

Marginal zone B-cell lymphoma of the pulmonary mucosa-associated lymphoid tissue: A case report

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Abstract. Marginal zone B-cell lymphoma of the pulmonary mucosa-associated lymphoid tissue (pulmonary MALT-MZL) is a common type of primary pulmonary lymphoma, but is rare as a pulmonary malignant tumor. In the present study, a 49-year-old male patient was admitted to The First Affiliated Hospital of Xi'an JiaTong University (Xi'an, China) with a pulmonary lesion in the right upper lung. The patient was diagnosed with pulmonary MALT-MZL subsequent to undergoing chest computed tomography (CT), a routine blood test, pathological and histological examinations, a transbronchial lung biopsy and bronchoscopy. A chest CT scan revealed right middle lobe consolidation and inflammatory signs, accompanied by mediastinal lymphadenopathy in the anterior basal segment of the upper lobe and CT angiogram signs. Bronchial stenosis and swollen mucosa were observed by bronchoscopy. The tissue section of the transbronchial lung biopsy specimens revealed diffusely infiltrated monocytoid B-cell lymphocytes and a lymphoepithelial lesion. The tissue was found to be positive for cluster of differentiation (CD)20, B-cell lymphoma 2 and CD79a expression, but negative for CD3, CD5, cyclin D1 and κ -light chain expression. CD21 and CD23, located in the residual follicular dendritic cells, were detected by immunohistochemical staining. The clinical manifestations of pulmonary MALT-MZL are non-specific and misdiagnosis frequently occurs in clinical practice. Therefore, an appropriate invasive biopsy procedure is necessary for early and accurate diagnosis of pulmonary MALT-MZL. Clinical presentation that includes periodic fever and distended bronchi in pulmonary consolidation may indicate a diagnosis of MALT-MZL. Pulmonary MALT-MZL belongs to the category of indolent lymphoma and accurate clinical diagnosis is challenging. The

results in the present study may provide additional evidence for the accurate diagnosis of this rare entity.

Introduction

Extranodal marginal zone B-cell lymphoma (MZL) of mucosa-associated lymphoid tissue (MALT), and splenic and nodal MZL are the three subtypes of MZL recognized by the World Health Organization (WHO) classification (1). Overall, MZLs share morphological and immunophenotypic features that are similar to those of the hypothesized common cell of origin, the marginal zone B-cell in secondary B-follicles.

Extranodal MZL, also termed MALT lymphoma, is a distinct subgroup of non-Hodgkin's lymphoma (NHL) that accounts for ~5% of all NHLs (1,2). Despite the stomach being the most frequently involved organ in extranodal MZL, the lung is one of the most common non-gastrointestinal sites of occurrence (3,4). Extranodal MZL accounts for <0.5% of all primary lung neoplasms, but more than two-thirds of primary pulmonary NHLs are extranodal MZLs (5-7). Pulmonary MALT-MZL exhibits no clear symptoms and thus, the disease is usually identified during routine chest X-ray examinations (8). Pulmonary MALT-MZL is diagnosed by imaging examination and biopsy (9,10) and the main treatment modalities for MALT-MZL include surgery, radiotherapy and chemotherapy (11,12). Pulmonary MALT-MZL exhibits a good prognosis, with a five-year survival rate of 93.6% (8,13).

Due to the non-specific clinical manifestations of pulmonary MALT-MZL, misdiagnosis is frequently observed in clinical practice. The present study describes the presentation and diagnosis of one patient with pulmonary MALT-MZL, and aims to provide evidence for the accurate diagnosis of pulmonary MALT-MZL. Written informed consent was obtained from the patient.

Case report

A 49-year-old male was referred to The First Affiliated Hospital of Xi'an JiaoTong University (Xi'an, Shaanxi, China) with a pulmonary lesion in the right upper lung observed on a chest radiograph that was performed during a routine health checkup at a local hospital. The patient had smoked for

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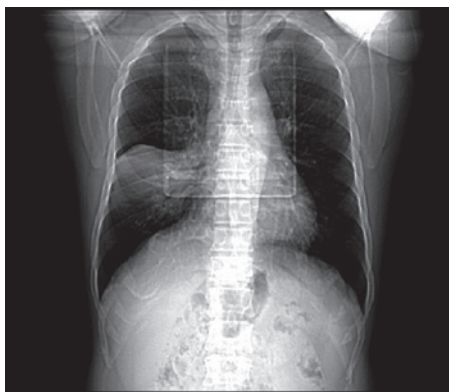


Figure 1. Chest radiograph revealing a lesion in the right upper lung.

