

Pleural Involvement in Pulmonary Sarcoidosis: A Case Report and Review of the Literature

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Case report

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Abstract

Background: Sarcoidosis is a chronic, multisystemic granulomatosis of unknown origin that can affect multiple organs throughout the body with variable progression and prognosis. Although the lungs and mediastinal lymph nodes are almost always affected in sarcoidosis, involvement of the pleura remains uncommon.

Case presentation: A 69-year-old female presented with dry cough, dyspnea on exertion and fatigue. She was diagnosed with pleural sarcoidosis based on the histological examination of the pleural biopsy and was treated with oral prednisone. Her complaints regressed two weeks later and the left pleural effusion almost disappeared four weeks later.

Conclusions: Pleural involvements in sarcoidosis should be considered in the differential diagnosis of pleural effusion and pleural nodules.

Background

Sarcoidosis is a multisystem disease characterized by noncaseating granulomatous inflammation.¹ Its exact etiology remains unknown and it can affect different organs, especially the lungs, lymph nodes, skin and eyes. Although lungs are involved in approximately 90% of patients with sarcoidosis, the pleurae are rarely affected in this perplexing disease.² The frequency of pleural sarcoidosis is less than 3% and pleural effusion, pleural thickening, pleural nodules, and pneumothorax are major forms of pleural involvements.^{3,4} However, it is relatively unusual that sarcoidosis can manifest as pleural effusion in association with pleural nodules. The present report describes a case of sarcoidosis with both pleural nodules and pleural effusion.

Case Presentation

A 69-year-old female was admitted to our hospital because of dry cough, dyspnea on exertion and fatigue for a month. She had no previous disease and no history of smoking. On admission, temperature, pulse, respiratory rate and blood pressure were 36.6°C, 79 beats/min, 21 breaths/min and 126/88 mm Hg, respectively. Serum electrolytes, brain natriuretic peptide, and liver & kidney function tests of were normal. The serum levels of carcino-embryonic antigen (CEA), neuro-specific enolase (NSE), CYFRA 21-1, squamous cell carcinoma antigen (SCCA), pro-gastrin-releasing peptide (Pro-GRP), and angiotensin converting enzyme (ACE) were 1.24 ng/ml (0-5.0 ng/ml) 15.78 ng/ml (0-16.3ng/ml) 1.54 ng/ml (0.1-3.3 ng/ml) 0.9 ng/ml (0-1.5 ng/ml) and 34.19 pg/ml (0-63 pg/ml) 44.3 U/ml (17.6-34 U/ml) respectively. On abdominal B-mode ultrasonography both the liver and the spleen were normal. A computed tomographic (CT) scan of the thorax demonstrated left pleural effusions and linear opacity (Fig.1). The exudative, yellow fluid with the predominance of lymphocytes (85%) was detected by thoracentesis. The concentrations of CEA, NSE, CYFRA 21-1, SCCA, and Pro-GRP in pleural effusion were 0.62 ng/ml (0-5.0 ng/ml) 0.86 ng/ml (0-16.3ng/ml) 2.95 ng/ml (0.1-3.3 ng/ml) 1.35 ng/ml (0-1.5 ng/ml) and 34.72 pg/ml

(0-63 pg/ml) respectively. In her left pleural effusion, the total protein value was 54.1 g/L (serum, 66.80 g/L) lactate dehydrogenase (LDH) value was 208 units/L (serum, 200.0 units/L), glucose value was 6.96 mmol/L (serum, 4.35 mmol/L), and adenosine deaminase (ADA) value was 47.5 IU/L (serum, 13.3 IU/L). Cultures of the pleural effusion were negative for acid fast bacilli (AFB), fungi, and other organisms. The cytological examination of exfoliated cells in pleural fluid revealed no malignant cells. A purified protein derivative (PPD) skin test was also negative and evidences of other organ involvements were not found. To evaluate the cause of pleural effusion, video-assisted thoracoscopy was performed and revealed a myriad of white nodules on the visceral and parietal pleura, as well as on the diaphragm (Fig.2). Histological examination of the pleural biopsy sample demonstrated non-caseating granulomas and real-time quantitative polymerase chain reaction (PCR) for mycobacterium tuberculosis was negative (Fig.3). These results were believed to be consistent with pleural sarcoidosis and this patient was started on prednisone 30 mg daily. All complaints regressed two weeks later and a follow-up CT four weeks later exhibited the left pleural effusion almost disappeared (Fig.4).

