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Erdheim-Chester Disease
: A Case Report

A 42-year-old man with Erdheim-Chester disease (EC) is presented. This is the first case of this disease reported in Korea. The patient complained of knee pain and plain roentgenogram of the bilateral legs revealed diffusely increased density, coarsened trabecular pattern, and cortical thickening in the diaphysis, and metaphysis as well as epiphysis. Magnetic resonance imaging revealed that the lesions showed low signal intensity on T1-weighted images and heterogeneously low and high signal intensity on T2-weighted images. Histological examination of the biopsy specimen showed a xanthogranulomatous lesion consisting aggregations of foamy histiocytes and Touton-type giant cells. Immunohistochemical staining showed positive reaction to anti-S-100 and lysozyme in the cytoplasm of the giant cells.

Key Words: *Erdheim-Chester disease; Histiocytosis; Immunohistochemistry*

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INTRODUCTION

Erdheim-Chester disease (EC) is a rare lipogranulomatosis or histiocytosis in adults which is characterized by an infiltration of foamy histiocytes in multiple organs especially in bone marrow (1-3).

EC is another confusing eponym used to describe a distinctive pathologic and radiographic entity with disparate clinical findings. Whether it is a distinct syndrome or merely part of the spectrum of histiocytosis has recently been questioned (4). Based on the literature, the clinical and histological features of this disease appear to resemble some Langerhans cell histiocytosis, in particular, Hand-Schuller-Christian disease as well as sinus histiocytosis with massive lymphadenopathy, and Rosai-Dorfman disease. However, the entity differs distinctively from those diseases in several ways. EC shows symmetrical distribution of bone lesions on roentgenogram, lack of Langerhans granules in the histiocytes aggregating in the lesion, lack of S-100 antibody staining in the histiocytes as well as lack of lymphocytophagocytosis of the histiocytes, distinguishing it from those diseases.

In this report, we describe a case of EC involving both femurs and tibias of a 42-year-old male patient. We also describe immunohistochemical properties of the characteristic infiltrating cells.

CLINICAL HISTORY

The 42-year-old man had suffered from pain in both knees for six months. Conservative management was done. Pain in both knees was aggravated and he was admitted to this hospital. Physical examination revealed swelling, tenderness, as well as local warmth in joint areas. His temperature was 38.5℃. Laboratory findings showed an elevated erythrocyte sedimentation rate (62/30 mm/hr, corrected sedimentation rate) and mild leukocytosis. X-rays were taken on both femurs and tibias. Plain radiographs of the left knee showed diffusely increased density, coarsened trabecular pattern, and cortical thickening in the diaphysis, metaphysis and epiphysis (Fig. 1). Magnetic resonance imaging revealed that the epiphysis was also involved with the partial preservation of posterior portion of the femoral and tibial condyles. Lesions showed low signal intensity on T1-weighted images, and heterogeneously low and high signal intensity on T2-weighted images (Fig. 2). Under the clinical impression of chronic osteomyelitis, a biopsy was done on the tibia. There were striking infiltrations of foamy, lipid-laden histiocytes as well as Touton type of giant cells (Fig. 3). Occasional lymphocytes and plasma cells were present. No eosinophils were identified. Necrosis of the trabecular bones and fibrosis was also noted. There

