A Case of Bronchus-associated Lymphoid Tissue Lymphoma in a Young Woman

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ABSTRACT —— ***Background.*** Pulmonary lymphoma in young patients under 40 years of age without immunological deficiency is rare. ***Case.*** A 27-year-old woman was admitted to our hospital with bilateral multiple pulmonary opacities on a chest radiograph. Computed tomography revealed an irregular marginal nodular shadow 2.8 cm in diameter in right S^4 with spiculation and multiple alveolar opacities in left S^{1+2}, S^4, S^{10} and right S^2. The tumors in the left lung were resected thoracoscopically, and were well defined and white in color. Pathologically, the specimens were diagnosed as extranodal marginal zone B-cell lymphoma of the bronchus-associated lymphoid tissue. The patient rejected immediate treatment and chose to be followed up until tumor progression was confirmed. ***Conclusion.*** We encountered a rare case of primary multiple pulmonary lymphomas of bronchus-associated lymphoid tissue in a young person. (*JJLC.* 2005;45:47-50)

KEY WORDS —— Pulmonary B-cell lymphoma, Bronchus-associated lymphoid tissue, Thoracoscopy

INTRODUCTION

Primary pulmonary lymphomas are rare and account for approximately 0.3% of all pulmonary neoplasms.[1,2] Among primary lymphomas, extranodal marginal zone B-cell lymphoma of the bronchus-associated lymphoid tissue (BALT) type appears to be the most common primary lymphoma of the lung.[3-6] A few cases of BALT lymphoma have been described in children with human immunodeficiency virus infection.[7] In general, BALT lymphoma in young patients under 40 years of age without immunological deficiency is rare. We encountered a case of primary multiple BALT lymphomas in a 27-year-old woman. This is the youngest nonimmunocompromised patient with BALT lymphomas ever to be reported in Japan.

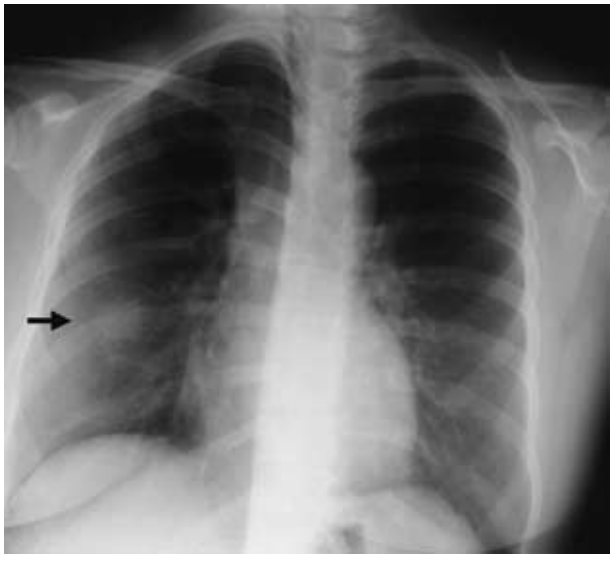

Figure 1. Chest radiograph at admission, showing a nodular shadow in the right middle lung field.

CASE REPORT

A 27-year-old woman was admitted to our hospital, with bilateral multiple infiltrative shadows in the right upper, middle and left lower lung fields on a chest radiograph taken at a regular medical examination (Figure 1). The results of laboratory tests, consisting of a complete blood count, biochemical examinations, tumor markers of carcinoembryonic antigen, squamous cell carcinoma-related antigens, neuron-specific enolase and progastric releas-

