Low Grade Primary Pulmonary Lymphoma Presenting as a Lung Abscess: A Case Report

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An 82-year-old man developed an abscess-like mass in the middle lobe of his right lung. It was initially misdiagnosed as a lung abscess and, therefore, mistreated. Repeated sono-guided fine needle biopsies confirmed the presence of low-grade primary pulmonary lymphoma, which was supported by the results from serial examinations. Following 6 courses of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), the patient's symptoms showed substantial improvement. A thoracic CT showed that the tumor had been reduced. Most low-grade primary pulmonary lymphoma manifest through an area of opacification with poorly defined margins and air bronchograms. We present the case of this unusual malignancy that mimicked a lung abscess. This case serves to remind clinicians to include low-grade primary pulmonary lymphoma in their differential diagnoses when suspecting lung abscess and when unable to determine positive results from treatment.
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Key Words: primary pulmonary lymphoma, mucosa-associated lymphoid tissue lymphoma, lung abscess

INTRODUCTION

The most common radiological pattern in primary pulmonary lymphoma is an area of opacification with poorly defined margins and an air bronchogram in roentgenogram or computerized tomography (CT) of the chest. Other

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radiographic patterns in primary lymphoma of the lung include nodules, diffuse bilateral air space consolidation, and segmental or lobar atelectasis[1]. It is rare for a patient to present with an abscess-like appearance in chest-enhanced CT. This reported case presented with clinical symptoms of low-grade fever, productive cough, and mild dyspnea. Initially, the patient received treatment for lung abscess; however, lung consolidation did not decrease in severity after administration of antibiotics. Repeated sono-guided fine needle biopsy confirmed the presence of primary pulmonary mucosa-associated lymphoid tissue lymphoma, supported by results from serial examination. In this report, we present a case with rare radiological presentation of primary pulmonary mucosa-associated lymphoid tissue lymphoma and briefly review previous literature.

CASE REPORT

An 82-year-old nonsmoking man with old pulmonary tuberculosis had received right nephrectomy for renal hemangioma more than 10 years ago. He was free of other systemic diseases. He attended our emergency room because of low-grade fever, productive cough, chest pain, and mild shortness of breath during the previous 2 days. His vital signs were a temperature of 37.8℃, blood pressure of 105/61 mmHg, a respiratory rate of 20 breaths/min, and a pulse rate of 90 beats/min. Auscultation of the chest revealed diminished breathing sound in right anterior wall. His heart sound showed no sign of murmur. No superficial lymph nodes were palpated, and no other abnormalities were identified during physical examination. Chest radiology showed a large opacified lesion in the right middle lobe (Figure 1A). Enhanced thoracic CT scan revealed an abscess-like appearance with an irregular margin and internal necrosis. No pleural effusion was noted (Figure 1B). He refused to undergo bronchoscopy. Ultrasound-guided fine needle aspiration from the cavity wall showed abundant polymorphonuclear leukocytes and no malignant cell in pathology. The patient's blood count included leukocytosis of 12000/mm^3 (4000/mm^3 to 10000/mm^3) with 83.1% neutrophils, 10.7 g/dL hemoglobin (reference 12 g/dL to 16 g/dL) with 88.7 fL MCV (reference 77 fL to 91 fL), and 21.93 mg/dL C-reactive protein (CRP)(reference 0 to 1 mg/dL). Results from the culture of

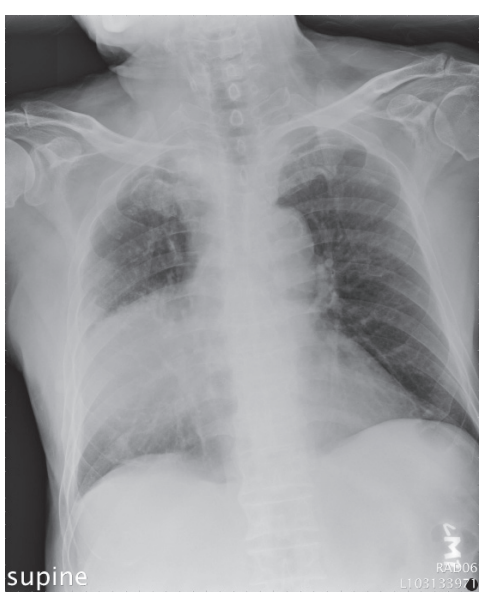

Figure 1A. Chest X-ray showed opacification over right lower lung region.

