Case Report
Coexistent sarcoidosis and tuberculous pleuritis: a case report

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Abstract: Background: Sarcoidosis is a multisystem granulomatous disorder characterized by the presence of non-necrotic granulomas pathologically. Tuberculosis belonging to the infectious diseases is caused by mycobacterium tuberculosis and characterized by granulomas with caseous necrosis. Although it is rare, tuberculosis and sarcoidosis may occur concomitantly. Case presentation: We report a rare case of a 49-year-old Chinese woman who presented with repeated low-grade fever and malaise that was initially diagnosed as tuberculous pleuritis. After the anti-tuberculosis treatment, the symptoms including fever and malaise were gone, and the pleural effusion did not relapse. However, the mediastinal lymphadenectasis did not lessen during the treatment. Later the patient felt dyspneic and the swollen superficial lymph nodes appeared. From the subsequent chest CT scans, a growing number of nodules were found in the lungs. Eventually the biopsy of lymph nodes in her right supraclavicular region confirmed the coexistence of sarcoidosis. Based on the result, corticosteroid therapy was introduced in the patient, and her swollen mediastinal lymph nodes shrunk and the pulmonary nodules were reduced obviously in the 2 month of follow-up. Conclusion: Rarely sarcoidosis and tuberculosis may coexist, and there remains a diagnostic challenge when tuberculosis and sarcoidosis occur concomitantly. If the possibility of tuberculosis can not be ruled out completely, tentative anti-tuberculosis treatment before the application of glucocorticoid is suggestive.

Keywords: Sarcoidosis, tuberculous pleuritis, mycobacterium tuberculosis

Introduction

Sarcoidosis is a systemic illness of unknown etiology characterized by non-caseating epithelioid granulomas in the affected tissues. It commonly affects the lungs and lymph nodes. Tuberculosis, caused by the infection of mycobacterium tuberculosis, is featured by the caseous necrotic granuloma. The two seemingly irrelevant diseases may coexist for some reason (Table 1) [1-6]. However, it is rare in clinical practice and easily ignored by respiratory physicians. Herewith, we report the case of sarcoidosis in a 49-year-old Chinese female with tuberculous pleuritis.

Case presentation

A 49-year-old Chinese female with a medical history of repeated low-grade fever and malaise for 1 month before her hospitalization for the pleural effusion on the left side and mediastinal lymphadenectasis (Figure 1) 17 months ago in the local tumor hospital. Thoracentesis was performed for the diagnosis. The pleural fluid was yellow, and Rivalta test was positive. The total number of WBCs in her pleural fluid was 1020×10⁶/L, in which lymphocytes accounted for more than 50%. A total protein concentration in the pleural fluid was 36 g/L, with a pleural fluid-to-serum protein ratio higher than 0.87. ADA was 60 U/L. The acid-fast stain was negative and exfoliative cytological examinations of the fluid for five times were all negative. After the sufficient drainage of the pleural effusion, the patient took the chest contrast-enhanced CT scan (Figure 2) which showed a normal lung field without pleural effusion but unchanged mediastinal lymph nodes. Then the bronchoscope was applied to the patient for further diagnosis (Figure 3). The result showed the bronchial lumen was normal, and malignant cells were not visible in the TBNA specimen of
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Table 1. Similar cases diagnosed as coexistence of sarcoidosis and tuberculosis from 1998 to 2017 in literature

<table>
<thead>
<tr>
<th>Year</th>
<th>Region</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Author</th>
<th>Journal</th>
</tr>
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<tbody>
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<td>2014</td>
<td>India</td>
<td>Female</td>
<td>38</td>
<td>Sanjay Kumar Mandal, et al. [1]</td>
<td>BMJ Case Rep</td>
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Figure 1. The CT scan images show pleural effusion on the left side and mediastinal lymphadenectasis.

Figure 2. The CT scan images show the pleural effusion on the left side disappears after the effusion drainage.

pleural effusion did not relapse in her regular review by the chest CT scans (Figures 4-6). However, the mediastinal lymphadenectasis did not lessen in the course of the treatment.

