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CASE REPORT

Challenges in the Diagnosis of Hematogenous Disseminated Pulmonary Tuberculosis with Multiple Organ Involvement

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SUMMARY

Background: **Tuberculosis is a public health problem worldwide, and China is a high-burden country. Hematogenous disseminated pulmonary tuberculosis is one of the most serious forms of tuberculosis, and diagnosing hematogenous pulmonary tuberculosis is a challenge, even for the most experienced clinicians, who may also feel perplexed. We report a case of hematogenous disseminated tuberculosis involving multiple organs that was initially misdiagnosed as metastatic malignancy. The diagnosis was finally confirmed by metagenomic Next-Generation Sequencing (m-NGS) of peritoneal and pericardial effusions, which detected Mycobacterium tuberculosis complex.**

Methods: **Appropriate laboratory tests, m-NGS, Chest and abdominal CT, Pericardiocentesis, and Peritoneal puncture.**

Results: **Chest and abdominal CT showed diffuse nodules in both lungs, pericardial effusion, bilateral pleural effusion, and abdominal pelvic effusion. Tuberculosis bacillus antibody was negative, erythrocyte sedimentation rate increased to 42 mm/H, and the carcinoembryonic antigen (CEA) increased to 7.1 ng/mL, peritoneal effusion adenosine deaminase increased to 65.17 U/L, pericardial effusion adenosine deaminase increased to 142.39 U/L. m-NGS of pericardial effusion and peritoneal effusion detected 886,963 M. tuberculosis complex.**

Conclusions: **Miliary tuberculosis is a severe and rare form of tuberculosis. Delayed diagnosis may be the most important factor leading to death from miliary tuberculosis. We report a case where Mycobacterium tuberculosis was identified through mNGS of pericardial and peritoneal effusions, enabling rapid diagnosis of disseminated tuberculosis. This case provides a new approach for the rapid diagnosis of disseminated tuberculosis.**

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KEYWORDS

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CASE REPORT

In this article, we report a case of a 50-year-old male. A month ago, he experienced loss of appetite and fatigue. Therefore, he went to the gastroenterology outpatient department for a gastroscopy. The result showed no obvious abnormalities in his stomach. Chest CT scan indicated multiple tiny nodules in both lungs. Due to their small size, these nodules did not draw the attention of the doctor or the patient. After returning home, the patient's symptoms did not improve and gradually developed abdominal distension and breathing difficulties. Three days ago, he returned to the gastroenterology department for hospitalization for treatment. The physical examination revealed an enlarged abdomen, and positive mobile dullness in the abdomen indicates the presence of fluid. The chest and abdominal CT scans showed diffuse nodules in both lungs, with the nodules having increased in size compared to before. There was a small amount of pleural effusion on both sides, as well as a large amount of pericardial effusion and abdominal and pelvic effusion (Figure 1A - F). The blood routine test indicated that the white blood cell count had risen to 11.2 x 10^9/L (normal range: 3.5 - 9.5 x 10^9/L), and the erythrocyte sedimentation rate had increased to 42 mm/H (normal range: less than 15 mm/H). The tuberculosis antibody test was negative, and the carcinoembryonic antigen (CEA) increased to 7.1 ng/mL (normal range: less than 5.0 ng/mL). The initial impression was lung cancer with multiple organ metastasis. Therefore, this patient was transferred from the gastroenterology department to the respiratory department for continued treatment. To alleviate the symptoms of cardiac tamponade and to clarify the nature of pericardial effusion and peritoneal effusion, we successively performed pericardiocentesis and peritoneal puncture for drainage. The results indicated that it was exudative effusion. The adenosine deaminase (ADA) level in pericardial effusion increased to 142.39 U/L (normal range: 3 - 22 U/L) and that in peritoneal effusion increased to 65.17 U/L (normal range: 3 - 22 U/L). The cytological examination of exfoliated cells from pericardial and peritoneal effusions did not reveal any tumor cells. At this point, we strongly suspected hematogenous disseminated pulmonary tuberculosis. In order to make a definitive diagnosis as soon as possible, we sent for the metagenomic next-generation sequencing (m-NGS) of pericardial effusion and peritoneal effusion. The next day, the results showed that 886,963 Mycobacterium tuberculosis complex were detected, confirming our diagnosis. Then this patient began a standardized anti-tuberculosis treatment and is still under follow-up.

