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ERDHEIM-CHESTER DISEASE DETECTED WITH ^{99M}TC MDP BONE SPECT/CT

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Erdheim-Chester disease (ECD) is a rare non-Langerhans' cell histiocytosis. Mild but permanent juxta-articular bone pain in mainly knees and ankles is the most frequent associated symptom. Despite the pathognomonic radiographic findings, most cases are still diagnosed by the pathologist. The lesions consist of lipid-storing CD 68 +/ CD 1a – non-Langerhans' cell histiocytes, most frequently localized in bone but also involving multiple organ systems in the body. We present a case report in which the diagnosis of ECD was established with ^{99m}Tc MDP bone SPECT/CT.

Key-word: Lipogranulomatosis.

Erdheim-Chester disease (ECD) or polyostotic sclerosing histiocytosis is a rare histiocytic disorder, which leads to xantogranulomatous infiltration by lipid-laden histiocytes of multiple organ systems (skin, lung, bone, heart, central nervous system, pituitary, retroperitoneum, (retro-) orbital tissue) (1).

The pathologist Jakob Erdheim and physician William Chester reported the first cases in 1930. They described the clinical and pathologic findings of 2 patients with distinctive lipoid granulomatosis and associated bone changes (2).

ECD remains sporadic with about 100 well-documented cases in literature (2).

Case report

A 51-year old woman with a 4-year history of intermittent joint pains, primarily in ankles and knees, presented at rheumatology with fever and swelling of the right elbow.

Blood sample result included an abnormal lipid metabolism with hypercholesterolemia (total cholesterol 248 mg/dl, nl range < 190 mg/dl; LDL 136 mg/dl, nl range < 115 mg/dl; triglycerides 335 mg/dl, nl range 150 mg/dl), elevated C-reactive protein (14,9 mg/l, nl range < 5 mg/l), elevated white blood cell count ($13,8 \times 10^3/mm^3$, nl range $3,6\text{-}9,6 \times 10^3/mm^3$), slightly elevated sedimentation rate (25 mm/h, nl range 0-20 mm/h), nl kidney function (creatinine 0,74 mg/dl, normal range 0,40-1,20 mg/dl), nl red blood cell count ($4,5 \times 10^6$, nl range $3,9\text{-}5,0 \times 10^6$).

X-ray of forearms and knees showed heterogeneous osteosclerosis, suggesting metastatic disease. ^{99m}Tc MDP bone scan revealed intense osteoblastic activity in the right maxilla, distal femora, proximal tibiae, ankles and tarsal bones. Additional SPECT-CT of the knees revealed heterogeneous sclerotic bone marrow lesions with epiphyseal sparing, corresponding with the areas of osteoblastic activity (Fig. 1).

MRI of the knee showed diffuse hyperintense lesions on the T1 sequence after the intravenous injection of Gadolium in femora, tibiae and fibulae, confirming the heterogeneous active detriment of the normal bone marrow (Fig. 2). Based on the symptoms and characteristic imaging, ECD was suspected.

Bone biopsy of the distal femur revealed an infiltration of lipid-storing macrophages with non-Langerhans' features (CD 68 +/CD1a –/S100 –), which is consistent with ECD (Fig. 3).

