Int J Clin Exp Med 2018;11(10):11222-11228
www.ijcem.com /ISSN:1940-5901/IJCEM0074853

Case Report

Coexistent sarcoidosis and tuberculous pleuritis: a case report

Yan Wang[1], Jinzhi Yin[1], Shili Yu[2], Ke Wang[1]

[1]Department of Respiratory Medicine, [2]Pathology Medicine, The Second Hospital of Jilin University, Changchun, Jilin, P.R.China

Received September 30, 2017; Accepted June 19, 2018; Epub October 15, 2018; Published October 30, 2018

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 tuberculousis

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 1020×10^6/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

Table 1. Similar cases diagnosed as coexistence of sarcoidosis and tuberculosis from 1998 to 2017 in literature

Year	Region	Sex	Age (years)	Author	Journal
1998	China	Female	35	CF Wong, et al. [5]	Chest
2005	South Africa			Oluboyo PO, et al. [6]	Cent Afr J Med
2010	Croatia	Female	43	Kornelija Mise, et al. [3]	Cases Journal
2014	Polan	Male	26	Wojciech J Piotrowski, et al. [4]	Am J Case Rep
2014	India	Female	38	Sanjay Kumar Mandal, et al. [1]	BMJ Case Rep
2017	North-Africa	Male	45	Carbonelli C, et al. [2]	Respiration

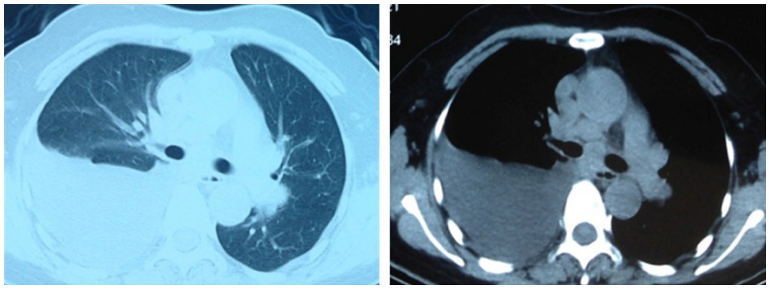

Figure 1. The CT scan images show pleural effusion on the left side and mediastinal lymphadenectasis.

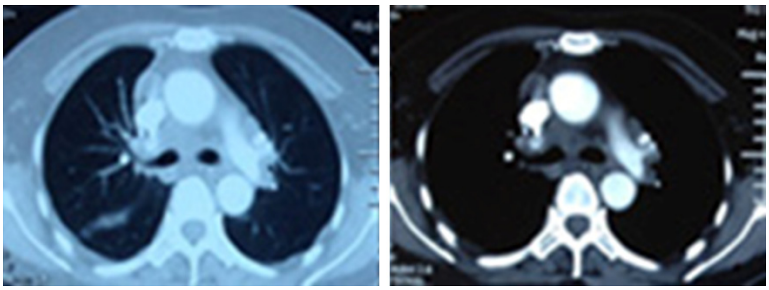

Figure 2. The CT scan images show the pleural effusion on the left side disappears after the effusion drainage.

lymph node from the right front juga or the right rear juga.

After excluding the possibility of malignant pleural effusion, the patient was transferred to the local hospital for infectious diseases and took further examination. The serum ACE was 53 U/L. The PPD skin test which showed the induration equaled to 13 mm was considered positive, and the interferon gamma release assay was also positive. According to the above clinical data, the patient was eventually diagnosed with the tuberculous pleuritis, and then treated with antitubercular drugs for 12 months. During the treatment, the symptoms including fever and malaise were gone, and the pleural effusion did not relapse in her regular review by the chest CT scans (**Figures 4**-**6**). However, the mediastinal lymphoadenectasis 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 supraclavicular 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 4.0×10^9/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_LCO

