A Case of Sarcoidosis Presenting With Diffuse Endobronchial Involvement and Pleural Effusion

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Abstract

Pleural effusion, diffuse endobronchial mucosal involvement and distal airway obstruction were observed in a 50-year-old woman. Chest X-ray revealed mediastinal lymphadenopathy and diffuse parenchymal infiltrates. Extensive extrapulmonary involvement was not present. Both transbronchial lung biopsy and pleural biopsy demonstrated non-caseating granulomas consistent with sarcoidosis. The patient was given prednisone which was continued for 18 months in gradually decreasing doses. This treatment resulted in marked improvement of bronchoscopic findings. The simultaneous presence of pleural effusion and endobronchial involvement in the same patient is a rare occurrence in sarcoidosis.

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Key words: *pleural effusion, non-caseating granuloma, endobronchial involvement*

Introduction

Sarcoidosis is a systemic disease of unknown etiology in which the lung is the most involved organ. Pleural effusion and diffuse mucosal involvement are unusual manifestations in sarcoidosis (1-6). We report a patient with sarcoidosis in whom both pathologies were present in the same individual. The association of these two events in a sarcoidosis patient with no systemic involvement is a rare occurrence (4,7).

Case Report

A 50-year-old woman was admitted to hospital because of dyspnea on exertion and dry cough for two months. Wheezing, weight loss (5kg in the past 4 months) and a right sided chest pain were also present. On physical examination, breath sounds were diminished at the right base and expiratory rhonchi were present. There were no skin lesions nor enlarged lymph nodes. Erythrocyte sedimentation rate (ESR) was found to be increased (105 mm/h). Tuberculin skin test was positive (17x25 mm). Other laboratory results were normal. The pleural effusion was an exudate with 660 leucocytes/ml and 360 erythrocytes/ml identified in the cell count. No malignant cells were encountered in the cytological examination.

Pulmonary function tests showed the following values: FVC 1.84 L (69% of predicted); FEV_1: 0.98 L (43% of predicted); FEV_1/FVC: 53% of predicted; and DLCO/VA: 3.72 (61% of predicted).

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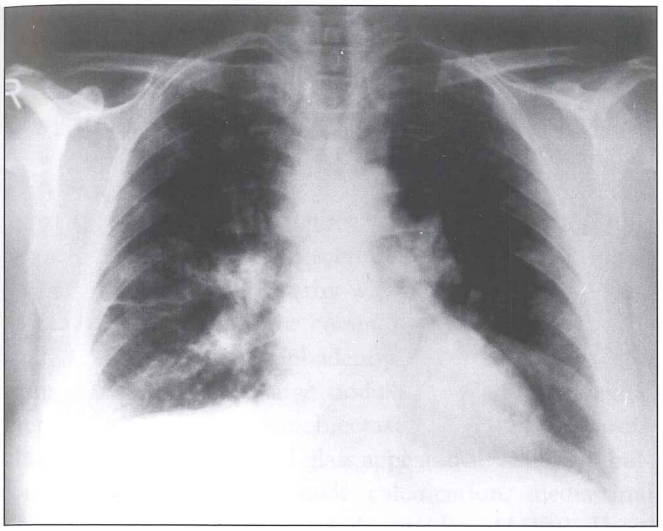

Figure 1. *Chest X-ray at admission showing right-sided pleural effusion and bilaterally hilar enlargement.*