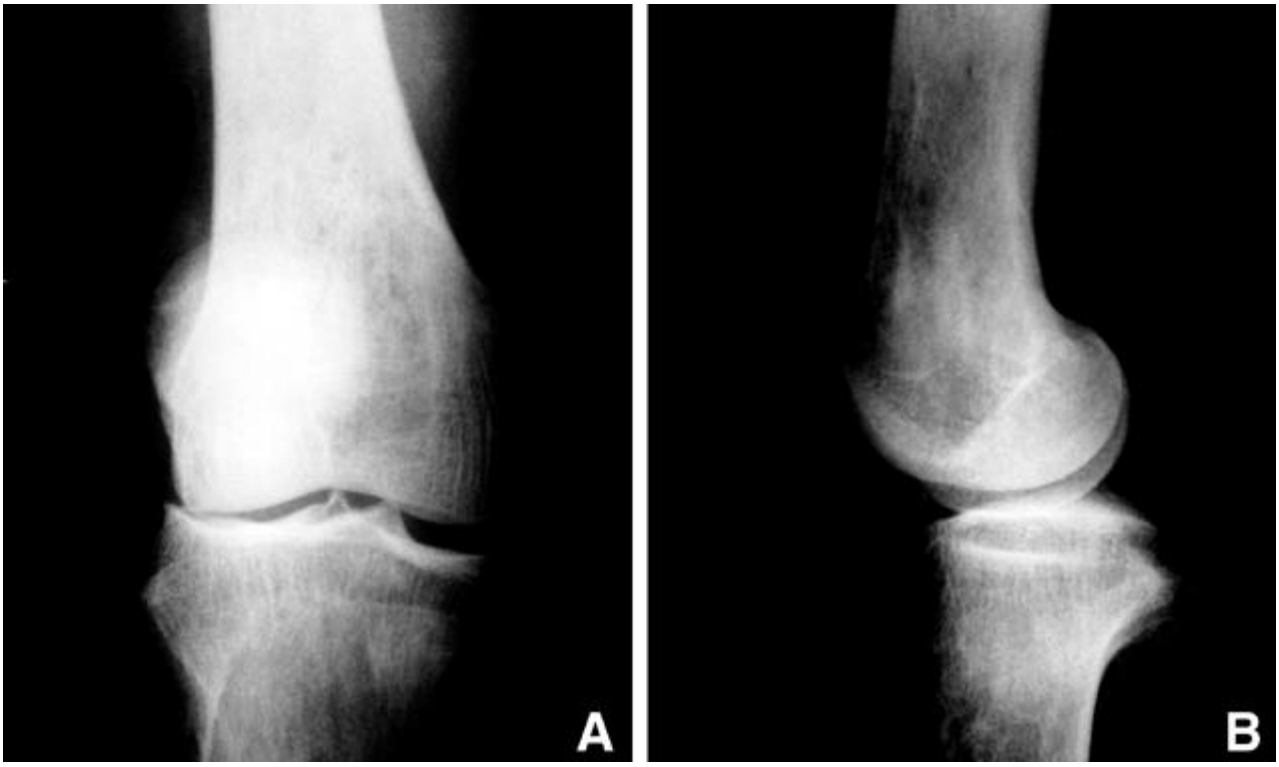

Fig. 1. A and B. Radiographs of left knee showed diffusely increased density, a coarsened trabecular pattern, and cortical thickening (A, A-P view, B, Lateral view).