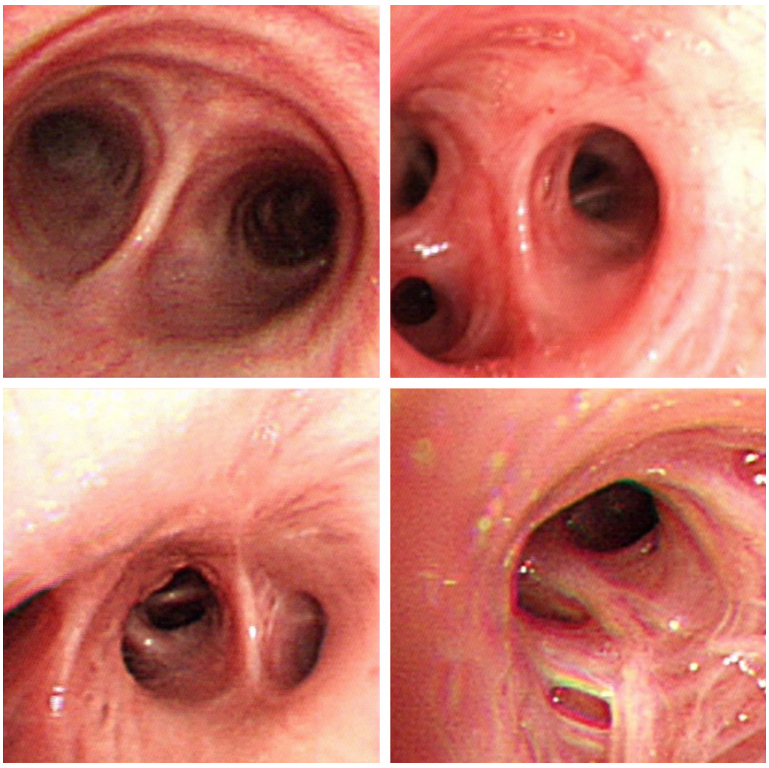

Figure 3. The bronchoscope shows the bronchial lumen is normal.

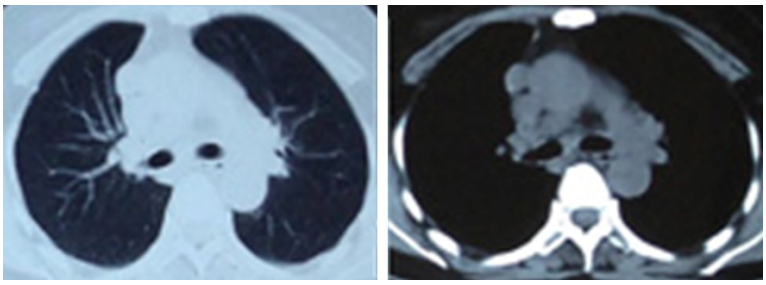

Figure 4. The CT scan images show that the swollen mediastinal lymph nodes remained the same as before, but pleural effusion did not relapse after the anti-tuberculosis treatment for 3 months.

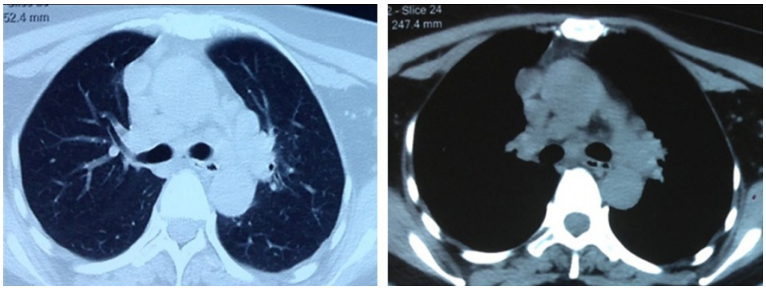

Figure 5. The CT scan images show that the swollen mediastinal lymphnodes remained the same as before, but pleural effusion did not relapse after theanti-tuberculosis treatment for 6 months.

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.

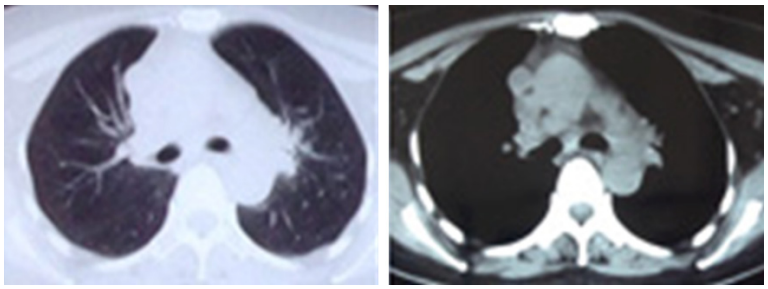

Figure 6. The CT scan images show thatthe swollen mediastinal lymph nodes remained the same as before, but pleural effusion did not relapse afterthe anti-tuberculosis treatment for 9 months.

