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Lung and Pleural Malignancies

Low-grade B-cell Primary Pulmonary Lymphoma of Mucosa-Associated Lymphoid Tissue (MALT) Type With Synchronous Involvement Of Lacrimal Gland

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Abstract
A 52-year-old male patient was admitted to our hospital with non-productive cough, dyspnea and chest pain. He had been previously hospitalized in our facility in 2001 for the evaluation of localized consolidation area on thorax CT. A diagnosis could not be reached by conventional methods, but he was diagnosed as MALT type lymphoma of the lacrimal gland and referred to the oncology clinic. He had received no medical care during the last five years, after which period the pulmonary lesion was stable. Histopathological examination of the resected consolidation area revealed extranodal marginal zone-B-cell lymphoma of MALT type.

Keywords: primary pulmonary lymphoma, MALT type lymphoma, lacrimal gland

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INTRODUCTION

Lymphomatous proliferation can involve the lungs in three ways: 1) by hematogenous dissemination of non-Hodgkin's lymphoma (NHL) or Hodgkin's disease (HD); 2) by contiguous invasion from a hilar or mediastinal site of nodal lymphoma; and 3) by primary pulmonary involvement. In the first two situations, there is progression or relapse of a known lymphomatous disorder, and the treatment focuses on this hematological disorder. But in the third situation, there are a number of diagnostic and therapeutic problems [1].

Primary pulmonary lymphoma (PPL) is a rare clinical entity, constituting 3-4% of extra-nodal NHL, less than 1% of NHL in general, and only 0.5-1% of primary pulmonary malignancies [1,2]. PPL includes three distinct entities: 1) Low-grade B-cell PPL; 2) High- grade B-cell PPL; and 3) Lymphomatoid granulomatosis [1]. Low-grade B-cell PPL is the most frequent form, accounting for 58-87% of cases in pathological series [3-5]. Nearly 90% of these cases correspond to mucosa-associated lymphoid tissue (MALT) type NHL [4,5]. Previous or synchronous MALT lymphomas at other extranodal sites may occur in the gastrointestinal system, orbit, lacrimal gland, and salivary gland, etc. [1].

In this paper, we present a demonstrative case of low-grade B-cell PPL with synchronous involvement of the lacrimal gland and discuss the diagnostic and therapeutic problems in light of the current medical literature.

CASE PRESENTATION

A 52-year-old male patient was admitted to our hospital with non-productive cough, dyspnea, and chest pain. In his past medical history, he had undergone gastroenterostomy operation because of peptic ulcus 24 years ago. He had a smoking history of 54 pack-years and he gave up smoking five years ago (February 2001) when he was hospitalized in our facility. At that time, he complained of nausea, loss of appetite, and fatigue. Because of a mass lesion on chest radiography he was referred to our hospital.

We reviewed his past files. Computed tomography (CT) of the thorax revealed a localized consolidation on the anterior segment of the right upper lobe and ground-glass opacity on the lingular segment (Figure 1). Three fiberoptic bronchoscopic examinations revealed a narrowed right upper lobe anterior segment bronchus. There was lymphoid infiltration on transbronchial lung biopsies on two occasions. Since the lesion was located centrally, it was not found suitable for a Tru-Cut transthoracic biopsy. During the evaluation period, a cranial magnetic resonance imaging study, which was provided for the evaluation of enophthalmos and ptosis, revealed a mass lesion of 22x10 mm in the lacrimal gland adjacent to the lateral posterior wall of the left orbit (Figure 2). After lacrimal gland biopsy, he was diagnosed as MALT type lymphoma. Since the pulmonary lesion was stable during the follow-up period of six months, no further diagnos-

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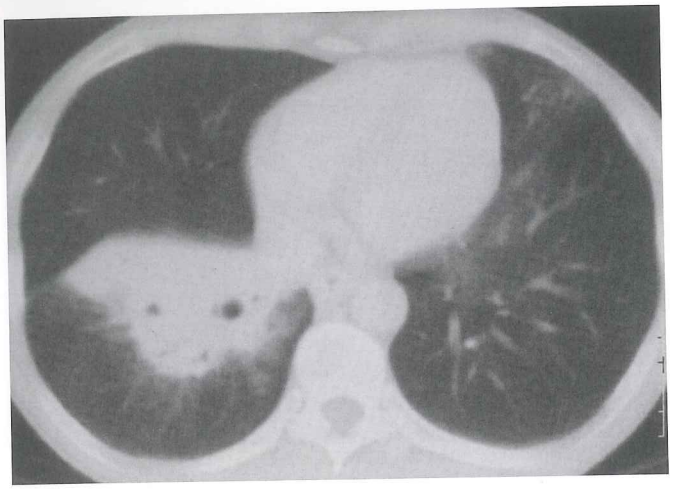

Figure 1. Localized consolidation on the right upper lobe anterior segment is seen on CT scan of thorax.

