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Pulmonary MALT lymphoma associated with interstitial pulmonary disease

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ABSTRACT

Interstitial lung disease (ILD) and low-grade Mucosa-associated B-cell lymphoma (MALT lymphoma) are two different disorders of the respiratory system. In some cases, pulmonary MALT lymphoma is seen presenting with interstitial lung disease. We report a case of 42-year-old man presenting with a pulmonary MALT lymphoma associated with interstitial lung disease.

1. Introduction

Interstitial lung disease (ILD) represents a large group of diseases causing inflammation, structural deterioration, and fibrosis in the lung parenchyma [1]. In some cases, the cause is not identified and they are called idiopathic. Primary pulmonary lymphoma (PPL) is a monoclonal lymphoid proliferation affecting the lungs in patients with no detectable extra thoracic lymphoma. It is an extremely rare disease [2]. It accounts for only 0.4% of all lymphomas, among which low-grade Mucosa-associated B-cell lymphoma (MALT lymphoma) is the most common. MALT lymphomas are most commonly seen in the stomach (50%), followed by the salivary glands, lungs, small bowel, and thyroid.

In some cases, pulmonary MALT lymphoma is seen presenting with interstitial lung disease [1]. We, here by, report a case of pulmonary MALT lymphoma underlying interstitial lung disease.

2. Case presentation

A 42-year old male, with no previous medical history, consulted in January 2018 for progressive dyspnea associated with paroxysmal dry cough. He reported a history of 9-year pack smoking, weaned since 2013.

On examination, temperature was 36.8 °C, blood pressure was 100/50 mm Hg, pulse rate was 75 beats/min, and respiratory rate was 20 breaths/min. There were no palpable lymph nodes. On pulmonary auscultation, there were fine crackles. Heart sound was normal. The remainder of his physical examination was unremarkable.

The chest x-ray revealed increased interstitial markings suggestive of interstitial lung disease (Fig. 1).

High resolution computed tomography (HRCT) showed thickening of septal lines, nodular and reticular patterns, ground glass opacity, and honey pattern, localized in the subpleural and basal lung parenchyma.

This interstitial lung disease finding was associated with centimetric mediastinal lymphadenopathy: paraaortic, subcarinal and hilar adenopathy with lymph nodes pf Barety space. (Fig. 2).

Pulmonary function tests showed a restrictive ventilation pattern with a total lung capacity of 61% of predicted values Diffusion

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capacity was reduced, with a transfer factor for carbon monoxide (DLCO) of 21% of predicted values.

A pulmonary arterial hypertension with systolic pulmonary artery pressure (SPAP) was equal to 45 mm Hg and right ventricular dilatation was found in the transthoracic cardiac echography.

The patient had no evidence of environmental, occupational or radiation exposures, infections and autoimmune diseases. Complete blood count was normal, but the blood biochemical panel showed an elevated lactate dehydrogenase (LDH) (224). The 18-item antinuclear antibodies (ANA) panel were negative. Lung biopsy was proposed, but rejected by the patient.

A bronchial fibroscopy was performed showing a normal macroscopic appearance of the airways. The bronchoalveolar lavage showed an increased total cell count (500 cells/l), lymphocytosis (12%), and neutrophilia (27.5%). Bacterial, fungal and viral infections were excluded.

Despite the normal-appearance of bronchial mucosa, biopsies were performed. Microscopic examination of the bronchial biopsy was characterized by lymphocytes with irregular nuclei and nucleolus infiltrated lung parenchyma. Immunohistochemically, tumor cells were found to be positive for CD20 and negative for CD3.

On extrapulmonary evaluation, no lymph nodes were found in the abdominal high resolution computed tomography. Furthermore, there was no evidence of lymphoma infiltration in the stomach, on gastric endoscopies with histological examination, as well as on the bone marrow biopsy.

The diagnosis of pulmonary MALT lymphoma was confirmed. The patient was treated with chemotherapy containing Rituximab plus cyclophosphamide, doxorubicin, vincristine, and Prednisolone (CHOP).

After 6 cycles of R–CHOP21 without regression on HRCT, the patient's symptoms deteriorated. He was hospitalized for acute respiratory deficiency 6 months after the last cycle. There was no evidence of infection. Pulmonary embolism was removed by CT angiography.

He received three bolus injections of corticosteroid then oral Prednisone (1mg/Kg daily), with no improvement of respiratory symptoms.

Repeated HRCT showed a progression of diffuse and bilateral fibrosis (Fig. 3) and he died due to respiratory distress within 12 months.

3. Discussion

We present the case of a patient complaining of a MALT lymphoma associated with progressive pulmonary interstitial and fibrosis opacity and poor prognosis.

