A Case of Baltoma Diagnosed by Transthoracic True-Cut Needle Biopsy

Fisun Karadağ, MD[1]; Mehmet Polatlı, MD[1]; Füruzan Kaçar, MD[2]; Orhan Çildağ, MD[1]

[1]Department of Chest Diseases, School of Medicine, Adnan Menderes University, Aydın, Turkey
[2]Department of Pathology, School of Medicine, Adnan Menderes University, Aydın, Turkey

Abstract

We describe a 73-year-old patient with symptoms of chest pain, hemoptysis, malaise and weight loss for two years. Airspace consolidations with air bronchograms in right middle and both lower lobes were observed radiologically. For fiberoptic bronchoscopy was non-diagnostic, transthoracic true-cut needle biopsy was performed under CT guidence. Histological examination of lung biopsy revealed replacement of normal lung parenchyma with diffuse infiltration of monotonous cells with scanty cytoplasma and little nuclear irregularity. In immunohistochemical examination it was detected that the LCA and B cell markers of the cells were stained positive for CD20 and CD79; whereas epithelial markers were stained negative for cytokeratin and EMA, and T cell markers were stained negative for CD3. The histopathological features were reported to be compatible with primary pulmonary BALT (bronchus-associated lymphoid tissue) lymphoma or baltoma.

We recommend that baltoma should be included in differential diagnosis of patients with slow-progressing pulmonary symptoms and airspace consolidation. Transthoracic true-cut needle biopsy under CT guidence might provide sufficient tissue in peripheral lung lesions for immunologic studies.

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Introduction

B-cell lymphoma of bronchus-associated lymphoid tissue (BALT) or baltoma may be defined as low-grade non-Hodgkin's lymphoma presenting in the lung either unilaterally or bilaterally and showing no evidence of involvement of other sites (other than hilar lymph nodes) at the time of presentation or in the following 3-month period. Such lymphomas represent less than 0.5 percent of all primary lung tumors (1).

The precise pathogenesis of primary pulmonary lymphomas is unknown. BALT is a normal constitutive feature of the lung's immune system in a range of different animal species (2). BALT has been referred to as a normal component of human lung in several immunological and pathological texts (2,3) but recent studies have questioned whether it is in fact a constitutive feature of human lung, suggesting that it may develop only after antigenic stimulation (4,5).

Corresponding Author: *Yard. Doç. Dr. Fisun Karadağ*
Adnan Menderes Üniversitesi, Tıp Fakültesi
Göğüs Hastalıkları AD, 09010 Aydın, Türkiye
Phone : +90 (256) 212 00 20/150
Fax : +90 (256) 214 64 95
E-mail : fisunkaradag@yahoo.com

Lymphoid proliferations of the lung represent a rare and vexing collection of lesions, including primary pulmonary lesions, spanning the gamut from reactive hyperplasia to high-grade malignant lymphoma. Pulmonary lesions with histologic characteristics such as infiltrate of mature lymphocytes and true germinal centers without lymph node involvement had been diagnosed as pseudolymphomas (6). However, recent advances in the production of monoclonal antibodies and in molecular biology have allowed specific and precise analyses of lymphoproliferative disorders of the lung, most of which have been classified as benign because of their indolent clinical course (7). Reclassification of many of these entities by immunohistochemical and molecular techniques and use of the Revised European-American Lymphoma (REAL) classification has contributed to pathologists' and clinicans' confusion (8). Previously described pseudolymphoma was shown to be a heterogenous disease group, including nodular lymphoid hyperplasia and low-grade ß-cell lymphoma arising from the bronchus-associated lymphoid tissue (8).

Baltomas are thought to arise in either mucosa-associated lung tissue or interbronchial nodes or lymphatic channels. This indolent form of lymphoma is often multicentric or diffuse and the monoclonal cells are most often small B lymphocytes. Lymphoid proliferation may present as isolated masses, peribronchial proliferation or interstitial infiltration (9).

