

—Report on Experiments and Clinical Cases—

Primary Pulmonary Mucosa-associated Lymphoid Tissue Lymphoma Combined with Idiopathic Thrombocytopenic Purpura and Amyloidoma in the Lung

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Abstract

Three abnormal shadows were detected in the right lung on chest X-ray films and computed tomography in a 75-year-old woman during follow-up for idiopathic thrombocytopenic purpura. Because a definitive diagnosis was not obtained through general examinations, exploratory thoracotomy was performed for diagnosis and treatment. The main lesion in the right middle lobe was diagnosed as mucosa-associated lymphoid tissue (MALT) lymphoma according to histopathological findings, cytogenetic studies and reverse transcriptase-polymerase chain reaction analysis, and nodular lesions in S³ and S⁷ were diagnosed with Congo-red staining as local deposition of amyloid. The patient had no recurrence of the MALT lymphoma of the lung or other organs for 4 years after surgery. To our knowledge, this is the first reported case of primary pulmonary MALT lymphoma combined with idiopathic thrombocytopenic purpura/lung amyloidoma.

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Key words: primary pulmonary mucosa-associated lymphoid tissue lymphoma, idiopathic thrombocytopenic purpura, amyloidosis

Introduction

Extranodal lymphomas are most frequently found in the gastrointestinal tract, and primary pulmonary lymphoma is extremely rare^{1,2}. Most primary lymphomas of the lung arise from the mucosa-associated lymphoid tissue (MALT) of the bronchus¹.

In this study, we report on a patient with a history of idiopathic thrombocytopenic purpura (ITP) in whom an MALT lymphoma arose from a primary focus in the lung with amyloidosis.

Generally, MALT lymphoma is associated with an autoimmune disease, such as ITP, caused by antiplatelet antibodies³. Amyloid L is derived from immunoglobulin light chain, which is thought to be

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produced by lymphoid cells⁴.

To our knowledge, only 1 patient with MALT lymphoma with ITP has previously been described⁵; this patient had Evan's syndrome. Our case is the first case reported in which the MALT lymphoma was complicated by ITP and amyloid deposition in the lung.

Case Report

A 75-year-old woman who had been followed up for ITP since 1988 was informed of the presence of abnormal shadows on a routine chest X-ray in 1995; middle lobe syndrome was suspected. Because the abnormal shadow in the middle lobe were larger on chest X-ray films in 1998, she was referred to the Saitama Cancer Center Hospital for examination and treatment. She had no symptoms, and the physical examination were normal. The ITP was under good control with steroid treatment.

Three lesions were found on chest X-ray films of the right lung (**Fig. 1**). The films showed a nodular shadow in the right middle lung field, suggesting atelectasis at the periphery. Above the lesion, another nodular shadow was detected. In addition, a round nodular shadow was detected to the right of the inferior thoracic vertebrae (**Fig. 1**).

Computed tomography of the chest showed a nodular lesion with diameter of 35 mm in the proximal right middle lobe which had caused atelectasis in the distal lung field (**Fig. 2b**). In the S³ (**Fig. 2a**) and S⁷ areas (**Fig. 2c**), nodular lesions 15 mm and 30 mm in diameter, respectively, were found. Bronchoscopy revealed obstruction in the right B⁴ area, and transbronchial lung biopsy (TBLB) was performed via the right B⁷ area. However, there was no tumor, the specimens contained no malignant cells, and the cytologic diagnosis of bronchoalveolar lavage fluid was class II. Most results of routine laboratory examination were within normal limits. The levels of tumor markers, such as carcinoembryonic antigen and CYFRA, were within the normal range (2.9 ng/ml and 0.8 ng/ml, respectively). On respiratory function testing, vital capacity (VC) was 2,390 ml, %VC was 117%, forced expiratory volume in 1 second (FEV_{1.0}) was

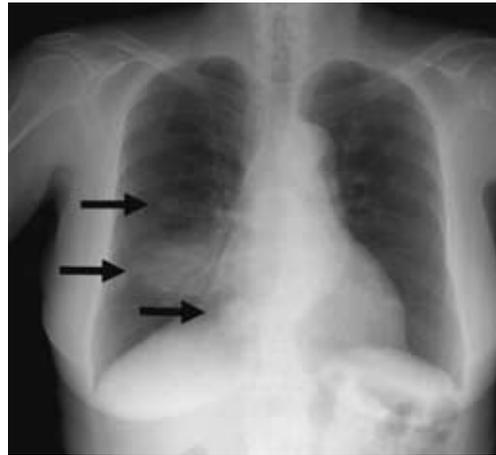


Fig. 1 Chest X-ray film
Three lesions were shown in the right lung.

1,660 ml, and %FEV_{1.0} was 69.4%.