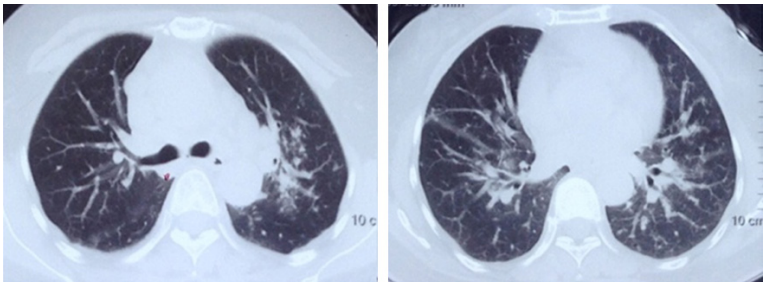

Figure 7. The CT scan images show scattered nodules on both sides of the lung and mediastinal lymphadenectasis, but there is no pleural effusion.

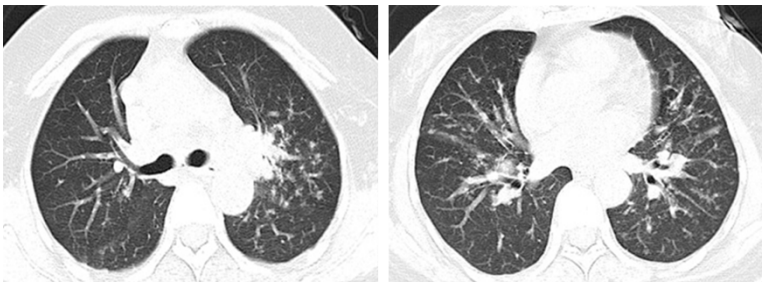

Figure 8. The CT scan images shows an obviously increase of the nodules compared to **Figure 7**.

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 mycobaterium tuberculosis due to immunodeficiency [11], in addition, the mycobaterium 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

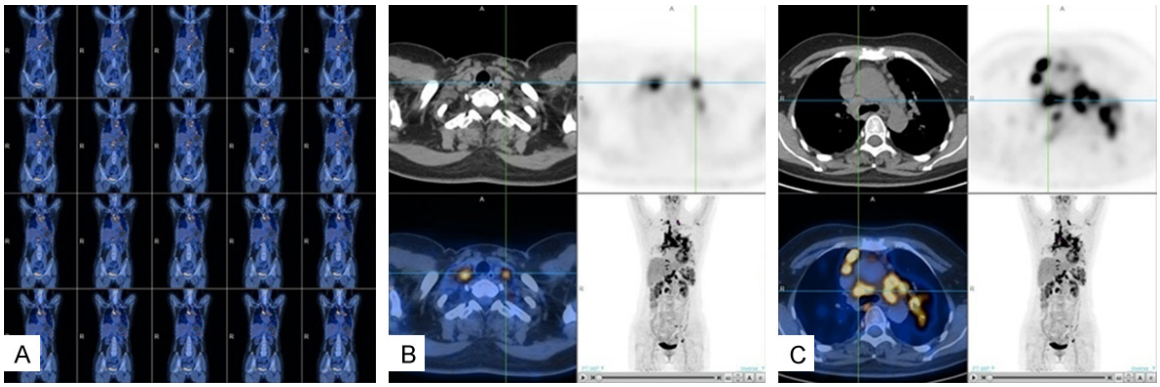

Figure 9. A. PET-CT images show the swollen lymph nodes in different regions of the body. B. PET-CT images show the swollen lymph nodes in bilateral supraclavicular regions. C. PET-CT images show the swollen lymph nodes in mediastinum.

