Sarcoidosis Complicated with Major Pulmonary Artery Obstruction and Stenosis

Koichi Hasegawa, Seiko Ohno, Mai Takada, Hiroshi Ogino, Shinsuke Shiotsu, Chieko Takumi, Noriya Hiraoka, Tomohiro Handa and Sonoko Nagai

Abstract

A 34-year-old woman with bilateral pulmonary infiltrates was diagnosed with sarcoidosis. She refused corticosteroid treatment despite a worsening of the pulmonary infiltrate, and thereafter developed dyspnea following hemoptysis 6 years later. The upper lobe branches of the pulmonary artery were obstructed and the left main pulmonary artery was narrowed by mediastinal soft tissue, thus complications of granulomatous mediastinitis and fibrosing mediastinitis were suspected. The mediastinal soft tissue regressed, following the administration of corticosteroids, whereas the vascular obstruction and narrowing remained unchanged. Although the obstruction or stenosis of major pulmonary vessels is rare in sarcoidosis, such potential developments should be considered when mediastinal soft tissue appears in follow-up examinations.

Key words: sarcoidosis, pulmonary artery obstruction, granulomatous mediastinitis, fibrosing mediastinitis

Introduction

Sarcoidosis is a chronic granulomatous disease of unknown etiology, commonly associated with intrathoracic lymphadenopathy and the lungs are the most affected organ (1). Disease progression is occasionally observed, which is frequently accompanied by fibrosis related to the pulmonary parenchyma. That fibrotic process leads to the destruction of the pulmonary vascular bed, which is believed to be one of the causes of pulmonary hypertension (PH) (2). In contrast to such small vessel destruction, narrowing or obstruction of the major pulmonary vessels is rare. This type of vascular complication is believed to be caused by several different mechanisms in sarcoidosis (3). This report presents a case of sarcoidosis with major pulmonary artery obstruction that is thought to have been caused by granulomatous mediastinitis and fibrosing mediastinitis.

Case Report

A 34-year-old woman presented at our hospital for a evaluation of bilateral infiltrate noted on chest X-ray images obtained during a health survey examination in 2004. She was a non-smoker with no past medical history and had worked as a bank clerk without exposure to causative antigens. The patient was asymptomatic and her vital signs, oxygen saturation, and other findings in a physical examination were normal. Chest X-ray imaging showed bilateral nodular infiltrate, while computed tomography (CT) of the chest showed peri-bronchovascular nodular infiltrate and small mediastinal lymph nodes (Fig. 1). A complete blood count (CBC) was normal, as were serum levels of electrolytes, calcium, angiotensin converting enzyme, and lysozyme. Fiberoptic bronchoscopy revealed a network formation of small vessels in the trachea. Bronchoalveolar lavage of the right S4a region showed a predominance of lymphocytes (84%), with a CD4/8 ratio of 2.44. These results suggested sarcoidosis and she was therefore referred to a sarcoidosis clinic. Although the pulmonary infiltrate worsened and she developed slight dyspnea on exertion, she rejected systemic corticosteroid treatment because of concerns about potential side-effects.

She returned to our hospital, six years after the referral,
Figure 1. Chest X-ray and CT findings at the first presentation. (A) Chest X-ray image showing bilateral nodular infiltrates. Chest CT images showing (B) small mediastinal lymph nodes and (C) small nodular infiltrates mainly in the peribronchovascular interstitium.

