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Case report

A young man with an unchanged consolidation in chest CT

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ABSTRACT

Primary pulmonary mucosa-associated lymphoid tissue (MALT) lymphoma is extremely rare. MALT lymphoma patients usually show no clinical symptoms or physical signs. Chest radiograph or computed tomography (CT) may confuse MALT lymphoma with other pulmonary diseases, which would lead to misdiagnosis or a delayed diagnosis. In the present study, a 33-year-old male patient had cough and fever. Chest CT showed consolidation on both sides. Those clinical symptoms disappeared after he had been misdiagnosed and treated for community-acquired pneumonia for three weeks. However, further chest CT still showed the consolidation without any change. Then an ultrasonic guided transthoracic needle biopsy was performed. Morphological changes indicated the diagnosis of extranodal marginal Zone B cell lymphoma of MALT. The patient was then treated with chemotherapy and rituximab. After this line of treatment, the consolidation decreased.

1. Introduction

Primary pulmonary lymphoma accounts for 0.5–1.0% of pulmonary malignancies and < 1.0% of all lymphomas [1]. It develops both in the normal MALT tissue and in a normal organ or tissue without MALT [2]. Patients with primary pulmonary lymphoma may show no symptoms or physical signs. There are no typical or significant changes in the chest radiograph or CT scan that can distinguish primary pulmonary lymphoma from other pulmonary diseases. Here we present a case of MALT lymphoma with an unchanged consolidation in the chest CT, diagnosed by ultrasonic guided transthoracic needle biopsy.

2. Case report

A 33-year-old male patient who had cough and intermittent for two months was admitted to our clinic. He had experienced fevers, yellow sputum, episodes of minimal hemoptysis and left chest pain recently. He had no history of weight loss, alcohol abuse, or smoking, and didn't expose to tuberculosis. His respiratory examination revealed diminished movement of lower left chest wall. Other general clinical examination results were normal. However, laboratory findings revealed that the white blood cells, C-reactive protein, erythrocyte sedimentation rate (ESR) and procalcitonin (PCT) were all raised. The results of both T-SPOT TB test and tumor markers were negative. Cell immunity and humoral immunity were normal.

His chest CT showed bilateral consolidation in the right upper and middle lobes and the left upper lobes (Fig. 1A). There was a little left pleural effusion. No mediastinal or hilar adenopathy was noted. He was first treated for community-acquired pneumonia for three weeks, and all symptoms were gone. Further blood lab examinations on white blood cells, neutrophil, C-reactive protein, ESR and PCT were all normal. However, the chest CT scan revealed less pleural fluid and an unchanged consolidation (Fig. 1B). Some causes of non-resolving pneumonia should be excluded. We decided to complete other examinations.

The bronchoscopy revealed diffuse mucosal swelling in both lobar branches, with neutrophils and some normal bronchial cells, but no malignancies or acid fast bacilli were found; while other tests for microbes showed negative results. Pleural fluid was aspirated from the left hemithorax and identified as exudative. Cells in the pleural fluid were predominantly lymphocytes, with lactate dehydrogenase (LDH) 299U/L, adenosine deaminase level 45.2U/L. No malignant cells or acid fast bacilli were detected in the pleural fluid. PET-CT indicated intense fluorodeoxyglucose (FDG) uptake in the right upper and middle lobes and left upper lobe (maximum standardized uptake value: 5.66–9.63). There were no signs of disease in other sites.

Then an ultrasonic guided transthoracic needle biopsy of the right upper consolidated area was performed. H&E staining showed that normal alveolar structure had completely disappeared and had been substituted by diffuse lymphoid cells with irregular nucleus. These