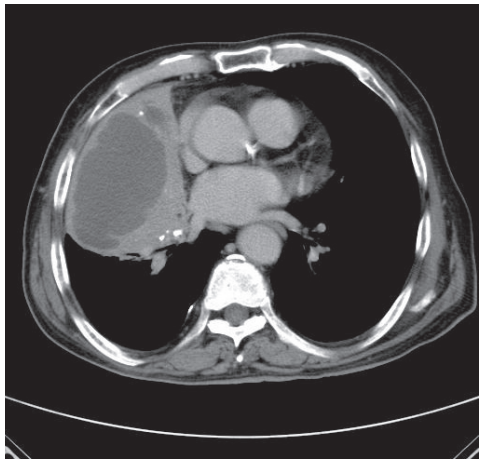

Figure 1B. Enhanced thoraic CT scan revealed consolidative change over right middle lobe region with internal large cystic component and peripheral calcified nodule.

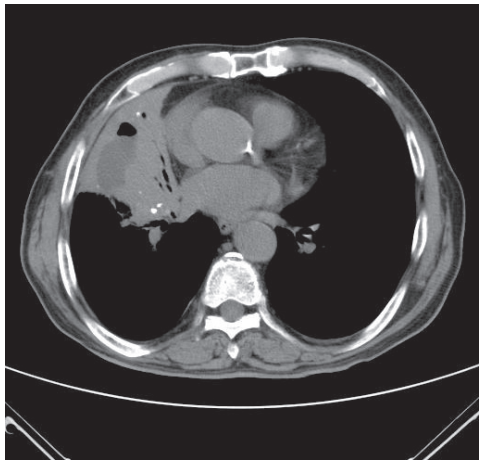

Figure 1C. Enhanced thoraic CT scan after administration of antibiotics revealed persistent consolidative change over right middle lobe region with central cavitation and air-fluid level.Air bronchogram and multiple calcifications over right middle lobe region were also identified.

sputum, and blood, and staining for acid-fast bacilli were all negative. The tumor markers carcinoembryonic antigen (CEA) and squamous cell cancer antigen (SCC) were within reference ranges. The patient's lactate dehydrogenase concentration was 133 U/L, and his HIV serology was negative. Immunoglobulins, antinuclear antibody, antineutrophil cytoplasmic antibody, and rheumatoid factor were all within reference ranges. Because these results were considered more compatible with a lung abscess than a malignant tumor, the patient was empirically treated with a 14-day course of Ceftazidime 2 gm every 8h. He was discharged home on mexifloxacin. An enhanced thoracic CT scan eight weeks later showed the persistent abscess-like lesion (Figure 1C). Because a pulmonary neoplasm was suspected, sonography-guided fine needle biopsy of the pulmonary mass was reperformed, and the pathology showed diffuse and small- to medium-sized atypical lymphocyte infiltration with oval to angulated nuclei, mild nuclear pleomorphism, and moderate amounts of cytoplasm in hematoxylin and eosin (H&E) staining (Figure 2). Immunohistochemical analysis revealed that the atypical lymphocytes were positive for CD20 (Figure 3) and Bcl-2 and negative for CD3, which indicated that the pulmonary lesion was a low-grade B cell lymphoma. Follicular cell lymphoma, small lympholytic lymphoma, and mantle cell lymphoma are less favored because of the lack of immunohistochemical positivity for CD5, CD10, CD23, and cycline D1. Pulmonary mucosa-associated lymphatic tissue lymphoma is first considered due to the histopathological and immunohistochemical findings mentioned above. To exclude

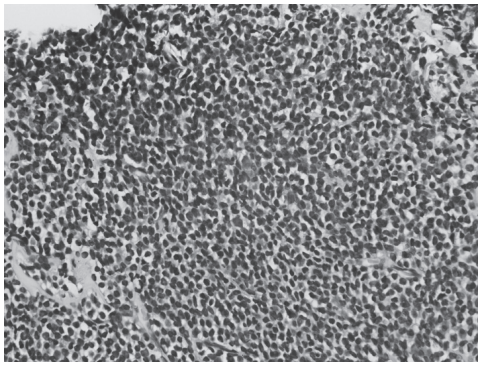

Figure 2. High power view (400X) of the lung lesions from the sonography-guided biopsy showed diffuse and small to medium-sized atypical lymphocytes infiltration with oval to angulated nuclei , mild nuclear pleamorphism ,and moderate amount of cytoplasm (the H&E stain).