Figure 2. Chest X-ray and CT findings at the second presentation. (A) Chest X-ray image showing bilateral infiltrates involving mainly the upper and middle lung fields. (B) Chest CT image showing bilateral areas of consolidation and small nodules. (C) Mediastinal soft tissue can be seen and (D) the inferior left pulmonary vein is narrowed.
complaining of a sudden onset of mild hemoptysis and shortness of breath. Examination findings revealed the patient to be in a tachypneic and hypoxic condition, with oxygen saturation of 95% while breathing 5 liters of oxygen per minute through a simple oxygen mask. Chest auscultation revealed mild bilateral rhonchi on expiration. The pulmonary infiltrate observed in chest X-ray images had progressed in comparison to the results obtained 6 years earlier, while they were unchanged from the chest X-ray findings obtained at a clinic 1 day before visiting this department. An electrocardiogram (ECG) showed right axis deviation and tall P waves in V1 and V2, with T wave inversion in V1, V2, and V3 also observed. Contrast-enhanced chest CT revealed dense homogenous tissue in the mediastinum that continuously extended to the bronchovascular interstitium. The bilateral upper lobe branches of the pulmonary artery were obstructed and the left main pulmonary artery was narrowed by that tissue. The left inferior pulmonary vein was also narrowed (Fig. 2, 3). The CBC and serum levels were unremarkable, other than elevated Krebs von den Lungen-6
Bed rest and adequate oxygenation improved the dyspnea and hypoxia within 3 days after admission, and the hemoptysis also disappeared without any intervention. Gallium scans (67 Ga) demonstrated a bilateral isotope uptake in the lung parenchyma and mediastinum (Fig. 4), and lung perfusion scintigraphy revealed bilateral perfusion defects in the upper lobes and diminished perfusion in the left lower lobe (Fig. 5). Fiberoptic bronchoscopy also showed the bilateral upper lobe bronchi to have narrowed. A transbronchial lung biopsy performed at left S3a demonstrated noncaseating epithelioid cell granuloma consistent with sarcoidosis (Fig. 6). Echocardiography findings showed an enlargement of both the right atrium and ventricle, and regional left ventricular hypokinesis was detected at the apex. The ejection fraction of the left ventricle was 62%. Doppler echocardiography revealed an estimated systemic pulmonary artery pressure of 51 mmHg. Right heart catheterization was performed, which showed an enlarged right ventricle, along with a mean right atrial pressure of 1 mmHg, mean pulmonary artery pressure of 18 mmHg, pulmonary capillary wedge pressure of 4 mmHg, cardiac output of 5.39 L/min, and pulmonary vascular resistance of 207 dyne.sec.cm⁻⁵. Coronary angiography showed no abnormalities, whereas left ventriculography demonstrated hypokinesis of the apex. The cardiac biopsy results were nonspecific.

The patient was thus found to have progressive pulmonary infiltrate and a mediastinal mass involving the pulmonary vessels. The patient was treated with 30 mg/day oral prednisolone, which led to an improvement in exercise tolerance and pulmonary infiltrate. The T wave inversion in V2 and V3 also normalized, and echocardiography showed improvement of wall motion of the left ventricle. Follow-up contrast-enhanced chest CT at 6 months after the initiation of treatment demonstrated the disappearance of the mediastinal soft tissue and pulmonary consolidation, with a slight architectural distortion and bronchiectasis remaining. Although the narrowing of the left inferior pulmonary vein was found to have improved (Fig. 7), the obstruction of the bilateral branches of the pulmonary arteries remained unchanged. Perfusion defects demonstrated by lung perfusion scintigraphy also persisted. Prednisolone was gradually tapered and the patient demonstrated a stable clinical course.

**Discussion**

Pulmonary involvement in sarcoidosis is common and intrathoracic lymphadenopathy is frequently recognized (1).
On the other hand, the present patient showed abnormal soft tissue infiltrating the mediastinum, which is different from the classic adenopathy observed in patients with sarcoidosis. Furthermore, the branches of the bilateral main pulmonary arteries were obstructed by that tissue, which resulted in regional pulmonary blood flow defects.

Obstruction or narrowing of large vessels is rare in sarcoidosis and it has been previously proposed to be caused by 3 possible mechanisms. Damuth et al. reported a case of sarcoidosis with major pulmonary artery stenosis that resulted in an elevated pulmonary arterial pressure. They attributed this to fibrosing mediastinitis, based on a hilar tomogram pattern and pulmonary angiography findings (3). In addition, that study noted compression by enlarged lymph nodes and granulomatous inflammation involving the walls of the large pulmonary arteries as 2 other possible mechanisms that might cause major pulmonary artery narrowing.

Granulomatous mediastinitis and fibrosing mediastinitis are chronic mediastinal diseases that are now considered to be two ends of the same disease spectrum (4). Although they are mainly caused by granulomatous infection, such as histoplasmosis or tuberculosis, sarcoidosis is one of the non-infectious causes and accounted for 11% of the confirmed cases in a review by Schowengerdt et al. (5). However, they also frequently involve vital structures in the mediastinum. Devaraj et al. described CT findings of 12 patients with fibrosing mediastinitis including 2 with sarcoidosis (6).