ILD and MALT lymphoma are two different disorders of the respiratory system. Clinical symptoms and radiographic abnormalities are inconstant, nonspecific and can be similar [1]. Treatment and prognosis of these two diseases are different and accuracy in diagnosis is necessary. Sometimes, differentiating between malignant lymphoma and ILD is difficult with ordinary explorations. For these reasons, surgical lung biopsies are the gold standard to make a certain diagnosis [1].

ILD is a large group of diffuse lung diseases affecting the interstitium [3]. Clinical symptomatology is various and nonspecific making it difficult to distinguish from other respiratory diseases. The most common symptoms are dry cough and shortness of breath. It is critical to distinguish the various forms of ILD to determine the correct management and to predict prognosis [3]. They can be subdivided into two groups: those with an obvious cause and those without called idiopathic interstitial pneumonia.

Initial investigations include pulmonary function tests, bronchoalveolar lavage, serologic tests to detect autoimmune disorders, and radiologic exploration. The HRCT of the chest is the gold standard for diagnosis and classification of ILD and can eliminate the need for

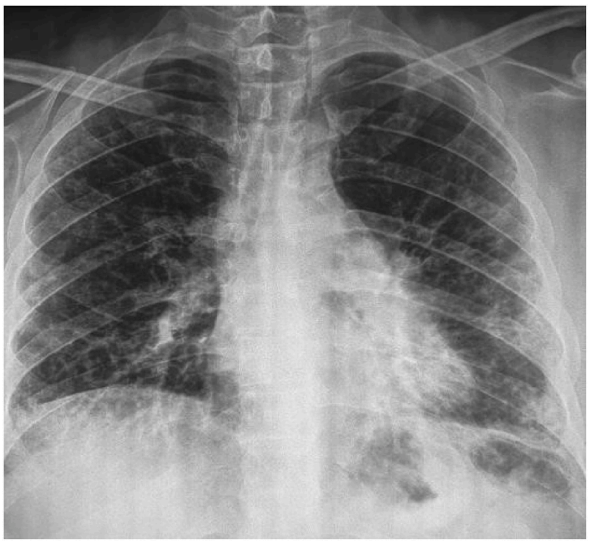

Fig. 1. X-ray chest: diffuse interstitial lung disease.

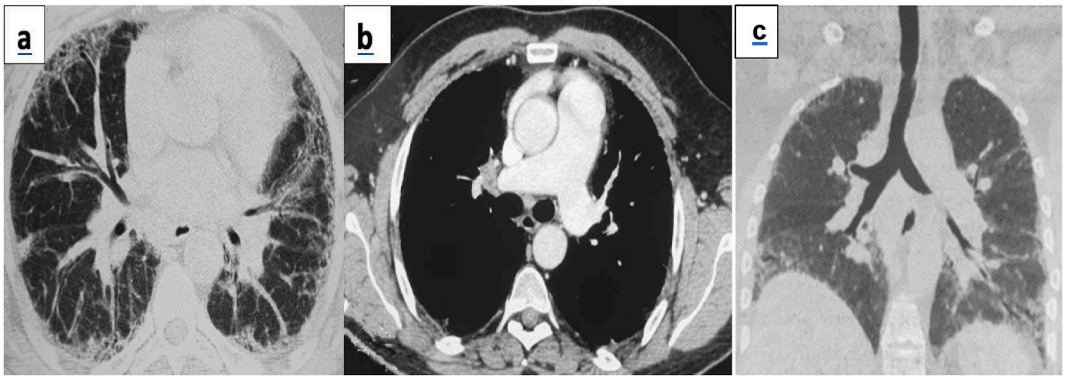

Fig. 2. a
- HRCT showed thickening of septal lines, reticular patterns, and honey pattern in the subpleural lung parenchyma.
b- Hilary lymphadenopathyc
- Sagittal view of HRCT showed the extensive crazy paving opacity and the subpleural and basal predominant features.

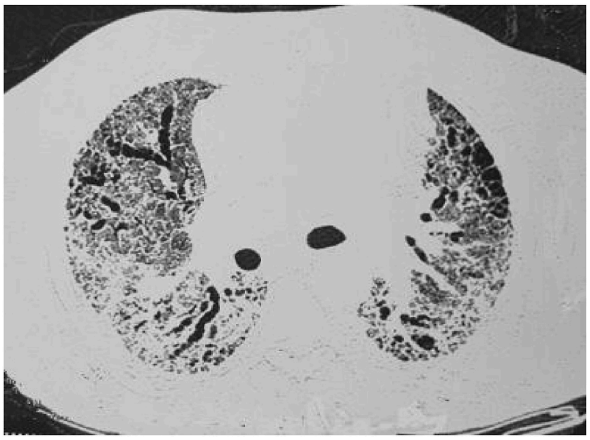

Fig. 3. HRCT showed diffuse and bilateral fibrosis.

invasive procedures in many cases.