DISCUSSION

Miliary tuberculosis is a severe and rare form of tuberculosis. It is the result of the extensive lymphatic dissemination of Mycobacterium tuberculosis bacteria. Its characteristic is the obvious microscopic nodules in gross pathology, which are similar in size and appearance to millet seeds, and the imaging manifestations are uniform in size, density and distribution [1,2]. The typical case of miliary disease may evolve over time [3]. This patient's chest CT scan one month ago showed ill-defined, less than 2 mm diameter atypical miliary nodules. In further examinations and diagnoses, a repeat chest CT scan revealed the classic miliary pattern. Therefore, it emphasizes the importance of regular repeat chest imaging examinations for patients suspected of having miliary tuberculosis. Miliary tuberculosis and metastatic cancer may be difficult to distinguish from each other, as both can present with similar multisystem symptoms and signs, many of which are not specific to cancer or chronic infections, such as progressive muscle atrophy, weight loss, night sweats and fever [4,5]. For this case, our lesson is that an elevated carcinoembryonic antigen is not a specific indicator of cancer, and a negative tuberculosis antibody test cannot rule out a tuberculosis diagnosis. In the differential diagnosis of bilateral pulmonary nodules mimicking metastasis, pulmonary tuberculosis should be considered. When miliary tuberculosis spreads throughout the body through blood or lymphatic fluid, it is called disseminated tuberculosis. Among them, peritoneal tuberculosis is a latent disease with subacute manifestations. If there is no suspicion, it may be difficult to diagnose. By aspirating the peritoneal fluid and then conducting microbiological examination, acid-fast bacilli (AFB) staining, and culture are usually carried out as a step in diagnosing peritoneal tuberculosis. It is well known that AFB staining and culture are not sensitive in identifying organisms [6, 7]. It has been reported that the sensitivity of staining is 3% and that of culture is 35%. Moreover, Mycobacterium tuberculosis needs to grow on traditional culture media for 4 to 8 weeks, resulting in further delay in diagnosis [8]. The definite diagnosis of tuberculous pericarditis also requires isolating Mycobacterium tuberculosis from pericardial effusion [9,10]. Elevated levels of ADA and interferon-γ in peritoneal fluid, pleural effusion, and pericardial effusion are helpful for diagnosing miliary tuberculosis [11-12]. By conducting mNGS testing on the serous cavity effusion, we were able to achieve a rapid diagnosis of hematogenous disseminated pulmonary tuberculosis.

CONCLUSION

Patients with miliary tuberculosis must receive standard anti-tuberculosis treatment promptly. Delayed diagnosis and thus delayed initiation of specific anti-tuberculosis treatment seem to be the most important factor contributing to the mortality of miliary tuberculosis. We report a case of disseminated pulmonary tuberculosis with multiple organ involvement, which was initially misdiagnosed as metastatic malignant tumor. Eventually, the tuberculosis complex was detected through m-NGS of

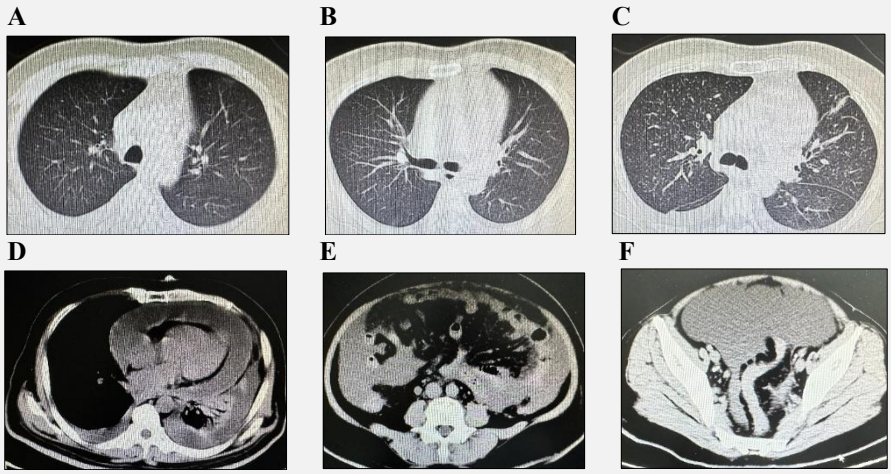

Figure 1. Chest and abdominal CT scans showed diffuse nodules in both lungs, a small amount of pleural effusion on both sides, a large amount of pericardial effusion, and abdominal and pelvic effusion (Figure 1A - F).

peritoneal and pericardial effusions, leading to a rapid and accurate diagnosis and shortening the diagnosis time to 24 hours. This provides a new idea for the rapid diagnosis of disseminated tuberculosis and reduces the need for more invasive examinations for patients, such as thoracoscopy, laparoscopy, bronchoscopy, etc. For patients with diffuse nodules in both lungs combined with multiple serous cavity effusions, we must consider the disease of disseminated pulmonary tuberculosis.

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Ethical Approval:
This study was approved by the ethics committee of the First Affiliated Hospital of Chongqing Medical and Pharmaceutical College. All procedures performed in the studies were in accordance with ethical standards. Informed consent was obtained from all individual participants included in this study.

Declaration of Interest:
No conflicts of interest.

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