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An unexpected diagnosis of a lung mass with endobronchial involvement

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Abstract

Mantle cell lymphoma is a subtype of B-cell non-Hodgkin's lymphoma. Most cases of the disease have extranodal involvement at the time of the initial diagnosis; however, endobronchial involvement is rare. A 51-year-old woman was referred to our hospital because a chest CT showed pathological tissue in the right hilum englobing the pulmonary artery, the left main bronchus and their main lobar branches appearing to be small in caliber, multiple lymphadenopathies up to 4 cm in size in the subcarinal region. A bronchoscopy revealed stenotic lumen with infiltrated hyperemic mucosa of the left upper lobar bronchus and the left lower lobar bronchus. She was diagnosed as having mantle cell lymphoma based on an endobronchial biopsy and transbronchial needle aspiration. The diagnosis was confirmed using immunohistochemical staining.

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Case Report

A 51-years old woman was referred to our department to perform a bronchoscopy. The patient was suffering from exertion dyspnea (2-3 mmRC) for about a month, so the attending physician prescribed a chest X-ray. She was no smoker, and she had no prior medical history, excepting recurrent angioedema treated with steroids. The chest X-ray showed a 7 cm diameter paramediastinal mass in the left hilar area, no other pathological findings (Figure 1A).

A chest-CT scan of was then prescribed, which showed pathological tissue in the right hilum (6.7 x 6 cm) englobing the pulmonary artery, the left main bronchus and their main lobar branches that appeared to be small in caliber, and multiple lymphadenopathies up to 4 cm in size in the subcarinal region (Figure 1 B,C).

On physical examination, vesicular murmur present over the entire lung range, no added pathological sounds; cardiac action rhythmic and normo-frequent, clear tones and free pauses; abdomen treatable, not painful or tender on superficial and deep palpation, no resistance; no palpable lymph nodes in explorable stations. Complete blood counts revealed a white blood cell count of 8700/mm^3, a hemoglobin level of 15.5 g/dL, a platelet count of 250,000/mm^3, an absolute neutrophil count of 5900/mL (67.5%), and a lymphocyte count of 2000/mL (23.4%). Renal function, electrolytes and inflammatory indices were normal. The patient underwent flexible bronchoscopy with sampling.

The examination showed the left main bronchus of normal caliber, while the spur of the left upper lobe was enlarged with infiltrated mucosa. The left upper lobar bronchus had a stenotic lumen with hyperemic mucosa that appeared to be infiltrated by heteroplasia, the left lower lobar bronchus was stenotic, and the apical segment of the left lower lobe (B6) could not be explored with the bronchoscope due to significant stenosis (Figure 2). Bronchial biopsies were performed from the left upper spur, upper and lower left lobar bronchus. Transbronchial needle aspiration (TBNA) was performed on subcarinal lymph node and then on the mass.

The result of the bronchial biopsies was bronchial mucosa with diffuse infiltration of atypical cells with small to medium irregular nuclear dimensions. Immunohistochemical reactions positive for CD20, CD5 and largely for Bcl-1. CD23, CkCAM, TTF-1, Synaptophysin, CD56 negative. Few plasma cells were present. No mitosis, Ki 67 proliferation index <10%. The findings suggested

diffuse infiltration of the bronchial mucosa with malignant low-grade B-cell non-Hodgkin's lymphoma (NHL) suggestive of mantle cell lymphoma (MCL). Further tests were performed with evidence of t(11;14) translocation. In summary: infiltrates of a MCL, according to WHO 2017, ICD-O9673/3. The Ki 67 proliferation index is <10% (Figure 3A). TBNA on subcarinal lymph node and hilar mass both show the same result: presence of small-medium sized lymphoid elements with immunophenotypic pattern: CD20+; CD3-; CD23-; CD5+; BCL1+; CkCAM5.2-. FISH was performed: BCL-1 translocation (Figure 3B). To complete the staging, the patient underwent a PET-CT scan showing supra- and subdiaphragmatic lymphadenopathies with increased metabolic activity referable to the known lympho-proliferative disorder.

The patient was then referred to the Department of Hematology for treatment.

