CASE REPORTS

Primary Pulmonary Lymphoma Presenting as a Pulmonary Mass With Cavitation

C. Martínez Rivera, M. Bonnin Vilaplana, C. Simón Adiego, A. Palacín Forgué, J. Puig Zuza, and I. Sampablo Lauro

Hospital Sagrat Cor, Barcelona, Spain.

Primary pulmonary lymphoma is a rare entity usually formed of B-type cells, usually low-grade and composed of mucosal- or bronchial-associated lymphoid tissue. High-grade primary pulmonary lymphomas usually occur in immunodeficient patients who mostly present with respiratory and nonspecific symptoms. A chest x-ray may show a pulmonary mass or atelectasis and pleural effusion. In such cases, the prognosis is worse than for low-grade pulmonary lymphomas; survival is 8 to 10 years and there is a higher probability of local progression or metastasis. We report the case of an immunocompetent 76-year-old patient who had a pulmonary mass with cavitation secondary to a large B-cell primary pulmonary lymphoma. After the fourth session of chemotherapy the pulmonary mass was reduced in size and an aspergilloma was seen to have developed in the residual cavity. A review of the literature revealed this case to be anecdotal as it is extremely infrequent for a primary pulmonary lymphoma to present in the form of a single mass with cavitation and with few symptoms.

Key words: *Cavitated mass. Primary pulmonary lymphoma. High-grade. B-cells.*

Masa cavitada como forma de presentación de un linfoma pulmonar primario

El linfoma pulmonar primario es una entidad poco frecuente, que en la mayoría de las ocasiones es de estirpe celular tipo B, predominantemente de bajo grado y de tejido linfoide asociado a la mucosa (MALT/BALT). Los linfomas pulmonares primarios de alto grado suelen presentarse en pacientes inmunodeprimidos. Habitualmente se presentan con síntomas respiratorios y generales. La radiografía de tórax puede mostrar una masa pulmonar o atelectasia y derrame pleural. El pronóstico es peor que en los linfomas pulmonares de bajo grado, con un tiempo de supervivencia de 8-10 años y una mayor probabilidad de progresión local o recidiva a distancia. Presentamos el caso de un paciente de 76 años no inmunodeprimido con una masa pulmonar cavitada secundaria a un linfoma pulmonar primario tipo B de células grandes. Después de la cuarta sesión de quimioterapia se objetivó una reducción de la masa pulmonar y en la cavidad residual se desarrolló un aspergiloma. Revisando la bibliografía se ha comprobado lo anecdótico del caso presentado, pues es extremadamente poco frecuente que un linfoma pulmonar primario se presente en forma de masa cavitada única y con poca repercusión clínica en cuanto a sintomatología general.

Palabras clave: *Masa cavitada. Linfoma pulmonar primario. Alto grado. Células B.*

Introduction

Primary pulmonary lymphomas only constitute 4% of extra-nodal, non-Hodgkin lymphomas (NHL), less than 1% of NHL in general, and between 0.5% and 1% of malignant pulmonary neoplasms. Fifty-eight to 87% of cases of this extremely uncommon disease are low-grade B-cell lymphomas, and 11%-19% are high-grade or large B-cell lymphomas. The prognosis for high-grade or large B-cell lymphomas is worse than for low-grade lymphomas and respiratory and general symptoms are usually present. High-grade lymphomas are often found in immunosuppressed patients or those with autoimmune diseases. In patients infected by the human immunodeficiency virus (HIV), multiple, cavitated nodules can be seen. This is rare in immunocompetent patients.

We report the case of a 76-year-old man with respiratory symptoms in the form of cough, mucous expectoration and dyspnea. A chest x-ray and computed tomography (CT) scan revealed a cavitated mass in the superior lobe of the right lung. Histological diagnosis showed a pattern of high-grade B-cell lymphoma with features indicative of transformation from a mucosa-associated lymphoid tissue (MALT) lymphoma.

In this case report, we review the literature on this type of lymphoma, stressing the extremely unusual nature of the clinical and radiological presentation of this case.

Correspondence: C. Martinez Rivera.
Hospital Sagrat Cor.
Viladomat, 288. 08029 Barcelona. España.
E-mail: med003790@saludalia.com

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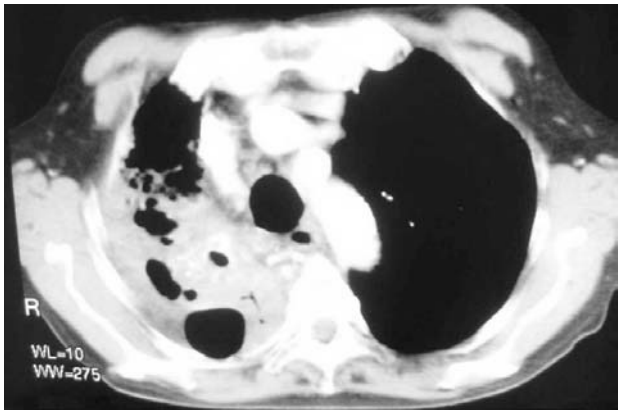

Figure 1. Thoracic computed tomography image showing a cavitated mass in the upper lobe of the right lung.