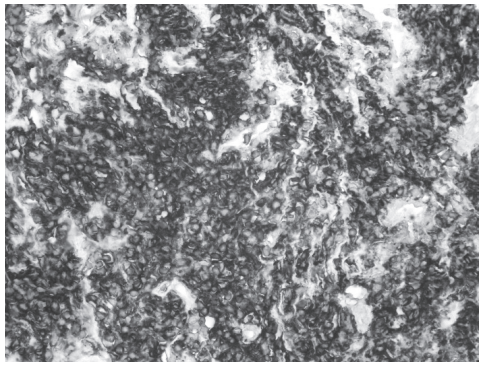

Figure 3. The tumor cells showed immunoreactivity for the B cell marker, CD20 (L26,X400).

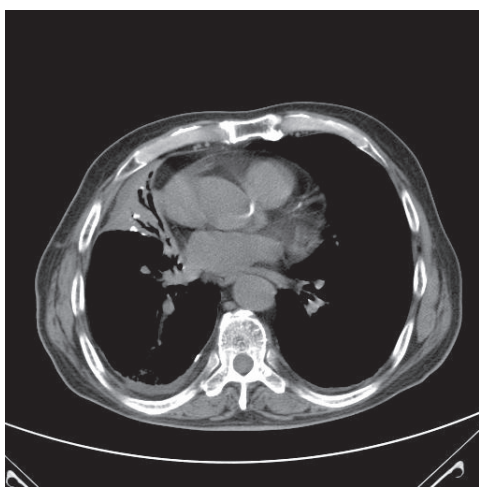

Figure 4. Follow-up axial CT image taken after CHOP-based chemotherapy for six cycles showed significant reduction in the size of the lesion.

extrathoracic disease, a bone marrow biopsy was performed, which showed no neoplastic infiltration. Abdominal CT was normal, except for the absence of the right kidney. The patient was staged IE according to the Ann Arbor staging system.

The patient was treated with a cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)-based chemotherapy regimen for 6 cycles, after which enhanced thoracic CT revealed marked reduction in the lung lesions (Figure 4).

DISCUSSION

Primary pulmonary lymphoma (PPL) is defined as a clonal lymphoid proliferation affecting one or both lungs with no detectable extrapulmonary involvement at diagnosis or during the subsequent 3 months. World Health Organization classifies PPL into B-cell primary pulmonary non-Hodgkin's lymphoma (NHL), and lymphomatoid granulomatosis [3]. B-cell primary pulmonary NHL is subdivided into low-grade B cell primary pulmonary lymphoma, high-grade B cell primary pulmonary lymphoma, primary pulmonary plasmacytoma, and intravascular pulmonary lymphoma types[2]. Primary pulmonary NHL is rare and accounts for only 0.4% of malignant lymphomas

and less than 1% of NHL[4]. Low-grade B cell lymphoma is the most common form of primary pulmonary NHL. Its most common subtype is marginal zone B cell lymphoma of mucosa-associated lymphoid tissue type (MALT lymphoma), which accounts for 58-87% of cases. Most affected patients are 50 to 60 years of age with equal incidence in both sexes. Approximately half of all patients have a history of smoking[2]. Most patients are asymptomatic at onset, especially low-grade types typically identified during routine health examination[5]. Pulmonary symptoms are nonspecific, such as cough, dyspnea, chest pain, and hemoptysis. Less than 25% of patients display systemic symptoms. Fewer (8%) present with both nonspecific and systemic symptoms. Our reported case displayed both types of symptoms.

Previous studies have reported that primary pulmonary lymphoma can manifest radiologically as solitary, multifocal, or bilateral nodules, a parenchymatous consolidation, localized or multiple infiltrates, atelectasis, or pleural effusion. The most common radiological pattern in primary pulmonary lymphoma is an area of opacification with poorly defined margins and an air bronchogram[1,2,4].

