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Case report

Spumous histiocytic oligoarthritis coexisting with systemic Langerhans' cell histiocytosis: Case report and literature review

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Abstract

A 27-year-old man consulted with clinical and radiological features of chronic erosive oligoarthritis of large joints (hips and knee), associated with diffuse lymph-node enlargement and diabetes insipidus. Lymph-node biopsy provided the diagnosis of systemic Langerhans' cell histiocytosis, for which synovial involvement remains a diagnostic challenge. Infectious diseases search and immunological tests were all negative. Skeleton radiographs, hip and cerebral magnetic resonance imaging showed, respectively, erosive arthritis of the hips and stigmates of pituitary-stalk involvement. Hip-synovium biopsy exhibited the main histological features of Erdheim–Chester disease, a non-Langerhans' cell histiocytosis. An extensive literature review found that Langerhans' cell histiocytosis and non-Langerhans' cell histiocytosis (mainly Erdheim–Chester disease) coexistence is rare and synovial involvements in them even more so, these latter presenting mainly as large joint monoarthritis. The absence of typical clinical and radiographic signs of Erdheim–Chester disease led to consideration of the rheumatologic diagnosis of unclassified non-Langerhans' cell histiocytosis (or Erdheim–Chester disease-type) oligoarthritis, associated with multiorgan Langerhans' cell histiocytosis. The differential diagnosis of large joint erosive arthritis should then include both entities, particularly when multiorgan manifestations are present. Non-Langerhans' cell histiocytosis synovial involvements responded poorly to vinblastine and corticosteroids, while Langerhans' cell histiocytosis involvements responded completely but transiently. Both entities regressed under cladribine, with only mild relapses of the non-Langerhans' cell histiocytosis involvements.

Keywords: Langerhans' cell histiocytosis; Synovitis; Erdheim–Chester disease; Arthritis; Cladribine

1. Introduction

Langerhans' cell histiocytosis (LCH) is a disease of the dendritic Langerhans'cell lineage. Like other entities corresponding to the heterogeneous group of non-Langerhans' cell histiocytosis (nLCH) including Erdheim–Chester disease (ECD), multicentric reticulohistiocytosis (MCRH), Rosai-Dorfman disease and juvenile xanthogranuloma that correspond to monocyte–macrophage disorders, its etiology and pathophysiology are poorly known and remain controversial [1]. However, LCH and certain nLCH, mainly ECD, share some similarities, suggesting a possible common cellular origin, background and/or pathogenic mechanisms. These entities are rare and exhibit a broad spectrum of specific or common but different organ tropisms of predilection, ranging from multisystemic life-threatening disease to localized and benign bone involvement. First–line therapy for LCH is consensual and consists of the combination of vinblastine and corticosteroids, while treatment of nLCH is less codified. Various chemotherapies and/or

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immunotherapies, including interferon-alpha, have been used with variable responses [1,2].

The performance of extensive English literature review using the Medline database found that the coexistence of LCH and nLCH group disorders (mainly ECD) in the same patient and their location on joints has rarely or exceptionally been reported. We report here and discuss about a patient, managements and nosological classifications of an oligoarthritis picture with histological features of ECD, mimicking inflammatory rheumatic diseases and coexisting with an histological proven systemic LCH.

2. Case report

A 27-year-old man, referred from Algeria to our department in September 2000, had a 10-year history of painless, enlarged cervical and axillary lymph-nodes associated with moderate occasional fever and anemia. A lymph-node biopsy performed in June 1996 showed unspecified histiocytic disease based on light microscopy histology. The patient received several cycles of oral or intravenous dexamethasone until July 2000, with only moderate and transient attenuation. His medical history was unremarkable except for a period of depression during the first years of the disease.

At admission, he complained of an 18-month history of inflammatory asymmetrical and intermittent pain in the knees, wrists and hips that had become constant during the last 6 months. Progressive polyuria–polydipsia syndrome was also noted. Physical examination revealed moderate general deterioration (Karnofsky index 70) and numerous enlarged (less than and greater than 1 cm) cervical and axillary lymph-nodes. Active and passive mobilizations of the hips were painful, predominantly on the left. Blood tests showed slightly elevated neutrophil count (10.4×10^9/L), anemia (hemoglobin, 95 g/dL), elevated inflammatory markers (C-reactive protein, 115 mg/L; erythrocyte sedimentation rate, 80 mm first hour), hypernatremia (150 mEq/L). Water-deprivation test confirmed diabetes insipidus. Other laboratory test results were unremarkable. Microbiology tests, including blood cultures, human immunodeficiency virus, tuberculosis, Lyme's disease, Whipple disease search and immunological assays (including rheumatoid factor, antinuclear and anti-cyclic citrullinated peptide antibodies) were all negative. HLA B27 research was also negative.