^{18}F-FDG-PET-CT was performed to detect visceral manifestation. Mild

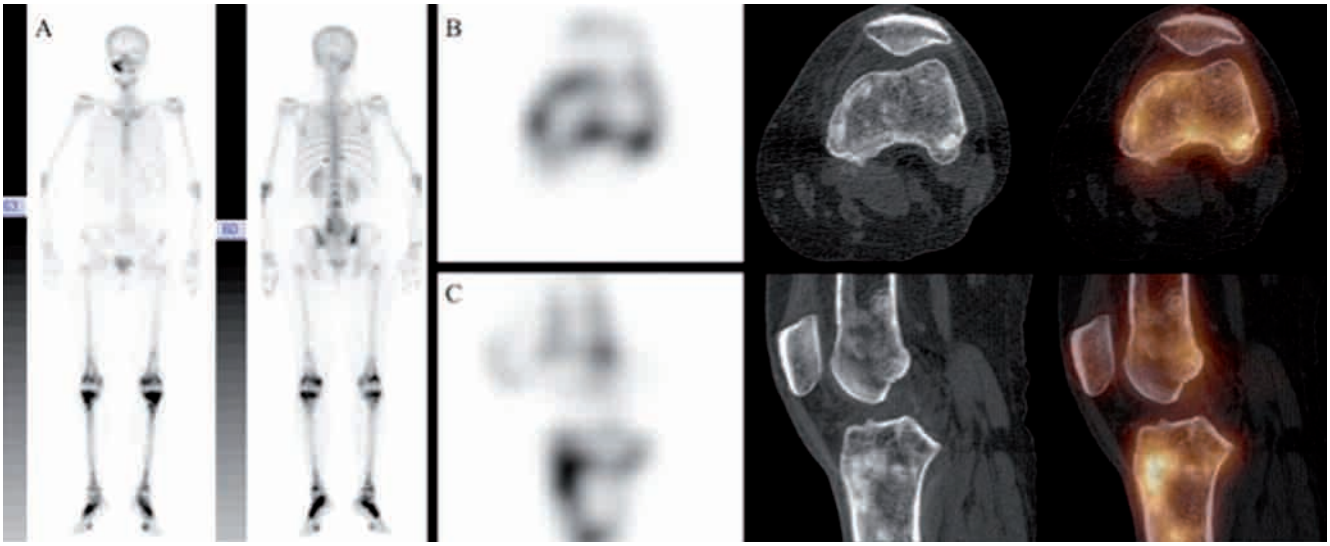

Fig. 1. — A. ^{99m}Tc MDP bone total body scan demonstrated intense osteoblastic activity in the right maxilla, distal femora, proximal tibiae, ankles and tarsal bones. B. (transverse slices) and C. (sagittal slices). Additional SPECT/CT revealed corresponding sclerotic bone marrow lesions with epiphyseal sparing.

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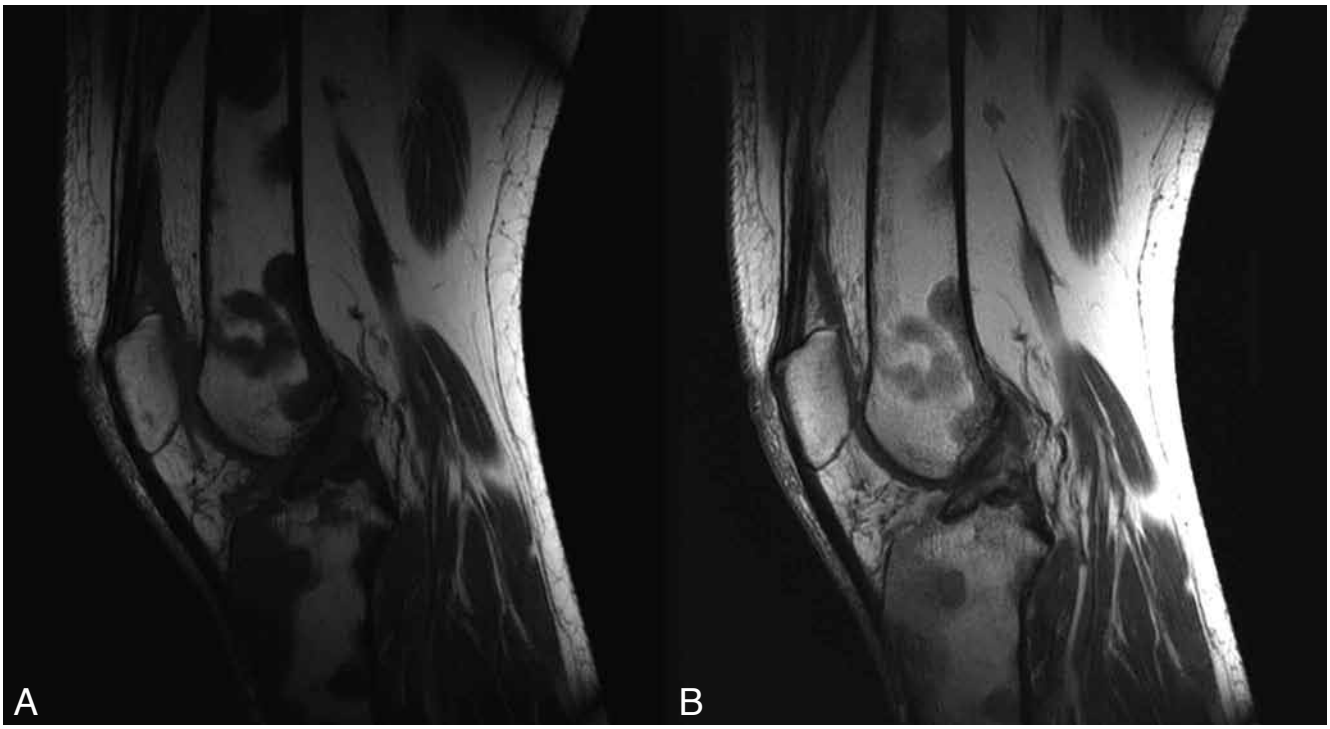

Fig. 2. — A. MRI of the knee shows irregular zones with low signal on the T1 non-contrast enhanced image, sparing the epiphysis. B. These lesions had contrast enhancement on the T1 sequence after intravenous injection of Gadolinium.