The radiological appearance of central necrosis in the consolidation is nonspecific and can be displayed in benign conditions such as abscess, lung infarction, antineutrophil cytoplasmic antibody (c-ANCA)-associated granulomatous vasculitis, and carcinomas. Cordier et al reported that a cavitary mass lesion in primary pulmonary lymphoma occurs in 1 in 70 cases[6]. Bazot et al described that primary pulmonary lymphoma shows cavitation in patients with HIV infection[7]. According to Cartier et al, this pattern of disease is rare in primary pulmonary NHL and more commonly occurs in primary pulmonary Hodgkin's disease[8]. It is unusual for primary pulmonary NHL to present as a necrotic mass. This aggressive type more commonly develops in patients who are immunocompromised. Three case reports showed high-grade primary pulmonary B cell lymphoma should be considered when a radiographic image shows a cavitated or necrotic mass because of its possible aggressive behavior[9-11]. Central ischemic change probably causes necrosis and cavitation in lymphoma. This change might be caused by rapid tumor growth and tends to occur in large nodules and masses. A cavity with air-fluid levels might present when there is communication between an adjacent bronchus and a necrotic mass. However, to our knowledge, MALT lymphoma of the lung, which manifests as a necrotic mass in CT, is rare. Our reported case displayed a mass-like area of consolidation over the right middle lobe with central necrosis in chest CT. The tumor showed a thick wall and irregular inner margin, characteristics that are more frequently displayed by malignant lesions[12]. In low-grade primary pulmonary B cell lymphoma, cavitation and necrosis rarely occur because of indolent disease with minor growth for a prolonged period. In our case, calcification of the

tumor suggested an indolent course. MALT lymphomas characteristically involve the airways and have intraluminal lesions that occasionally create a ball-valve effect and cause distal parenchyma destruction and necrosis[13].

Current treatment options for primary pulmonary lymphoma are surgery, chemotherapy, and radiotherapy. The respective efficacies of these treatment strategies remain under debate. Evynden et al reported no differences in survival among patients treated with surgery or chemotherapy or a combination of both[14]. Troch et al[15] suggested that a "watch-and-wait" policy should be adopted for the initial management of primary pulmonary lymphoma of MALT type without symptoms. Evynden et al further showed that complete resection of a tumor is associated with a 10-year survival of almost 90%[14]. Chemotherapy is suitable for patients presenting with diffuse involvement of one or both lungs and extrapulmonary involvement, relapse, or progression. Patients undergoing chemotherapy with CHOP have similar outcomes to those treated with other regimens, such as an alkylating agent (chlorambucil alone) or the cyclophosphamide, vincristine, and prednisone (CVP) regimen[5]. Our study patient was aged and unwilling to undergo surgery. After 6 courses of CHOP chemotherapy, his symptoms showed marked improvement and, in thoracic CT, the tumor had decreased. The outcome of MALT-type primary pulmonary lymphoma is generally favorable. More than 80% of cases have a 5-year survival rate, and the reported median survival rate is more than 10 years[2].

Because the clinical symptoms of primary pulmonary lymphoma are nonspecific, delayed diagnosis is common. Biopsy is required for early diagnosis. Although investigators have reported the diagnosis of primary pulmonary lymphoma using bronchoalveolar lavage, bronchial biopsy, and transcutaneous biopsy, most cases require thoracoscopic or open lung biopsy[5].The interval between the first clinical or radiological manifestation and diagnosis ranges from 5 months to 8 years[2]. Our patient had a delay in diagnosis because of previous inconclusive biopsy results.

Previous studies have reported relatively few cases of primary pulmonary lymphoma in Taiwan. One prospective study at a single center in Taiwan reported 22 patients with primary pulmonary lymphoma between 1992 and 2005[16]. The histological subtypes and clinical features of the Taiwanese primary pulmonary lymphoma patients were similar to those described in other reports. In chest radiology, lesions most frequently manifested as nodules or mass lesions.

Primary pulmonary lymphoma yields various radiographic findings. In this case report, we describe a patient with a necrotic mass in the right middle lobe that mimicked an anaerobic lung abscess radiographically. When a radiographic image shows a lung abscess following treatment with antibiotics, it tends to persist and might increase in size. Therefore, the possibility of low grade

primary pulmonary lymphoma must be considered in differential diagnosis.