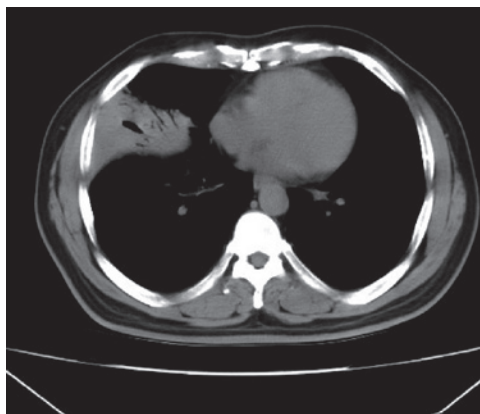


Figure 2. Chest computed tomography revealing a lesion in the anterior segment of the upper lobe of the right lung.

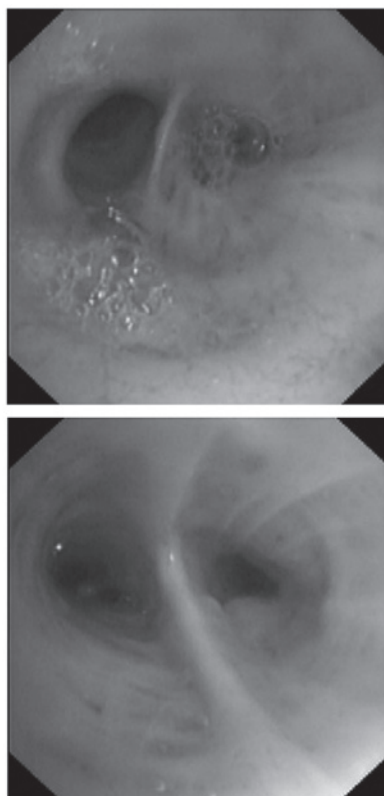


Figure 3. Bronchoscopy revealing mucosal edema and mild stenosis in the right main bronchus.

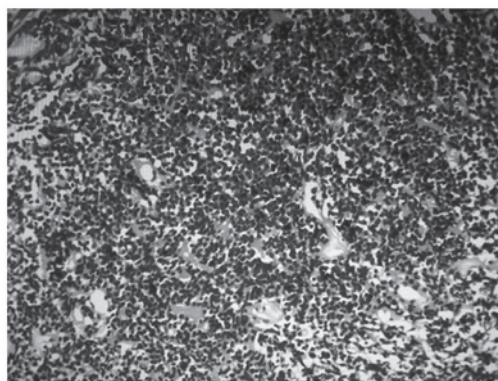


Figure 4. Immunohistochemical staining revealing positivity for CD20, B-cell lymphoma 2 and CD79a (magnification, x20).

>20 years and reported no history of respiratory illness, such as tuberculosis. The vital signs of the patient were normal, and a physical examination revealed no abnormalities.

The laboratory data were within the normal ranges, with the exception of a tumor marker, carcinoembryonic antigen (CEA), which possessed a level of 5.24 ng/ml (normal range, 0-3.4 ng/ml). Pulmonary function testing revealed no ventilatory defects. A chest radiograph revealed a nodule in the right upper lung (Fig. 1). A chest computed tomography (CT) scan revealed signs of inflammation accompanied by mediastinal lymphadenopathy in the anterior segment of the right upper lobe (Fig. 2). Additionally, flexible bronchoscopy was performed to identify the endobronchial lesion. At bronchoscopy, mucosal edema and slight stenosis were observed in the right main bronchus (Fig. 3). Immunohistochemical staining revealed diffuse strong positive staining for cluster of differentiation (CD)20, B-cell lymphoma-2 and CD79a, and the samples were negative for CD3, CD5, cyclin D1 and κ -light chain expression (Fig. 4). Considering the clinical outcomes, the pulmonary lesion was diagnosed as extranodal MALT-MZL. No evident absorption of the lesion was identified on CT scan following combined treatment with mezlocillin and sulbactam (3.75 g every 8 h) for 1 week. Bronchoscopic examination and pathological analysis revealed no evidence of bleeding or lumps, which confirmed the diagnosis of extranodal MALT-MZL. Subsequently, the patient was transferred to the Hematology Department, but refused further treatment. No follow-up examinations were performed.