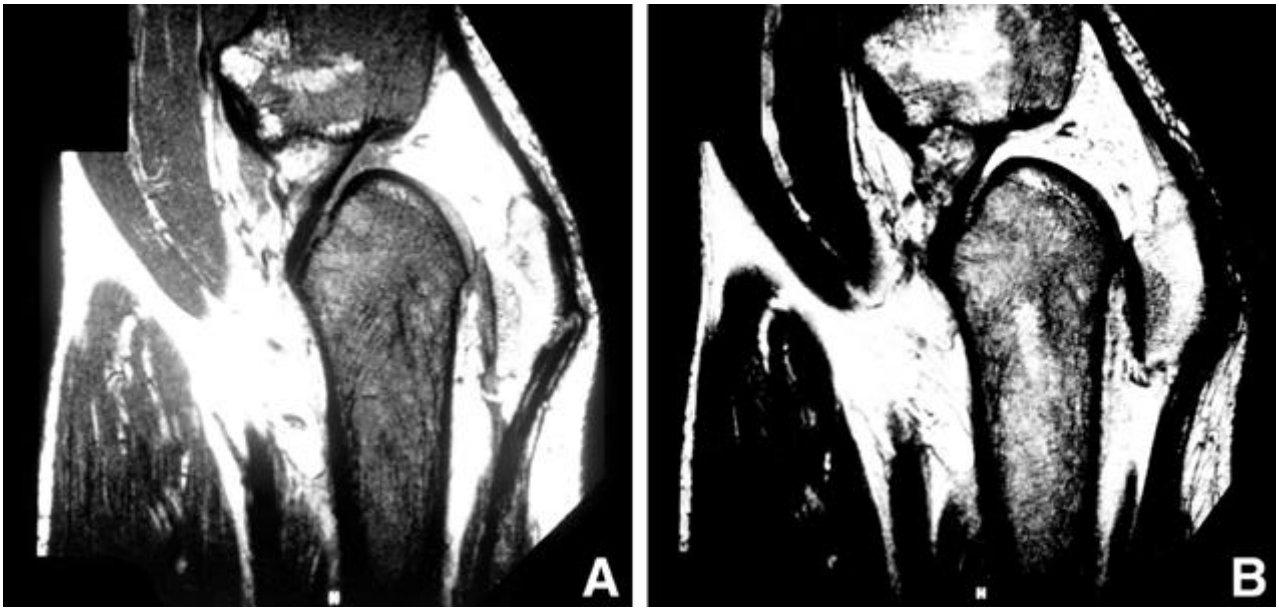

Fig. 2. A: T1-weighted sagittal image of the knee shows diffusely low signal intensity of the marrow cavity in the femur and the tibia. B: T2-weighted coronal image of the knee shows heterogenously low and high singal intensity.

were no granulomas, and stain results for fungi and acid-fast bacilli were negative. After antigen retrieval using the microwave on the citrate buffer, diffuse cytoplasmic staining against S-100 protein and lysozyme on the cytoplasm of the giant cells were revealed (Fig. 4). Pathologic findings were believed to represent Erdheim-Chester disease. The patient was treated with vinblastine, cyclophosphamide and methylpredinisone. Following chemotherapy, temperature returned to normal and knee pain subsided.

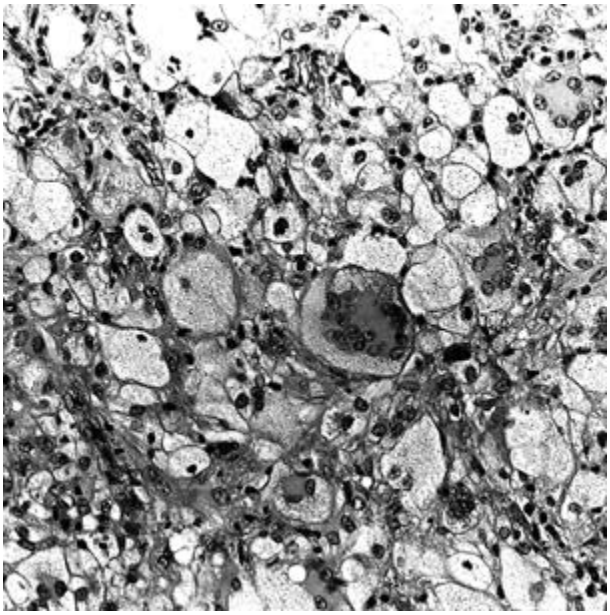

Fig. 3. There are diffuse lipid laden histiocytic infiltration with Touton-type giant cells. Also noted are mild marrow fibrosis with lymphoplasma cell infiltration (H&E, ×200).