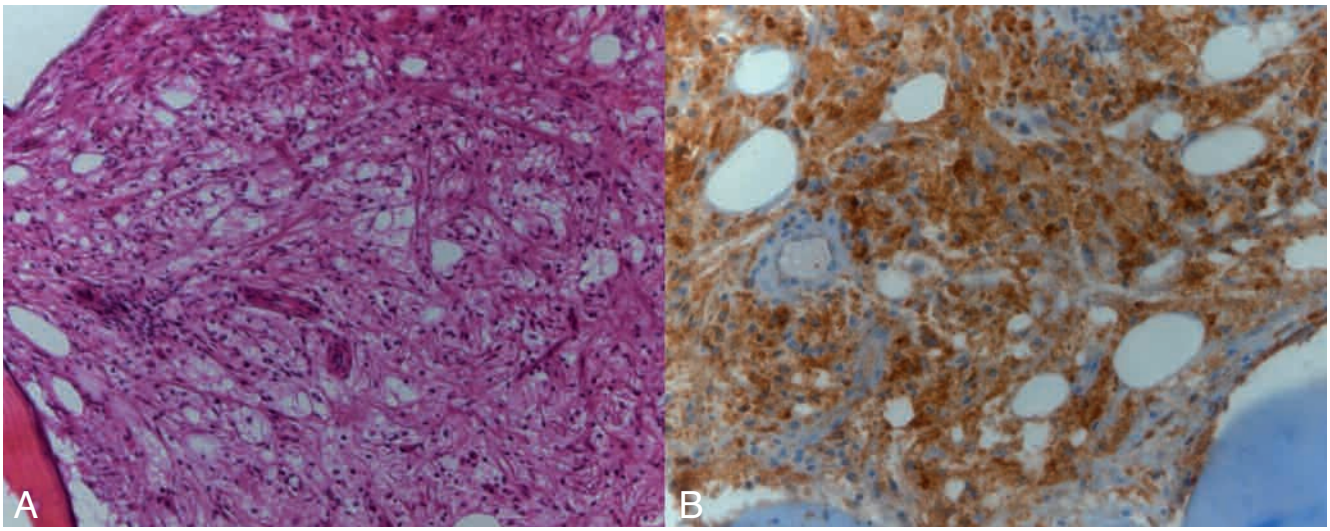

Fig. 3. — A. Bone biopsy demonstrated a diffuse infiltration of the normal bone marrow by lipid-laden histiocytes. B. These histiocytes were identified as macrophages as they were CD 68-positive on immunohistochemistry.

involvement of the lungs included a thickening of the interlobular septa; in the abdomen perinephric stranding, an atypical sign of retroperitoneal fibrosis, was present (Fig. 4). All visceral and skeletal lesions were hypermetabolic (Fig. 5).

Discussion

ECD is a rare form of non-Langerhans' cell histiocytosis affecting middle-aged adults (mean age of 53 years) without gender predisposition (3). The condition seems non-familial and no predisposing factors are defined (2). The precise origin of this disease is not yet fully understood; currently it has not been classified as cancer, neither as an infectious or autoimmune disease.

Diagnosis of ECD remains challenging. Mild permanent juxta-articular bone pain is the most frequent symptom and mainly affects the lower limbs. Other symptoms depend on the type of affected extra-skeletal tissue. In order of frequency of occurrence these comprehend retroperitoneal fibrosis, diabetes insipidus, exophalmia, xanthomas, neurologic signs (ataxia), dyspnea, kidney failure, hypopituitarism, liver failure. Of all cases 70-80% have skeletal involvement and more than 50% have visceral involvement (4).

