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Scientific letters

Unilateral Lung Infiltrate: A Rare Form of Presentation of Primary Pulmonary Lymphoma☆

Infiltrado pulmonar unilateral: una forma rara de presentación de un linfoma pulmonar primario

Dear Editor,

Primary pulmonary lymphoma accounts for 3%–4% of extranodal non-Hodgkin's lymphoma, less than 1% of non-Hodgkin's lymphoma, and only 0.5%–1% of primary pulmonary cancers.[1] The most common presentation is bilateral pulmonary infiltrate, whether in the form of nodules or a cavitated mass. Other less common presentations are air bronchogram, ground glass areas, pleural effusion, and atelectasis.[2,3] However, a unilateral presentation is rare. Diffuse large B-cell lymphoma (DLBCL) accounts for approximately 15% of cases of non-Hodgkin's lymphomas.[1]

We report the case of a 75-year-old man who consulted due to asthenia, anorexia, and weight loss of about 10 kg in 3 months, accompanied by pleuritic pain in the left hemithorax and intermittent dyspnea. He also reported a perforating injury in the left hemithorax that occurred several years ago. No toxic habits or exposure to physical or chemical agents were recorded, and personal history included arterial hypertension, type 2 diabetes mellitus, ischemic heart disease, and atrial fibrillation with permanent anticoagulation. The only finding of interest on examination was cachexia with hypoventilation in both lung bases and basal oxygen saturation of 98%. A raised left hemidiaphragm associated with a basal area of pulmonary consolidation and extensive pleural thickening, consistent with diffuse pleural fibrosis, were observed on chest X-ray. Clinical laboratory tests revealed normocytic anemia consistent with chronic disorders, neutrophilia without leukocytosis, slightly elevated beta-2-microglobulin, and hypoalbuminemia with no evidence of clonal spikes. Chest computed tomography (CT) revealed a tumor measuring 5.3×9.6 cm, adjacent to the descending thoracic aorta, with contrast medium uptake, apparently in contact with the left lower lobar bronchus, associated with an extensive area of pleural calcification. No associated lymphadenopathies were observed (Fig. 1). The remaining exploratory studies were normal. A positron emission tomography/CT (PET/CT) was performed in order to determine the nature of the lesion and to complete the study. This procedure revealed increased metabolic activity in the lesion, with an increased cellular proliferation rate, and possible infiltration of the D9 vertebra and posterolateral region of the chest wall. Fiberoptic bronchoscopy was ruled out, as the lesion would have been inaccessible with this technique. CT-guided core needle biopsy was performed, and histological results showed Epstein–Barr virus (EBV) positive DLBCL-NOS. The patient was referred to the medical oncology clinic to plan treatment and follow-up.

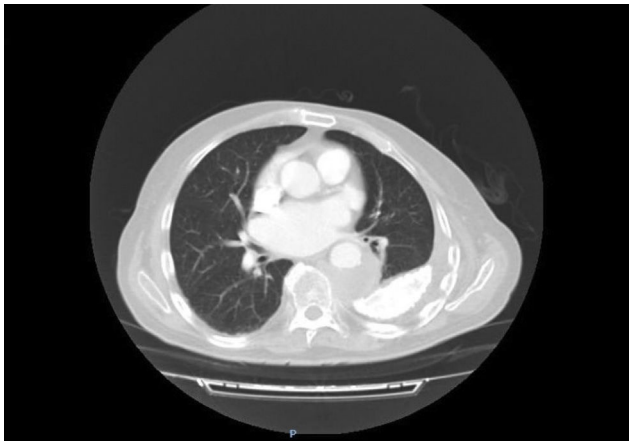

Fig. 1. Chest CT slice showing the lesion. An adjacent area of para-aortic pulmonary consolidation and left posterior pleural calcification can be observed.

Primary pulmonary lymphomas (PPL) are very rare, and account for less than 1% of cases of pulmonary neoplasms. PPLs are understood to be a disease exclusively involving the lung, with no evidence of extrathoracic, mediastinal, lymphatic or bone marrow involvement.[4] Presentation tends to be bilateral, usually in the form of masses or nodules that generally cavitate (around 50% of cases), and less frequently as ground glass areas, or with pleural involvement, air bronchogram, reticular images, or lobar atelectasis.[3] DLBCL is the most common form of non-Hodgkin's lymphoma (NHL), and accounts for 15%-25% of cases, depending on the series.[1,4] This type of lymphoma constitutes a heterogeneous group with its own clinical, morphological, genetic and biological signature. The most common extranodal site is the gastrointestinal tract. It is diagnosed more frequently in men over 60 years of age, although it has been reported in patients younger than 30. Half of these tumors are diagnosed in a disseminated stage, and the other half as localized disease, in other words, contained within the area of 1 radiation field. DLBCL is locally very invasive. EBV-positive DLBCL is a specific variant that was added to the World Health Organization classification system in 2016. It can occur at any age, and is generally diagnosed in patients with no history of immunodeficiency or other lymphomas.[1] This entity can overlap with lymphomatoid granulomatosis, the difference being in the appearance of EBV-positive B cells (which are scant otherwise). Our case is unusual due to the very rare manifestation of EBV-positive DLBCL as primary pulmonary lymphoma, along with the unilateral, non-cavitated pulmonary consolidation. We were unable to

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establish any association with the residual area of chronic pleural calcification, despite an extensive review of the literature.