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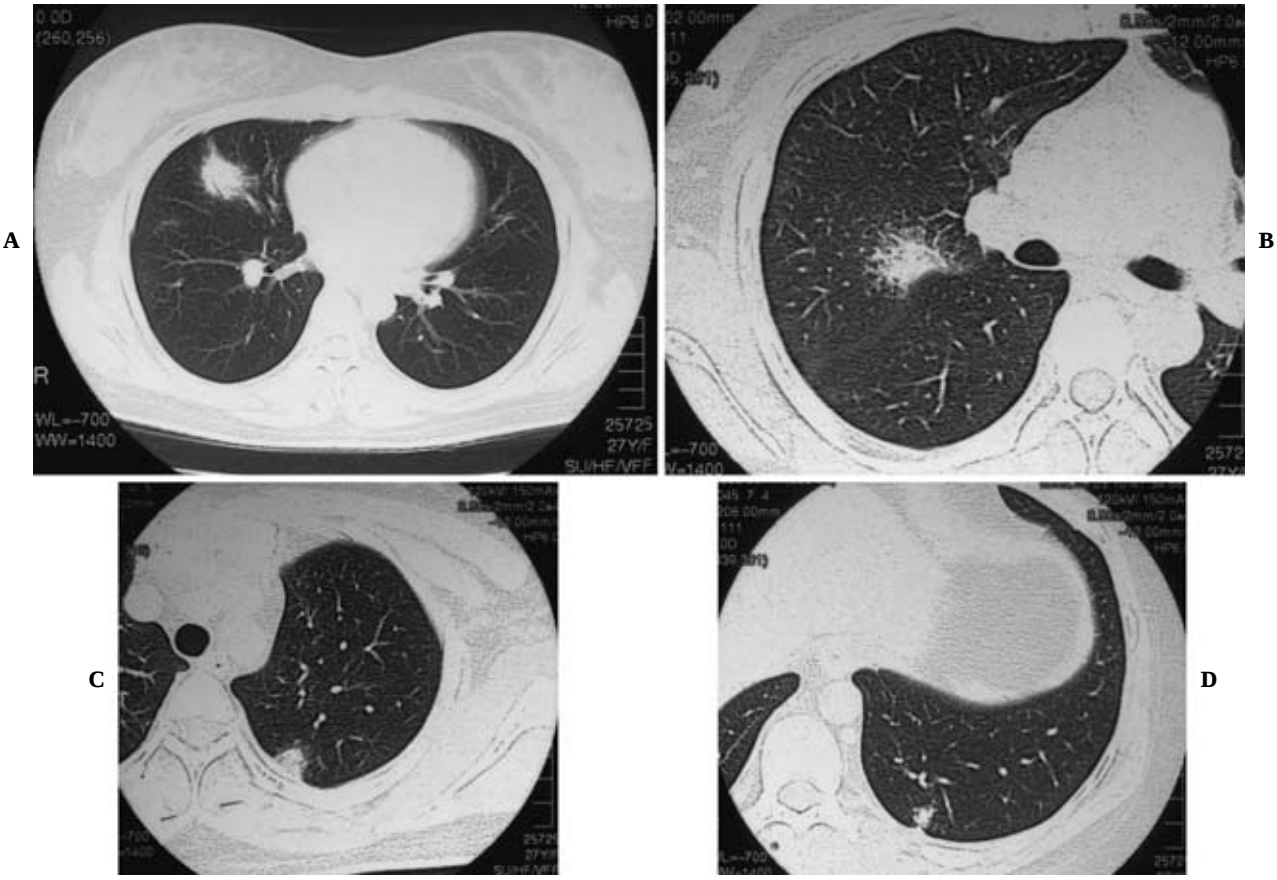

Figure 2. Computed tomographic scan of the chest at admission, showing nodular shadows on the right S^4 (**A**), S^2 (**B**), left S^{1+2} (**C**) and S^{10} (**D**).

ing peptide were within normal limits.

Computed tomography (CT) of the chest demonstrated an irregular marginal nodular shadow 2.8 cm in diameter in right S^4 with spiculation and localized alveolar opacities in left S^{1+2}, S^4, S^{10} and right S^2 without mediastinal lymphadenopathy (Figure 2). Bronchoscopy was performed and the macroscopic findings were normal. Therefore, the specimens of the transbronchial biopsy from the right S^4 were diagnosed as lymphoid cell infiltration, and lymphoma was suspected.

Video-assisted thoracoscopic resection of the nodules in the left lung was performed to obtain a precise diagnosis. Thoracoscopy revealed well-defined whitish nodules on the left S^{1+2}, S^4 and S^{10} segments (Figure 3). Limited wedge resections were performed thoracoscopically. The postoperative course was uneventful.