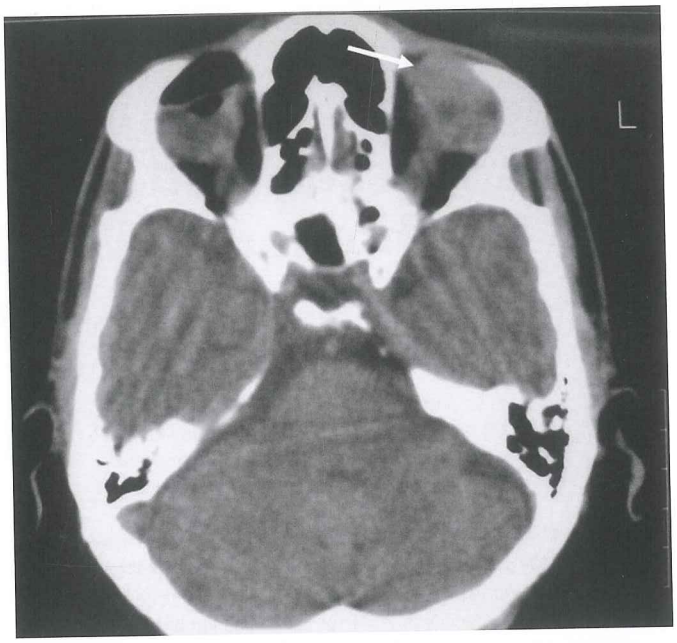

Figure 2. Mass lesion in the lacrimal gland is seen on CT scan of orbit.

tic procedure was performed. The patient was referred to the oncology clinic and treated with chemotherapy (3 cures combination regimen with cyclophosphamide, adriamycin, oncovin, and prednisone) and radiotherapy. During the last five years he received no medical care.

On physical examination, vital signs were within normal limits. There was bronchial sound on the left hemithorax. There was no gross pathology related to eyes. Other systemic examinations were normal. Routine laboratory investigations including complete blood count, biochemistry, and urine analysis were within normal limits other than a low hemoglobin level of 12 g/dl. Erythrocyte sedimentation rate was slightly increased (45 mm/hr).

Computed tomography (CT) of the thorax revealed a localized consolidation on the anterior segment of the right upper lobe and ground-glass opacity on the lingular segment, which was nearly identical when compared with the scans obtained five years previously (Figure 3). Fiberoptic bronchoscopy revealed a narrowed right upper lobe anterior segment bronchus. Bronchial lavage was non-diagnostic. Ophthalmic examination was normal without any evidence of recurrence. Abdominal ultrasound was normal.

The patient was operated and the localized consolidation area was resected. The histopathological examination revealed extranodal marginal zone-B-cell lymphoma of MALT type. In immunohistochemical study, tumoral cells were positive for CD45 and CD20, and negative for CD3. Atypical lymphocytes infiltrating the bronchial wall and the pulmonary parenchyma are seen in Figure 4. The patient was referred to the oncology clinic for chemotherapy.

DISCUSSION

MALT is a lymphoid tissue specialized in mucosal defence. It is absent in physiological circumstances, but develops during chronic antigenic stimulation [1]. For example, as a result of chronic *Helicobacter pylori* infection, MALT can develop in the stomach and undergo secondary lymphomatous transformation arising from marginal zone-B cells. No triggering antigens have been identified in the lung, but chronic antigenic stimulation in certain autoimmune diseases (such as systemic lupus erythematosus, multiple sclerosis, Hashimoto's thyroiditis, and Sjögren's syndrome), smoking, and infections are considered to affect the onset of pulmonary MALT lymphomas [6]. In the presented case, smoking may have been the etiological factor for the development of pulmonary MALT lymphoma.

Low-grade B-cell PPL is the most frequent form, accounting for 58-87% of cases in pathological series [3-5]. Nearly 90% of these cases correspond to MALT type NHL [4,5]. Patients tend to be in their fifth, sixth or seventh decades, with a slight male preponderance. The most common presentation is a mass discovered on a chest radiograph in an asymptomatic patient. When present, the symptoms are nonspecific, such as cough, mild dyspnea, chest pain, and occasionally hemoptysis. Fever and weight loss occur in less than one-quarter of the patients [3,7].

The most common radiographic presentation in chest X-ray is a localized alveolar opacity, with a diameter less than 5 cm and blurred or well-defined contours, in 50-90% of the cases. It is associated with an air bronchogram in nearly half of the cases [7-9]. CT is more sensitive than standard chest X-ray. CT demonstrated the presence of usually bilateral (60-70%) and multiple (70-77%) lesions [10,11]. Less than 10% of the patients have bilateral diffuse reticulonodular

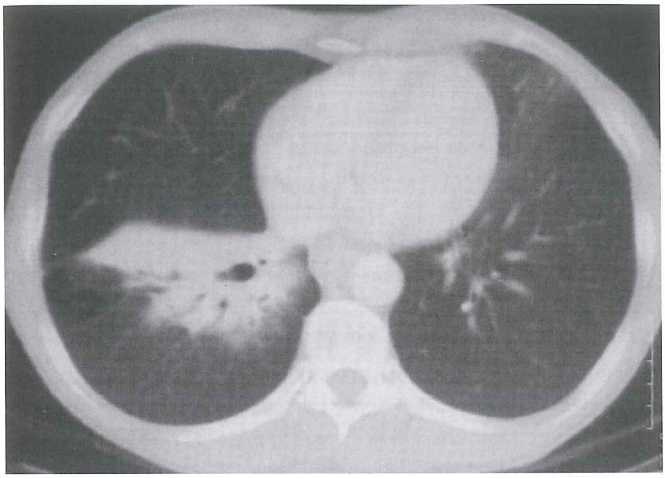

Figure 3. Localized consolidation area, which was stable after five years, is seen on CT scan of thorax.

