Elevated Serum CA19-9 Level and Regional Lymphadenopathy in a Young Man with Allergic Bronchopulmonary Aspergillosis

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A 21-year-old man with bronchial asthma who suffered from productive cough; his chest X-rays and computed tomographic (CT) scans revealed central atelectasis and pulmonary infiltrates with paratracheal and hilar lymphadenopathy. The serum CA19-9 level was elevated. He was suspected to have malignant neoplasms on admission, but he was diagnosed with allergic bronchopulmonary aspergillosis (ABPA) by Rosenberg’s criteria. After steroid therapy, his symptoms and radiographic findings improved and the serum CA19-9 level decreased. ABPA should be considered in the differential diagnosis of asthmatic patients with or without lymphadenopathy and an elevated serum CA19-9 level.

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Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity reaction to the fungus Aspergillus that was first described by Hinson et al in 1952 (1). It has been recognized more frequently in recent years with the diagnosis based on a combination of clinical, immunologic and radiologic criteria (2). The generally recognized features of ABPA include bronchial obstruction (asthma), peripheral blood eosinophilia, elevated serum immunoglobulin E (IgE) concentration, immediate skin reactivity to Aspergillus antigen, precipitating antibodies against Aspergillus antigen, transient or fixed pulmonary infiltrates and central bronchiectasis. In spite of these features, the diagnosis of ABPA is sometimes difficult, because of the various stages and severity of the disease. We encountered a case of ABPA presenting with mediastinal and hilar lymphadenopathy and elevated serum CA19-9 level.

Case Report

A 21-year-old nonsmoking man with bronchial asthma was admitted to our hospital because of productive cough with pulmonary infiltrates. There was a history of mild asthma since childhood, which was treated on an outpatient level without steroid therapy and good condition for the past a year. The patient was well until a month before admission, when he experienced the onset of an increase in productive cough. At that time, abnormal shadows on a routine chest X-ray were noted. The patient was admitted to our hospital because his symptoms did not improve. There was no history of fever, chill, stridor, dyspnea, chest pain, sweats, hemoptysis, body weight loss, exposure to industrial dusts or animals or a risk for human immunodeficiency virus infection. His temperature was 36.5°C; pulse was 80/min. Blood pressure was 140/80 mmHg. On physical examination, the patient appeared well. No surface lymphadenopathy was found. The chest, abdomen and extremities were normal and neurologic examination was negative. The results of laboratory tests were as follows: erythrocyte sedimentation rate (ESR) was 45 mm/h, hematocrit value was 40% and white blood cell count was 9,100/jul with eosinophils, 16.2%. C-reactive protein was 1.4 mg/dl. Serum angiotensin-converting enzyme and serum chemistry values were normal. Serum carcinoembryonic antigen and neuron-specific enolase concentrations were within normal limits, but CA19-9 level was elevated to 160 U/ml (normal, 0 to 37 U/ml). Pulmonary function tests revealed a moderate mixed obstructive and restrictive pattern: a forced vital capacity of 2.19 l (55.4% of predicted), a forced expiratory volume in one second of 1.10 l (50.2% of predicted). An electrocardiogram was normal. A chest X-ray film on admission showed atelectasis of right upper lobe, a round opacity at the left hilum and infiltrations in the left upper lobe (Fig. 1). In addition, chest postcontrast computed
tomographic (CT) scans revealed central bronchiectasis and paratracheal and hilar lymphadenopathy (Fig. 2). Gallium scintigrams revealed abnormal uptake in the right mediastinum and the left hilum. Initial antibiotic treatment (FMOX, flomoxef sodium) proved ineffective. Suspicion of pulmonary tuberculosis, lymphoma, lung cancer or other neoplastic diseases prompted further evaluation. Bronchoscopic examination revealed non-specific inflamed mucosa, which narrowed the lobar and segmental bronchi of the bilateral upper lobe and the obstruction of right B2 due to persistent mucoid plugging. Brushing samples at obstructive bronchus were negative on culture including acid-fast bacilli and fungus. Pathological examination of bronchial biopsy specimens showed granulation tissue and infiltration of mononuclear cells and eosinophils, but no malignant features. Abdominal CT scans showed no particular lesions. At this point, the features of this case fitted the spectrum of allergic bronchopulmonary fungal disease, prompting serologic tests for Aspergillus antibodies. The serologic profiles showed a total serum IgE level of 2,700 U/ml (normal, 0 to 250 U/ml), positive IgE Aspergillus-specific antibody and positive Aspergillus fumigatus–precipitating antibody by gel diffusion. The patient was diagnosed with ABPA according to Rosenberg’s criteria. With the treatment of 20 mg of prednisolone (0.5 mg/kg) for 10 days, his symptoms improved rapidly with resolution of the atelectasis, infiltrates and lymphadenopathy, but the bronchiectasis remained. In addition, the serum eosinophilia disappeared and the serum IgE and CA19-9 level decreased to within normal limits. IgE Aspergillus-specific antibody declined to negative but Aspergillus fumigatus – precipitating antibody remained positive.