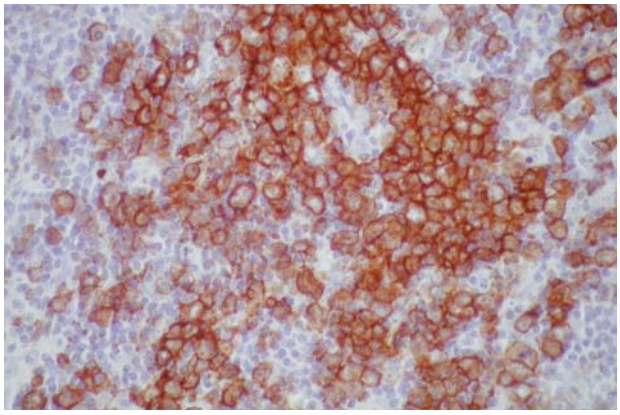

Figure 2. B-lymphocytes (CD20-type marker) can be seen in the tissue sample.

Clinical Observation

The patient was a 76-year-old man, with no known allergies and no smoking or drinking habits, who had a medical history of hypertension, hypolipemia, and incipient vascular dementia. At the age of 18 he developed a respiratory infection, with hemoptoic expectoration, which required treatment for 2 years. He did not know what diagnosis was given. The patient came to the emergency room because of cough with sputum expectoration in the previous month accompanied by dyspnea in the previous 15 days. He also reported that mild retrosternal, thoracic pain that increased on coughing or taking a deep breath had developed in the previous 2 or 3 days. Wasting syndrome was not evident and fever was denied. The physical examination revealed a good general state of health, with normal results for hydration and skin color, and no fever. Palpation detected no involvement of lateral-cervical, axillary, or supra-clavicular lymph nodes. Heart sounds were normal. Respiratory auscultation revealed diffuse crackles in the right lung field, predominating in the base. The abdomen was soft and palpable. There was no swelling of liver or spleen. The neurological examination gave normal results.

Laboratory tests were carried out on admission to hospital. Glucose and liver and kidney function tests were normal. The lactate dehydrogenase concentration was 808 U/L, C-reactive protein was 11.9 mg/L, and β_2 microglobulin was 5 mg/dL. The hematocrit, red cell count, white cell count, and leukocyte composition were normal. The chest x-ray showed a mass with well-defined edges and internal cavitation situated in the apex of the right lung, and displacing the trachea. The Mantoux test was negative after 48 hours.

Tumor markers—prostate-specific antigen, carcinoembryonic antigen, and alfa fetoprotein levels—were normal. HIV serology was negative. The immunoglobulin G Epstein-Barr antibody titer was high (5.5), but the immunoglobulin M Epstein-Barr antibody titer was normal (0.1)

The results of sputum culture and the 3 direct Koch bacillus examinations were not specific for any bacterial or mycobacterial agent.

Because a pulmonary neoplasm was suspected, CT and fiberoptic bronchoscopy were carried out. The CT scan confirmed the presence of a dense cavitated mass in the upper lobe of the right lung. The CT image revealed infiltration of the posterior mediastinum by the pulmonary mass and by diseased mediastinal lymph nodes (Figure 1). Fiberoptic bronchoscopy showed stenosis of the right main bronchus due to extrinsic compression and an exophytic mass at the entrance of the upper lobar bronchus of the right lung that prevented the bronchoscope from passing and bled easily. A biopsy of bronchial tissue in this area revealed the presence of an atypical lymphoid infiltrate of B-cell phenotype. An attempt to obtain more biopsy material for immunohistochemical testing failed. Bronchial aspirate was obtained for direct examination for BK virus and for cytology, both of which gave negative results. Following this a CT-guided fine-needle aspiration of the pulmonary mass obtained little material, mostly consisting of atypical lymphoid cells. The amount of material obtained was insufficient to allow specific classification by immunohistochemical techniques.