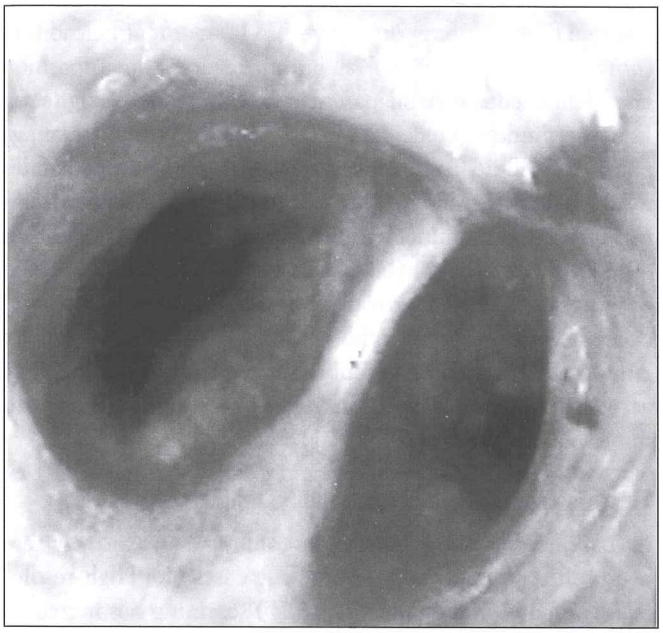

Figure 3. *Endobronchal appearence of right lower lobe basal segment showing mucosal irregulatarity and lesions.*

Chest X-ray revealed bilateral hilar lymph node enlargement, a right pleural effusion and diffuse parenchymal infiltration with a reticulo-nodular pattern (Figure 1). Thorax computerized tomography (CT) showed multiple mediastinal lymphadenopathies, right pleural effusion with thickening of the pleura and parenchymal patchy and nodular lesions (Figure 2). Abdominal ultrasound demonstrated 3-4 enlarged lymph nodes approximately 1.5 cm in size at the portal hilus. On bronchoscopy, the bronchial mucosa easily hemorrhaged and small, white mucosal lesions were observed in some places and the orifices of the right upper lobe anterior segment, of the middle lobe and of the basal segments of

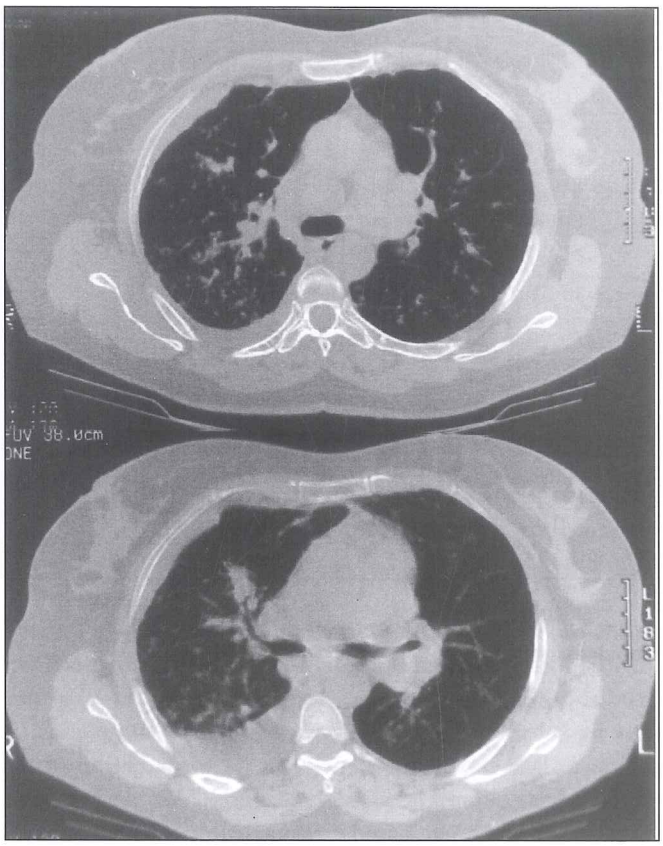

Figure 2. *Computed chest tomography at the level of main stem bronchial origins showing predominantly right-sided pleural thickening, effusion and peribronchial nodulary lesions.*