The patient felt dyspneic one month after drug withdrawal, then she visited the doctor in the local hospital again. Her chest CT scan (Figure 7) showed mediastinal lymphadenectasis and scattered nodules on both sides of the lung, but no pleural effusion. The patients refused to take further diagnosis and treatment. Within the next month, the patient felt increasingly dyspneic, and gradually increased masses appeared in the right supraventricular region and the left inguinal region. Then she took another chest CT scan (Figure 8) which confirmed an obviously increase of the nodules. Finally the patient was admitted to our hospital and took the further examination for an explicit etiology.

Upon admission, routine investigation revealed total count of white blood cells $4.0 \times 10^9/L$ with 73.3% neutrophils and 17.2% lymphocytes; her hepatic function, renal function, blood glucose, blood ions, myocardial enzyme and brain natriuretic peptide were all normal. The serum ACE increased to 175.4 U/L which was much higher than the previous test result. The blood-gas analysis revealed PH 7.42, PO$_2$ 88 mmHg, PCO$_2$ 42 mmHg, SO$_2$ 90%. The bronchial dilation test was negative, and the pulmonary diffusion function was moderate dysfunctional by D$_{L}$CO
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The bronchoscope shows the bronchial lumen is normal.

The bronchoscope shows the bronchial lumen is normal.

The CT scan images show that the swollen mediastinal lymph nodes remained the same as before, but pleural effusion did not relapse after the anti-tuberculosis treatment for 3 months.

The CT scan images show that the swollen mediastinal lymph nodes remained the same as before, but pleural effusion did not relapse after the anti-tuberculosis treatment for 6 months.

55%. The PPD test became negative for the induration diameter 4 mm, and the interferon gamma release assay was also negative.

According to the results above, especially the masses in lymph node regions and the high-level serum ACE, we suspected the possibility of sarcoidosis and malignant tumors. Then the patient took the PET-CT scan (Figure 9) which showed a large number of swollen lymph nodes in her body and prompted a high possibility of sarcoidosis, but lymphoma still could not be excluded. A further lymph node biopsy was conducted in her right supraclavicular region. The histology (Figure 10) showing granulomatous inflammation without necrosis in the proliferative fibrous tissue suggested sarcoidosis.

Combined with the medical history, treatment and laboratory examinations, the diagnostic conclusion of sarcoidosis was made eventually. Then the patient was treated with oral prednisone with initial dose of 0.5 mg/(kg. d). Another chest CT scan (Figure 11) was taken after one month of prednisone treatment. The result showed the bilateral diffuse nodules decreased significantly and the swollen mediastinal lymph nodes shrunk slightly. After two months of prednisone treatment, the patient’s mediastinal lymph nodes shrunk significantly (Figure 12).

In summary, the final diagnostic conclusion for the patient is coexistence of pulmonary tuberculosis and sarcoidosis.
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Figure 6. The CT scan images show that the swollen mediastinal lymph nodes remained the same as before, but pleural effusion did not relapse after the anti-tuberculosis treatment for 9 months.

Figure 7. The CT scan images show scattered nodules on both sides of the lung and mediastinal lymphadenectomy, but there is no pleural effusion.

Figure 8. The CT scan images show an obviously increase of the nodules compared to Figure 7.

Discussion

Sarcoidosis is a chronic granulomatous disease which is characterized by the pathological change of non-caseous epithelia granuloma, while tuberculosis is characterized by the caseous necrotic granuloma. There seems to be no correlation between the two diseases, however, they actually can coexist in one patient [1-3]. At present, researchers have revealed that mycobacterium tuberculosis detected in part of sarcoidosis patients has been confirmed as the antigenic driving factor of sarcoidosis and may induce the granuloma reaction of sarcoidosis [4, 7-9]. This phenomenon is regarded as 'tuberculous sarcoidosis' [10]. Moreover, sarcoidosis patients are prone to be infected by mycobacterium tuberculosis due to immunodeficiency [11], in addition, the mycobacterium tuberculosis always invade the sarcoidosis granuloma more often [12]. These traits may be one of the important reasons why sarcoidosis and tuberculosis appear at the same time and tuberculosis may be secondary to sarcoidosis.