Finally, 45 days after the first visit, a diseased right lateral-cervical lymph node not present on the first visit appeared. Following excision of the node, histology showed a proliferation of lymphoid cells, many of which were phenotype B ($CD20^+$), with a high proliferation index. Soft tissues had been infiltrated and nerves surrounded. The examination also revealed the presence of small lymphocytes of mature appearance including T-lymphocytes and to a lesser extent, mature B-lymphocytes (Figure 2). On the basis of these findings the patient was diagnosed with a large B-cell or high-grade lymphoma although, given the presence of small B-lymphocytes of mature appearance, the possibility of a transformation from MALT lymphoma to large B-cell lymphoma was considered. Chemotherapy with cyclophosphamide, Adriamycin, vincristine, and prednisone was administered every 14 days in 6 cycles. After the fourth cycle complications occurred. A thrombocytopenia of autoimmune origin developed, and the patient suffered an episode of incipient hemoptysis. A chest x-ray and CT scan revealed a mycetoma. *Aspergillus fumigatus* grew in cultures of bronchial aspirate and sputum. At the moment of writing this report treatment with itraconazole at a dosage of 200 mg per day has been started. Once the platelet count has improved, embolization and surgery of the aspergilloma will be considered.

Discussion

The modern definition of primary pulmonary lymphoma specifies that it is a clonal, lymphoid proliferation affecting a single lung or both and that has

not spread outside the lungs on diagnosis or does not spread in the following 3 months.[1] When the lung is the main organ affected by a NHL, the term primary pulmonary lymphoma also includes multifocal MALT NHL, lung disease with hilar or mediastinal lymph node involvement, and lymphomatoid granulomatosis (whose clonal nature is debatable).[2]

Primary pulmonary lymphomas are very uncommon. They constitute only 3%-4% of extra-nodal NHL, less than 1% of NHL in general, and only 0.5%-1% of malignant pulmonary tumors.[2]

According to the World Health Organization's classification system, primary pulmonary lymphomas can be divided into B-cell primary pulmonary NHL, and lymphomatoid granulomatosis.[3] The first group subdivides into low-grade B-cell primary pulmonary lymphomas (58%-87%), high-grade B-cell primary pulmonary lymphomas (11%-19%), primary pulmonary plasmacytoma, and intravascular pulmonary lymphomas.[2] Ninety percent of low-grade B-cell, primary pulmonary lymphomas are composed of MALT or bronchus-associated lymphoid tissue.

The incidence of high-grade B-cell primary pulmonary lymphomas may have been underestimated as they spread rapidly into mediastinal and extra-thoracic locations.[4] It has been observed that in 50% of cases they can coexist with MALT, B-cell lymphomas. These mixed or transitional forms have given rise to the hypothesis that high-grade B-cell lymphomas may be the result of the transformation of a low-grade lymphoma. This is subject to debate, as cytogenic differences have been found between the 2 types of lymphoma that would seem to rule out this possibility.[5] However it has been proved conclusively that high-grade B-cell primary pulmonary lymphomas often occur in immunocompromised patients. The age at which the illness starts is about 60, except in the case of patients with HIV infection.[2,6]

Patients usually present with respiratory symptoms, fever, and weight loss.[2,6] The chest x-ray shows a pulmonary mass or atelectasis. Pleural effusion is also common. Patients with HIV infection usually have multiple nodules that may be cavitated.[7] Bronchoscopy often reveals stenosis due to infiltration or an exophytic mass.[6] A histological diagnosis can be obtained by bronchial or transbronchial biopsy or by transthoracic fine-needle aspiration. Cells show mitotic activity, and lymphoid infiltrate can affect bronchial, vascular, or pleural structures. Necrosis may be evident. Given the high degree of cell atypia it is usually necessary to use immunohistochemical techniques to rule out a diagnosis of carcinoma, melanoma, or sarcoma when there is a fibroblastic reaction. Angiotropic lesions may be an indication of lymphomatoid granulomatosis.[2,8]

Survival is shorter for high-grade B-cell lymphomas than for low-grade ones. The average survival period is 8-10 years.[9] However it is shorter for patients with underlying diseases like HIV infection or for patients who have had organ transplants. Progression and remission, whether local or distant, are more common than in patients with low-grade B-cell lymphomas.

In the case we report a series of factors coincided to give an unusual presentation. There were very few repercussions in the form of general symptoms and the patient did not present with fever or wasting syndrome. Although it is not particularly uncommon to see images of a single, unilateral mass, the fact that the mass was cavitated in an immunocompetent individual makes it especially rare within the literature we reviewed (MEDLINE, 1985-2003). Cavitated masses occur in patients with HIV infection and are multiple and bilateral.[7] We have only found 2 cases of patients with single cavitated pulmonary masses. The first, a younger patient initially diagnosed with Wegener's granulomatosis, was diagnosed by lung biopsy.[10] The second patient was diagnosed by fine-needle aspiration of the pulmonary mass.[11]

This experience leads us to the conclusion that when a radiographic image shows a cavitated pulmonary mass the possibility of a high-grade B-cell primary pulmonary lymphoma has to be considered in the differential diagnosis whether or not there is an underlying disease involving autoimmunity or immunodepression.

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