Open lung biopsy is usually suggested for definite differential diagnosis of pulmonary lymphoproliferative disorders if transbronchial biopsy and transthoracic fine-needle aspiration biopsy could not provide sufficient tissue for immunologic studies (1,10).

We present a case of baltoma diagnosed by transthoracic true-cut needle biopsy along with review of literature aiming to contribute to diagnostic approach of practising pulmonologists.

Case Report

A 73-year-old female was admitted to our institution in February 2002, with a 2-year history of bilateral chest pain, hemoptysis, malaise and weight loss. She had never smoked. She had been treated for arrythmia and glaucoma. She had been investigated in a hospital 2 years ago for left hilar, right perihilar densities and right lower lobe consolidation (Figure 1a), but diagnostic tests including fiberoptic bronchoscopy had been non-diagnostic. Open lung biopsy had been suggested for definite diagnosis, but se had refused.

Pathological findings on physical examination were decreased chest expansion and dullness to percussion with decreased breath sounds over both hemithorax inferiorly. Bibasilar end-inspiratory crackles were also present. Cardiac sounds were arrythmic. There was no palpable peripheral lymphadenopathy (LAP).

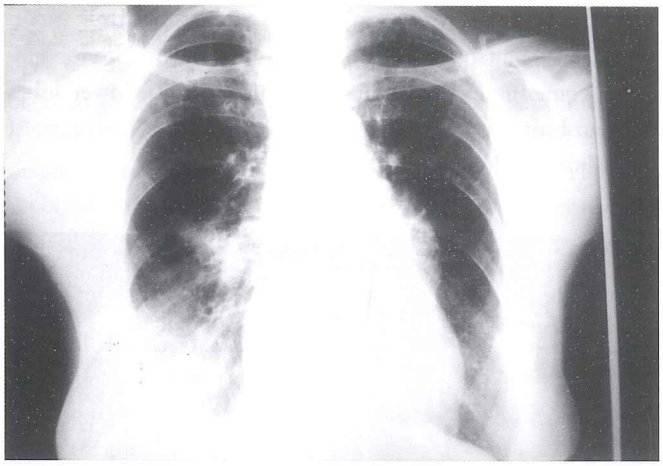

Figure 1a. *Previous chest x-ray (August, 2000) showing left hilar, right perihilar densities and right lower lobe consolidation.*

Laboratory studies included the following: Hemoglobin 12.8 mg/dl, WBC 10.800/mm^3 (PNL 52.7%, lymphocyte 35.2%, monocyte 9.6%, eosinophil 1.6%). Erythrocyte sedimentation rate was 74 mm/h. Biochemical tests were normal except elevated serum globulin (4.2 g/dl). Serum C-reactive protein was high whereas rheumatoid factor was negative. No bacteria, fungus or acid-fast bacilli were detected in sputum examination and cultures. Cytological examination of sputum showed inflammatory reaction rich in neutrophils and lymphocytes. Tuberculin skin test was 8 mm positive (with BCG vaccination). Atrial fibrillation was observed in ECG. Spirometry yielded restrictive pattern with FVC (forced vital capasity) 33%, FEV_1 (forced expiratory volume in one second) 32% and FEV_1/FVC 79%.

There was significant progression in radiologic findings meanwhile. Chest radiography on admission to hospital revealed left hilar density and bilateral lower lobe consolidations (more prominent on right side) not obscuring contours of heart (Figure 1b).