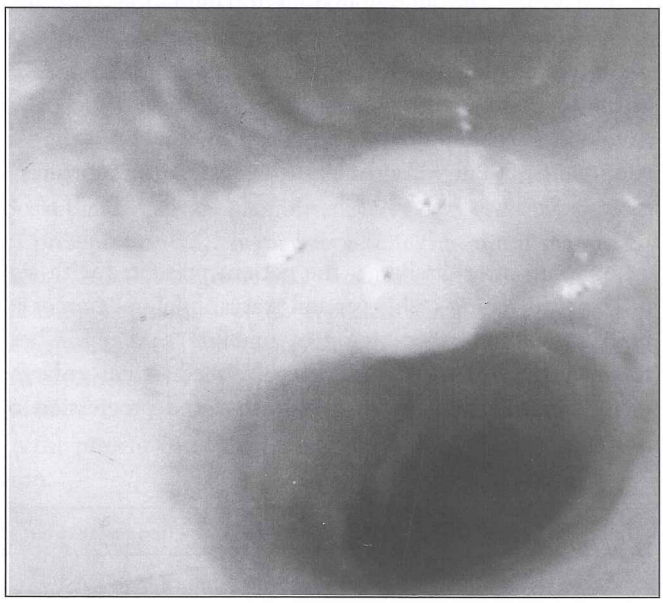

Figure 4. *Endobronchial polipoid lesions at the carina between left upper and lower lobe.*

the lower lobe were narrowed. Similar mucosal lesions were present at the carina of the left upper lobe (Figure 3 and 4). Bronchial mucosa biopsy demonstrated granulomas, cal-

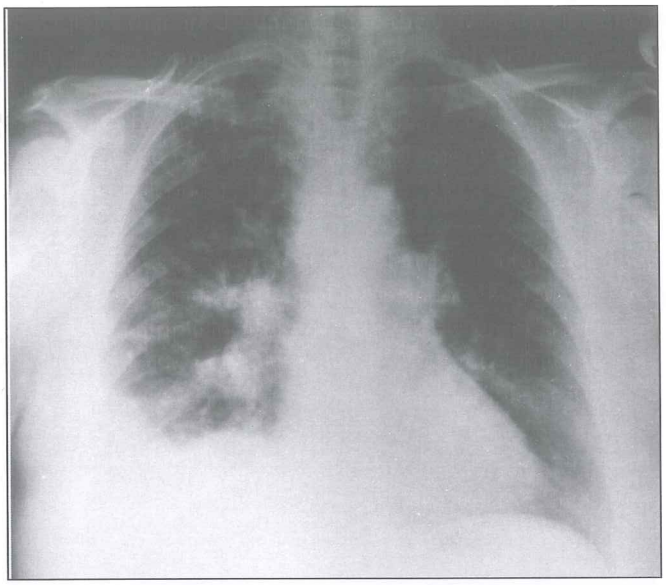

Figure 5. *Chest X-ray of the patient at the end of the first month of antituberculosis therapy.*

