Case report

Diffuse Interstitial Lung Disease as a First Manifestation of Waldenström's Macroglobulinemia: Case Report and Review of the Literature

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ABSTRACT

Waldenström's macroglobulinemia (WM) is a lymphoid malignancy characterized by infiltration, mainly of the bone marrow and lymph nodes, by small mature lymphocytes showing plasmacytoid differentiation, associated with an IgM monoclonal band, and in general, a low degree of aggressiveness. We present the first case reported in the Spanish literature of interstitial lung disease presenting as WM and we review the literature.

Enfermedad pulmonar intersticial difusa como primera manifestación de macroglobulinemia de Waldenström: descripción de un caso y revisión de la literatura

RESUMEN

La macroglobulinemia de Waldenström (MW) es una neoplasia linfoides caracterizada por una infiltración principalmente de la médula ósea y del ganglio linfático por linfocitos pequeños maduros o con diferenciación plasmocitoide, con banda monoclonal IgM asociada, y en general un bajo grado de agresividad. Presentamos el primer caso publicado en la literatura española de enfermedad pulmonar intersticial difusa como forma de presentación de una MW y realizamos una revisión de la literatura.

Introduction

Waldenström's macroglobulinemia (WM) is a lymphoid malignancy characterized by infiltration of the bone marrow, lymph nodes or other tissues by small mature lymphocytes showing plasmacytoid differentiation. It is associated with the presence of an IgM monoclonal band and generally has a low degree of aggressiveness. The incidence of pulmonary manifestations is low, and it is even rarer for pulmonary disease to constitute the onset of the disease. We present the first case reported in the Spanish literature of interstitial lung disease as the initial presentation of WM and a review of the literature.

Clinical Characteristics

A 73-year-old male ex-smoker was referred to our hospital with chronic cough. Pulmonary auscultation revealed bilateral basal fine end inspiratory crepitations. No lymphadenopathy or hepatosplenomegaly was observed. The chest X-ray showed mild diffuse opacity on both lower fields. High-resolution computed tomography (CT) showed interstitial involvement with mainly peripheral thickening of the interlobular septa of the left lung, associated with bilateral, patchy areas of ground glass opacities, mainly in the peripheral regions (Fig. 1A).
Table 1
Case Study of Pulmonary Involvement as First Manifestation of Waldenström’s Macroglobulinemia.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Ref.</th>
<th>No. of cases</th>
<th>Respiratory symptoms</th>
<th>Radiological findings</th>
<th>Diagnostic method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hull (1982)</td>
<td>2</td>
<td>1</td>
<td>Dyspnea, cough</td>
<td>Infiltration</td>
<td>BMB, TBB</td>
</tr>
<tr>
<td>Bruno (1968)</td>
<td>3</td>
<td>1</td>
<td>Dyspnea</td>
<td>Mass, pleural effusion</td>
<td>TBB, OLB</td>
</tr>
<tr>
<td>Winterbauer (1974)</td>
<td>4</td>
<td>2</td>
<td>Dyspnea, cough or asymptomatic</td>
<td>Infiltration</td>
<td>BMB, autopsy</td>
</tr>
<tr>
<td>Moeschlin (1966)</td>
<td>5</td>
<td>1</td>
<td>Dyspnea, cough</td>
<td>Infiltration</td>
<td>OLB</td>
</tr>
<tr>
<td>Strunge (1969)</td>
<td>6</td>
<td>1</td>
<td>Dyspnea, hemoptysis</td>
<td>Infiltration, mass, pleural effusion</td>
<td>Autopsy</td>
</tr>
<tr>
<td>Fadil (1998)</td>
<td>7</td>
<td>1</td>
<td>Dyspnea, cough</td>
<td>Infiltration, pleural effusion</td>
<td>BMB, TBB</td>
</tr>
<tr>
<td>Bull (1984)</td>
<td>8</td>
<td>1</td>
<td>Dyspnea on effort</td>
<td>Pleural biopsy</td>
<td>VTLD</td>
</tr>
<tr>
<td>Case described</td>
<td>1</td>
<td></td>
<td>Cough</td>
<td>Interstitial lung disease</td>
<td>VTLD</td>
</tr>
</tbody>
</table>


**Discussion**

Lymphoproliferative lesions affecting the lung are rare. Among these, primary lymphomas, defined as clonal lymphoid proliferation isolated from the lung, are even more uncommon, representing an estimated 1% of all lymphomas and 0.5% of all lung tumors. Pleuropulmonary involvement in WM is infrequent and the most typical respiratory symptoms are dyspnea and cough. In the early case descriptions, only pneumonia and pleural effusion were identified as pulmonary manifestations of WM, but later reviews have shown that the spectrum of respiratory involvement is wider. Interstitial pulmonary involvement, as such, is exceptional and may be underreported.

After performing a search of the literature in the PubMed and Medline databases, we only found 7 articles describing cases in which the disease presented as a pulmonary event (Table 1). Among these, we did not find any cases similar to the one discussed here, which presented initially as diffuse interstitial lung disease.

Although there are studies that support bronchoscopy (transbronchial biopsy and bronchoalveolar lavage) as methods for the diagnosis of lymphoproliferative disorders of the lung, others claim that the efficacy of these methods is poor, with diagnostic yields of between 15% and 30%. These results suggest that surgical biopsy may be the procedure of choice for the diagnosis of lymphoma in potentially operable patients. In our case, given the good clinical status of the patient and as a minimally invasive approach using video-assisted thoracoscopic surgery, we did not opt for surgical biopsy.

The pathological findings suggested a differential diagnosis of lymphoid interstitial pneumonia, lymph node hyperplasia or even hypersensitivity pneumonitis.

In this patient, the laboratory findings of monoclonal gammopathy suggested a diagnostic hypothesis of a lymphoproliferative process. This was subsequently confirmed with the histological testing. In WM, the lymphoid infiltration may have a histological component of plasmacytoid lymphocytes or small mature lymphocytes. For this reason, immunohistochemistry or flow cytometric immunophenotyping is essential for differentiating this entity from other lymphoproliferative processes, such as lymphocytic lymphoma or follicular lymphoma (grade I) that also involve the proliferation and accumulation of small lymphocytes.

Finally, the test results and a review of the literature confirmed a non-low grade Hodgkin’s lymphoma with plasmacytoid differentiation, compatible with a diagnosis of WM.

**References**