Recurrence of Inflammatory Pseudotumor of the Lung after Eleven Years of Remission

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Abstract

The standard treatment of inflammatory pseudotumor of the lung is surgical excision. However, little data is available on steroid therapy in patients with the unresectable disease. Here, we report a patient with recurrent inflammatory pseudotumor of the lung with pleural involvement who had been successfully treated with corticosteroid eleven years previously. Like the previous treatment, retreatment with corticosteroid proved to be effective for the recurred lesion. In addition, the patient had developed extramammary Paget’s disease and bladder cancer after the initial onset of inflammatory pseudotumor. Steroid therapy could be an optional modality in treating unresectable inflammatory pseudotumor, although long-term follow-up is definitely necessary.

Key words: inflammatory myofibroblastic tumor, plasma cell granuloma, recurrence, steroid therapy


Introduction

Inflammatory pseudotumor of the lung is a rare disease that most often affects children and young adults (1). It consists of a spectrum of fibroblastic or myofibrotic proliferations with a varying infiltrate of inflammatory cells, including plasma cells, lymphocytes, and histiocytes. Multiple synonyms, such as plasma cell granuloma or inflammatory myofibroblastic tumor, have been utilized. In this context, inflammatory pseudotumor is very likely composed of multiple distinct entities with differing etiology, ranging from reactive proliferation to low-grade neoplasm (2).

The natural history of inflammatory pseudotumor of the lung is extremely diverse. The lesions are usually solitary and well-circumscribed masses. Most of the lesions remain stable in size or grow slowly, but some of them invade local mediastinal structures or the chest wall (3-6). The disease can relapse, be multifocal and give distant metastases (6).

The standard procedure, for both diagnosis and treatment, is surgical excision (3-6). The prognosis of patients who underwent complete surgical resection has been reported to be excellent (5, 6). However, surgery is not indicated in some of the cases because of various medical reasons, and there have been a few reports in English regarding steroid therapy in patients with unresectable lesions (7-10). In addition, little is known about the long-term results from steroid therapy. Here, we report a recurrent case of inflammatory pseudotumor of the lung eleven years after successful steroid therapy, who also developed extramammary Paget’s disease and bladder cancer after the initial onset of inflammatory pseudotumor.

Case Report

A 76-year-old man was admitted to Toranomon Hospital in November 2006 because of a back pain and a new pulmonary lesion on chest radiograph. He had been well until December 1992, when a right back pain and a low-grade fever developed. Chest radiograph, obtained by another hospital, showed a mass and extensive pleural thickening in the right lung, and he was referred to our hospital in January
1993. He had a history of pulmonary tuberculosis at the age of 16 years, which was treated by artificial pneumothorax. He had smoked 40 cigarettes a day for 40 years. The complete blood count was normal. The erythrocyte sedimentation rate was 21 mm per hour (reference range, <10), and the C-reactive protein level was 2.1 mg/dL (reference range, <0.3). Immunological tests showed elevated serum immunoglobulin G (IgG) level of 2,419 mg/dL (reference range, 870-1,700), but serum IgM and IgA levels were normal. CT scan of the chest revealed a mass with irregular margin measuring 4×4 cm in diameter in the right lower lobe that was contiguous to a marked pleural thickening with calcification (Fig. 1A). Interlobular septal thickening was also seen. Both the mass and pleural thickening were heterogeneously enhanced by contrast material. Gallium scintigraphy demonstrated intensive accumulation of the isotope in the right lower lung field and increased uptake in the whole right lung field. Since transbronchial lung biopsy and CT-guided needle biopsy were not diagnostic, an exploratory thoracotomy was performed. Histological examination of the excised specimen showed an inflammatory fibrosing process composed of lymphoplasmacytic infiltrates and intra-alveolar organization beneath the fibrous pleural thickening (Fig. 2A). Immunohistochemically, plasma cells were positive for both kappa and lambda light chains. IgG-4 positive plasma cells were sparsely infiltrated in the lesion (Fig. 2C). Staining for the anaplastic lymphoma kinase (ALK1) was negative. A polymerase chain reaction using formalin-fixed paraffin embedded specimens showed no rearrangement of the immunoglobulin heavy chain gene, indicating a polyclonal nature. A pathological diagnosis of inflammatory pseudotumor was made.

Because complete resection was difficult and a rapid growth of the tumor had been observed for three months, a high dose of steroid therapy was chosen to treat the patient. In March 1993, intravenous methylprednisolone 500 mg per day was administered for three consecutive days, followed by oral prednisolone 60 mg daily. After the steroid therapy, the symptoms disappeared and a marked shrinkage of the mass and pleural thickening was achieved (Fig. 1B). Serum levels of the erythrocyte sedimentation rate, C-reactive protein, and IgG recovered to normal. Prednisolone was gradually tapered, but re-growth of the tumor developed at 10 mg of prednisolone every other day in December 1993. The dosage of prednisolone was increased to 20 mg daily, and radiographic improvement was obtained again. In March 1994, oral cyclophosphamide 50 mg daily was added to reduce prednisolone. Finally, prednisolone was stopped in No-
November 1995, and subsequently cyclophosphamide was discontinued in March 1996. After treatment, CT scans of the chest, taken annually, showed no significant changes.

In 2001, erythematous keratotic papula developed on the skin of the lower abdomen and gradually worsened with accompanying hemorrhage. In December 2003, the skin lesion was surgically resected and a diagnosis of extramammary Paget’s disease was made.