Discussion

The clinical features of pleural involvement in our patient seem to be interesting for several reasons. Firstly, this case of sarcoidosis is presented with both pleural effusion and pleural nodules. Pleural involvement in sarcoidosis was first recognized by Schaumann in 1933.⁵ It can be manifested by pleural effusion, pleural nodules, pleural thickening, pneumothorax, hydropneumothorax, and chylothorax.³ The true incidence of pleural involvement in sarcoidosis remains unclear because some cases of pleural sarcoidosis are asymptomatic.⁶ Chusid and colleagues reported that pleural involvements were histologically confirmed in 5 of 950 (0.5%) patients with sarcoidosis.⁷ Soskel et al. stated that pleural involvement occurred in about 3% of sarcoidosis.³ The first case of histologically proven pleural effusion caused by sarcoidosis was reported by Talbot et al.⁸ Sarcoidosis-related pleural effusions were considered to be less than 3% of this entity and, when present, occur slightly more commonly in the right pleural cavity, although sometimes they can be bilateral.³ The typical finding in pleural effusions caused by sarcoidosis is a paucicellular exudate with the predominance of lymphocytes.⁹ The mechanism of pleural effusion formation may be analogous to that of other infiltrative diseases. Increased capillary permeability due to involvement of the pleura, obstruction of superior vena cava, lobar atelectasis, and trapped lung have been considered as a cause of pleural effusions secondary to sarcoidosis.^{10,11} Pleural nodules, another manifestation of pleural sarcoidosis, were infrequent although the use of CT and thoracoscopy has increased awareness of this unusual site of involvement in sarcoidosis. These are often described as innumerable white nodules on both the parietal and visceral pleura.^{12,13} Sarcoidosis-related pleural effusions and pleural nodules are unusual, and they occur concurrently in one patient, as described in our case, are even more uncommon.

Secondly, pleural involvement is the initial manifestation of sarcoidosis. Pleural manifestations caused by sarcoidosis may arise at the onset of this disease which is first diagnosed, as the case we have described, or at any time during the course of the known sarcoidosis.¹⁴ The development of pleural

involvement in sarcoidosis seems to have no definite prognostic value.¹⁵ Thirdly, the pleural effusion and pleural nodules are associated with neither hilar adenopathy nor pulmonary infiltrate. The most common radiographic finding of sarcoidosis is bilateral hilar adenopathy. Other clinical features consist of interstitial lung disease, pulmonary nodules, skin lesions, and eye symptoms.¹³ Pleural sarcoidosis usually correlates with extrapulmonary involvement or extensively parenchymal lesions of the lung.^{7,9,16} In the present case, of great interest is pleural involvements are not associated with hilar adenopathy or pulmonary infiltrate.

Finally, the pleural involvement of sarcoidosis responds well to corticosteroids. Systemic corticosteroids are the mainstay of treatment of sarcoidosis. Corticosteroids hamper the formation of granulomas and, as a result, are largely efficient against most active clinical manifestations.¹⁷ They are required for recurrent or symptomatic patients of sarcoidosis with pleural involvement.¹⁸ Asymptomatic pleural effusions are likely to resolve spontaneously. The time of spontaneous resolution ranges from 1 to 3 months.¹⁸ Our case responded well to oral corticosteroid therapy, resulting in marked improvement in both symptoms and chest radiological findings. Sarcoidosis related pleural effusions which resolve incompletely and develop to trapped lung may be relieved by decortication.¹¹

