Tuberculous pericarditis mimicking multiple tumors in pericardial effusion

Caie Li¹,* , Qiming Zhao²,* , Xiangyang Wu³ and Jing Yu⁴

Abstract
Tuberculosis is still the leading cause of pericardial disease in developing nations. A definite diagnosis of tuberculosis is usually relatively difficult, especially when its manifestations are not typical. We report a 19-year-old man who presented with chest obstruction, shortness of breath, edema of the lower extremities, and mild fever for 14 days. The manifestations of tuberculosis pneumonia were not typical, except for a small high-density shadow in the left upper lung field near the pleura, with a small amount of pleural effusion on chest computed tomography. The tuberculin skin test, acid-fast stain of sputum and pericardial effusion, and bacterial culture showed negative results. Echocardiography showed three free-floating irregular masses in a large amount of pericardial effusion. The masses and exudates were removed by pericardiectomy. The masses were composed of hyperplastic granulation tissue and dead tissue without a normal architecture, mixed with numerous caseous substances, which confirmed the diagnosis of tuberculous pericarditis. This is a unique report of a patient who presented with tuberculous pericarditis with multiple solid masses in a large amount of pericardial effusion, without typical clinical manifestations of tuberculosis.

Keywords
Tuberculosis, cardiac tamponade, pericarditis, pneumonia, caseous granuloma, fever

Date received: 28 September 2018; accepted: 7 February 2019

¹Lanzhou University Second Hospital, Lanzhou, Gansu, China
²Department of Cardiac Surgery ICU, Lanzhou University Second Hospital, Lanzhou, Gansu, China
³Second Department of Cardiac Surgery, Lanzhou University Second Hospital, Lanzhou, Gansu, China
⁴Department of Cardiology, Lanzhou University Second Hospital, Lanzhou, Gansu, China

*These authors contributed equally to this work

Corresponding author:
Jing Yu, Department of Cardiology, Lanzhou University Second Hospital, No. 82 Cuiyingmen Street, Lanzhou 730030, Gansu, China.
Email: yujing2304@126.com

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (http://www.creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).
Introduction

Although tuberculous pericarditis is relatively rare in developed countries, it is still one of the most important causes of pericarditis in developing countries in which tuberculosis remains a major public health problem. We report an unusual case of tuberculous pericarditis in a patient who presented with multiple tumors in pericardial effusion, which were finally proven to be caseous granuloma.

Case report

A 19-year-old man presented to our hospital with chest obstruction, shortness of breath, edema of the lower extremities, and mild fever since 14 days previously. He seldom coughed, and had no sputum or night sweat. The patient had no history of pulmonary tuberculosis or a history of close contact with patients with tuberculosis. On a physical examination, he was well-nourished and was mildly febrile (38.2°C). He had a regular heart rate of 110 beats/minute, respiratory rate of 20 breaths/minute, and blood pressure of 105/65 mmHg, together with slight edema of the lower extremities. A chest exam had no positive findings. On auscultation, heart sounds were low with no murmur. A blood test on admission showed high white cell counts (12.5 × 10^9/L) with a high neutrophil percentage (81%), and a high C reactive protein level (121.81 mg/L) and erythrocyte sedimentation rate (75 mm/hour). A chest computed tomographic (CT) scan showed a small high-density shadow in the left upper lung field near the pleura, a small amount of pleural effusion, and a large amount of pericardial effusion (Figure 1). A cardiac magnetic resonance imaging examination found similar results as the CT scan. Echocardiography showed three free floating irregular masses in a large amount of pericardial effusion (Figure 2).

The tuberculin skin test, sputum culture, T cell spot test, and detection of tumor markers, including alpha-fetoprotein, carcinoembryonic antigen, epithelial membrane antigen, neuron-specific enolase, and cytokeratin 19 (CY211), were negative. We performed pericardiocentesis under the suspicion of pericarditis with cardiac tamponade. The fluid was clear and yellowish in appearance. A cytological examination, gram stain, acid-fast stain, and bacterial and fungal cultures yielded negative results. Fever persisted, despite the use of antibiotics (cefoperazone-sulbactam), and...
symptoms of cardiac tamponade were aggravated, with a rapid heart rate, paradoxical pulse, and jugular venous distention. The irregular masses with pericardial effusion persisted under echocardiography (Figure 3). We then performed pericardiectomy for the patient, and removed pericardial effusion and several masses. The yellowish irregular masses were soft and fragile. The largest mass (Figure 4) was then submitted for a histological examination. A microscopic

**Figure 2.** Echocardiographic finding on admission. Free-floating irregular masses in a large amount of pericardial effusion can be seen.