In October 2006, the patient noticed right chest pain. Chest radiograph showed a new shadow in the right lung, and he was admitted to our hospital. The erythrocyte sedimentation rate was 12 mm per hour and C-reactive protein level was 0.3 mg/dL. Serum IgG and IgG4 levels were 1,299 and 56 mg/dL (reference range: 4.8-105), respectively. Chest CT scan revealed a new consolidation measuring 3×3 cm in diameter in the right middle lobe adjacent to the pleura (Fig. 1C). Gallium scintigraphy was not examined. A video-assisted thoracoscopic biopsy was performed. Pathological evaluation showed prominent plasma cell infiltration with intra-alveolar organization (Fig. 2B). Some of the plasma cells were IgG4-positive (Fig. 2D). ALK1 staining was negative. These findings were identical to those obtained at the initial thoracotomy in 1993. A thick-walled cavity developed after surgery. The patient was treated daily with 30 mg of oral prednisolone, and the cavity changed into a thin-walled cystic lesion (Fig. 1D). Prednisolone was discontinued in September 2007, and no recurrence has been observed to date.

In December 2008, macroscopic hematuria occurred. A bladder mass was found by cystoscopy, and the patient was diagnosed as having bladder cancer. After removing the tumor by transurethral resection, he is being observed without treatment.

Discussion

Inflammatory pseudotumor may arise at any anatomical site, and is considered to be composed of a variety of etiological entities ranging from inflammation to neoplasm (2). Some researchers regard it as a true neoplasm because of the tendency for local recurrence and the presence of ALK gene rearrangement on chromosome 2p23 in a subset of inflammatory myofibroblastic tumors (11). The ALK gene encodes for a receptor tyrosine kinase, and ALK gene rearrangements were first documented in anaplastic large cell lymphoma (12). The ALK abnormality generally leads to ALK protein overexpression and is detectable by immunohistochemistry. Although our patient had recurrence, immunohistochemistry for ALK protein was negative.

In contrast, other investigators believe that inflammatory
Inflammatory pseudotumor is an immunologic response to an infectious or non-infectious insult (13). A history of antecedent infection was present in approximately one-third of the reported cases (14). Recently, immunohistochemical studies have suggested that IgG4-related immunopathologic process is likely involved in the pathogenesis of inflammatory pseudotumor (15). The association of IgG4 dysregulation and inflammatory pseudotumor was first reported in sclerosing pancreatitis (16). IgG4 is the least abundant of the IgG subclasses, accounting for less than 6% of the total IgG fraction in the serum of a healthy subject (17). Serum IgG4 is elevated in the limited number of conditions such as atopic dermatitis and pemphigus vulgaris (18, 19).

The present patient had a past history of pulmonary tuberculosis, and laboratory data showed the presence of an inflammatory condition. Furthermore, immunohistochemical staining revealed mild infiltration of IgG4-positive plasma cells in the lesion. These findings and favorable responsiveness to oral corticosteroid suggest an inflammatory/reactive pathogenic process in the present case.

Inflammatory pseudotumor of the lung is often asymptomatic (3, 4). Symptomatic patients may complain of cough, dyspnea, chest pain, and hemoptysis, depending upon the lesion location. The present patient suffered from chest pain at the initial and recurrent time due to the pleural involvement.

Radiographic findings of inflammatory pseudotumor are typically solitary, peripheral, sharply circumscribed masses with an anatomic bias for the lower lobe (20). Initial CT findings of our patient were the mass with irregular margin contiguous to the extensive pleural thickening. Pleural calcification was also seen due to old tuberculosis. The radiologic differential diagnosis in the present case included lung cancer, malignant methotelioma, and pyothorax-associated lymphoma.

Because it is difficult to diagnose inflammatory pseudotumor by a small biopsy, surgical excision remains the most accurate diagnostic method (4-6). Matsubara et al (14) proposed a classification of inflammatory pseudotumor of the lung into three histologic categories: organizing pneumonia type (44%), fibrous histiocytoma type (44%), and lymphoplasmacytic type (12%). Although there is considerable histologic overlap among the three types, pathological features of our patient were consistent with those of the organizing pneumonia type.

The treatment of choice for inflammatory pseudotumor of the lung is surgery (3-6). The prognosis of patients who undergo radical resection is superb. Nevertheless, relapse can occur even many years after resection (6). Radiotherapy and steroids have been employed for functionally inoperable patients, those with unresectable lesions or with disease relapse. Experience in radiotherapy for inflammatory pseudotumor is limited, with both success and failure (21).

Several reports have demonstrated the efficacy of steroid therapy to inflammatory pseudotumor of the lung (7-10). Because the present patient had extensive pleural invasion, steroid therapy was initiated and resulted in remarkable shrinkage of both the mass and pleural thickening. In this context, Ishioka et al (10) also reported a case of inflammatory pseudotumor of the lung with pleural thickening treated with prednisolone.

Importantly, individuals with inflammatory pseudotumor of the lung may be associated with malignant tumors (13, 22). Pettinato et al (13) reported two cases of inflammatory pseudotumor who had a history of neoplastic disease involving the lung. Copin et al (22) demonstrated a case of squamous cell carcinoma within inflammatory pseudotumor and non-Hodgkin lymphoma developing after radiation therapy to inflammatory pseudotumor. In the present case, extramammary Paget’s disease and bladder cancer developed 10 and 15 years, respectively, after the diagnosis of inflammatory pseudotumor.

In summary, we reported a case of inflammatory pseudotumor of the lung with pleural involvement, which dramatically responded to corticosteroid. Although the tumor recurred 11 years after the initial steroid therapy, retreatment with corticosteroids was effective again. In addition, the patient had experienced two types of malignant tumor during the course of inflammatory pseudotumor. Steroid therapy could be an option in treating unresectable inflammatory pseudotumor of the lung, and in such cases, long-term follow-up is required.

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References