Gallium scintigraphy exhibited no abnormal accumulation in other organs. We suspected the nodular lesions were primary lung carcinoma or metastatic lung tumors, and decided to perform exploratory thoracotomy for definitive diagnosis.

In 2000, surgery was performed. Under general anesthesia, the patient was intubated with a double-lumen endotracheal tube and was placed in the left lateral position. Many small nodules were found on the middle lobe pleura, and we suspected these small nodules represented pleural dissemination. However, pathological examination of frozen sections confirmed that these specimens were nonmalignant. Subsequently, partial resection of the S⁷ mass was performed for rapid diagnosis with frozen specimens. However, malignancy was not found. Frozen specimens from the main lesion in the middle lobe showed an accumulation of lymphocytes, suggesting a non-Hodgkin's lymphoma. Initially, right middle lobectomy was planned. However, middle lobectomy was expected to be difficult because the tumor involved the middle and lower lobes, and was near the pulmonary artery. Ultimately, lobectomy of the right middle and lower lobes was performed. The S³ lesion was in a relatively deep area, and enucleation was carried out. Because hilar and mediastinal lymph nodes were not enlarged and to avoid excessive surgical stress, lymph node dissection was not done.

Pathological examination showed that many

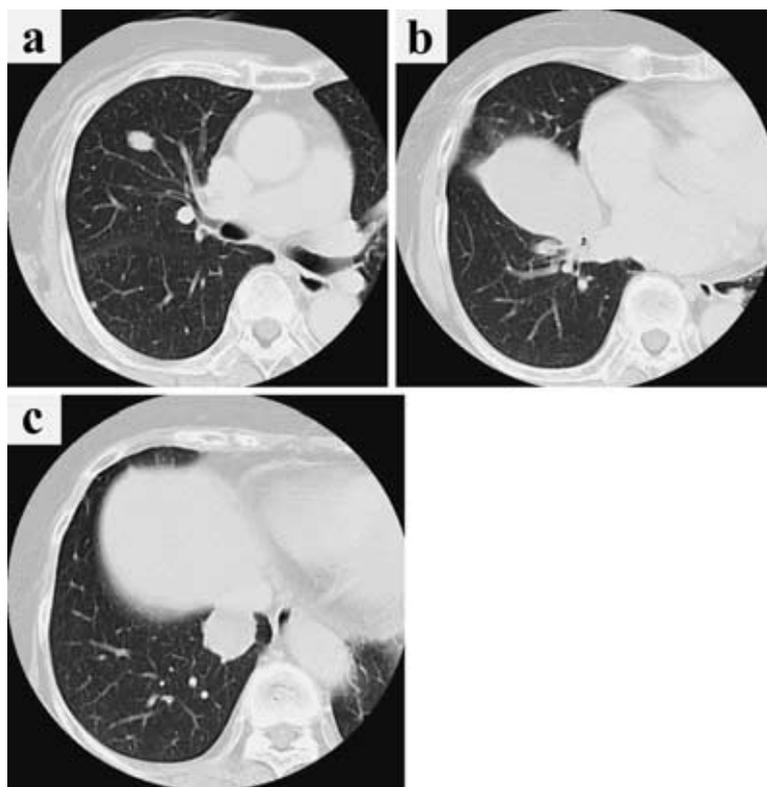


Fig. 2 Chest computed tomography

- (a) Right S³: nodule with a diameter of 15 mm
 (b) A nodular shadow measuring 35×25 mm in the right middle lobe, and the periphery was suggestive of atelectasis.
 (c) Right S⁷: nodule with a diameter of 30 mm

B-cells had diffusely infiltrated the main middle lobe lesion and that a lymphoepithelial lesion was presented in a part of the bronchial mucoepithelium (Fig. 3a). Immunohistochemical studies demonstrated that these lymphoid cells expressed L26 and CD79 a were negative for CD3 and CD45RO. In addition, reverse transcriptase-polymerase chain reaction analysis of the specimens from the middle lobe tumor revealed monoclonal rearrangement of immunoglobulin heavy chain genes. Cytogenic studies of the middle lobe tumor showed no t(11; 18)(q21; q21) translocation. The S³ and S⁷ lesions which were stained with Congo-red and apple-green birefringence under polarized light (Fig. 3b), were diagnosed as amyloid deposition. In a portion of the middle lobe lesion, a structure-free deposit was noted in the presence of diffuse infiltration of B lymphocytes. The definitive diagnoses were primary pulmonary MALT lymphoma of the lung for the middle lobe lesion and pulmonary amyloidosis for

both the right S³ and S⁷ nodules. Four years after surgery, the patient has had no recurrence of MALT lymphoma in the lung and other organs.

