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Pulmonary manifestation of lymphomatoid granulomatosis[☆]



Granulomatosis linfomatoide: afectación pulmonar

To the Editor,

We report the case of a 57-year-old woman, former smoker, with a history of non-pathological cervical and axillary lymphadenopathies, non-necrotizing granulomatous mastitis and acute dorsal myelopathy. She was admitted for bronchopneumonia, and underwent bronchoscopy with transbronchial biopsies, which were inconclusive, and bronchoalveolar lavage (BAL) showing 65% lymphocytes and a normal CD4/CD8 ratio. The patient was readmitted due to right pleural effusion, categorized as lymphocytic exudate with no malignant cellularity, hepatosplenomegaly, and signs of pulmonary hypertension. Low levels of IgG subclasses were reported and treatment was initiated with prednisone. The patient subsequently developed dyspnea, anorexia and asthenia. Chest computed tomography showed peribronchial pulmonary nodules with undefined borders, air bronchogram sign, and tendency to converge into large masses in the lower lobes. These masses were surrounded by ground glass opacities and mediastinal lymphadenopathies, indicative of lymphomatoid granulomatosis. Ground glass opacities and lymphadenopathies,

however, are not typical of lymphomatoid granulomatosis, and may have been associated with the patient's smoking habit (Fig. 1). Lung function tests showed moderate restriction, with 36% diffusion, and laboratory reports revealed leukopenia due to lymphopenia. A bone marrow biopsy and a second bronchoscopy were performed, from which BAL showed predominant lymphocytes and a normal CD4/CD8 ratio. No additional data could be obtained from biopsy of a paratracheal lymphadenopathy. Culture and cytology were negative. A lung biopsy was obtained, after which the patient showed clinical and radiological worsening.

The result of the bone marrow biopsy suggested a T-cell-rich large-B-cell lymphoma. Chemotherapy was initiated, without improvement. Pathology results from the lung biopsy were inconclusive. The patient continued to worsen rapidly and progressively until she died. Autopsy confirmed diffuse T-cell and histiocytic-rich large-B-cell lymphoma, associated with Epstein-Barr virus (EBV), with perivascular involvement and changes indicative of lymphomatoid granulomatosis.

Lymphomatoid granulomatosis was first described in 1972 by Liebow et al.¹ It occurs primarily in patients aged between 40 and 60 years, and mainly in men (2:1). It is an angiocentric and angiodestructive process, affecting extranodal regions that in 90% of cases involves the lung. This disease of the B-cells is thought to be associated with EBV infection, large-B-cell lymphoma, and immunosuppressive states.² Typical lung involvement is characterized by nodular lesions, with lymphocytic invasion of the blood vessels, that may converge and cavitate.^{2,3} It is diagnosed from histology findings, including polymorphic lymphoid infiltrates, transmural infiltration of the arteries and veins by lymphoid cells, and focal areas of necrosis.⁴

The treatment of lymphomatoid granulomatosis is controversial, and varies according to the histological grade. In the absence of symptoms and if the histological grade is low, the patient should be monitored. Other cases are treated with prednisone and cyclophosphamide, although standard therapy for non-Hodgkin lymphoma has also been attempted.

Satisfactory therapeutic outcomes have recently been achieved with interferon-alfa-2b and rituximab.⁵ The prognosis of lymphomatoid granulomatosis varies: spontaneous remission is observed in 20% of cases, while in others, mean survival is 2 years, with a 5-year mortality of 63%–90%.