REFERENCE

1.Lee KS, Kim Y, Primack SL: Imaging of pulmonary lymphomas. Am J Roentgenol 1997; 168: 339-45.
2.Cadranel J, Wislez M, Antoine M: Primary pulmonary lymphoma. Eur Respir J 2002; 20: 750-62.
3.Harris NL, Jaffe ES, Diebold J, et al: Lymphoma classification-from controversy to consensus: the R.E.A.L. and WHO Classification of lymphoid neoplasms. Ann Oncol 2000; 11: 3-10.
4.Kim JH, Lee SH, Park J, et al: Primary pulmonary non-Hodgkin's lymphoma. Jpn J Clin Oncol 2004; 34: 510-4.
5.Wannesson L, Cavalli F, Zucca E: Primary pulmonary lymphoma: current status. Clin Lymphoma Myeloma 2005; 6: 220-7.
6.Cordier JF, Chailleux E, Lauque D, et al: Primary pulmonary lymphomas. A clinical study of 70 cases in nonimmunocompromised patients. Chest 1993; 103: 201-8.
7.Bazot M, Cadranel J, Benayoun S, Tassart M, Bigot JM, Carette MF: Primary pulmonary AIDS-related lymphoma: radiographic and CT findings. Chest 1999; 116: 1282-6.
8.Cartier Y, Johkoh T, Honda O, M?ller NL: Primary pulmonary Hodgkin's disease: CT findings in three patients. Clin Radiol 1999; 54: 182-4.
9.Martínez Rivera C, Bonnin Vilaplana M, Simón Adiego C, Palacín Forgué A, Puig Zuza J, Sampablo Lauro I: Primary pulmonary lymphoma presenting as a pulmonary mass with cavitation. Arch Bronconeumol 2004; 40: 94-6.
10.Brown S, Horton J, Rosario D, Dorsey DA, Hetz S, King CS: High-grade primary pulmonary B cell lymphoma presenting as a necrotic mass. Respir Care 2011; 56: 871-3.
11.Tao H, Nakata M, Saeki H, Kurita A, Takashima S: Unsuspected primary pulmonary malignant lymphoma. Jpn J Thorac Cardiovasc Surg 2002; 50: 533-6.
12.Honda O, Tsubamoto M, Inoue A, et al: Pulmonary cavitary nodules on computed tomography: differentiation of malignancy and benignancy. J Comput Assist Tomogr 2007; 31: 943-9.
13.Ansari S, Dubaybo H, Levi E, Dubaybo BA: Development of Bullous Disease during Treatment of Pulmonary Marginal Zone B-Cell Lymphoma. Case Rep Pulmonol 2012; 2012, Article ID 146081, 5 pages, 2012. doi:10.1155/2012/146081
14.Vanden Eynden F, Fadel E, de Perrot M, de Montpreville V, Mussot S, Dartevelle P: Role of surgery in the treatment of primary pulmonary B-cell lymphoma. Ann Thorac Surg 2007; 83: 236-40.
15.Troch M, Streubel B, Petkov V, Turetschek K, Chott A, Raderer M: Does MALT lymphoma of the lung require immediate treatment? An analysis of 11 untreated cases with long-term follow-up. Anticancer Res 2007; 27: 3633-7.
16.Hu YH, Hsiao LT, Yang CF, et al: Prognostic factors of Chinese patients with primary pulmonary non-Hodgkin's lymphoma: the single-institute experience in Taiwan. Ann Hematol 2009; 88: 839-46.

[病例報告]

以肺膿瘍表現之原發性低度惡性肺部淋巴瘤

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一位 82 歲男性於右肺中葉罹患疑似膿瘍的腫塊。此病灶一開始被誤診為肺膿瘍，因而沒有進行正確治療。超音波指引細針取樣確認為低度惡性肺部淋巴瘤的診斷，經過一系列檢查後支持這是個原發性病灶。接受六個療程的癌德星、阿黴素、長春新鹼、及強體松(CHOP) 化療後，患者的症狀明顯改善。胸腔電腦斷層掃描也顯示腫瘤已經縮小。低度惡性原發性肺部淋巴瘤為罕見的惡性腫瘤，大多數的影像學特徵為邊緣不清的混濁區域及空氣支氣管徵象。我們提出案例的表現卻與肺膿瘍的病徵極相似。此個案可以提醒醫師在疑似肺膿瘍的診斷中，若治療無成效時，應考慮病灶為低度惡性原發性肺部淋巴瘤的可能性。

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