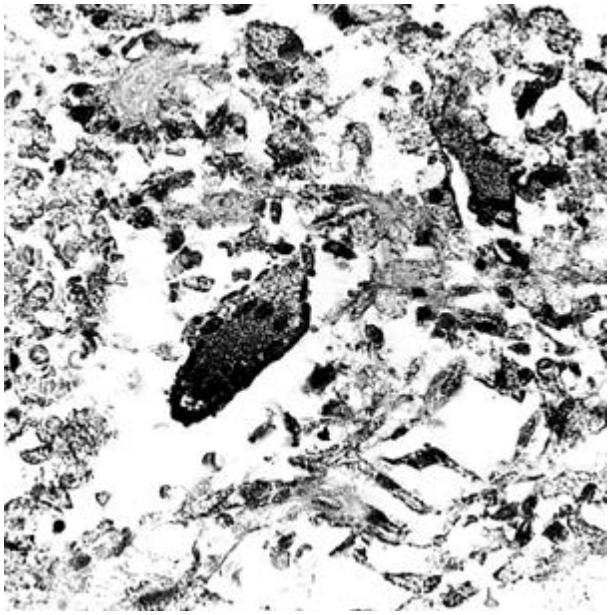

Fig. 4. Immunohistochemical staining against S-100 protein reveals cytoplasmic staining at the Touton-type giant cells (× 200).

DISCUSSION

Erdheim-Chester disease is an unusual lipogranulomatosis which was originally described by American pathologist Chester and Viennese pathologist Erdheim in 1930 (5). In his report, Chester described two cases of a rare lipogranulomatosis which was distinguishable from Hand-Schuller-Christian disease and primary lipid disorders (5).

The clinical characteristics of EC are not well understood. Nearly all reported patients were older than 40 years (3). The disease is characterized by bilateral, symmetric mixed osteolytic sclerotic lesions of the metaphyseal regions of the long bones. Additional lesions may be present in the ribs, sacrum, craniofacial bones, and lumbar vertebrae. Involvement of craniofacial bones is sometimes associated with diabetes insipidus. Clinical manifestations range from joint pain and keloid formation to systemic involvement of the heart, liver, spleen, pancreas, pericardium, lungs, adrenal glands, lymph nodes, retroperitoneal tissues, aorta, peritoneum, bowel serosa, pituitary, orbit, and bone (3, 6).

The typical and virtually diagnostic changes of EC are seen in the major long tubular bones of the appendicular skeleton. Most commonly, the long bones of the upper and lower extremities are symmetrically involved. Diffuse or patchy increased density, coarsened trabecular pattern, medullary sclerosis, and cortical thickening usually affect the diaphyses and metaphyses (3, 7). Epiphyseal involvement is less comon. Approximately one-third of cases have a mixed osteolytic and sclerotic pattern (4). Sclerosis is produced by a thickened trabecular pattern and endosteal cortical thickening.

Histologically, the xanthogranulomatous lesions are infiltrates of foamy lipid-laden histiocytes and giant cells, with medullary fibrosis as well as osteosclerosis (2). The majority of cells have microscopic features of ordinary histiocytes (no nuclear grooves are seen) not Langerhans cells (8). Benign fibrous histiocytoma is also listed for the differential diagnosis. However, in benign fibrous histiocytoma, no Touton type giant cell is present.

Immunohistochemically, it has also been reported that Langerhans cell histiocytosis cells react with antibodies against S-100 protein and lack reactivity with anti-α-1-antichymotrypsin and anti-α-1-antitrypsin antibodies, which antibodies show a remarkable positive reaction to ordinary histiocytes (8). It is well known that the majority of histiocytes in EC are negative for S-100 protein and positive for α-1 antitrypsin, α-1 antichymotrypsin and lysozyme. In this case, giant cells were positively stained with anti-S-100 antibodies after antigen retrieval treatment using a microwave oven in citrate buffer. Lysozyme is also positive in the cytoplasms of the giant cells. In recently reported cases of EC, histiocytes in the lesions also show positive staining with anti-S-100 antibody (9, 10). Ultrastructurally, they have features of ordinary histiocytes with numerous lysozymes and lipid vacuoles. No Birbeck granules are reported in this EC.

EC must be distinguished from other histiocytic cell prolfierations, such as conventional Langerhans cell his-

tiocytosis, storage disorders, predominately Gaucher's disease, bone infarcts, and secondary foamy histiocytic reactions superimposed on other bone lesions such as fibrous dysplasia. Paying close attention to the very unique radiological presentation of EC is the best way to diagnose this entity correctly. Immunohistochemical finding of small clusters of cells positive for S-100 protein and ultrastructural findings are helpful in differential diagnosis with other histiocytic lesions.

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