

Linfoma pulmonar MALT: reporte de un caso y revisión de la literatura

Pulmonary Malt Lymphoma: A Case Report and Review of the Literature

Carolina Amado¹, Tiago Valente¹, Gisela Ferreira², Margarida Cruz¹

¹ Internal Medicine Department. Centro Hospitalar do Baixo Vouga. Aveiro (Portugal)

² Hematology Department. Centro Hospitalar do Baixo Vouga. Aveiro (Portugal)

ABSTRACT

Pulmonary mucosa-associated lymphoid tissue lymphoma (pMALToma) is an extranodal low-grade B-cell lymphoma which originates from bronchial and/or parenchyma MALT. The authors report a case of an 81-year-old female with incidental finding of multiple bilateral pulmonary consolidations. After being submitted to an extensive workup, the diagnosis of pMALToma was finally established. The authors intend to highlight this rare entity and its challenging workup. It is characterized by non-specific clinical manifestations and diverse imaging findings frequently leading to the need to perform more invasive techniques for a final diagnosis.

Keywords: Mucosa-associated Lymphoid Tissue, Pulmonary Lymphoma, Neoplastic disease.

INTRODUCTION

Pulmonary MALT lymphoma (pMALToma), although rare, represents more than 70% of primary pulmonary lymphoma cases¹ and 0.5%-1.0% of all primary lung cancers^{2,3}. It is characterized by a clonal lymphoid proliferation affecting the parenchyma and/or bronchi of one or both lungs without detectable extra-pulmonary involvement until 3 months after the diagnosis².

The disease is slow growing, affecting patients in their fifth and sixth decades of life, with no gender predominance⁴, and with a chronic inflammatory or infectious background².

PATIENT AND OBSERVATION

The authors present the case of an 81-year-old female non-smoker, with previous relevant history of unstratified chronic pulmonary disease, cardiac failure, and multiple cardiovascular risk factors. She was evaluated weeks after being hospitalized due to decompensated cardiac failure in the setting of an Influenza A respiratory infection. In between, the patient performed a lung CT due to undetermined pulmonary disease showing multiple and bilateral pulmonary consolidations, the largest sized 2x2.3 cm (fig.1 - A). The patient was asymptomatic: no fever, cough, lymphadenopathy, night sweats nor weight loss. Blood analysis showed neither infection nor positive autoimmunity parameters. Hematologic parameters, lactate dehydrogenase, renal/liver function tests and HIV/HCV/HBV serologies were normal. A new high resolution lung CT showed stable disease (fig.1 - B). The patient was then submitted to a flexible bronchoscopy which revealed a diffuse hyperemia at the bronchial mucosa with no other relevant endoscopic abnormalities. A CT-guided trans-bronchial mucosa needle biopsy was performed and allowed the identification of small lymphocytic proliferation, centroblasts with plasmocitoid differentiation, positive to CD20 and BCL-2, with Ki-67 of 20%, in keeping with a MALT lymphoma. Bone marrow aspirate and biopsy were negative for lymphoma involvement and abdominal and pelvic CT showed no relevant findings. After the establishment of the diagnosis of pMALToma, the patient underwent 4 cycles of rituximab over one month with toler-

ability. She presented partial response on control TCAR, and a new therapeutic strategy is on hold.

DISCUSSION

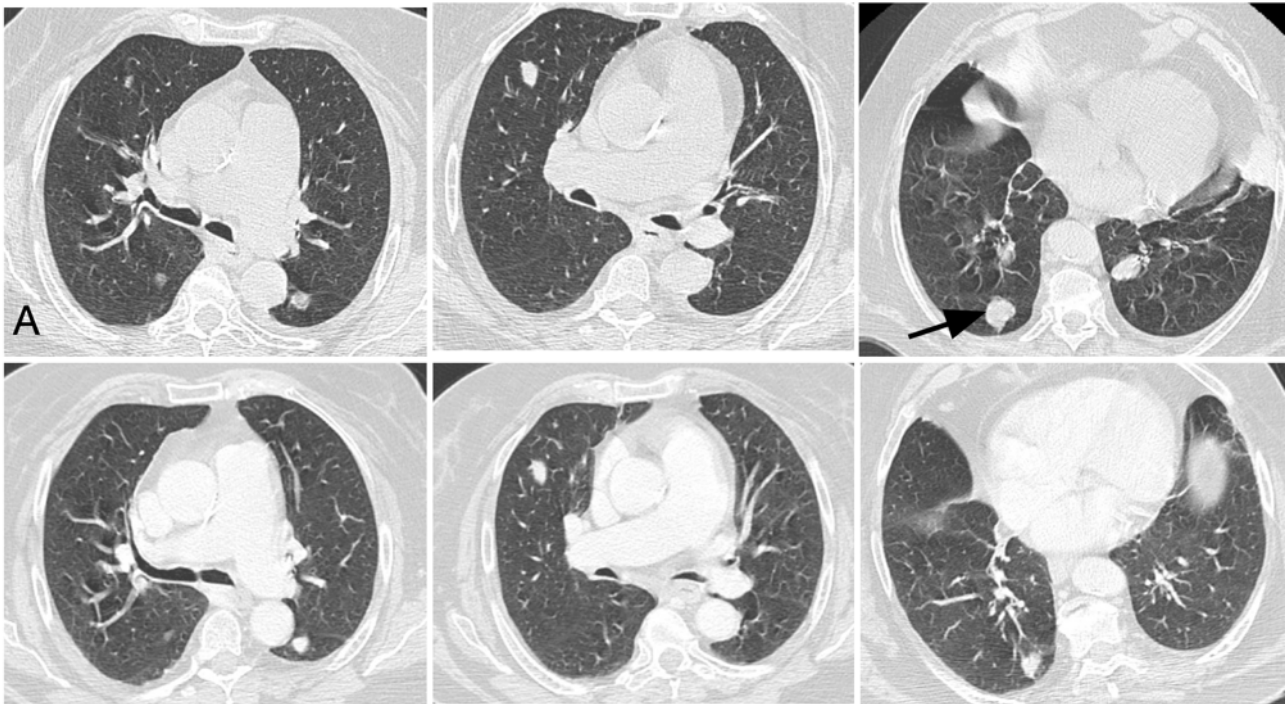
Despite being rare, pMALToma is the most common type of primary pulmonary lymphoma¹ resulting from the uncontrolled proliferation of the mucosal B-cell lymphocytes². Its prevalence among patients with chronic immune system stimulation supports the belief that MALT lymphoma is not a normal constituent of the lung⁵ and it may result from the chronic antigen stimulation with eventual replication errors^{1,2,4-5}. Nonetheless a causative antigen associated with pMALToma is yet to be found^{1,2,4}. An European study found a possible relation with *Achromobacter xylosoxidans*, but more studies are necessary to prove the casual association^{3,4}. Disorders such as systemic lupus erythematosus or Sjogren's syndrome are recognized risk factors for developing pMALToma⁴. However, neither of those two were diagnosed during the patient's workup and bacterial.