Discussion

MCL is a type of B-cell NHL characterized by t(11;14)(q13;q32) and Cyclin D1 over-expression [1]. MCL represents about 4-6% of all lymphomas and about 3-10% of all NHL. Patients with MCL at diagnosis have a median age of 63 years with a male predominance (male-female ratio 4:1). Almost all cases are already in an advanced stage at the time of diagnosis (stage III-IV) with an extranodal involvement, such as the gastrointestinal tract, spleen with splenomegaly, bone marrow, liver, Waldeyer's ring, skin, lacrimal glands, and central nervous system [2,3]. Although the extranodal involvement is frequent, pulmonary and especially bronchial involvement are rare and, in particular, the bronchoscopic findings are unclear and specific for a hematological disorder.

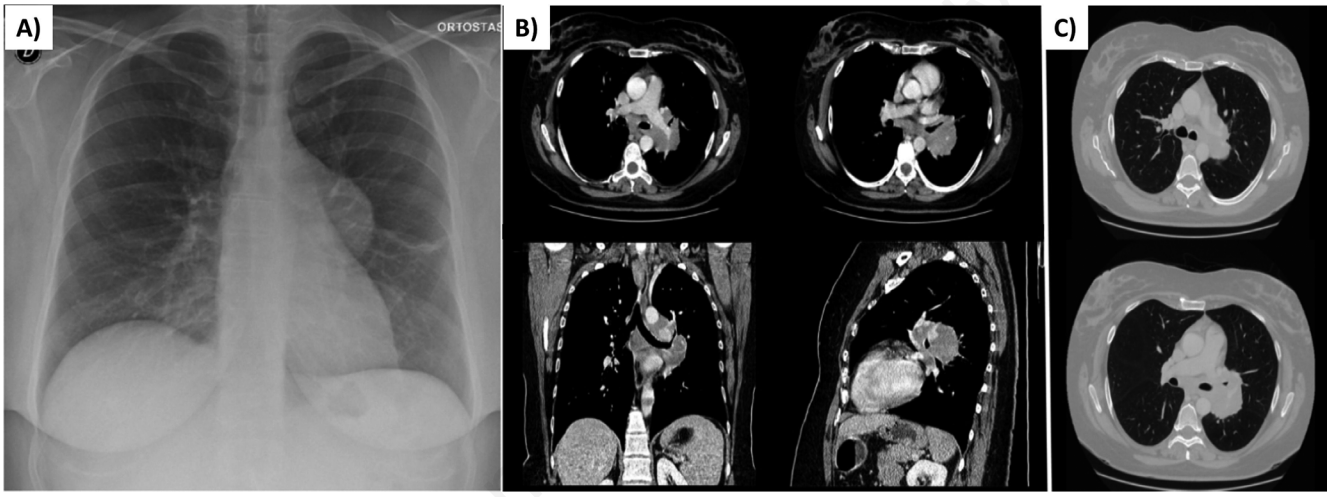

Figure 1. A) Chest X-ray: left hilar lesion; mediastinum (B) and lung parenchyma (C) on chest CT-scan.