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Pulmonary Meningotheliomatosis

Meningoteliomatosis pulmonar

Dear Editor:

The differential diagnosis for diffuse bilateral pulmonary micro nodules is extensive and typically includes infections, inflammatory disorders and malignancy. Meningothelial-like nodules of the lung, which are the result of proliferation of epithelioid cells within the interstitium, can also present as solitary pulmonary nodule, or as diffuse micro nodules, as in our patient. Although initially characterized as "minute pulmonary chemodectomas", these nodules were subsequently found to lack neuroendocrine properties.[1–4] The case adds to the growing literature on the natural history of pulmonary meningotheliomatosis (PM), as it remains an elusive clinical entity.

We report the case of a 58-year-old female, non-smoker, who presented to our clinic with an "abnormal" CT scan of the chest. The patient had presented to the emergency department a week previously for abdominal pain for which a CT abdomen/pelvis was obtained. The abdominal imaging was unremarkable except for lung nodules visualized at the bases. This prompted a dedicated chest CT scan and referral to our clinic. Her only symptom was intermittent dry cough for 3 months before presentation. Her physical examination, pulmonary function tests, routine blood work and rheumatology studies were unremarkable.

CT (computed tomography) scan chest showed multiple bilateral micronodules, some of which had ground glass appearance while others were more well-defined (Fig. 1A). Both upper and lower zones were involved although there was a basal predominance. Bronchoscopy with bronchoalveolar lavage (BAL) was unremarkable and showed normal macrophage predominance. Transbronchial biopsy was non-diagnostic. A video assisted thoracoscopic (VATS) biopsy was performed, the histopathology of which revealed multiple pulmonary meningothelial lesions (Fig. 1B). A final diagnosis of pulmonary meningotheliomatosis (PM) was made based on radiology and histopathological features.

Meningothelial lesions of the lung were first described by Korn et al. in 1960, and were initially characterized as "minute pulmonary chemodectomas".[1] Since immunohistochemical studies showed it lacked neuroendocrine properties, the condition was renamed "minute pulmonary meningothelial-like nodules".[3,4] Other term that surfaced in our review of literature includes "diffuse pulmonary meningotheliomatosis", particularly when there are numerous pulmonary micronodules causing symptoms.[2,5] For purpose of uniformity, we will refer to this entity as "pulmonary meningotheliomatosis" (PM) henceforth.

Data from large retrospective studies so far show that it most commonly presents in the sixth decade of life.[2,6,7] The age range can be between 20 and 80 years of age.[6,7] The condition seems to have a strong female predilection.[2,6,7] Although mostly diagnosed incidentally on pathology specimens, in patients with diffuse micronodules, non-specific symptoms (e.g.: cough, shortness of breath, fatigue) and pulmonary function abnormalities have been reported.[2]

PM can present as a solitary nodule, or more commonly as multiple, sub-centimeter, ground glass nodules on the CT scan.[2,7,8] While majority of the cases have reported basal predominance, this does not seem to be universal.[8] Although surgical lung biopsy seems to have a higher yield for diagnosis, transbronchial biopsy has also been utilized successfully.[5,9] When it presents as diffuse micronodules, such as in our patient, it closely resembles more common etiologies such as granulomatous infections or metastatic malignancy, from which it needs to be distinguished. Therefore, given its rarity and lack of a characteristic radiological pattern, diagnosis of PM requires histopathology.

The etiology and risk factors for proliferation of meningothelial-like nodules remain unclear. It is more commonly associated with chronic lung insults than with acute lung injury.[6] One of the most commonly reported association for meningothelial lesions has been with pulmonary thromboembolic disease.[2] This was highlighted again in the retrospective study by Mukhopadhyay et al. where the highest incidence of meningothelial lesions was in patients with thromboembolic disease/infarcts (5/12; 42%).[6] Interestingly, 26% of patients were also found to have smoking related interstitial lung disease such as respiratory bronchiolitis-associated interstitial lung disease/desquamative interstitial pneumonia.[6] However, relationship with smoking remains unclear and causality cannot be inferred based on available data. Pulmonary meningothelial nodules have also been found in higher incidence in patients with malignant pulmonary tumors than in those with benign disease (7.3% versus 2.5%; $P = .044$).[7] In the analysis of 121 patients by Mizutani et al., meningothelial lesions were found more often in patients with lung adenocarcinoma than with other primary pulmonary malignant tumors.[7] A similar trend was noted in the study by Mukhopadhyay et al. but was not statistically significant.[6] Thus, based on most of the studies, the meningothelial proliferation likely occurs in the setting of a chronic lung disease, as a reaction to hypoxia, ischemia or an underlying malignancy.

On histopathology, PM is characterized by an interstitial proliferation of epithelioid cells with oval, bland nuclei with stippled chromatin. These cells are arranged in nests within the alveolar septa, usually expanding it, and they are usually found around pulmonary veins.[2] As they expand, they may connect to each other with intervening collagen.[2] However, proximity to