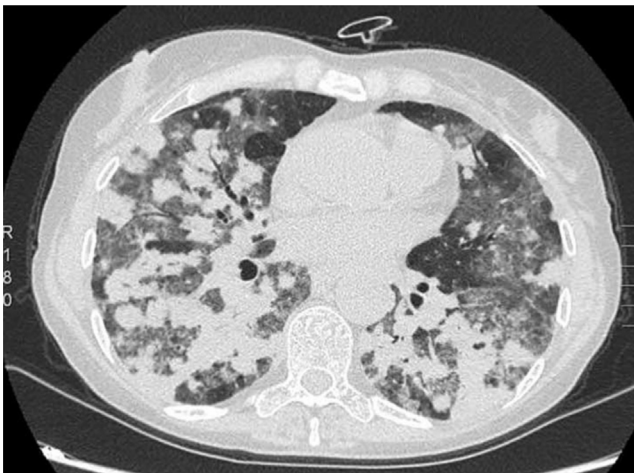


Fig. 1. Chest computed tomography, axial slice. Parenchymal window.

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Pulmonary Lymphomatoid Granulomatosis. A Rare Entity in the Differential Diagnosis of Pulmonary Nodules[☆]



Granulomatosis linfomatoide. Una entidad infrecuente a tener en cuenta en el diagnóstico diferencial de la imagen en suelta de globos

Dear Editor,

Lymphomatoid granulomatosis (LG) is an uncommon entity, classified by the WHO among the group of B-cell lymphoproliferative syndromes associated with Epstein–Barr virus (EBV) infection.¹ As lung is affected in more than 90% of cases, clinicians must establish a differential diagnosis against other diseases such as Wegener's granulomatosis, lymphoma or pulmonary metastases.

We report the case of a 76-year-old patient, with no toxic habits, hypertensive, with the chance finding on a chest X-ray of a “balloon release” image, finally diagnosed as LG. The patient was asymptomatic. No significant findings were observed on physical examination and lung auscultation was normal. Minimal leukocy-



Fig. 1. Chest X-ray, showing a chance finding of images of bilateral nodules resembling a “balloon release”, predominantly in the mid and lower fields.

tosis was seen on clinical laboratory testing, which was normal for tumor markers. Imaging tests showed the presence of bilateral pulmonary nodules, predominantly in the lower lobes (Fig. 1), some with air bronchogram sign and occasional central cavities. Transbronchial and transthoracic biopsies were performed, but did not yield a diagnosis. An atypical surgical resection of a pulmonary node was performed, showing polymorphous lymphocytic infiltrate with an angiocentric and angiodestructive pattern, consisting of aberrant CD20 positive lymphoid cells on a background of small sized lymphocytes. An EBER probe was used to demonstrate the presence of EBV-infected cells, establishing a definitive diagnosis of grade 2 LG.²

In view of the radiological progression over the previous months, treatment was started with prednisone and IFN α -2b. Initial response was good, but after 18 months of treatment, the patient died from the disease.

LG generally occurs between the ages of 50 and 70 years, mainly in men.

It is one of the B-cell lymphoproliferative syndromes associated with EBV infection, and appears more frequently in immunosuppressed patients, and in association with the administration of azathioprine and methotrexate.^{2,3}

The most frequently affected organ is the lung, but it can also affect the skin, the kidneys and the nervous system.

Patients may be asymptomatic at the time of diagnosis, but up to 60% can present non-specific symptoms such as cough, fever, rash, subcutaneous nodules, asthenia and anorexia, dyspnea, chest pain, ataxia or peripheral neuropathy.

Imaging tests typically show bilateral nodules and masses with peribronchovascular distribution, mainly in the lower lobes, which may converge or form central cavities. FDG uptake on PET is variable.⁴

Histopathological diagnosis is based on the triad of polymorphic lymphoid infiltrates, vasculitis, and focal necrosis.

The WHO proposes a histological classification according to the prominence of B-cells, from grade 1 to 3. The characteristics of these cells are similar to those of diffuse B-cell lymphoma.¹

Treatment requires discontinuation of potentially causative medications, plus chemotherapy with IFN α -2b⁵ or rituximab.

The decision to treat must be based on the presence of symptoms, extensive involvement, or high-grade histopathological lesions.

Although rates of spontaneous remission of up to 20% have been reported, most cases progress, and mean survival is between 1 and 6 years.

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