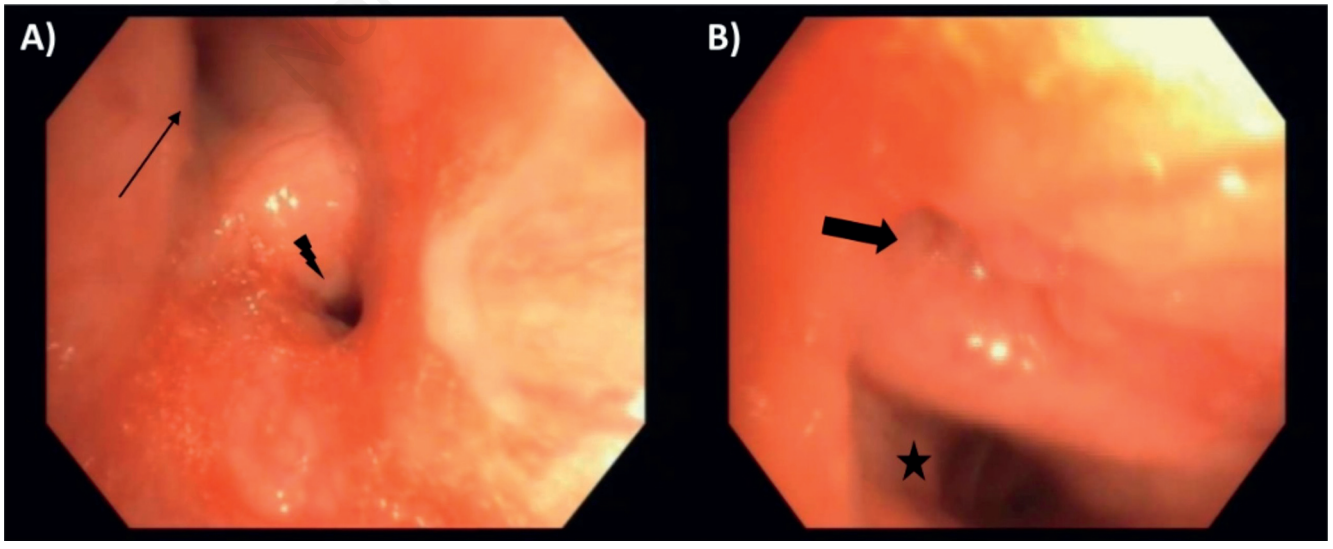

Figure 2. A) Upper lobe bronchus (thin arrow) and lower lobe bronchus (lightning bolt). B) B6 stenosis of left lower lobe (thick arrow) and left basal pyramid (star).

MCL is a type of mature B-cell NHL, characterized by the proliferation of B-cells like those found in follicular mantle zones, a subset of which arise from memory B-cells. Tumor cells are typically CD5, CD19, CD20 positive, CD10 and CD23 negative. The vast majority overexpress cyclin D1, which is not typically expressed in normal lymphocytes. Cyclin D1 over-expression is associated with a translocation between the CCND1 gene on chromosome 11 and the IGH gene on chromosome 14 [t(11;14)(q13;q32)]; however, this translocation is present at karyotype in only 50%-65% of patients [1].

The only symptom presented by our patient was dyspnea on exertion (2-3 mMRC). She did not complain of any other respiratory or systemic symptoms that might lead to the suspicion of lymphoproliferative disease. Indeed, her history did not include the so-called «B symptoms» of NHL, i.e., unexplained fever (TC>38°C), night sweats, weight loss (at least 10% of body weight in the last six months). B symptoms are more common in patients with aggressive NHL subtypes, especially in those with hepatic and extranodal involvement. Conversely, when present in indolent lymphomas they are usually associated with advanced disease and/or large tumor masses [4]. The patient's dyspnea can be very well explained by endobronchial involvement, as segmental bronchus B6 of the left lower lobe was occluded and all segmental bronchi of the ipsilateral upper lobe had stenotic lumen.

Another consideration concerns the patient's pathological history. She suffered from recurrent angioedema for about two years. This disorder was always treated with systemic steroids with clinical benefit. Acquired angioedema is a rare phenomenon in association with lymphoproliferative disorders. Related lymphoproliferative disorders range from monoclonal gammopathy of unknown significance MGUS (35%) to NHL (20%) [5,6]. B-cell NHL is the most common lymphoma to give rise to angioedema, especially recurrent angioedema, and angioedema may precede or follow the diagnosis of NHL. There are few reported cases in which acquired angioedema is the first manifestation of NHL. The pathogenesis of angioedema in B-cell NHL is unclear but it is suggested that activation of the classical complement pathway by immune complexes or monoclonal antibodies produced by tumor tissue may lead to C1-INH consumption. Thus, serum levels of C1, C1q, C2, C4 and protein levels of C1-INH are lower than normal [7].

Endobronchial involvement of MCL is rare. Bronchoscopic findings in literature described irregular bronchial or tracheal surface lesions and polyposis-like lesions. Endobronchial lymphoma is classified into two patterns: diffuse submucosal infiltration (type I) and localized solitary mass (type II) [8,9]. Interestingly, the cases described previously in the literature all showed a type I pattern. Several possible mechanisms of endobronchial metastases have been reported, such as bronchial invasion by a mediastinal mass, lymphatic spread into the peribronchial connective tissue, transbronchial aspiration of tumor emboli and direct haematogenic metastases [10-12]. Our patient presented a different and apparently unique endoscopic pattern. In fact, in addition to the presence of an evident mucosal alteration, characterized by mucosa with an irregular surface, enlargement and infiltration of the upper left lobe spur, there was involvement of the ostium of B6 lower left lobe with an almost complete occlusion of the bronchial lumen, such as to make it impossible to explore this bronchus. To date, no cases of mantle cell lymphoma with endobronchial involvement causing occlusion of the bronchial lumen have been described in the literature.