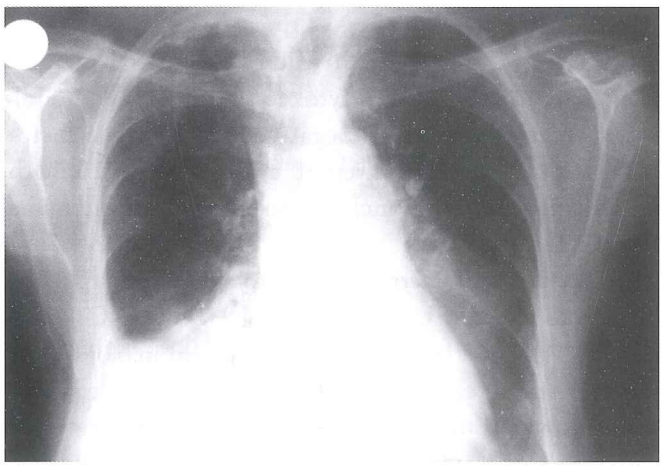

Figure 1b. *Chest x-ray on admission (February, 2002) showing left hilar density and bilateral lower lobe consolidations.*

Thorax computed tomography (CT) yielded multiple mediastinal LAP, airspace consolidations in right middle lobe lateral segment next to the chest wall and both lower lobes with air bronchograms and minimal pleural effusion on right hemithorax (Figure 1c).

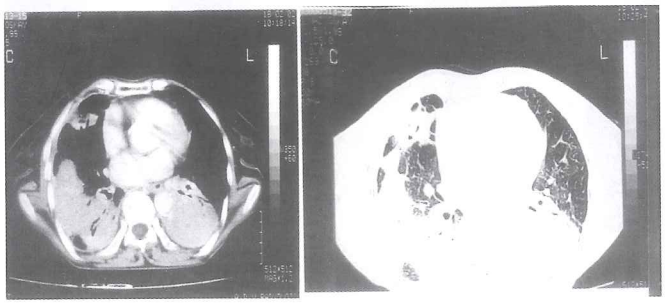

Figure 1c. *Thorax computed tomography (CT) shows airspace consolidation in right middle lobe lateral segment next to the chest wall and both lower lobes with air bronchograms.*

In fiberoptic bronchoscopy bronchial mucosa of lower lobes was hyperemic and edematous but no endobronchial lesion was observed. Histopathological examination of bronchial aspiration and mucosal biopsy was reported to be non-diagnostic. For the lesions were peripherally located adjacent to the chest wall, a CT-guided transthoracic biopsy was performed from right lower lobe with a true-cut needle instead of a fine-needle, in order to obtain a tissue sample for immunohistochemical studies; and no complication developed.

Histological and immunohistochemical findings: Histological examination of lung biopsy revealed replacement of normal lung parenchyma with diffuse infiltration of monotonous cells with scanty cytoplasma and irregular nuclei. Neoplastic cells have relatively round nuclei with inconspicuous irregularities (centrocyte-like cells). In immunohistochemical examination it was detected that the LCA and B cell markers of the cells were stained positive for CD20 and CD79; whereas epithelial markers were stained negative for cytokeratin and EMA, and T cell markers were stained negative for CD3. The histopatholoical features were reported to be compatible with B-cell lymphoma of bronchus-associated lymphoid tissue (Figure 2a-b).

The patient was transferred to Hematology Clinic for staging and chemotherapy. Upper abdominal USG and CT were normal. There was bone marrow involvement in biopsy. She received four cycles of CMOP (cyclophosphamide, mitoxantrone, vincristin, prednisolone) chemotherapy protocole with diagnosis of stage IV baltoma and significant radiologic and clinical response was achieved (Figure 3a-b).