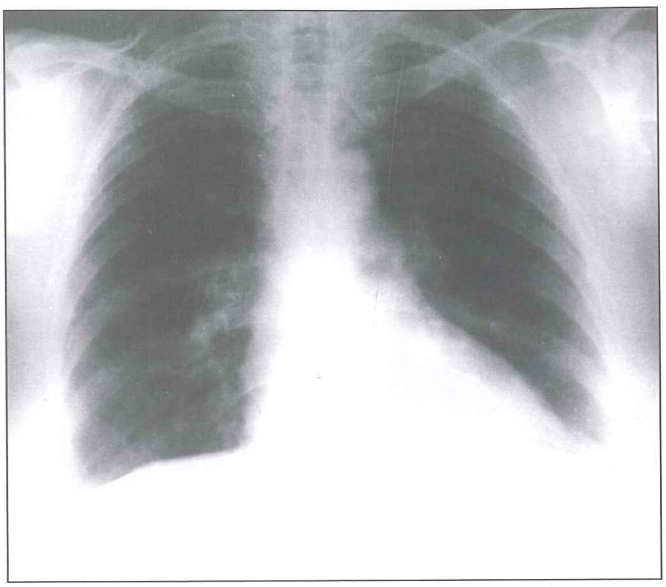

Figure 6. *Chest X-ray of the patient at the end of corticosteroid therapy.*

cium oxalate crystals in giant cells, a desquamation of the surface epithelium and a thickened basal membrane, findings which were evaluated as compatible with a granulomatous infection. But the cells were not stained with Ziehl Nielsen. The pleural effusion was a yellow exudate and contained lymphocytes, polymorphonuclear leucocytes and reactive mesothelial cells. Pleural biopsy revealed a fibrinous pleuritis and granulomatous inflammation. The histology of the pleural biopsy specimen did not reveal any etiology for the pleural effusion. However, based on the possibility of a pulmonary tuberculosis infection which also involved the pleura, treatment with isoniazid (H) 300mg/d, rifampicin 600mg/d, ethambutol 1g/d, and morphozinamide 3g/d was started.

One month after discharge, the patient presented with significant worsening of his general status, bilateral tremor in both hands and complaining of inability to sleep. Chest roentgenogram showed cardiomegaly, mediastinal enlargement, bilateral hilar lymphadenopathy, and progression of the pleural effusion and parenchymal infiltrates (Figure 5). ESR was found to be decreased to 74 mm/h. Bronchial lavage and pleural fluid cultures were negative for acid-fast bacilli. Antituberculous therapy was discontinued and the patient was started on oral corticosteroid treatment (prednisolon 40mg/d). Chemoprophylaxis with H 300mg/d was also given because of tuberculin skin test positivity. Two months later, physical examination was normal and ESR had decreased to 23mm/h. At the end of 18 months the clinical, radiological as well as bronchoscopic findings were found to be much improved (Figure 6 and Table 1).

Discussion

Involvement of the pleura in sarcoidosis is a relatively rare event and occurs in about 3% of the cases (1). High-resolution computed tomography (HRCT) scanning has increased the ability to detect pleural thickening. The manifestations of pleural sarcoidosis include pneumothorax, hemothorax, chylothorax, pleural thickening and pleural effusion. Pleural effusion is the most commonly encountered pleural manifes-

Table 1. The improvement of the pulmonary function tests within time

Treatment	At the beginning	3th month	8th month	11th month	15th month
FEV_1 (L)	0.98 43%	1.89 84%	1.99 96%	2.07 101%	2.23 109%
FVC (L)	1.84 69%	2.57 97%	2.62 107%	2.64 109%	2.74 113%
FEV_1/FVC	53%	73%	76%	78%	81%
PEF (L/sec)	2.54 43%	4.35 74%	4.65 82%	4.55 81%	5.20 93%
$FEF_{\%25-75}$ (L/sec)	0.49 15%	1.51 47%	1.65 53%	1.90 62%	2.22 72%
DLCO/VA	3.72 61%	5.91 96%		6.24 102%	

L: Litre

tation and can be detected in over 30% of patients with sarcoid involvement of the pleura (2, 3).

Clinical signs are variable and 30-60% of sarcoidosis patients are asymptomatic. Patients with bronchial and pulmonary parenchymal involvement present with cough and dyspnea and bronchial hyperractivity may be present (1). In 90-95% of cases, chest roentgenogram is abnormal. Mediastinal lymphadenopathy with or without hilar lymphadenopathy is the most common finding. Pleural effusion, unilateral hilar lymphadenopaty, segmental infiltrations or mass lesions, large nodular opacities mimicking metastases, cavities, bronchiectasis secondary to bronchostenosis, diffuse ground-glass appearance, advanced bullous emphysema, lymph node calcification, mediastinal fibrosis are rare manifestations of sarcoidosis (1-3%). These atypical forms of the disease are mostly encountered in patients older than 50 years of age (1).