The diagnosis of sarcoidosis involving the pleura is based on finding the histologic evidence of noncaseating granuloma, the hallmark of sarcoidosis, and on excluding other granulomatous diseases, such as tuberculosis, fungal disease, and granulomatous polyvasculitis.² In addition, some disorders including congestive heart failure and neoplasia, may be concomitant with sarcoidosis, must be ruled out. However, because the clinical and pathological features of sarcoidosis and tuberculosis may mimic each other, the differentiation between the two entities remains a challenging problem. when the caseous necrosis is absent in biopsy samples, the real time PCR quantification for mycobacterium tuberculosis genome is a valuable test for differentiation between sarcoidosis and tuberculosis.¹⁹

Medical thoracoscopy, a relatively less invasive and more efficient diagnostic method, plays a significant role in the diagnosis of pleural involvement in sarcoidosis, especially of pleural effusions and pneumothorax. It allows physicians to directly access and assess the pleural cavity, including the parietal, visceral and diaphragmatic pleura, and to obtain adequate tissue sampling. Additionally, pleural fluid can be aspirated without complications during thoracoscopy. Therefore, thoracoscopy, an appropriate alternative technique, can provide doctors with important evidences to convince pleural sarcoidosis. Although thoracentesis or closed pleural biopsy can also help to diagnose, it is not easy for physicians to get the accurate pathologic evidence.

Conclusions

In summary, this case illustrates an unusual form of pleural involvement of sarcoidosis with pleural effusion plus pleural nodules. A definitive diagnosis of pleural sarcoidosis relies on the histological identification of noncaseating granulomas in the pleurae and on the exclusion of all other possible

causes. Although rare, pleural involvements in sarcoidosis should be considered in the differential diagnosis of pleural effusion and pleural nodules. As is the case with other forms of pulmonary involvement in sarcoidosis, these manifestations respond well to corticosteroids. It is believed that careful evaluation and vigorous treatment of pleural involvement in sarcoidosis is imperative.

Abbreviations

CEA=carcino-embryonic antigen, NSE=neuro-specific enolase, SCCA=squamous cell carcinoma antigen, Pro-GRP=pro-gastrin-releasing peptide, ACE=angiotensin converting enzyme, ADA=adenosine deaminase, PPD=purified protein derivative, LDH=lactic dehydrogenase.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

We have obtained written informed consent from the patient for publication of this case report and the related images.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable requests.

Competing interests

The authors declare that there is no potential conflict of interest related to this article.

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Authors' contributions

JML, FS, HYP and YXJ collected the case information and XQJ, LXW and DGL drafted the manuscript. All the authors read and approved the final manuscript.

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Not applicable.