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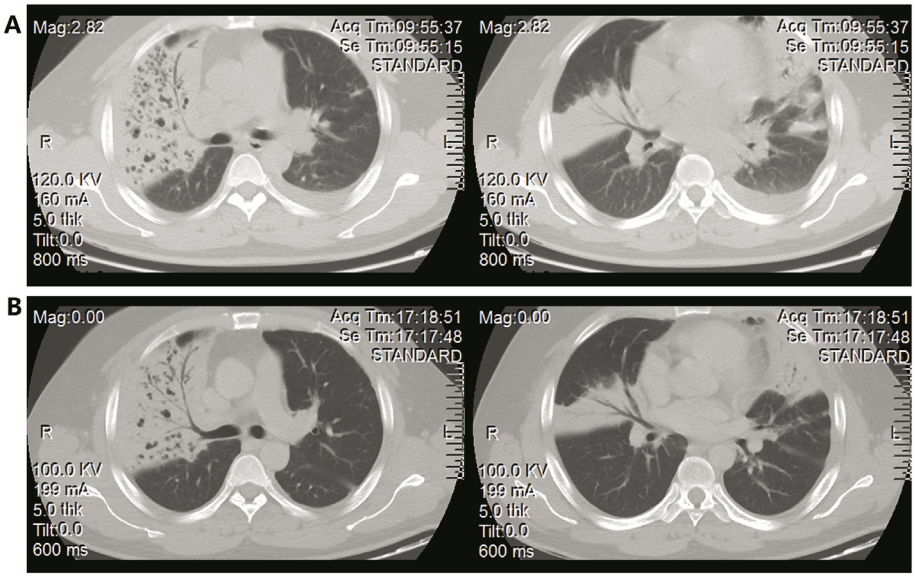

Fig. 1. The chest CT showed bilateral areas of consolidation and little pleural effusion in the left (A). After antibiotic treatment, the chest CT scan revealed less pleural fluid and unchanged consolidation (B).

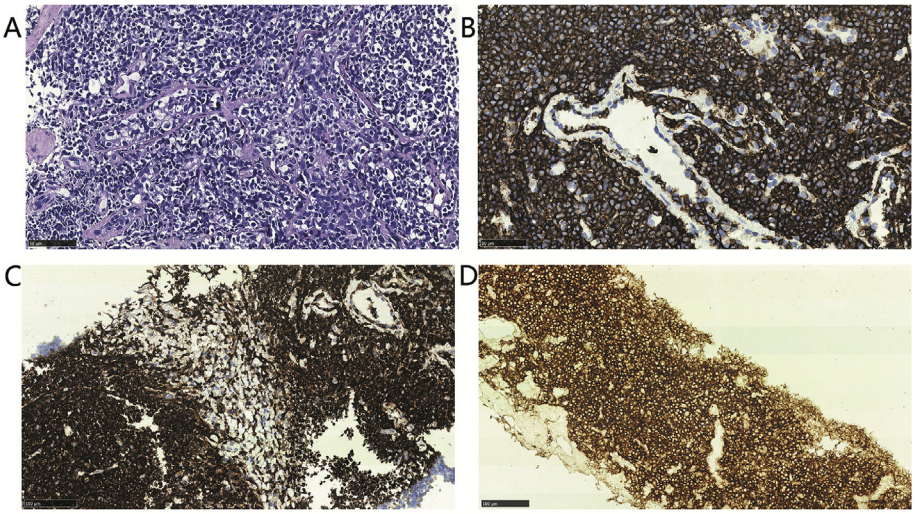

Fig. 2. H&E staining showed that the normal alveolar structure had completely disappeared, being substituted by diffuse lymphoid cells infiltration. These lymphoid cells included small and round lymphoid cells, centrocyte-like cells and monocytoid-resembling lymphocytes. (Magnification ×40) (A); Immunohistochemical test indicated that the cells were positive for CD20 (B), Bcl-2 (C), CD79a (D).

lymphoid cells included small round lymphoid cells, centrocyte-like cells and monocytoid-resembling lymphocytes (Fig. 2 A). Immuno-histochemistry cell staining showed positive results for CD20, CD79a, PAX-5, LCA, Bcl-2, and ki67 (LI about 10%) (Fig. 2 B, C and D), and negative results for CD5, CD23, CyclinD1, CD10, CD56, TdT, MUM1, CgA, Syn and NSE. These morphological changes match a diagnosis with extranodal marginal Zone B –cell lymphoma of mucosa-associated lymphoid tissue (MALT).

