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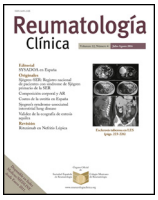

Case report

Rheumatoid Arthritis and Pulmonary Nodules: An Unexpected Final Diagnosis☆

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ABSTRACT

We report the case of a 50-year-old female smoker with an 11-year history of seropositive rheumatoid arthritis (rheumatoid factor and anti-cyclic citrullinated peptide antibodies) receiving triple therapy. She developed pulmonary nodules diagnosed as Langerhans cell histiocytosis by lung biopsy. We found no reported cases of the coexistence of these two diseases. Smoking abstinence led to radiologic resolution without modifying the immunosuppressive therapy.

Artritis reumatoide y nódulos pulmonares: un diagnóstico final inesperado

Palabras clave:
Artritis reumatoide
Histiocitosis de células de Langerhans
Nódulos pulmonares

RESUMEN

Se presenta el caso de una mujer de 50 años, fumadora, con artritis reumatoide seropositiva (FR y CCP) de 11 años de evolución en tratamiento con triple terapia, y aparición de nódulos pulmonares con diagnóstico final de histiocitosis de células de Langerhans por biopsia pulmonar. No hemos encontrado casos descritos de la coexistencia de ambas enfermedades. La abstinencia tabáquica llevó a la resolución radiológica sin necesidad de modificar la terapia inmunosupresora.

Case Report

The patient was a 50-year-old woman who smoked 20 cigarettes/day. She had been diagnosed with seropositive (rheumatoid factor [RF] and anti-cyclic citrullinated peptide antibodies [anti-CCP]), erosive rheumatoid arthritis (RA) in 1999. She was being treated with methotrexate (MTX) since 2000, in combination with salazopyrin and hydroxychloroquine since February 2009, at which time, she had achieved complete remission. In March 2010, in relation to a self-limiting case of a cold, her primary care physician had asked for a chest radiograph, which showed possible images of nodules, predominantly in the upper lobes. The patient was asymptomatic and the physical examination was normal. She had an immunological study in which she tested positive for RF and anti-CCP and negative for antinuclear antibodies and antineutrophil cytoplasmic antibodies; the Mantoux text was positive, and chest computed tomography revealed multiple bilateral pulmonary nodules measuring about 0.5 cm, some showing cavitation, especially in images from the upper and middle lobes, but the lower lobes were also involved (Fig. 1A). The bronchoscopy was normal, with negative results in the smear, bronchoalveolar lavage fluid culture and cytology of the bronchial aspirate for

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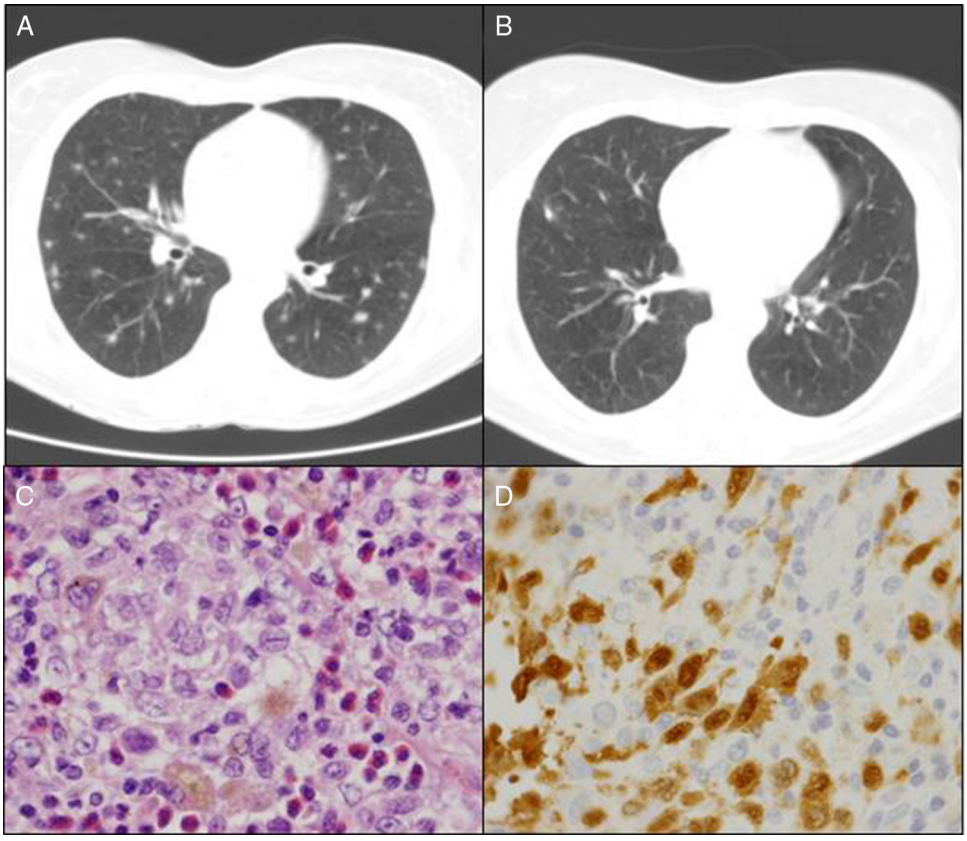