**Figure 3.** Echocardiographic finding before pericardiectomy. Irregular masses with pericardial effusion persisted.
examination showed that the masses were composed of hyperplastic granulation tissue and dead tissue without normal architecture, mixed with numerous caseous substances (Figure 5). These characteristics suggested tuberculosis, although acid-fast bacteria were not isolated from the specimen, even after culture. Tuberculous pericarditis was finally verified, and anti-tuberculous meditation with isoniazid, rifampicin, pyrazinamide, and ethambutol was then started. The fever subsided soon after treatment. The C-reactive protein level and erythrocyte sedimentation gradually returned to normal. The patient was discharged 2 weeks after surgery.

This research was in accordance with ethical principles for medical research.

Figure 4. One of the masses in the pericardial space. The tissue is yellowish, soft, and fragile.

Figure 5. Microscopic finding. Hyperplastic granulation tissue and dead tissue without a normal architecture, mixed with numerous caseous substances.
involving human subjects outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Lanzhou University Second Hospital (approval number: 2018A-008). Informed consent to report this case was obtained from the patient.

**Discussion**

In this report, we describe a case of tuberculous pericarditis that mimicked multiple tumors in pericardial effusion. We could not determine the reason for formation of the rare solid masses in the pericardial cavity in our patient. We assume that this specific phenomenon is mainly due to the relatively strong immunity of young people. Our patient was 19 years old, well-nourished, and had no obvious weight loss. Therefore, in the early exudative stage of tuberculous pericarditis, there was likely to be a large number of neutrophils, T cells, and macrophages, and fibroblasts engulfed the tubercle bacilli to form a granuloma, along with exudation of red blood cells, and fibrinous and collagenous substances. We also hypothesize that the granuloma was enlarged in size at this stage. Furthermore, the initial granuloma might have had a loose organization, gradually solidified, and appeared as a semi-disc shape with cardiac movement, which repeatedly compressed the space between the visceral and parietal pericardium. This hypothesis is supported by the fact that in human immunodeficiency virus-infected patients with tuberculous pericarditis, the rate of formation of a granuloma either systematically or within the pericardium is much less than that in those without human immunodeficiency virus infection. A relatively strong immunity may also be one of the main reasons for the lack of typical clinical manifestations of tuberculous pneumonia in our patient. Interestingly, most of the similar cases that were reported previously were teenagers or school age children, whose immunity is relatively strong.

Tuberculous pericarditis presents clinically in three forms, including pericardial effusion, constrictive pericarditis, and a combination of effusion and constriction. Pathologically, four stages are recognized as follows: i) fibrinous exudation and early-stage granuloma, with abundant mycobacteria, and some macrophages and T cells; ii) serosanguinous effusion and lymphocytic exudate, with emerging monocytes and foam cells; iii) absorption of effusion and formation of caseous granuloma, with fibrosis of the pericardium; and iv) calcification of the pericardium and formation of constrictive scarring. Our case was clinically classified into the pericardial effusion phase and was pathologically classified as between stages 1 and 2. However, our case showed multiple masses floating in a large amount of pericardial effusion, without typical symptoms of pulmonary tuberculosis, which is relatively rare.

A subpleural nodule, persistent mild fever, and poor response to treatment of antibiotics led us to suspect tuberculosis in our patient. However, the diagnosis of tuberculosis infection was difficult because the tuberculin skin test, acid-fast stain, and the T cell spot test failed to confirm our suspicion. Negative results of a bacterial culture also failed to support the diagnosis of tuberculosis. Echocardiography of our patient at admission showed three free-floating irregular masses within a large amount of pericardial effusion. These findings suggested a neoplasm on the pericardium or in the pericardial cavity, such as a metastatic tumor, pericardial mesothelioma, or teratoma. Although a metastatic tumor appeared slightly likely because of the high-density shadow in the lung, the age of the patient and a lack of symptoms of malignant cancer did not support this possibility. With regard to the possibility
of a pericardial mesothelioma or teratoma, we measured tumor markers in blood serum, including alpha-fetoprotein, carcinoembryonic antigen, epithelial membrane antigen, neuron-specific enolase, and cytokeratin 19, which were negative. We even performed a cardiac magnetic resonance imaging examination for the patient, and did not find any more evidence than the CT scan. Although these tests did not support the possibility of a pericardial mesothelioma or teratoma, they could only be excluded by a histological examination.

