

PULMONARY MANIFESTATIONS REVEALING ROSAI-DORFMAN DISEASE

M. Campana¹, J. Goupil de Bouillé², A. de Muret³, E. Diot², P. Dumont⁴, L. Plantier⁶, P. Diot^{1,5}, S. Marchand-Adam^{1,5}

¹CHRU Tours service de pneumologie; ²service de médecine interne; ³service d'anatomopathologie; ⁴service de chirurgie thoracique, Hôpital Bretonneau et Trousseau, Tours, France; ⁵Centre d'Etudes des Pathologies Respiratoires, INSERM U-1100/EA-6305 37032, Faculté de médecine, Université François Rabelais, 37032, Tours, France; ⁶service de Physiologie-Explorations Fonctionnelles, AP-HP, Hôpital Bichat-Claude Bernard, Université Paris Diderot

ABSTRACT. Rosai-Dorfman disease is a rare non-Langerhans cell histiocytosis, mainly involving cervical nodes. We present the case of a patient with a pulmonary form of Rosai-Dorfman disease without peripheral or intrathoracic lymph nodes, characterized by the presence of pulmonary nodules and cysts associated with bilateral pleural effusions. (*Sarcoidosis Vasc Diffuse Lung Dis* 2015; 32: 275-277)

KEY WORDS: histiocytosis, pulmonary fibrosis, cyst

Rosai-Dorfman disease is a rare non-Langerhans cell histiocytosis, mainly involving cervical nodes. We report the case of a man who presented with isolated pulmonary localization, without lymph node involvement.

In 2008, this 67-year-old man consulted for dyspnea with a two-year history of impaired general condition. His main medical history was a colonic adenocarcinoma cured by partial colectomy in 2003. In 2006, he had presented with an autoimmune hemolytic anemia treated successfully by a three-month course of systemic corticosteroids. Since this episode, and despite short courses of corticosteroids, he had experienced severe recurrent episodes of exudative pleural effusions, polyarthritides and Raynaud's phenomenon.

An initial assessment was conducted in 2008. Physical examination revealed a stage I MMRC dys-

pnea and bilateral crackles on lung bases. CT scan of the thorax showed an interstitial pneumonitis with sub-pleural interlobular septal thickening and micronodules, bilateral pleural effusion and mediastinal lymph nodes (2R, 2L, 4R and 7). Fiberoptic bronchoscopy did not reveal any endobronchial lesion. Bronchoalveolar lavage found 170000 cells/ml with 42% lymphocytes, 40% macrophages and 18% neutrophils. Spirometry results were normal. Antinuclear antibodies were positive at 1/1600 with anti-histone and anti-nucleosome specificity, and cryoglobulinemia type 3 was demonstrated. There was no elevation of IgG4. Mediastinal nodes were biopsied by mediastinoscopy. There was no specific lymphadenitis and no histiocytic infiltration. Systemic lupus erythematosus and cryoglobulinemia were ruled out and no diagnosis was established. However, corticosteroid therapy was begun at a dose of 20 mg per day associated with mycophenolate mofetil 2 gr/day, resulting in improvement of dyspnea, and loss of pleural effusions, arthritis and Raynaud's phenomenon.

From 2008 to 2012, corticosteroids were gradually tapered to 5mg/day. A new chest CT scan found that three pulmonary micronodules in the two

Received: 22 December 2014

Accepted after revision: 5 January 2015

Correspondence: Sylvain Marchand-Adam,
Service de Pneumologie, Hôpital Bretonneau,
2bis boulevard Tonnellé, 37044 Tours Cedex 9, France
Tel. 33 (0)2 47 47 37 87
Fax 33 (0)2 47 47 38 82
E-mail: s.marchandadam@univ-tours.fr

lower lobes had increased in size, reaching a diameter of 10 mm (Fig. 1A and 1B) with no change in mediastinal lymph nodes. Thickening of the pleura had occurred and lung cysts had also appeared (Fig. 1C and 1D). PET scan revealed significant uptake of 18FDG (SUV_{max} 2.1) in the pleura and nodules,

with no mediastinal lymph node or extra-thoracic uptake. A surgical biopsy of the lung nodules was performed. Histological analysis showed infiltration by histiocytes of pleural lymphatics, along interlobular septa and bronchioles (Fig. 1E). These histiocytes exhibited emperipolesis (Fig. 1F). Immunohis-