Fig. 1. (A) Pulmonary computed tomography (CT) at the time of diagnosis. (B) Pulmonary CT 6 months after the patient had quit smoking. (C) Langerhans cells (hematoxylin–eosin). (D) Positive immunohistochemical technique for CD1a (100×).

malignant cells. The patient was referred to undergo lung biopsy. Videothoracoscopy revealed that the lung parenchyma had small scattered subpleural lesions, and the pathological study showed the presence of foamy histiocytes with grooved nuclei, with other multinucleated and somewhat elongated histiocytes occupying the alveolar spaces (Fig. 1C). Immunohistochemical techniques identified cells that were positive for CD1a (Fig. 1D) and for S100, as well as langerin in the histiocytes described, all of which was consistent with Langerhans cell (LC) histiocytosis (LCH). At that time, it was recommended that she quit smoking and the same immunosuppressive therapy was maintained. During that entire period, she had no joint or respiratory symptoms and underwent radiographic follow-up 6 months later. The images showed residual pulmonary cysts and the nodules had disappeared (Fig. 1B). After 5 years of follow-up with no new incidences, the patient continues to receive triple immunosuppressive therapy.

Discussion

Histiocytes are cells of the immune system that include both macrophages and dendritic cells (non-macrophage antigen-presenting cells). Histiocytoses are rare diseases, LCH being the most representative, characterized by the infiltration of LC, a type of dendritic cell found predominantly in the pulmonary alveoli and in the skin, with its distinctive "racket"-shaped cytoplasmic Birbeck granules. The term LCH was coined in the attempt to confer a better classification and identification of the patients, as it combines previous entities (eosinophilic granuloma, histiocytosis X, etc.) in which the lesions were due to a proliferation and infiltration of the same cell type, the identification of LC being the diagnostic criteria called for since then.[1] The pathogenesis is unknown, there being either a reactive or clonal proliferative response, with different degrees of phenotypic aggressiveness in the infiltrated organs or systems (Table 1). Pulmonary Langerhans cell histiocytosis (PLCH) is the most representative form in adults and is usually recognized as a separate entity.

This disorder occurs in young adult smokers, and smoking cessation can lead to partial or total remission of the pulmonary lesions. In the early stages, it is characterized by bronchoalveolar inflammatory changes and, in the most advanced phases, by cystic lung destruction. The clinical manifestations vary widely: dyspnea,

Table 1
Classification of Histiocytosis.

Simplified classification of histiocytosis[a]
1. *Langerhans cell histiocytosis (LCH)*
2. *Hemophagocytic lymphohistiocytosis (HLH)*
3. *The rare histiocytic disorders (RHD)*
Juvenile xanthogranuloma
Erdheim-Chester disease
Multicentric reticulohistiocytosis
Rosai-Dorfman disease
The malignant histiocytosis
Classification of *Langerhans cell histiocytosis*
1. *Isolated disease in a single organ or system*[b]
Pulmonary LCH (85% of the cases of pulmonary LCH in adults)
Bone (single or multiple)
Skin/hypothalamus/hypophysis/lymph nodes/liver, spleen, thyroid glands
2. *Multisystem disease*[c]*: affecting two or more organs*

[a] Source: https://www.histiocytesociety.org.

[b] Previous nomenclature: histiocytosis X, eosinophilic granuloma. Hashimoto Pritzker disease: in the newborn, skin lesions and self-healing course.

[c] Previous nomenclature: Letterer–Siwe disease: aggressive infantile disorder with fever, lymphadenopathy, hepatosplenomegaly, bone and lung involvement. Hand–Schuller–Christian: triad of exophthalmos, diabetes insipidus and bone lesions, typical infantile disease, rare in adults.