Radiological hallmarks (X-ray/CT) include symmetric heterogeneous

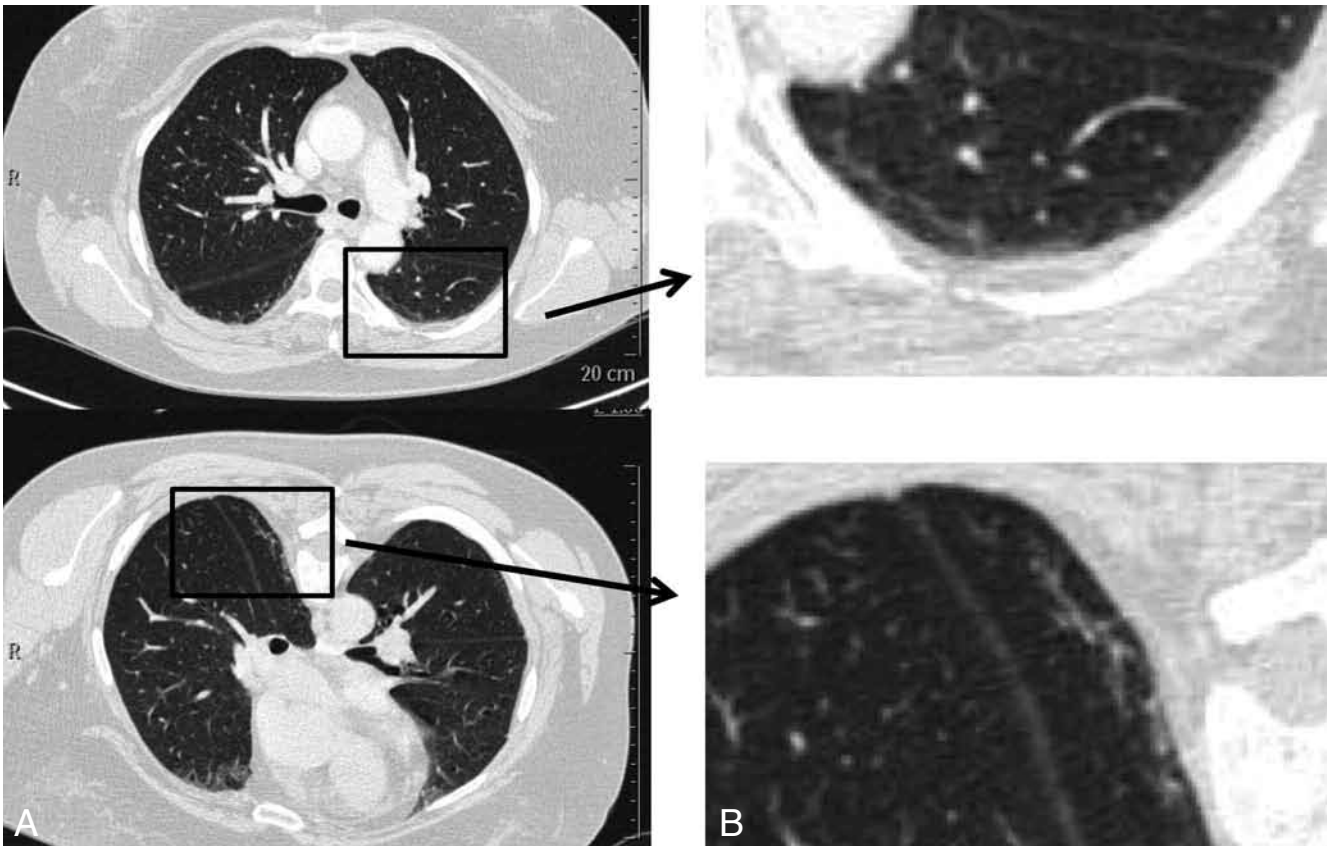

Fig. 4. — A. (supine position) B. (prone position) HRCT of the lung showed mild involvement of the lungs: thickening of the interlobular septa.