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Figures

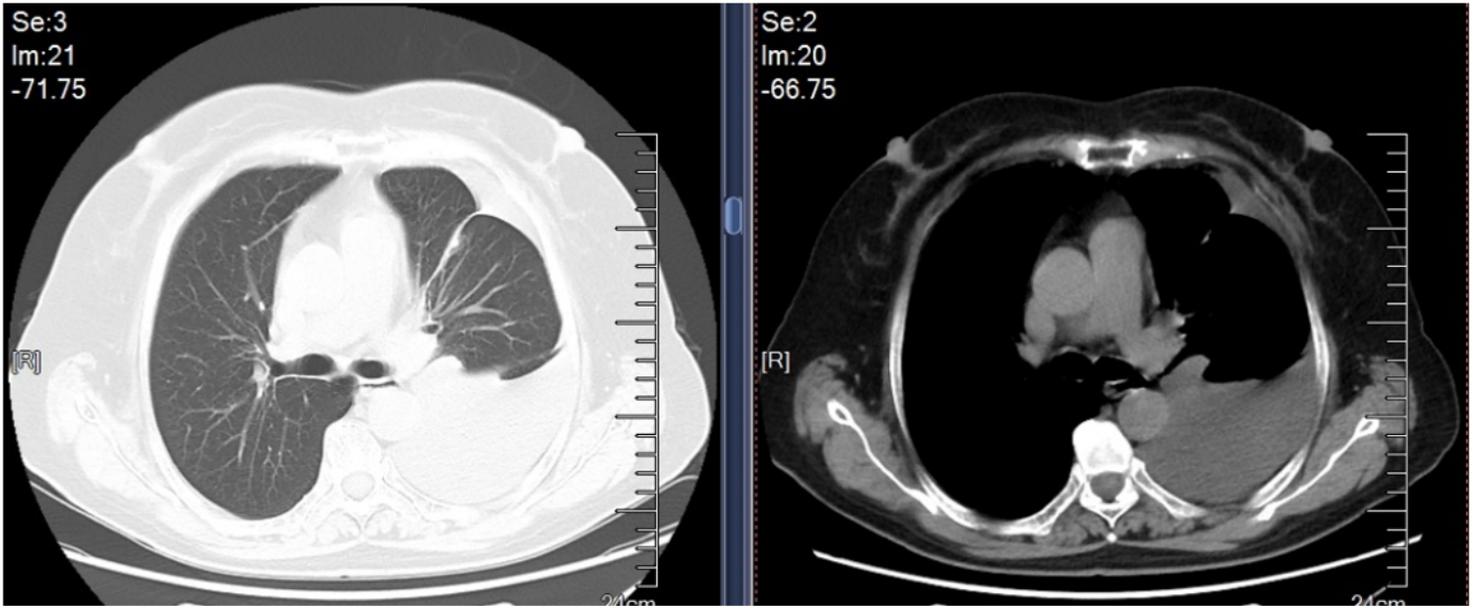


Figure 1

Chest CT scan showed left pleural effusions and linear opacity.