Bronchoscopy is normal in 55% of cases with sarcoidosis and bronchial mucosal biopsy reveals granulomas. The most common endoscopic finding is a thickened, oedematous and hyperemic mucosa, encountered in almost half of the patients. The diagnostic yield of a biopsy obtained from such a mucosal lesion is twice higher than that of biopsies obtained from normal mucosa (9). Mizushima et al. reported a case with sarcoidosis accompanied by pleural effusion and multiple bronchial stenoses. On bronchoschopy, they noted that the middle and lower lobe bronchi of the right lung could not be observed due to stenoses. Bronchial mucosa easily hemorrhaged and a scar-like appearance was observed.

In the present case, bronchial mucosa had a haemorrhagic appearance and the mucosal lesions were predominant in the right bronchial system. The basal segment orifices of the right lower lobe were narrowed and bronchial mucosal biopsy revealed granulomas. The occurrence of bronchial stenoses is uncommon in patients with sarcoidosis. The use of corticosteroids appears disputable. Endoscopic bougie dilatation is effective in some cases (8).

In 1-3% of the cases, pleural effusion can be detected on chest roentgenogram and the majority of these patients are Stage II or III sarcoidosis cases. Thorax CT is more sensitive in demonstrating minimal pleural effusion and thickening. Pleurisy associated with sarcoidosis can be an exudate or transudate (6). The frequency of occurrence of pleural effusion in patients with sarcoidosis has been reported as 0.16% (1/624) by Tommasini et al. as 0.7% (2/270) by Salazar et al. as 4% (6/150) by Sharma and Gordonson and 6.6% (15/227) by Wilen et al. (4, 5, 7). The relative frequency of the pleural effusion to occur on the right versus the left side or to be bilateral is reported as 13: 8: 5; the transudate/exudate ratio is given as 9: 5; and a predominance of lymphocytes is reported in most cases (7). The present case was a right-sided effusion which was transudate in nature and contained predominantly lymphocytic cells. Salazar et al. reported that pleural effusions were associated with extensive pulmonary or extrathoracic involvement and were present at the onset of sarcoidosis (4). In the present case, extrathoracic involvement was absent, but diffuse pulmonary parenchymal infiltration was detected.

In Mizushima's case, pleural effusion was a yellow exudate which was predominatly lymphocytic (CD4/CD8 ratio=3.4). The patient showed spontaneous resolution in the follow-up (7). In our case, no spontaneous regression was observed. Furthermore, progression was noted within the first month of antituberculous therapy.

Sarcoidosis with bilateral pleural effusion and endobronchial involvement was also reported by Hernandez et al. (8). In this patient, bronchoscopy revealed a diffuse infiltrated mucosa and epitheloid granulomas were observed in the mucosal biopsy specimen. Pleural biopsy with video-assisted thoracoscopy and bronchial mucosa biopsy revealed non-caseated granuloma formation.

Ataç et al. reported a male patient with sarcoidosis who presented with pleural effusion, lympadenopathy, splenomegaly and pulmonary hypertension. A biopsy obtained from the cervical lymphadenopathy revealed granulomatous inflammation. The patient was started on antituberculous therapy, but sarcoidosis was considered in the differential diagnosis when clinical deterioration developed in the follow-up period. In this patient, pleural effusion developed 7 months after the initial diagnosis (10). As recently reviewed by Soskel and Sharma, pleural effusion has no specific pattern of presentation (2). It may represent the initial manifestation of sarcoidosis, or it may occur later in the course of the disease. Tommasini et al. reported acase with sarcoidosis diagnosed more than two years prior to the onset of pleural involvement (5).

In the present case, pleural effusion was the initial manifestation.

Pleural effusion associated with sarcoidosis has been reported to have a favourable prognosis and corticosteroids may prove to be of benefit (2, 4). Spontaneous resolution has also been noted (7). In most cases histological differantiation of sarcoidosis and tuberculosis is difficult. Detailed diagnostic evaluation is required since pleural effusion due to sarcoidosis shows regression under steroid therapy. If an extensive differential diagnosis is carried out and steroids started early in the course of the disease, a significant improvement is

observed in sarcoidosis patients. Corticosteroid therapy for at least one year is required in such cases in order to prevent the development of bronchial stenosis or stricture.

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