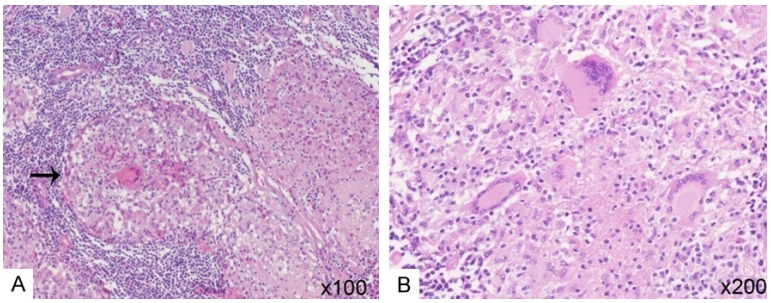

Figure 10. A. The non-necrotic granuloma consisted of many epithelioid cells exist in the lymph nodes. B. Many epithelioid cells accompanied by few Langerhans cells and lymphocytes exist in the granuloma.

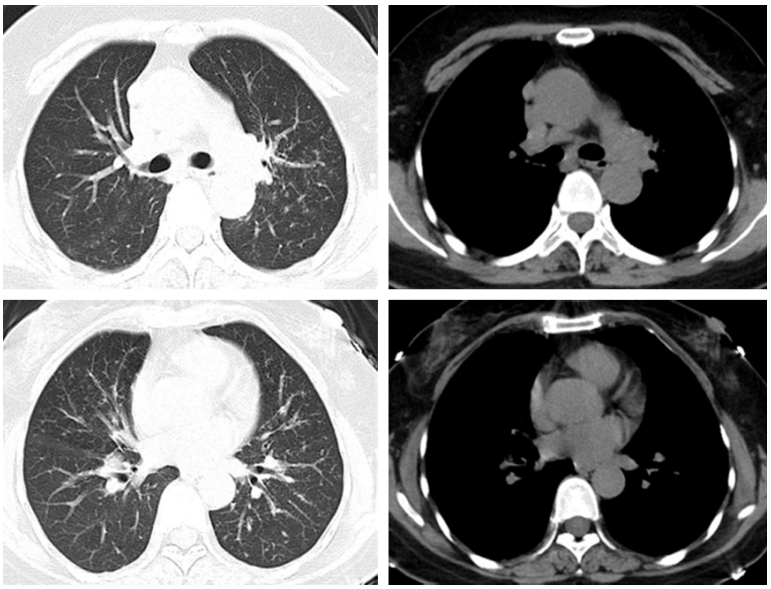

Figure 11. The CT shows the bilateral diffuse nodules decrease significantly and the swollen mediastinal lymph nodes shrink slightly after 1 month of glucocorticoid.

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 supraclavicularlymph nodes. Because the swollen mediastinal lymph nodes had kept for more than one year, and the

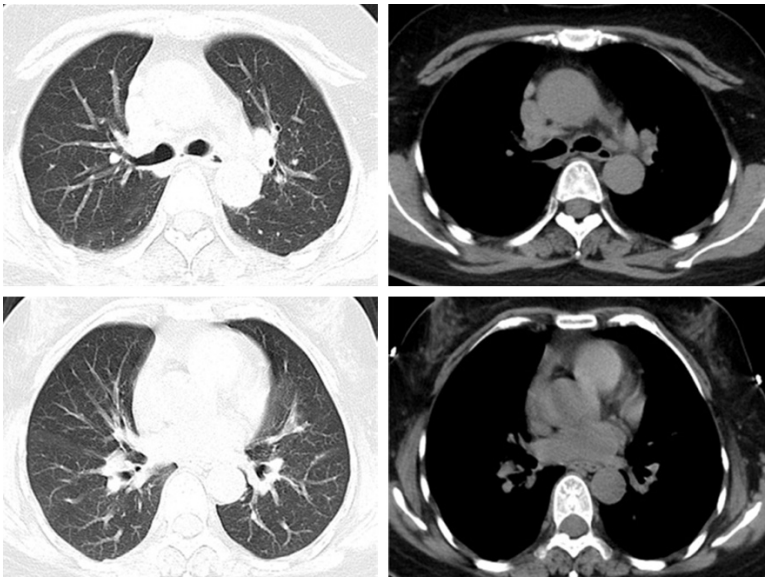

Figure 12. The CT shows the swollen mediastinal lymph nodes shrink obviously after 2 month of glucocorticoid.