We also considered the possibility of fibroma, which can also not be confirmed without a histological examination. Because most tests that focus on detecting tubercle bacilli have a poor sensitivity,1 negative results of these tests are insufficient to rule out the possibility of tuberculosis. Furthermore, benign tumors are not necessarily associated with increased tumor markers. Therefore, multiple diagnoses are possible. Because the symptoms of cardiac tamponade became aggravated, we performed pericardiectomy for the patient and removed the masses. The patient’s diagnosis was finally confirmed by pathology, which showed a caseous granuloma mixed with dead tissue in the pericardial floating masses.

Definitive diagnosis of tuberculous pericarditis is based on one of the following criteria: i) tubercle bacilli are found in pericardial effusion, either in a stained smear or after culture; ii) tubercle bacilli or a caseous granuloma is found in a histological examination; and iii) polymerase chain reaction of a specimen from a pericardial biopsy is positive.1,2 Our case was negative for tubercle bacilli on a pericardial biopsy, but there was the presence of caseous granuloma on a microscopic examination, which was adequate to confirm the diagnosis of tuberculosis.

There were at least four similar, but different, cases of tuberculous pericarditis reported in Africa and Asian, all of which were pediatric cases. One case from Taipei was a 10-month-old girl whose echocardiography showed a solid mass that originated from thickened pericardium, which compressed the whole heart.6 Echocardiography of a 14-year-old Korean boy showed free-floating, multiple, round, discoid masses in a large amount of pericardial effusion.3 A 16-year-old African boy was hospitalized for signs of cardiac tamponade with a 30-mm circumferential echogenic “porridge-like” pericardial effusion with signs of cardiac tamponade in echocardiography.4 Echocardiography of an 8-year-old Indian boy showed an intrapericardial mass that compressed the right atrium and superior vena cava.5 In all of these cases, symptoms and signs were improved by pericardiectomy. Our case is similar with the second reported case,3 but the typical clinical manifestation of tuberculous pneumonia was absent in our case, which made the differential diagnosis difficult. The porridge-like effusion in the third case4 may be similar to the previous state of solid masses found in our case and other cases.

We present a unique report of a patient who presented with tuberculous pericarditis with multiple solid masses in a large amount of pericardial effusion, without typical clinical manifestations of tuberculosis. The unusual presentation of tuberculous pericarditis can help clinicians to differentiate pericarditis from a pericardial tumor.

Acknowledgments
We thank Wensheng Chen and Yalin Wei for the assistance provided during treatment of the patients.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.
Funding
This research was supported by Cuiying Graduate Supervisor Applicant Training Program of Lanzhou University Second Hospital (for Qiming Zhao).

ORCID iD
Caie Li http://orcid.org/0000-0001-6268-3327

References
1. Mayosi BM, Burgess LJ and Doubell AF. Tuberculous pericarditis. Circulation 2005; 112: 3608–3616.
2. Ntsekhe M and Mayosi BM. Tuberculous pericarditis with and without HIV. Heart Fail Rev 2013; 18: 367–373.
3. Yoon SA, Hahn YS, Hong JM, et al. Tuberculous pericarditis presenting as multiple free floating masses in pericardial effusion. J Korean Med Sci 2012; 27: 325–328.
4. Massoure PL, Bonnaert G, Caumes JL, et al. Porridge-like tuberculous cardiac tamponade: treatment difficulties in the Horn of Africa. Gen Thorac Cardiovasc Surg 2010; 58: 276–278.
5. Garg A, Rajamouli DS, Eknath JU, et al. Tuberculous pseudo-tumor of the pericardium: a case report. Indian J Thorac Cardiovasc Surg 2013; 29: 262–264.
6. Lin JH, Chen SJ, Wu MH, et al. Fibrinofibrous pericarditis mimicking a pericardial tumor. J Formos Med Assoc 2000; 99: 59–61.