Discussion

In 1983, Isaacson and Wright (14) reported two cases of MALT lymphoma arising from the gastrointestinal tract for the first time. Subsequently, a variety of studies identified additional MALT lymphoma cases worldwide (3,14,15). MALT lymphoma has been classified in the WHO and revised European-American classifications of lymphoid neoplasms as extranodal MALT-MZL (1,4,7). This extranodal lymphoma with low-grade features infiltrates the marginal zone of reactive B-cell follicles and arises most commonly from the MALT of the stomach, but also from the lungs, salivary glands and thyroid gland (4).

Pulmonary extranodal MZL is a rare entity that accounts for <0.5% of primary pulmonary malignancies and <1% of all lymphomas (5-7). The incidence of lung adenocarcinoma, which usually arises from peripheral small bronchi or alveolar epithelial cells, is increasing worldwide. The etiology of pulmonary extranodal MZL has yet to be elucidated (7), but chronic immune stimulation resulting from infection or auto-immune disorder may be associated with the pathogenesis of extranodal MZL. In addition, previous studies have identified the strong association between *Helicobacter pylori* infection and gastric extranodal MZL (2,4).

It has been indicated that approximately half of patients are asymptomatic at presentation, with abnormal radiological findings being identified by chest radiography. For the initial staging and follow-up in patients with malignant lymphoma, ¹⁸Fluoro-2-deoxyglucose-positron emission tomography (¹⁸FDG-PET) has been widely used (16). Although a previous study (17) indicated that there is a limited role for PET in extranodal MALT lymphoma patients due to the lack of FDG avidity, a later study by Elstrom *et al* (16) indicated that the issue is controversial, in particular, the accuracy of ¹⁸FDG avidity in MZL. In the study by Elstrom *et al*, at least one site of involvement was detected by PET-FDG in only 67% of MZL patients (16). Increased FDG uptake was detected in the majority of a small cohort of nodal MZL patients, but not in patients with extranodal disease, suggesting that the FDG-avidity depends on the tumor location or the MZL subtype (18).

In addition, symptomatic patients present with non-specific pulmonary symptoms, including cough, dyspnea, chest pain and hemoptysis. The B symptoms are uncommon and are observed in only a minor proportion of patients (4,7,19,20).

In the current study, the patient with pulmonary extranodal MZL was asymptomatic and the pulmonary lesions were incidentally found during physical examinations at a local hospital. The major radiographic patterns of pulmonary extranodal MZL have been reported as nodules, consolidation, ground-glass opacity and centrilobular nodules with linear branching opacities, also termed a tree-in-bud sign (4,7,15,20). In a previous study on the CT findings of MZL, single or multiple nodules or areas of consolidation were the main patterns, while none exhibited involvement of the main bronchus (15). In a later study, only two of the 61 enrolled patients were found to possess masses of various sizes in the main bronchus (19). Therefore, the characteristics of the present patient are observed extremely rarely in clinical settings as the patient presented with endobronchial edema and inflammatory symptoms, without lung parenchymal lesions being observed during bronchoscopy, which highly enhanced the difficulty of diagnosis and delayed the administration of the corresponding therapies.

Extranodal MZL can be clinically diagnosed by bronchoscopic, transbronchial or percutaneous needle biopsies, with a surgical lung biopsy being required in numerous cases (4,15,19). An infiltrate of small to medium-sized lymphocytes with irregular nuclei and abundant cytoplasm is characteristic of extranodal MZL, with reactive follicles also usually observed. Lymphoepithelial lesions, in which tumor cells infiltrate the bronchial, bronchiolar and alveolar epithelium, are characteristic of MZL, but not pathognomonic (2,4,7). Immunophenotyping studies aid in the confirmation of diagnosis, particularly when performed on small biopsy specimens,

and aid in the differentiation of extranodal MZL from diffuse large B-cell, small lymphocytic, mantle cell and follicular lymphomas (2,4,7,19). Pulmonary extranodal MZL is an indolent disease and exhibits a favorable prognosis, with a five-year survival rate of ~90% (4,7,20), but extra-pulmonary lesions and lymph node involvement are poor prognostic factors (20).

In the present study, since the male patient was asymptomatic, which significantly increased the difficulty of the clinical diagnosis, the male patient was required to undergo a series of clinical examinations, comprising chest radiography, chest CT, bronchoscopic examinations, immunohistochemical staining and transbronchial lung biopsy. Combining these clinical results and subsequent analysis outcomes, an accurate diagnosis of pulmonary extranodal MALT-MZL was finally confirmed.

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