Furthermore, a bone marrow biopsy was performed and the results showed no neoplastic invasion. Leukemia immunophenotyping was normal. No *Helicobacter pylori* or other infections were found at gastroscopy. Therefore, this young male patient was diagnosed with Primary MALT lymphoma stage IE according to the Ann Arbor classification (Table 1).

The patient was treated with five cycles of chemotherapy, including cyclophosphamide, vincristine, adriamycin and prednisone and rituximab, and complained of no clinical symptoms. He came for clinical and radiological follow-up visits every three months; the consolidation decreased in his CT photograph. There have been no symptoms and no progression since then.

Table 1
Clinical Stags of Pulmonary Non-Hodgkin's Lymphoma.

Stage	Extent of Disease
IE	Lung only involved, could be bilateral
II1E	Lung and hilar lymph nodes involved
II2E	Lung and mediastinal lymph nodes involved
II2EW	Lung and adjacent chest wall or diaphragm involved
III	Lung and lymph nodes below the diaphragm
IV	Diffuse disease

A Modified Ann Arbor classification.

3. Discussion

MALT lymphoma is known as a kind of non-Hodgkin's lymphoma (NHL) and accounts for 7–8% of NHLs. It belongs to the marginal-Zone B cell lymphomas but is different from the nodal and splenic forms. It was originally described at extranodal sites in relation to mucosae or glandular epithelia and usually occurs in the gastrointestinal tract, salivary glands, thyroid, ocular adnexa, kidney, breast, lung and so on [3]. The most common type is gastric MALT lymphoma (about 50% of

MALT lymphomas), while the primary lung MALT lymphoma is very rare. MALT lymphoma is considered to have high correlation with chronic antigenic stimulation (especially *Helicobacter pylori* to gastric MALT lymphoma), chronic inflammation and autoimmune disease. It was reported that smoking or autoimmune diseases, such as systemic lupus erythematosus, may be associated with pulmonary MALT lymphomas [4]. The chromosome translocations such as t (11; 18) (q21; q21), t (1; 14) (p22; q32) and t(14; 18) (q32; q21) also take part in the pathogenesis of MALT lymphomas [5].

The primary pulmonary MALT lymphoma is usually observed in patients aged 50–60 years, and is rarely observed in patients aged around 30 years. The incidence is independent of gender. MALT lymphoma is an indolent lymphoma which can last for a long time, with a tendency to disseminate late. It may not even progress for a decade [6]. And the 5-year relative survival of patients with MALT lymphoma is about 89% [7].

Half of the MALT lymphoma patients have no symptoms or physical signs. The patients may have cough, dyspnea, shortness of breath, chest pain, hemoptysis, fever and so on [8]. There are no specific symptoms that are essential for the diagnosis. But it tends to disseminate to other parts of the lung and the mucosa of other organs, such as the stomach and the salivary glands. Results from the common laboratory examination including routine blood tests are usually normal. The bone marrow biopsy is important, and the results may be abnormal when the patient has neoplastic infiltration. There are no typical or significant changes in chest radiograph or CT scan which distinguishes it from other pulmonary lymphomas. It can present as mass or mass-like consolidation and multiple nodules (about 70%). An air bronchogram (about 50%), ground-glass opacities and pleural effusion can also be seen in the case. The characteristics of all the changes are an indolent process, which may not develop for several years. The role of bronchoalveolar lavage (BAL) was unclear. It was reported that lymphocytes of BAL were more than 20% and CD19/20 positivity may suggest MALT lymphoma [9]. Bronchoscopy brushing is only useful when the bronchus is involved.

Histopathologic examination is the gold standard for the diagnosis of MALT lymphoma. Biopsy such as transbronchial biopsy, CT scan-guided or ultrasonic-guided transthoracic biopsy would be necessary. The histology characteristics of MALT lymphoma are centrocyte-like cells, which are small to medium-sized lymphocytes with abundant cytoplasm and small irregular nuclei. Alternatively, the neoplastic cells may resemble monocytoid lymphocytes, which have distinct cell borders, or they may resemble small mature lymphocytes. Infiltration of the epithelium by neoplastic cells can lead to lymphoepithelial lesions. This can also occasionally be seen in inflammation including reactive pulmonary infiltrates. In pulmonary MALT lymphoma, neoplastic cells could infiltrate lymphatic vessels, spreading along bronchovascular bundles, interlobular septa and pleura and then form pulmonary parenchyma lesions.