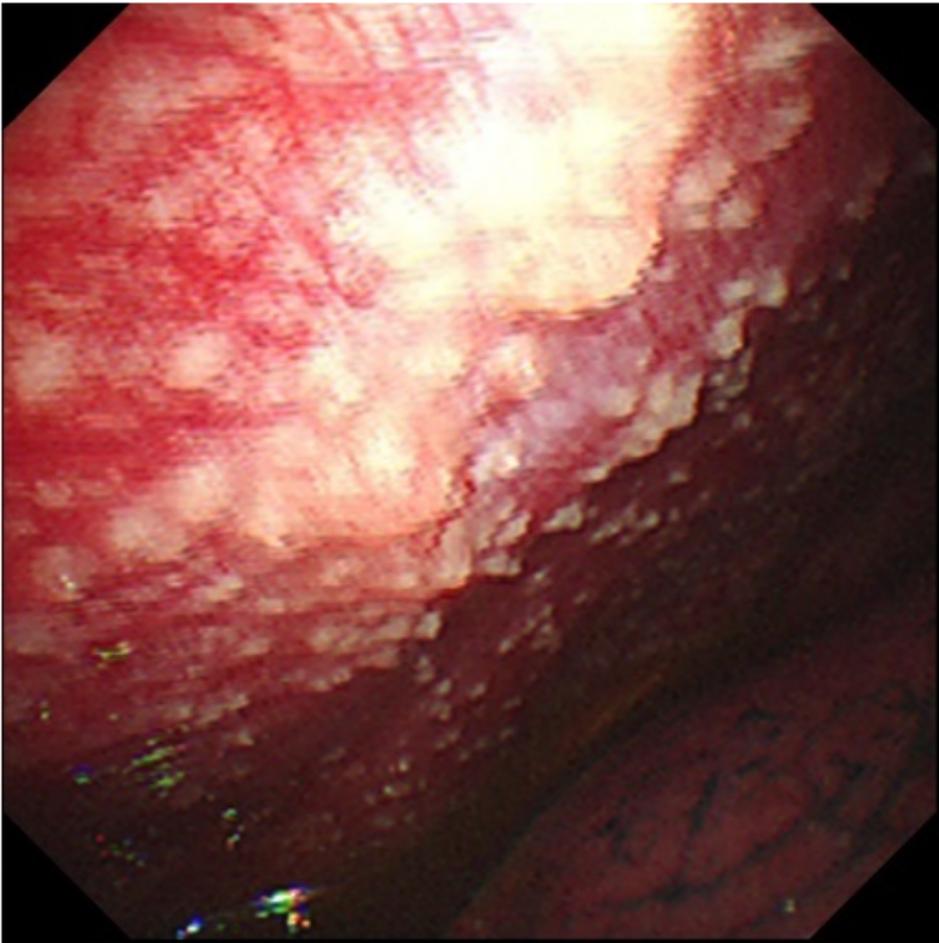


Figure 2

Thoracoscopy demonstrated amounts of white nodules on the pleurae.