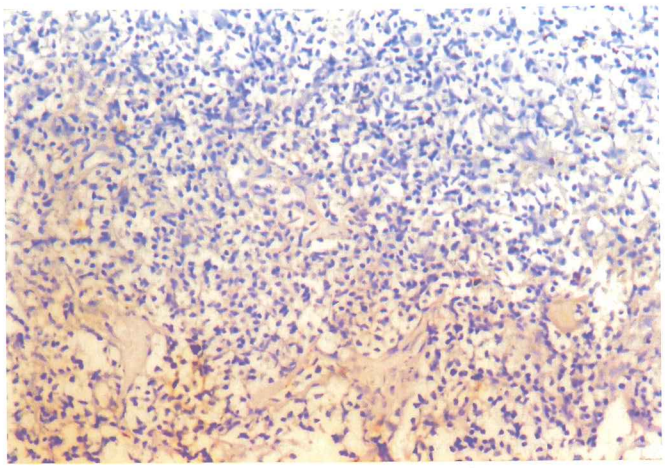

Figure 2a. *Photomicrograph of transthoracic needle aspiration biopsy showing lymphoma infiltrate in the lung parenchyma. Some of the neoplastic cells are centrocyte-like cells, and some are presenting plasmacytoid differentiation (H&Ex200).*

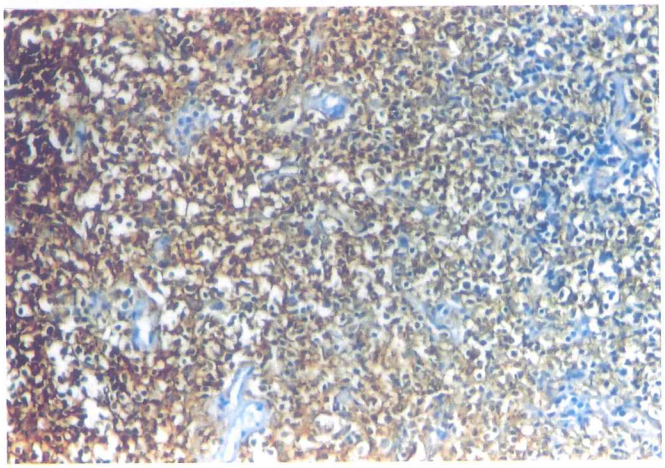

Figure 2b. *Neoplastic cells are showing CD79 positivity (CD79x200).*

Discussion

B-cell lymphoma of bronchus-associated lymphoid tissue, also called baltoma is a spesific type of low-grade lymphoma which mainly develops outside of lymph nodes (3). These tumors are rare and are often recognized on routine chest radiographs of middle-aged patients since they produce minimal symptoms (11). Patients may have cough, chest pain, hemoptysis, dyspnea. Systemic symptoms of lymphoma such as fever, night sweats and weight loss may be present (11,12). The presented patient had both pulmonary and systemic symptoms; she had applied for medical help with bilateral chest pain, hemoptysis, malaise and weight loss. She had become symptomatic two years ago, but fiberoptic bronchoscopy was non-diagnostic and she had refused open lung biopsy.

The radiographic characteristics of pseudolymphomas, in which baltomas are included, have been reported in the radiologic literature. Chest radiographic appearance is non-diagnostic: diffuse infiltrates, reticulonodular infiltrates, small