Discussion

MALT lymphoma is an extranodal non-Hodgkin's B-cell lymphoma arising from MALT, as defined by Iassacson in 1983⁶. MALT lymphomas are now classified in the Revised European American Lymphoma classification as extranodal, marginal zone, B-cell lymphomas⁶. Primary pulmonary MALT lymphoma accounts for 3% to 4% of extranodal lymphoma and 0.5% to 1% of primary pulmonary malignancies⁷. The present case met criteria for primary pulmonary lymphoma defined by Stalzman as a tumor that "originally involves only the lung, or the lung and its regional lymph nodes, and in which there is no evidence of dissemination of the tumor for at least 3 months after the diagnosis is

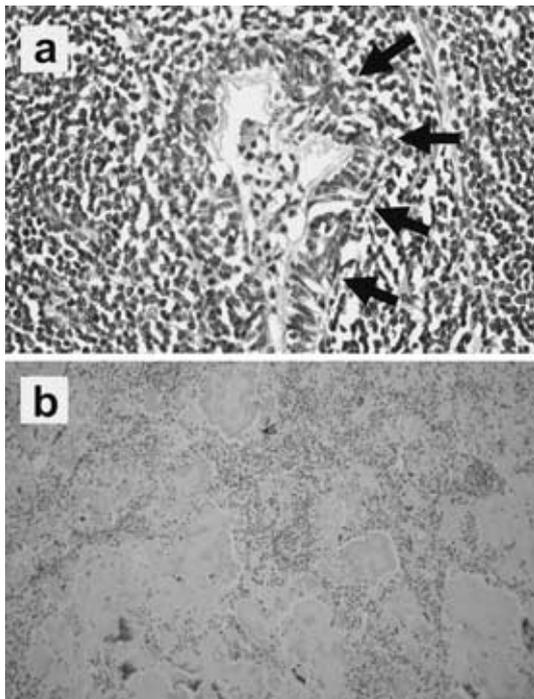


Fig. 3 Histological findings

(a) Lymphoepithelial lesion was found in a part of the bronchial mucosal epithelium in the right middle lobe lesion. (H-E stain, $\times 40$)

(b) S³ and S⁷ lesions were stained with Congo-red and showed apple-green birefringence under polarized light. (Congo-red stain, $\times 10$)

established"¹³.

Because definitive diagnosis is difficult, even if invasive examinations, such as bronchoscopy and percutaneous needle biopsy are performed, in many patients, primary pulmonary MALT lymphoma is diagnosed with pathological examination, immunohistochemical studies, cytogenetic studies, and RT-PCR analysis after exploratory thoracotomy. Kamiuehara *et al* summarized 53 cases of primary pulmonary lymphoma in Japan and found that definitive diagnosis established made during surgery in 72.2% of the patients, at autopsy in 5.6% of the patients, and during transbronchial/percutaneous lung biopsy in 20.3% of the patients⁸.

Although there is no consensus on treatment for primary pulmonary lymphoma, surgical resection is generally carried out in cases of localized tumor. However, according to recent reports, surgical resection is not always superior to chemotherapy and radiotherapy for primary gastrointestinal MALT lymphoma^{9,10}. Some case reports have

demonstrated that adjuvant chemotherapy is not related to prognosis in MALT lymphoma¹²; therefore, we did not perform adjuvant chemotherapy. The prognosis of primary pulmonary MALT lymphoma is generally favorable in most series, with 5-year survival rate of more than 80% and median survival time of more than 10 years⁷.

Our case is unusual because the patient had a history of ITP in addition to amyloid deposition in the lung. Although gastric MALT lymphoma can occur with ITP³, there has been only one case report of primary pulmonary MALT lymphoma combined with Evan's syndrome¹¹.

ITP is considered to be an autoimmune thrombocytopenia associated with production of antiplatelet antibodies. Sakai *et al* have reported that immunoglobulin G- κ type M-protein is produced by MALT lymphoma⁵. Therefore, an antiplatelet antibody produced by plasma cell-like lymphoma cells may have caused ITP; however, the details of the mechanism remain unclear. Localized amyloid deposition arising from MALT lymphoma is extremely rare with a frequency of less than 1%¹². Amyloid L is derived from immunoglobulin light chain, and a case report has shown that lymphoid cells produce amyloid⁴.

Some autoimmune diseases, such as systemic lupus erythematosus, multiple sclerosis, Hashimoto's thyroiditis and Sjögren's syndrome are associated with MALT lymphoma, and the onset of these autoimmune diseases is related to self antigens²⁷. To our knowledge, there have been no previous case reports of primary pulmonary MALT lymphoma with ITP and amyloidosis, as demonstrated in our patient. Therefore, the present case allows us to consider the relationship between MALT lymphoma and antiplatelet antibodies/local amyloid deposition.

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