Complete skeleton radiographs including spine and sacroiliac joints were normal except for the hips, which showed bilateral superior and internal joint-space narrowing associated with numerous femoral head and acetabular subchondral erosions. Body computed-tomography scan was normal. Cerebral MRI found only mild thickening of the posterior part of the pituitary-stalk with loss of its normal 'bright signal' on the T2-weighted sequences. Axillary lymph-node biopsy exhibited characteristic features of LCH, i.e., numerous $CD68^+$, protein $S\text{-}100^+$ and $CD1a^+$ histiocytes with indented nuclei (Fig. 1) filling the lymph-node sinus, along with abundant neutrophils, lymphocytes, rare eosinophils and some giant multinucleated cells.

Hip MRI showed bilateral gadolinium-enhanced synovial and intra-articular signs, typical of an inflammatory process on T1-weighted and T2-weighted sequences respectively, and numerous subchondral erosions (Fig. 2).

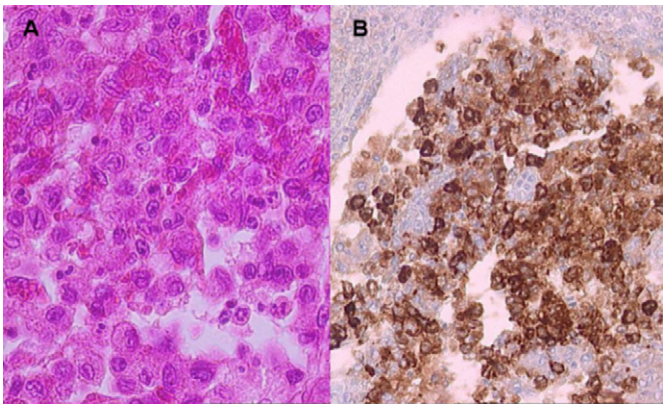

Fig. 1. Langerhans' cell histiocytosis in a lymph-node section. A. Numerous Langerhans'cells with indented nuclei containing typical linear grooves (hematoxylin–eosin, magnification × 400). B. Note the intense labeling of CD1a on Langerhans'cells (immunoperoxidase deposits, magnification × 200).

^{99m}Tc-bone scintigraphy detected bilateral elevated uptake at the superior acetabular pole of both hips, more pronounced on the left, while the rest of the skeleton was normal.

Left hip-synovium biopsy showed massive synovial infiltration by numerous foamy histiocytes with round nuclei (Fig. 3), exhibiting CD68 immunolabeling. CD1a immunolabeling was negative throughout the sample, but weak and very scattered immunolabeling of protein S-100 was observed. Microbiology cultures and search were negative, including for tuberculosis and Whipple disease.

Under first-line therapy with vinblastine plus prednisone (see Appendix 1), started in October 2000, in combination with DDAVP (desmopressin) nasal spray, all clinical and biological symptoms resolved except hip pain and stiffness, which diminished only slightly, requiring permanent symptomatic

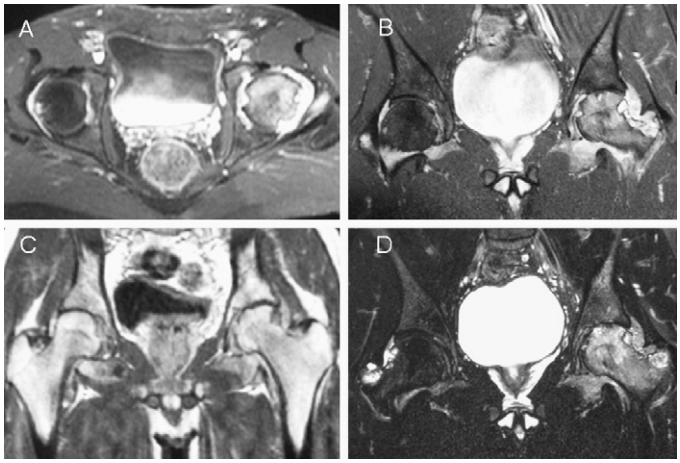

Fig. 2. MRI of the hips. Gadolinium-enhanced axial (A) and frontal (B, C) T1-weighted, and frontal T2-weighted (D) sequences. Note the rapid gadolinium enhancement of bilateral synovial thickening (pannus) and intra-articular joint effusion on T1-weighted sequences (A, B versus C), with high signal intensity on T2-weighted sequences, indicative of an inflammatory process, associated with numerous subchondral erosions on both femoral heads and acetabula (C and D).