Eleven of the 12 patients in their series had evidence of complications due to fibrosing mediastinitis, including pulmonary artery narrowing in 5. Pulmonary vein involvement by fibrosing mediastinitis has also been reported in sarcoidosis. Yangui et al. reported a case of sarcoidosis with pulmonary vein stenosis and pulmonary edema secondary to fibrosing mediastinitis (7), while Toonkel et al. also noted a case of pulmonary vein obstruction due to fibrosing mediastinitis that led to PH in a sarcoidosis patient (8).

Although specimens from the mediastinum of the current patient could not be obtained; both the clinical course, which was chronic in nature and CT findings similar to those reported in the review of Devaraj et al. (6), thus suggesting that granulomatous mediastinitis and fibrosing mediastinitis were the cause of the obstruction and stenosis of the large pulmonary vessels. Furthermore, the findings showing a relatively high pulmonary artery pressure and right heart strain were thought to be a consequence of the involvement of the pulmonary arteries in this case.

The pathogeneses of these mediastinal processes are unknown and even those that complicate histoplasmosis, the leading underlying cause in North America, have not yet been clearly elucidated. The complication of these diseases is uncommon in patients with histoplasmosis, with only 3 of 100,000 have been reported to develop fibrosing mediastitis during an outbreak of this fungal infection (9). The low complication rates suggest that the development of these dis-
eases is related to a host-specific abnormal immune response, which is supported by the report by Peebles et al. (10) that found an association with human leukocyte antigen-A2. Sarcoidosis is a chronic granulomatous disease with a variable presentation and clinical course. This variability could be partly related to genetic factors in the affected patients (1), while it may also contribute to the persistent granulomatous inflammation and inappropriate fibrosis seen in these mediastinal diseases.

The patient subsequently presented with acute dyspnea and hypoxia improved without specific treatment, which could be attributed to hemoptysis and an excessively disproportional blood flow. A possible explanation is that the ventilation of the lower lobes, where most pulmonary blood flowed in this patient, had been impaired by hemoptysis, and then hypoxia developed due to a worsening of the ventilation-perfusion mismatch. Hypoxic pulmonary vasoconstriction might have also contributed to the hypoxia, which was alleviated by adequate oxygenation after admission. Hypoaxia was reported in 6% of patients with sarcoidosis (11) and even a small amount could provoke severe hypoxia, especially in patients with regional pulmonary blood flow defects, as seen in the present case.

Oral corticosteroid treatment is indicated for progressive pulmonary sarcoidosis (12), while its effects on granulomatous mediastinitis or fibrosing mediastinitis complicating sarcoidosis are unclear. Systemic corticosteroid administration has been reported to be effective to relieve the symptoms in 2 cases (7, 8), which were also associated with a regression of mediastinal soft tissue and reduced pulmonary arterial pressures. On the other hand, corticosteroid treatment did not normalize the narrowed major vessels in all cases. In addition, the effectiveness of angioplasty and stenting of the pulmonary artery narrowing has been reported (13). Corticosteroid treatment was partially effective in the current patient, i.e., the mediastinal mass largely disappeared and pulmonary vein narrowing improved, though the pulmonary artery obstruction and pulmonary perfusion defects did not recover. These results may be due to the nature of the disease, which consisted of a mixture of granulomatous inflammation and fibrosis, and thus suggesting that corticosteroid therapy is effective for acute granulomatous inflammation, while it has little effect once fibrosis develops.

In summary, this report described a case of sarcoidosis with pulmonary artery obstruction that was speculated to have been caused by granulomatous mediastinitis and fibrosing mediastinitis. It is important to be aware that this mediastinal process can develop in sarcoidosis and may lead to irreversible complications, including vascular obstruction. Contrast-enhanced chest CT is helpful to recognize the process, while attending physicians should be careful not to delay the initiation of effective treatment in order to prevent the occurrence of irreversible fibrotic changes.

The authors state that they have no Conflict of Interest (COI).

References