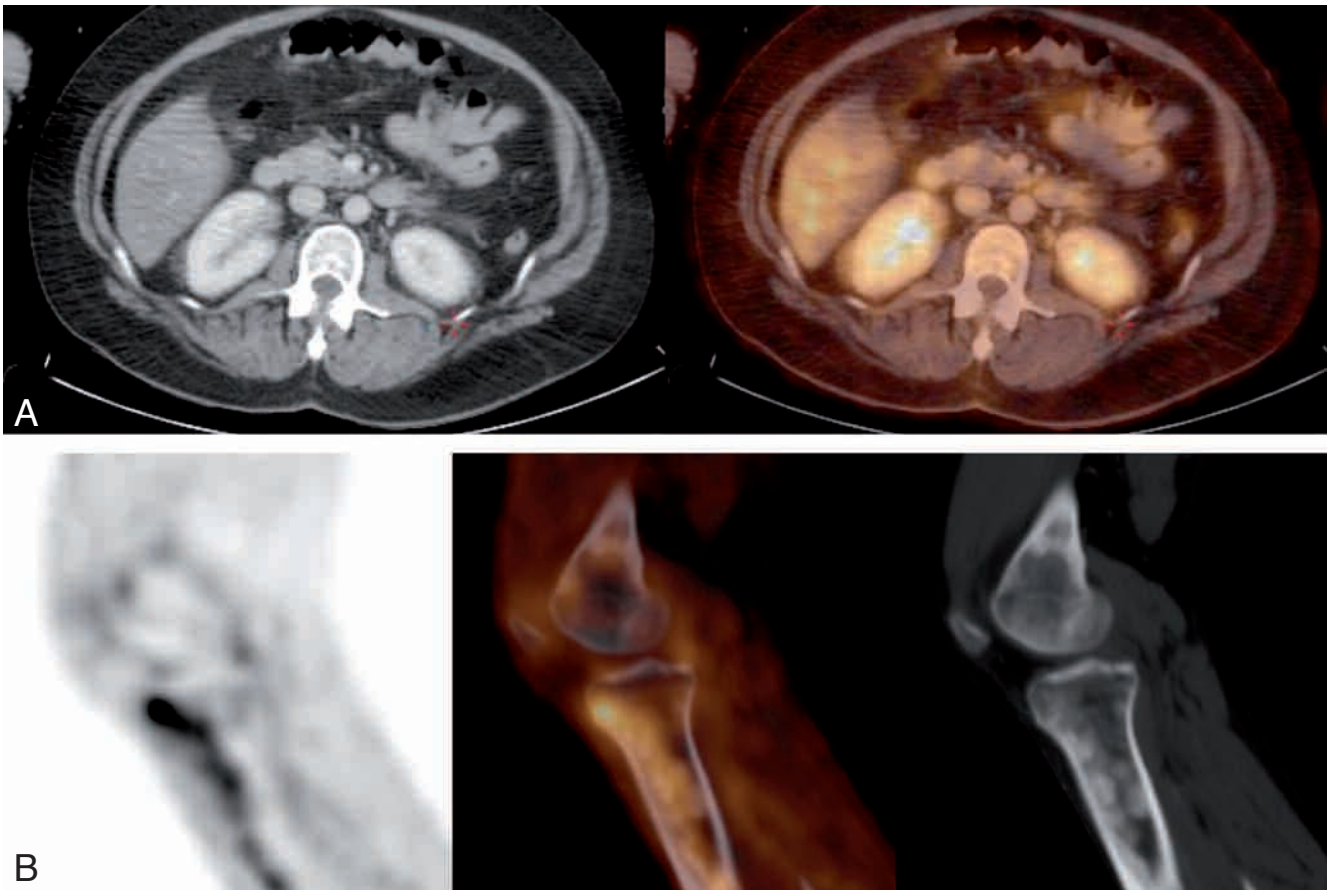

Fig. 5. — A. ^{18} F FDG PET/CT revealed metabolic active perinephric stranding, an atypical sign of retroperitoneal fibrosis. B. All visceral and skeletal lesions were hypermetabolic.

osteosclerosis of the diaphysis and metaphysis of the long bones with epiphyseal sparing (4, 5). Bone scintigraphy shows a corresponding symmetric increased tracer uptake in the diaphysis and metaphysis of primarily the long bones (6, 7). MRI depicts a replacement of the normal fatty bone marrow by a heterogeneous high intensity signal infiltrate on T1 sequence after intravenous injection of gadolinium, sparing the epiphysis (5).

Biopsy reveals a diffuse infiltration of bone and soft tissues by foamy histiocytes, further characterized by immunohistochemistry as non-Langerhans' cell (S 100 – and CD 1a –) macrophages (CD 68 +) (3).

As seen in our patient, blood samples often disclose an abnormal lipid metabolism, a moderate anaemia (related to the severity of the destruction of normal bone marrow, chronic inflammation and renal insufficiency), an increased sedimentation rate and C-reactive protein (signs of active inflammation).

Because of the rarity of this disease, no clinical trials have been conducted and treatment plans are mainly based on anecdotal experience. Treatment options are not curative but attempt to control the disease extension and include chirurgical debulking, systemic steroids, interferon alpha, various cytotoxic agents, radiation therapy and stem cell transplantation.

18F FDG PET/CT not only allows accurate staging of the disease (visceral and skeletal involvement), it is also an extremely useful tool to monitor treatment efficiency (8).

The prognosis of patients with ECD is related to the extent of disease at presentation and especially the severity of visceral involvement. Most patients with extra-skeletal disease die within 3 years after diagnosis due to congestive heart failure, lung fibrosis or renal insufficiency (4).

Conclusion

ECD is a rare form of non-Langerhans' cell histiocytosis, which still remains frequently unrecognized. The typical symmetric long bone involvement and the FDG-avidity of these osteoblastic lesions should however lead to the correct diagnosis in the era of hybrid imaging with ^{99m}Tc MDP bone SPECT/CT or ^{18}F FDG PET/CT.

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