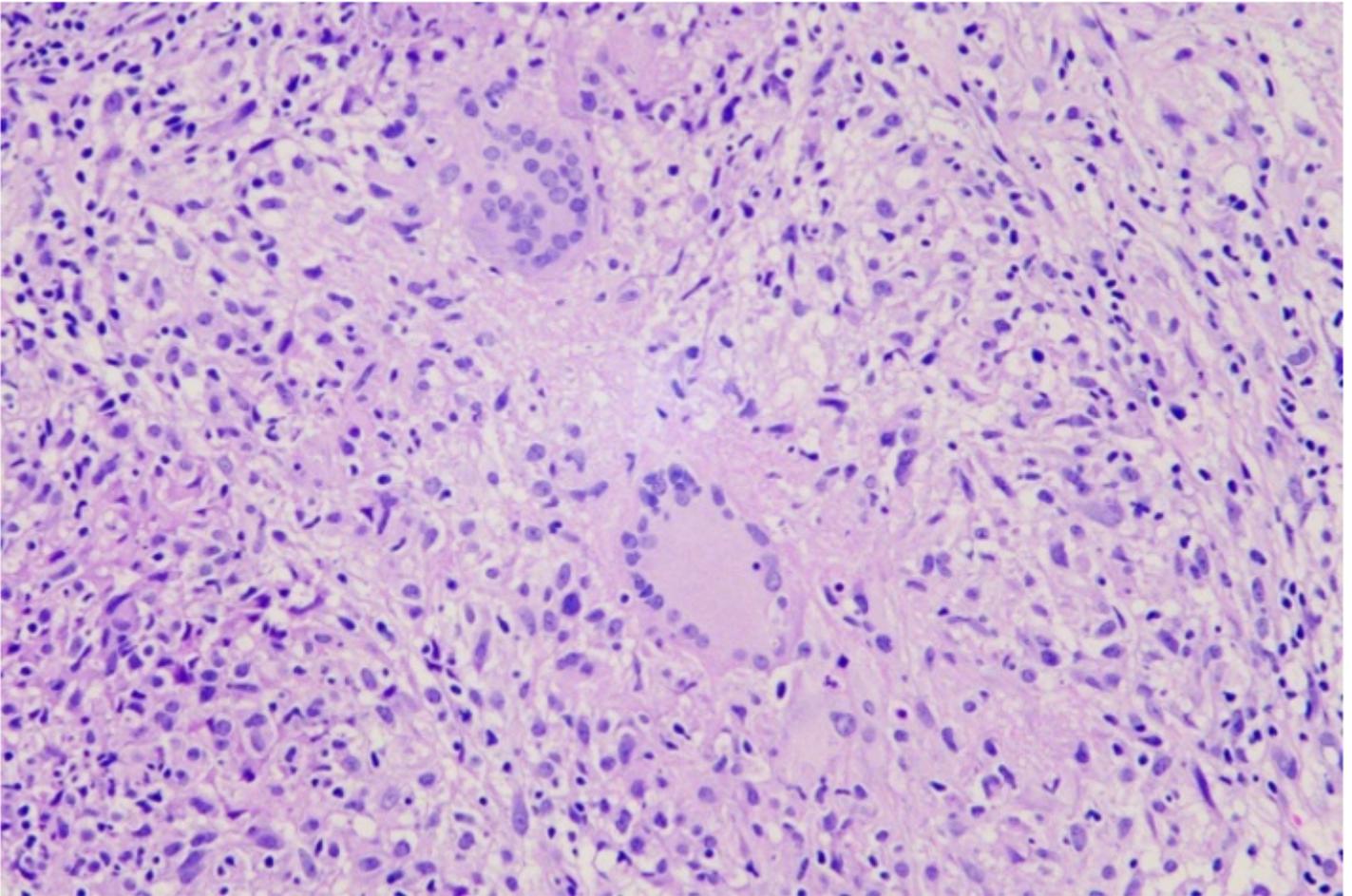


Figure 3

Histologic finding of noncaseating granulomas (hematoxylin-eosin, original magnification x400).

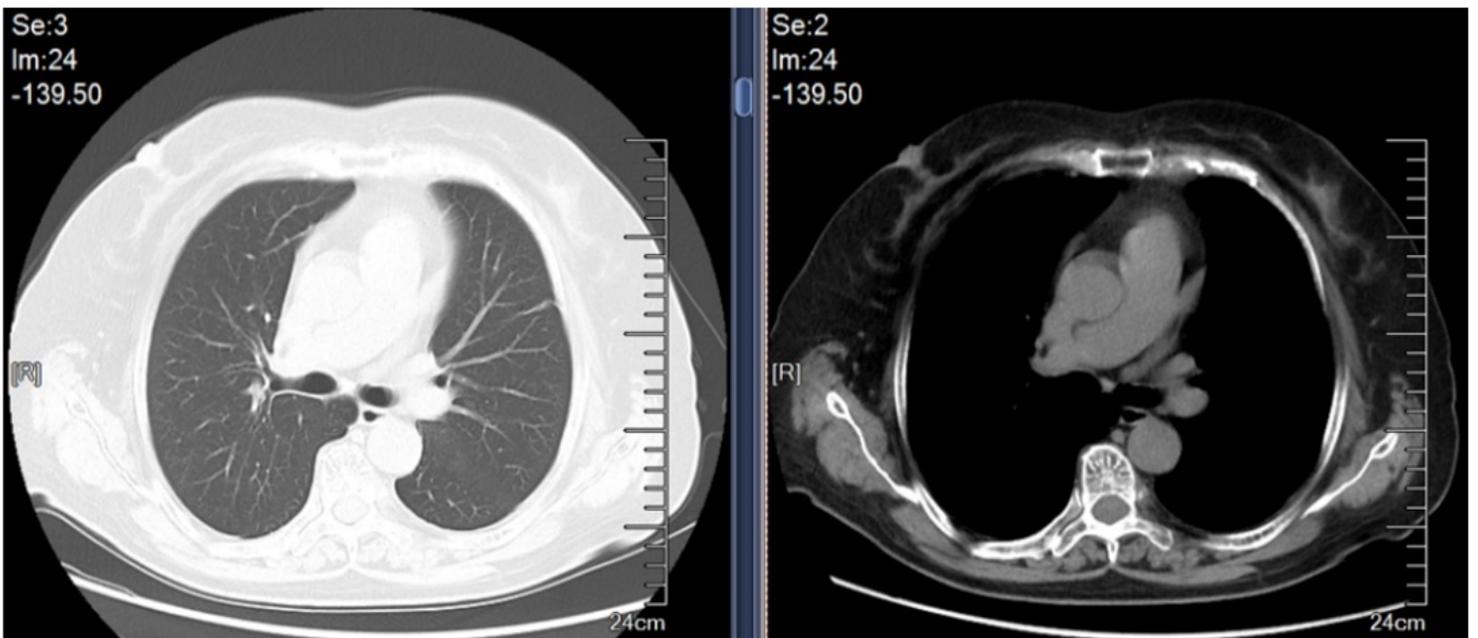


Figure 4

Follow-up chest CT showed a complete withdrawal of the left pleural effusion.