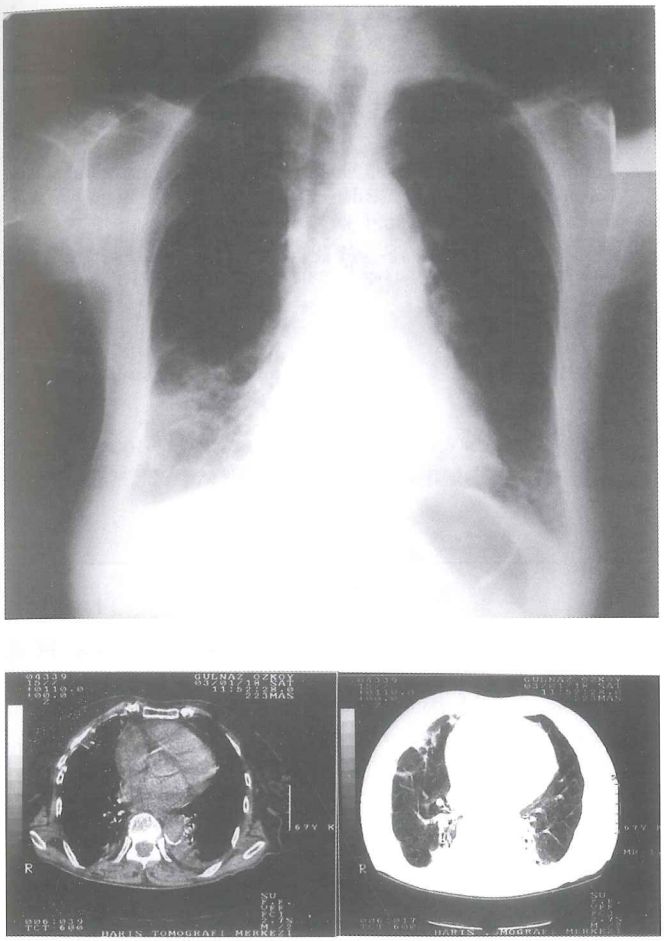

Figure 3a-b. *Chest x-ray and thorax CT after chemotherapy. Significant regression is observed in lesions.*

and large nodules and effusions may be seen (11,13). The most common CT appearance of baltoma is consolidation with air bronchograms (14,15). Lee at al (6) described CT findings of 10 patients (age range 43-73 years). Seven presented with abnormal chest radiograph in routine examination without any pulmonary symptoms. Symptoms in the remaining patients were cough, dyspnea, fever and sputum. None of them had any underlying diseases. CT scans demonstrated 60% airspace consolidation, 60% single or multiple nodules, 70% focal areas of ground-glass attenuation adjacent to consolidation or nodules with irregular margin and 30% mediastinal lymphadenopathy. There was no definite regional predominance in the distribution of disease. Air bronchogram inside the lesions was found in 90% of cases. Bilateral airspace consolidations with air bronchograms were detected in radiologic tests of the presented case, concordant with previous case reports.

Open lung biopsy is not inevitable in diagnosis of pulmonary lymphomas. Diagnosis is both practically feasable and reproducable by transbronchial biopsy or transthoracic needle aspiration biopsy as well (16). Wong et al (13) evaluated the yield and safety of transthoracic fine needle aspiration in focal lung lesions of hematologic malignancy. The underlying malignancy was lymphoma in 42 patients (63%) and the yield of needle biopsy was 68%. Complications of pneumothorax and bleeding occured in 25% of all biopsies. They concluded that transthoracic fine-needle aspiration biopsy should be considered a useful diagnostic tool. Kuruvilla et al (17) and Sprague et al (18) also reported cases of primary pulmonary lymphoma diagnosed by transthoracic fine-needle aspiration biopsy. Indeed true-cut needle might provide bigger tissue sample than fine needles, sufficient for differential diagnosis and immunologic studies in peripheral lesions adjacent to chest wall. Our patient had refused open lung biopsy before, but we could achieve definite diagnosis by transthoracic true-cut needle biopsy under CT guidance.

Microscopically baltomas have the features common to MALT (mucosa-associated lymphoid tissue) lymphomas in general but adapted to their bronchopulmonary location. The infiltrate is basicly interstitial. The neoplastic cells have a variable morphology that corresponds to the variants of the centrocyte-like cells. They are small with irregular indented nuclei although the irregularity may vary from slight to marked and cytoplasm is variable in amount. Variable numbers of blastic cells may be present and plasma cell differentiation is often a feature. If lymphoepithelial lesion exists, diagnosis is easier. Immunocytochemistry is important in establishing the B lineage of the lymphoma cells (1,10). The presented case has typical histopathologic findings of baltoma.

We recommend that baltoma should be included in differential diagnosis of patients with slow-progressing pulmonary symptoms and airspace consolidation. Transthoracic true-cut needle biopsy under CT guidance might provide sufficient tissue sample in peripheral lung lesions for immunologic studies.

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