Signs and symptoms are unspecific, with more than 50% of the patients clinically asymptomatic at the diagnosis², as in the presented case report. Occasionally patients may present with cough, mild dyspnoea, chest pain and rarely hemoptysis⁵.

Directed Investigations are usually initiated after abnormal findings on chest X-ray or CT¹. CT is more sensitive than standard radiography. It has demonstrated that most MALT lesions are multiple bilateral nodules (>60-70% of cases) with air bronchograms and no topographic predominance^{2,4}. Other rare findings may appear on CT images leading to a easier misdiagnosis³. Hilar and mediastinal lymphadenopathy is present in 30% of patients and pleural effusions are seen in 10% of cases. Although underutilized, PET-CT may help the diagnosis².

Tissue biopsy with posterior histopathologic examination and immunohistochemical staining is the gold standard for diagnosis^{4,5}, and it should be done using minimally invasive techniques, such as bron-

Figure 1. A - Sections of lung HRCT showing multiple and bilateral pulmonary consolidations, the largest sized 2x2.3 cm (arrow).
B - Sections of lung HRCT showing stable disease comparing with A.



choscopy and/or CT-guided needle biopsy. No specific immunohistochemical marker has been identified, however MALT lymphoma are usually positive for CD20 and BCL-2, as presented in the case⁵.

Most patients have a favorable prognosis^{4,6} with a 5-year survival rate over 84%^{3,5}. Due to the low incidence of the disease, there is no evidence-based therapeutic strategy based on randomized clinical trials^{2,5}. Watchful waiting can be an adequate initial approach in many patients because of its indolent nature^{3,4,6}. Radiotherapy and surgery are the preferred option for treatment of localized disease. Systemic therapies with chemo- or immunotherapy are preferred in symptomatic systemic disease or with overt progression, deep invasion, bulky disease, impending organ damage or patient's preference⁶. Although rituximab-chlorambucil has been used as the first choice (level of recommendation I A)⁶, rituximab alone can obtain a 70% response in MALT lymphoma⁷.

pMALToma is a rare indolent disease with a highly variable clinical and imagiological presentation and unknown pathophysiology. There are no international recommendations guiding the therapeutic approach, therefore treatment is based on expert opinion, with chemo- or immunotherapy being the proposed approach in symptomatic systemic disease or with overt progression, deep invasion, bulky disease, impending organ damage or patient preference.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this work.

SOURCE OF FUNDING

This research had no funding sources.

ETHICAL ASPECTS

All participants submitted a consent form to be included in this study

REFERENCES

1. Raphaël Borie, Marie Wislez, Martine Antoine, Jacques Cadranel. Lymphoproliferative Disorders of the Lung. *Respiration*. 2017;94(2):157-175.
2. Carlos Couto, Vera Martins, Vicência Ribeiro, Cristina Rodrigues, Joana Nogueira, Ana Oliveira, Jorge Roldão Vieira. Primary Pulmonary MALT Lymphoma: A Case Report and Literature Review. *Biomed Hub*. 2019;4:502488.
3. Lin Wang, Guanzhi Ye, Zhonghe Liu, Lin Shi, Cheng Zhan, Jie Gu et al. Clinical Characteristics, diagnosis, treatment, and prognostic factors of pulmonary mucosa-associated lymphoid tissue-derived lymphoma. *Cancer Medicine*. 2019;8:7660-7668.
4. Raphaël Borie, Marie Wislez, Martine Antoine, Christian Copie-Bergman, Catherine Thieblemont, Jacques Cadranel. Pulmonary Mucosa-associated Lymphoid Tissue Lymphoma Revisited. *European Respiratory Journal*. 2016;47:1244-1260
5. Khushali Jhaveri, Derek J Dimas, Abhay Vakil, Salim Surani. Primary Pulmonary Involvement in Mucosa-associated Lymphoid Tissue Lymphoma. *Cureus*. 2019;11(7): e5110.
6. E. Zucca et al. Marginal Zone Lymphomas: ESMO Clinical Practice Guidelines of diagnosis, treatment, and follow-up. *Annals of Oncology*. 2020;31:1
7. Annarita Conconi, Giovanni Martinelli, Catherine Thieblemont, Andrés JM Ferreri, Liliana Devizzi, Pedro Peccatori et al. Clinical Activity of Rituximab in Extranodal Marginal Zone B-cell Lymphoma of MALT Type. *Blood*. 2003;102:2741-2745.