Prednisolone was gradually reduced and ceased after 4 weeks and he has remained well for 3 years.

**Discussion**

ABPA is a serious respiratory disease that causes severe fibrosis of the lungs unless it is detected early and treated aggressively with corticosteroids (3). The prevalence of ABPA is uncertain, but it has been reported in 6 to 20% of patients with asthma (4). ABPA is equally distributed between male and female asthma patients and is generally diagnosed in the late teens or twenties (5). Most patients have combined symptoms of cough, sometimes productive of brown plugs, fever, dyspnea, malaise, chest pain, sweating and occasionally hemoptysis. The radiographic findings vary widely and may be normal or may include combined shadows of migratory or fixed infiltrates,
atelectasis, hyperinfiltration and evidence of central bronchiectasis and pulmonary fibrosis, often with honeycombing. Rarely, cavernous destruction of the lung has been reported (6). Although any pulmonary lobe may be involved, there is an upper-lobe predominance.

Recent refinements in serologic techniques (2) have simplified confirmation of this diagnosis. But the symptoms and radiographic findings of ABPA are so various that its diagnosis is sometimes difficult, unless specific serologic tests to determine ABPA are performed. Indeed, in this case we first suspected pulmonary tuberculosis and malignant neoplasms, because of atelectasis, lymphadenopathy and the elevated serum CA19-9 level.

In varied radiographic abnormalities, “pseudo-hilar adenopathy”, which is widening of the hilum in a pattern closely resembling hilar lymphadenopathy, has been described in ABPA (7). This simulation of adenopathy results from deposition of mucus in centrally dilated bronchi. In our case, however, postcontrast CT scans suggested true lymphadenopathy. Although uncommon, true hilar lymphadenopathy has been reported (5, 8, 9). The pathological diagnosis of lymphadenopathy was not performed in this case, but we suspected it was caused by reactive hyperplasia of the lymph node. Indeed, this lymphadenopathy was diminished after steroid therapy.

CA19-9 (sialyl Lewis), a tumor-associated carbohydrate antigen, is known to be a useful marker for gastrointestinal malignancies, particularly pancreatic adenocarcinoma (10, 11). Some reports also show evidence of an elevated serum CA19-9 level in lung cancer (12, 13). However, this carbohydrate antigen is also elevated in serum obtained from patients with nonmalignant lung diseases such as idiopathic pulmonary fibrosis (IPF), bronchiectasis, diffuse panbronchiolitis (DPB) (14) and cystic fibrosis (15). Immunohistochemical studies have revealed expression of CA19-9 on the following hypertrophic cells: bronchial glands in bronchiectasis and DPB, bronchiolar epithelial cells, which cover the surface of fibrosing alveolar septa and remodeling septal structures in IPF (14). In this case, immunohistochemical study showed no expression of CA19-9 in bronchial biopsy specimens, but the CA19-9 level recovered to normal range after steroid therapy. This indicates that the high serum concentration of CA19-9 was probably due to hypersecretion of mucus glycoprotein, secreted from hypertrophic glands or/and epithelial cells in the bronchioles. The extravasation into the circulatory system was caused by pathogenic change accompanying chronic inflammation.

The clinical features of ABPA vary with the stage and severity of the disease and may not all appear simultaneously. However, to our knowledge, this is the first report of ABPA with paratracheal and hilar lymphadenopathy and an elevated serum CA19-9 level. The patients with ABPA can continue to have clinically nonspecific features that are capable of progressing insidiously, causing severe lung damage. Thus, early detection and initiation of treatment greatly improves the prognosis. Finally, ABPA should be considered in the differential diagnosis of asthmatic patients with or without hilar and mediastinal lymphadenopathy and an elevated serum CA19-9 level.

References