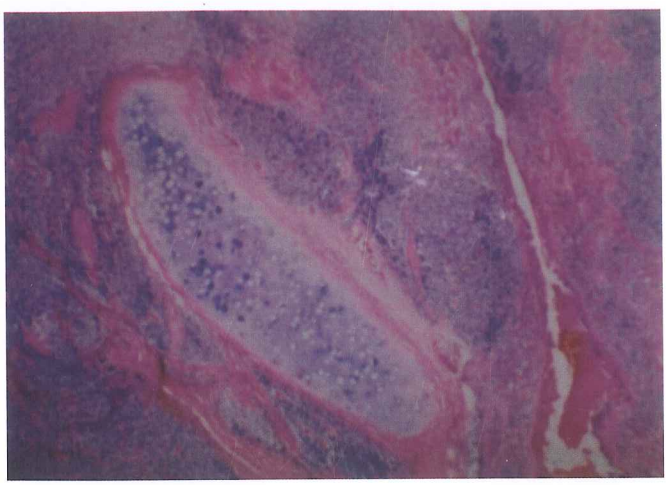

Figure 4. Atypical lymphocytes infiltrating the bronchial wall and the pulmonary parenchyma (HE X 40).

opacities, atelectasia or pleural effusion [7-9]. In the presented patient, chest X-ray revealed a mass lesion on the right lung. CT scans demonstrated a localized consolidation area on the right lung and ground-glass opacities on the lingular segment of the contralateral lung. The localized consolidation area was proven as MALT-type PPL, but we did not perform a surgical procedure for the contralateral lung. Like the primary lesion, the ground-glass opacities were almost identical to those observed five years earlier.

The diagnosis of MALT-type PPL is based on histological examination of surgical samples or bronchial, transbronchial or transthoracic biopsy material [1]. Fiberoptic bronchoscopy usually shows a normal macroscopic aspect [7]. But sometimes, abnormalities ranging from mucosal inflammation to bronchial stenosis can be observed, as in the presented case. The diagnostic yield of bronchial or transbronchial biopsy is high when there are visible endobronchial lesions or radiographic abnormalities. However, the absence of specific signs in most of the samples necessitates further diagnostic investigations [3,7,9,10]. The value of bronchoalveolar lavage (BAL) in the diagnostic work-up of PPL has not been adequately assessed, but it has been proven useful in isolated cases [12,13]. BAL can be helpful, particularly if it shows lymphocytic alveolitis (lymphocytes >20% of total cells), which is found in two-thirds of the patients [7]. The majority of patients needed surgical approaches for definite diagnosis, as in our patient.

Concomitant involvement of other mucosal lymphoid sites, such as gastrointestinal system, orbit, lacrimal gland, and salivary gland, is present in 25-35% of the cases [14]. In our patient, orbita was also involved. In addition, there was a history of gastroenterostomy operation 24 years ago, which might also have been due to MALT type lymphoma.

There is no consensus on the treatment of low-grade B-cell PPL. Current treatment options are surgery, chemotherapy, and radiotherapy [3,5,8,15]. The efficacy of these treatment modalities cannot be analyzed due to the lack of comparative series. Some authors even propose simple clinical monitoring [15]. Nevertheless, surgical resection is commonly preferred for localized tumors [3,5,8,15]. Exclusive chemotherapy is generally used for patients with bilateral or extrapulmonary involvement, relapse or progression. In our patient, pulmonary lymphoma was diagnosed five years after the diagnosis and treatment of lacrimal gland lymphoma. The pulmonary lesion was stable after five years, which may be attributed in part to the chemotherapy given for the treatment of the lacrimal gland lymphoma, but is more likely due to the good prognosis of PPL. The outcome of MALT-type PPL is generally favorable in most series, with a five-year survival rate of more than 80% and a median survival time of more than 10 years [5,7,9,15].

In conclusion, in spite of being a rare pulmonary malignancy, low-grade B-cell PPL must be kept in mind in the differential diagnosis of pulmonary mass lesions on chest X-rays. Presence of air bronchograms is a diagnostic clue on CT scans. Surgical excision of these lesions is useful both for diagnosis and treatment. Concomitant involvement of other mucosal lymphoid sites is common. The prognosis is good with a mean survival time of more than 10 years.

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