The cut surfaces of the nodules revealed round whitish tumors, and macroscopic observation of the adjacent bronchi showed no ectasis or thickening. Histologically, the tumor was composed of a diffuse proliferation of

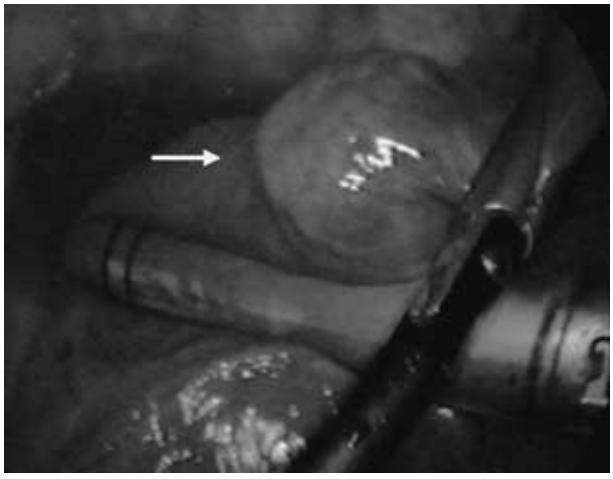

Figure 3. Intraoperative thoracoscopic findings of left S^{1+2}.

medium-sized atypical lymphoid cells forming some lymphoepithelial lesions, but the resected specimens showed no closed bronchus or unusual bronchial glands (Figure 4). The immunohistochemical findings showed that the atypical lymphoid cells were diffusely positive for L-26,

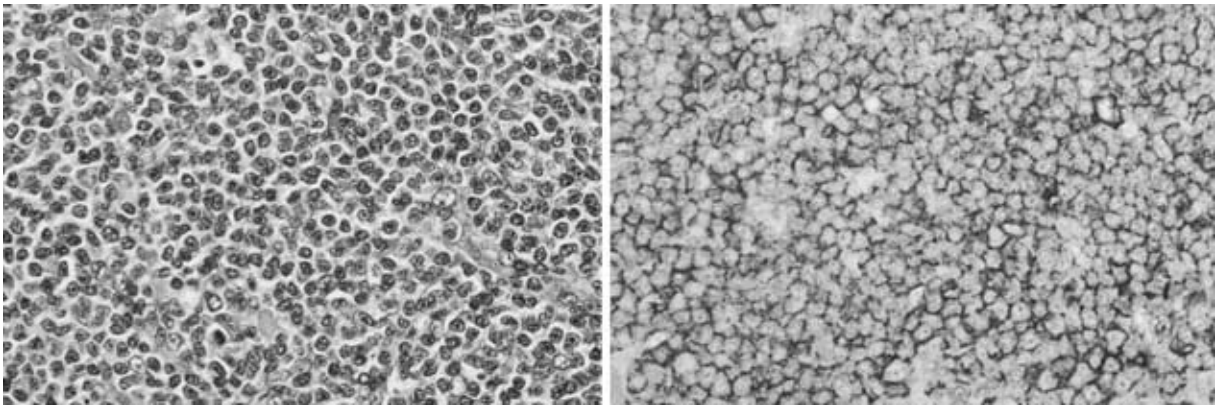

Figure 4. Resected specimens of left lung lesions. The tumor is composed of a diffuse proliferation of medium-sized atypical lymphoid cells forming some lymphoepithelial lesions. Immunohistochemical findings demonstrated that the medium-sized atypical lymphoid cells were diffusely positive for L-26（**A**: H. E. stain×150, **B**: L-26×300）.

LCA, and bcl-2, weakly positive for CD79a, but negative for UCH-1 and CD10. Pathologic study confirmed extranodal marginal zone B-cell lymphoma of the BALT.

Whole-body gallium-67 scintigram findings revealed no accumulation except in the bilateral lung fields. No atypical lymphoid cells were found in the bone marrow by sternal puncture. Gastrointestinal fiberscopic study showed no remarkable findings, and *Helicobacter pylori* were not found in the gastric mucosa. Finally, the diagnosis was made of pulmonary multiple lymphomas of BALT. The lymphomas were evaluated as stage I -E according to the Ann Arbor staging system modified by Ferraro et al.[1]

Resection of the right pulmonary tumors by thoracotomy or systemic chemotherapy with the administration of anti-CD20 antibodies was recommended, but the patient rejected immediate treatment. After 14 months of follow up, the tumors had not changed in size, and imaging studies showed no new lesions.