No specific immunohistochemical marker has yet been identified for MALT lymphoma. The NCCN Guidelines (Version 2.2016) of Non-Hodgkin's Lymphomas recommend markers for an immunohistochemistry (IHC) panel of Non-gastric MALT Lymphomas, including CD20, CD3, CD5, CD10, CD21 or CD23, CCND1, BcL2. CD5, CD23 and cyclinD1, IHC results are useful to differentiate MALT lymphoma from other low-grade B-cell lymphomas such as small lymphocytic lymphoma, chronic lymphocytic leukemia and mantle cell lymphoma, whereas CD10 and BcL-6 are identified in follicular lymphoma. In this case, the immunohistochemistry showed CD20, CD79a and Bcl-2 were positive, whereas CD5, CD23, CyclinD1, CD10, CD56, CgA, Syn and NSE were negative. A high expression of Ki-67 indicates a large number of cells in the proliferation cycle and correlates positively with the malignant degree of non-Hodgkin's lymphoma [10]. In the end, CgA, Syn and NSE positive were observed in small-cell carcinoma. Detection of Ig gene and chromosome of MALT 1 gene rearrangements would be helpful to the diagnosis [11].

After the diagnosis of pulmonary MALT lymphomas, an evaluation should be given. The following examinations should also be completed: A physical exam with performance status; complete blood count and measurements of serum lactate dehydrogenase; a CT scan of abdomen and pelvis; gastroscopy examination for *Helicobacter pylori* or other infections; and bone marrow biopsy. Hepatitis B testing should be done before immunotherapy and chemotherapy [12]. For clinical pulmonary MALT lymphoma staging, we always use the Ann Arbor classification (see Table 1). The value of the PET scan in the evaluation is controversial. A low-grade lymphoma has little FDG uptake, especially in the stomach [13], whereas some researchers think it may be helpful for initial staging and follow-up of patients [14]. So a PET scan is not used routinely for staging in lymphoma. Nonetheless, the treatment should be done whether there is a result for PET-CT or not [12].

The main treatment modalities for MALT lymphoma include surgery, radiotherapy, chemotherapy and rituximab [15,16], but the most effective course of treatment is still being debated. For patients with limited pulmonary diseases, surgical excision may be an appropriate choice. NCCN recommend that patients with stage I-II non-gastric MALT lymphoma should be given involved-site radiotherapy (ISRT) (24–30 Gy); however, this is unsatisfactory for primary pulmonary MALT lymphoma. Patients with pulmonary MALT lymphoma or extranodal involvement also could be observed [16]. Although chemotherapy is the traditional therapy for MALT lymphomas, which regimens to choose, the long-term effect and other data should be evaluated, especially in a localized disease. Rituximab is a choice for selected patients [17]. In our case, the patient was given chemotherapy regimens, such as cyclophosphamide, vincristine, adriamycin and prednisone, combined with rituximab, and no progression has been observed until now.

In conclusion, primary pulmonary MALT lymphoma is extremely rare and has no typical clinical symptoms or signs. Changes in the chest radiograph or CT scan may confuse it with other pulmonary diseases, which could lead to misdiagnosis or a delay in diagnosis. Histopathologic and genetic examinations contribute to the diagnosis of MALT lymphoma. Therefore, the diagnosing and staging is challenging. Although the disease was indolent and had a favorable prognosis, treatment was tailored to fit the individual patient. When we encounter an unchanged consolidation in chest CT or non-resolving pneumonia, we should keep in mind pulmonary MALT lymphoma, and a biopsy is necessary.

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Author contributions

Yang Zhao conceived and designed the study; Yang Zhao collected the data, and Guo wei analyzed the data; Yang Zhao and Guo wei

prepared the figures; Yang Zhao wrote and revised the manuscript.

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