The chest CT-scan features of pulmonary lymphoma are variable, but three patterns are classically described. The most common pattern is that of poorly defined scattered nodules with predominant distribution in the lower lobes, which frequently include airway bronchogram, cavitations with or without hydroaerial levels. The second most common pattern is a bronchovascular/lymphangitic process that presents with large linear and reticulonodular thickenings extending from the hilum towards the periphery, with a perivascular and peribronchial distribution. These lesions, when extensive, may appear very similar

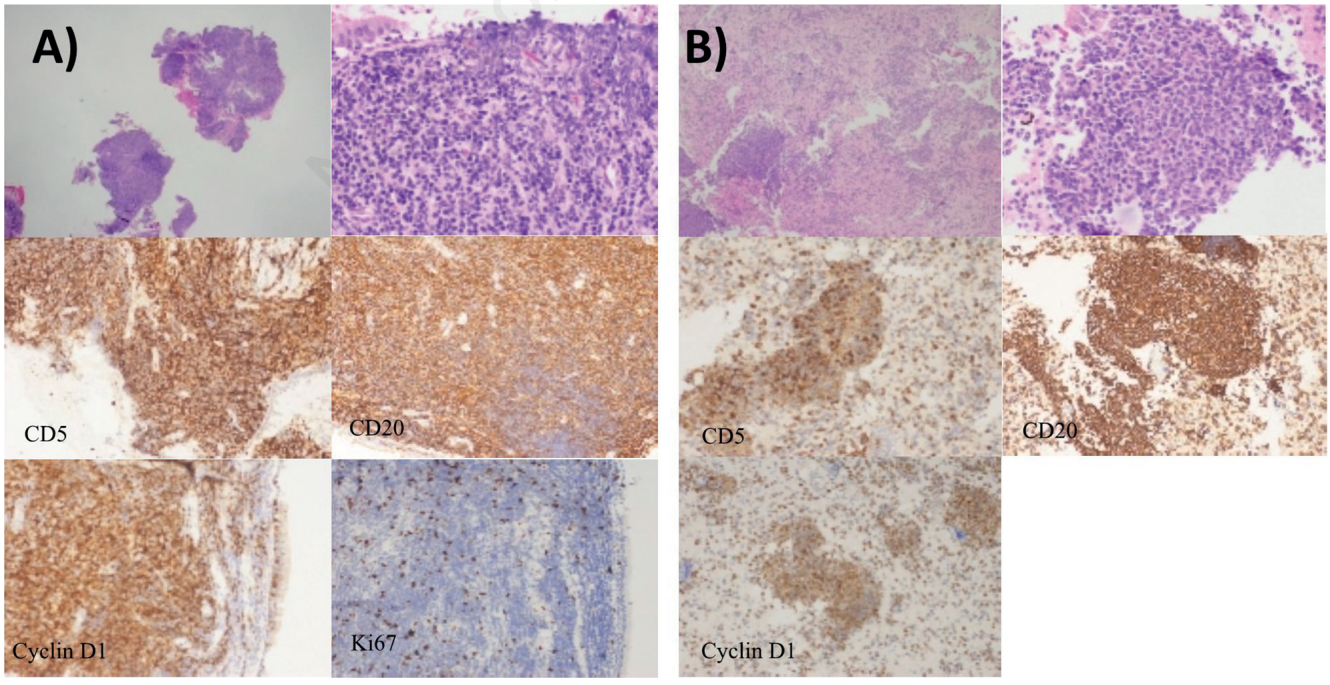

Figure 3. A) Histology (bronchial biopsy) and B) cytology (TBNA) with immunohistochemical reactions.

to bronchopneumonic consolidation. The third pattern is described as an alveolar pattern and is effectively indistinguishable from pulmonary consolidation of another nature. It may be a segmental or lobar process. The only distinguishing feature is the absence of volume loss, which is compatible with a consolidative process. Ground-glass opacification is a decidedly uncommon pulmonary presentation of lymphoma and is not classically described. Airway obstruction caused by endobronchial growth of lymphoma is also a very rare occurrence. It is well recognized that airway obstruction may be due to primary tracheal lymphoma or tracheobronchial compression «ab extrinsic» from lymphadenopathy [2,13].

Conclusions

The endobronchial involvement of MCL is rare. Bronchoscopic findings revealed a diffuse irregular surface of the tracheal and bronchial mucosa and a complete bronchial occlusion not still described in the literature. The diagnosis of MCL is based on biopsy findings of lymph nodes, involved tissues, and bone marrow. Most cases in the literature show a typical morphology of small to medium-sized infiltrating cells and positive results on immunohistochemistry, especially for cyclin D1. In the present case, histopathological diagnosis was possible on an endobronchial biopsy, showing that endobronchial biopsy is a useful diagnostic procedure if endobronchial involvement of the disease is suspected.

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