of these led to a cure of this disease.[4] Use of alendronate led to a decrease the biomechanical markers of bone turnover.[14] As our patient did not have multiorgan involvement but mild bone pain, we started a 70 mg/week single dose alendronate treatment. Although there was an improvement in bone densities and clinical relief there was no detectable, improvement in X-ray findings. Long term follow-up results will be reported in the future.

In conclusion, ECD is a lipoidosis causing bilateral symmetrical sclerosis of long bones which should be kept in mind when dealing with a patient presenting with bone pain and sclerosis.

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