Tuberculous pleuritis, belonging to a kind of tuberculosis, may coexist with sarcoidosis as well in theory. Although such cases are rare in practice, the reason for pleuritis caused by either mycobacterium tuberculosis or by sarcoidosis, should be clarified in sarcoidosis patient. The biopsy of pleura by medical thoracoscope is considered as a reliable diagnostic method. However, when the hospital is lack of medical thoracoscope or the patient is unsuited for medical thoracoscopy examination, the diagnosis should be made according to the patient’s condition, imaging manifestation, laboratory indexes and diagnostic treatment results. The PPD test and the interferon gamma release assay are usually positive, and the effusion ADA always exceeds 40 IU/L [13] in patients of tuberculous pleuritis. On the contrary, the PPD test and the interferon gamma release assay are often negative, and the effusion ADA is always less than 40 IU/L [13] in sarcoidosis patients. In addition, the serum ACE may increase in sarcoidosis patients. Generally, the pleural effusion in sarcoidosis patients is little and more often in the right pleural cavity [14, 15], and the ratio of CD4+/CD8+ is obviously higher than that in tuberculous pleuritis [16, 17]. When it is hard to diagnose especially
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due to the lack of pathologic evidence, tentative anti-tuberculosis treatment can be applied. In the most cases, tentative anti-tuberculosis treatment is ineffective for the sarcoidosis patients.

In this case, the thoracoscope examination was not allowed to perform because there was no pleural fluid when the patient was admitted to our hospital. In spite of the lack of pathological evidence, we took into prudent consideration of the characteristics of the pleural effusion, the PPD test and interferon-gamma release assay results, and the tentative anti-tuberculosis therapeutic effect. All the clinical evidence pointed to tuberculous pleuritis initially. However, after 12 months anti-tuberculosis treatment, the swollen mediastinal lymph nodes were not shrunken, and diffused nodules appeared in the lung gradually. It was highly suspected that another disease might coexist in this case. Sarcoidosis was eventually verified by the biopsy of her supraclavicular lymph nodes. Because the swollen mediastinal lymph nodes had kept for more than one year, and the

Figure 9. A. PET-CT images show the swollen lymph nodes in different regions of the body. B. PET-CT images show the swollen lymph nodes in bilateral supraclavicular regions. C. PET-CT images show the swollen lymph nodes in mediastinum.

Figure 10. A. The non-necrotic granuloma consisted of many epithelioid cells exist in the lymph nodes. B. Many epithelioid cells accompanied by few Langhans cells and lymphocytes exist in the granuloma.

Figure 11. The CT shows the bilateral diffuse nodules decrease significantly and the swollen mediastinal lymph nodes shrink slightly after 1 month of glucocorticoid.
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pulmonary infiltration appeared afterwards, we considered the pathogenetic condition of sarcoidosis in this patient was not self-limiting, and the diagnosis of tuberculous pleuritis was tenable. The patient responded well to glucocorticoid, however it should be noticed long time administration of glucocorticoid may render her highly susceptible to mycobacterial infection again or lead to the reactivation of latent bacilli.

In conclusion, this case was diagnosed as coexistence of sarcoidosis and tuberculosis. Sarcoidosis and tuberculosis may coexist due to some common driving factor between these two diseases; if the possibility of tuberculosis can not be ruled out completely, tentative antituberculosis treatment before the application of glucocorticoid is suggestive.

Acknowledgements

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We contacted the patient by telephone if she would agree to sign the consent agreement for the publication of the case report. Unfortunately, we were unable to obtain the written consent from the patient. The patient declared consent verbally on phone, but she refused to come to sign the document due to long distance travel. Therefore, it is burdensome to obtain the signed consent for us. However, this case report will raise the clinicians’ awareness of the coexistence of tuberculous pleuritis and sarcoidosis, and improve their diagnosis accuracy. Therefore, it is important for the clinicians and patients to know the clinical phenomenon and the importance of the clinical application.

Disclosure of conflict of interest

None.

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