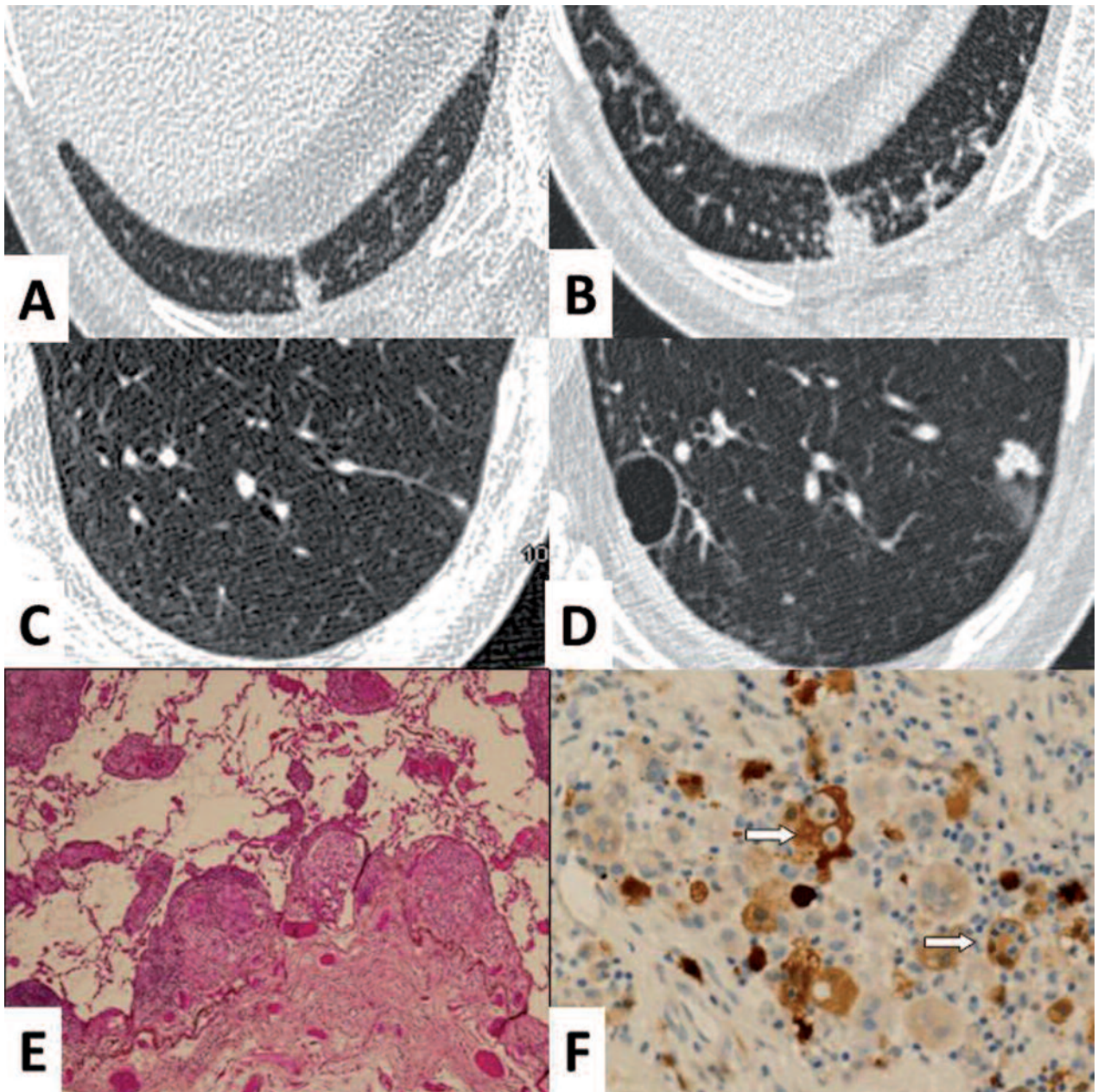


Fig. 1. Representative high resolution CT images of chest (Fig. 1A, 1B, 1C, 1D) and microscopic appearance of the lung lesion (Fig. 1E, 1F). Evolution of a pulmonary nodule in the right lower lobe under corticosteroid therapy between 2008 (A) and 2011 (B). Evolution of pulmonary cyst and a nodule in the left lower lobe between 2008 (C) and 2011 (D). Colonization of subpleural lymphatics and septa by histiocytes (hematoxylin and eosin) (E). PS100 immunostaining highlights histiocytic infiltration with emperipolesis (arrow) (F)

tochemistry analysis revealed CD68 positive, PS100 positive (Fig 1F), CD1a negative. All these tests confirmed a diagnosis of Rosai-Dorfman disease.

DISCUSSION

We present the case of a patient with a pulmonary form of Rosai-Dorfman disease, characterized by the presence of pulmonary nodules and cysts associated with bilateral pleural effusions without peripheral lymph nodes.

Rosai-Dorfman disease (RDD) is defined as a non-Langerhans histiocytosis of unknown origin, usually located mainly in the cervical lymph nodes¹. Its presentation includes a number of clinical and paraclinical signs, such as deterioration of the general condition, arthritis, inflammation, autoimmune hemolytic anemia, positive rheumatoid factor, polyclonal hypergammaglobulinemia, as in our patient, and the appearance of flu-like syndrome with the occurrence of large cervical (90%), axillary (24%), and mediastinal (15%) lymph nodes. It may be associated with hyper-IgG4 syndrome. None of these signs are specific and diagnosis can only be established by biopsy demonstrating histiocytic infiltration with emperilopesis, which is a pathognomonic element associated with positive immunomarking for CD68 + PS100 + and negative for CD1a (1).

Involvement of the mediastinal lymph nodes is the most common thoracic manifestation (15% of patients). Our patient had no specific mediastinal lymph node involvement but demonstrated an adenitis reaction on samples taken during mediastinoscopy. He subsequently developed episodes of bilateral pleural effusions responsive to corticosteroid, and pulmonary nodules and cysts. The presence of pleural effusions has been described in RDD as the result of an invasion of the pleural lymphatics

by histiocytes causing a loss of pleural resorption (2). "Pseudo-tumor" nodular presentation in the lungs as in our case has only been described on two previous occasions, in the form of hypermetabolic pulmonary nodules on PET scan (3,4). Cystic presentation has also been rarely reported. The mechanism of the formation of lung cysts in our patient does not seem to be an evolution of a granuloma, as observed in pulmonary Langerhans histiocytosis. It seems rather to be the consequence of the histiocytic infiltration of lymph along the broncho-vascular axes and bronchiolar obstruction as observed in lymphangioleiomyomatosis or lymphoid interstitial pneumonitis (5-8).

In the majority of RDD cases no active treatment is required. Therapeutic indications should be reserved for progressive tumor forms or those which are life-threatening or associated with autoimmune complications (1).

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