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

This work was supported by the funds from the National Development and Reform Commission of Jilin Province (2016C043-3); and the Science and Technology Agency of Jilin Province (201603034YY) to Ke Wang.

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 aburdensome 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.

Address correspondence to: Ke Wang, Department of Respiratory Medicine, The Second Hospital of Jilin University, 218 Ziqiang Street, Nanguan District, Changchun130041, Jilin Province, China. Tel: +86-18643111766; Fax: +86-431-88796820; E-mail: kewangm1@hotmail.com; wke@jlu.edu.cn

References

[1] Mandal SK, Ghosh S, Mondal SS and Chatterjee S. Coexistence of pulmonary tuberculosis and sarcoidosis: a diagnostic dilemma. BMJ Case Rep 2014; 2014:

[2] Carbonelli C, Giuffreda E, Palmiotti A, Loizzi D, Lococo F, Carpagnano E, Lacedonia D, Sollitto F and Foschino MP. Coexistent sarcoidosis and tuberculosis: a case report. Respiration 2017; 93: 296-300.

[3] Mise K, Goic-Barisic I, Puizina-Ivic N, Barisic I, Tonkic M and Peric I. A rare case of pulmonary tuberculosis with simultaneous pulmonary and skin sarcoidosis: a case report. Cases J 2010; 3: 24.

[4] Piotrowski WJ, Gorski P, Duda-Szymanska J and Kwiatkowska S. Mycobacterium tuberculosis as a sarcoid factor? A case report of family sarcoidosis. Am J Case Rep 2014; 15: 216-220.

[5] Wong CF, Yew WW, Wong PC and Lee J. A case of concomitant tuberculosis and sarcoidosis with mycobacterial DNA present in the sarcoid lesion. Chest 1998; 114: 626-629.

[6] Oluboyo PO, Awotedu AA and Banach L. Concomitant sarcoidosis in a patient with tubercu-

losis: first report of association in Africa. Cent Afr J Med 2005; 51: 123-125.
[7] Babu K. Sarcoidosis in tuberculosis-endemic regions: India. J Ophthalmic Inflamm Infect 2013; 3: 53.
[8] Saboor SA, Johnson NM and McFadden J. Detection of mycobacterial DNA in sarcoidosis and tuberculosis with polymerase chain reaction. Lancet 1992; 339: 1012-1015.
[9] Brownell I, Ramirez-Valle F, Sanchez M and Prystowsky S. Evidence for mycobacteria in sarcoidosis. Am J Respir Cell Mol Biol 2011; 45: 899-905.
[10] Shah JR, Hede J and Mathur RS. Diagnostic criteria of tuberculous sarcoidosis. Lung India 2009; 26: 86-88.
[11] Costabel U and Hunninghake GW. ATS/ERS/WASOG statement on sarcoidosis. Sarcoidosis statement committee. American thoracic society. European respiratory society. world association for sarcoidosis and other granulomatous disorders. Eur Respir J 1999; 14: 735-737.
[12] Cosma CL, Humbert O and Ramakrishnan L. Superinfecting mycobacteria home to established tuberculous granulomas. Nat Immunol 2004; 5: 828-835.
[13] Gupta BK, Bharat V and Bandyopadhyay D. Role of adenosine deaminase estimation in differentiation of tuberculous and non-tuberculous exudative pleural effusions. J Clin Med Res 2010; 2: 79-84.
[14] Soskel NT and Sharma OP. Pleural involvement in sarcoidosis. Curr Opin Pulm Med 2000; 6: 455-468.
[15] Navaneethan SD, Venkatesh S, Shrivastava R, Mehta J and Israel R. Recurrent pleural and pericardial effusions due to sarcoidosis. PLoS Med 2005; 2: e63.
[16] Aguiar LM, Antonangelo L, Vargas FS, Zerbini MC, Sales MM, Uip DE and Saldiva PH. Malignant and tuberculous pleural effusions: immunophenotypic cellular characterization. Clinics (Sao Paulo) 2008; 63: 637-644.
[17] Kumagai T, Tomita Y, Inoue T, Uchida J, Nishino K and Imamura F. Pleural sarcoidosis diagnosed on the basis of an increased CD4/CD8 lymphocyte ratio in pleural effusion fluid: a case report. J Med Case Rep 2015; 9: 170.