DISCUSSION

Bronchial-associated lymphoid tissue（BALT）is a lymphoid tissue specializing in bronchial mucosal defense.[8,9] The stomach was the most frequent site of mucosa-associated lymphoid tissue（MALT）lymphoma and it has served as a model for pulmonary BALT lymphoma.[10] The lung is the second most common extranodal site.

Under chronic antigenic stimulation, MALT can develop in the stomach and undergo secondary lymphomatous transformation arising from marginal zone B-cells. Thus far no triggering antigens have been identified in the lung, but chronic antigenic stimulation in certain autoimmune disorders is considered to influence the onset of pulmonary BALT lymphoma. A few cases of BALT lymphoma have been described with human immunodeficiency virus infection.[7,11]

BALT lymphomas have been reported in association with disorders of the immune system, such as Sjögren syndrome and Hashimoto thyroiditis, suggesting that dysregulation of T-cell function may be involved in the genesis of BALT lymphoma in these patients.

We could not discover any chronic antigenic stimulation, such as smoking, exposure to chemicals, infections or immune disorders in our patient. The mechanism by which BALT developed and underwent secondary lymphomatous transformation in our patient is not clear.

In patients with BALT lymphoma, the age distribution curve had its peak between the sixth and seventh decades.[1,5,6,9] Few cases of primary BALT lymphoma have been described in patients under 40 years of age. Patients in their twenties with BALT lymphoma are very rare.

Recently Cadranel et al[4] reported that the usual radiological finding was a localized alveolar opacity, with a diameter of under 5 cm and blurred or well-defined contours; it was associated with an air bronchogram in nearly 50% of cases, and computed tomography usually demonstrated bilateral and multiple lesions. Less than 10% of patients have bilateral diffuse reticulonodular opacities, atelectasis or pleural effusion. However it was reported that radiographic abnormalities were more commonly unilateral than bilateral.[1,4] Our case was asymptomatic and had bilateral and multiple opacities.

The results of bronchial endoscopy are usually normal, although abnormalities ranging from mucosal inflamma-

tion to bronchial stenosis are occasionally observed. The diagnostic yield of bronchial examinations, especially transbronchial biopsy of visible endobronchial lesions, is higher than that of bronchial endoscopy. The bronchoscopic specimens obtained from our patient were small, and we were only able to diagnose lymphoid cell infiltration, with suspected lymphoma.

Ahmed et al[5] showed that 42% of patients had a history of earlier biopsies by bronchoscopy that were either inconclusive or revealed a benign inflammatory process. The definitive diagnosis in these cases was obtained after a median delay of 3 months when persistent symptoms or the increasing size of pulmonary infiltrates led to surgical lung biopsy. Therefore, video-assisted thoracoscopy is the most useful diagnostic procedure unless the pulmonary nodules are considered malignant, in which case it may also be a therapeutic procedure.

Kurtin et al[6] reported that survival in BALT lymphoma was 71.7% at 10 years, and that overall survival was significantly worse than in an age- and gender-matched control population. Patients over 60 years of age at the time of diagnosis were 4.5 times more likely to die compared with patients under 60 years of age at diagnosis. However, most previous observations indicate a slow rate of progression and a favorable course in BALT lymphoma, including studies showing 2-year and 5-year survivals of 100% and 95-84%, respectively.[1,3-5] As a result, the optimal management of BALT lymphoma with regard to surgery, chemotherapy and radiation therapy alone or in combination, or abstention from therapy, has not yet been defined.

We informed our patient about the benefits of further surgical treatment of the right lung or systemic chemotherapy with anti-CD20 antibodies. She opted against immediate treatment, and chose instead to wait until further observation showed tumor progression, thereby avoiding hair loss and any adverse effect of chemotherapy on a possible pregnancy. The patient showed no evidence of progression of the disease either on clinical examination or on positron emission tomography scans during a 14-month follow up period.

We described a case of primary pulmonary lymphoma of BALT in an otherwise healthy 27-year-old Japanese woman. This is the youngest patient without immunological deficiency ever reported with a BALT lymphoma in Japan. Thoracoscopy was found to be the most advantageous diagnostic procedure.

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