In approximately a third of cases, clinical and radiological findings are insufficient to make an accurate diagnosis [3]. In these cases, histologic examination of a biopsy specimen is required to confirm the diagnosis and to rule out any malignant diseases [1]. A transbronchial biopsy is usually insufficient. Surgical lung biopsies are the gold standard to obtain a confident histologic diagnosis of ILD [3]. In our case, the lung biopsy indicated was refused by the patient.

Taking into consideration the various clinical, radiological, and histologic patterns of ILD, a consensus approach by a multidisciplinary team is required to make a confident diagnosis [3]. The prognosis of ILD is poor, particularly when fibrosis occurs [1].

B-cell lymphoma represent the majority of PPL, among which MALT lymphomas are the most common (70%–80%) [4]. This affection can develop in immunocompromised as well as immunocompetent people. In the literature, few cases of pulmonary MALT lymphoma associated with interstitial lung disease have been reported [1].

Clinical presentation of MALT lymphoma is variable, mostly because of the differences in signs associated with the different extra nodal organs [5]. Most patients present with localized disease, small tumor burden, and excellent performance status [4]. Furthermore, 30%–40% of patients are asymptomatic, and when symptoms appear, they are nonspecific such as dyspnea, cough, chest pain and hemoptysis [4].

Imaging manifestations of MALT lymphoma are heterogeneous, but most commonly appear as single or multiple, bilateral nodules or masses measuring from 2 to 8 cm commonly located in the lower lobes [4,6]. Cavitation is common, particularly in larger lesions [2]. Interstitial infiltration and pleural effusion are detected in 10% and 12%of the cases, respectively [7]. In HRCT, ILD is characterized by bilateral peripheral and basal reticular opacities, bronchiectasis areas, a honeycomb pattern, and ground glass opacity [3]. For these reasons, and because of the possible similarity of radiologic findings and clinical manifestations, lymphoma is considered in the differential diagnosis of ILD [4]. To make a diagnosis, tissue samples are required to use in bronchoscopy, computed tomography guided biopsies, or surgical lung biopsy. However, current evidence suggests that endobronchial ultrasound-guided transbronchial needle aspiration can be useful in patients with suspected lymphoma [8]. In the present case, the diagnosis of lymphoma was performed by bronchial biopsy.

The prognosis of MALT lymphoma is excellent [4]. MALT lymphoma usually remains localized for a prolonged period within the tissue of origin, but dissemination can occur. Thus, long-term follow-up is recommended.

There is no standard therapy strategy or guidelines for pulmonary MALT lymphoma [5]. Treatment options are surgery, radiotherapy, or chemotherapy. Some physicians opt for the watch-and-wait strategy in asymptomatic patients and chlorambucil-based chemotherapy with or without immunotherapy when symptoms are present [6]. The overall survival rate for patients with MALT lymphoma [9] ranges from 85% to 95% at 5 years and 90% at 9 years.

Association of primary MALT lymphoma with ILD may be coincidental, but MALT lymphomas are reported to be usually associated with chronic antigenic stimulation in response to cytogenetic abnormalities, autoimmune disease, or chronic pulmonary infection [4].

In our patient, pulmonary function tests revealed restrictive ventilatory defects and transthoracic cardiac echography showed chronic cor pulmonale appearance. Therefore, we concluded that the respiratory symptoms of the patient were caused by ILD more than MALT lymphoma.

Furthermore, Suzuki et al. reported that chemotherapy can worsen pulmonary fibrosis, causing respiratory failure and death in a patient with idiopathic pulmonary fibrosis associated with primary tracheal MALT lymphoma [10]. This finding was in agreement with our study findings.

4. Conclusion

In conclusion, Pulmonary MALT lymphoma underlying interstitial lung disease is rare. MALT lymphoma is a differential diagnosis of ILD, and lung biopsies should be performed to make an accurate and timely diagnosis. The prognosis is bad when these two diseases are associated.

Conflicts of interest

The authors declare no competing interests.

Authors' contributions

Imen Touil: conception, drafting the article and final approval of the version to be published, Hassen Ibn Hadj Amor: drafting the article and approval of the final version. Yosra Brahem: conception and drafting of the article, Soumaya Bouchareb: contributed to the design and drafting of the article, Nadia Keskes Boudawara: contributed to the conception, drafting of the article, and approval of the final version, Jihen Ayeb: conception and drafting of the article, Jalel Knani: contributed to the design, revision, and approval of the final version, Leila Boussoffara: contributed to the conception, revision, and approval of the final version.

Declaration of competing interest

No disclosure of relationship with industry.

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