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CASE REPORT

A Case of Multi-Organ Tuberculosis Misdiagnosed as Lung Cancer and a Literature Review

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Background: Tuberculosis (TB) is a very common and easily diagnosed as a malignancy. However, studies have described the difference between TB and lung cancer. Single-organ TB and lung cancer are often easily distinguished clinically. Atypical systemic hematogenous disseminated TB (HDTB) is uncommon, including rare cases involving multiple organs such as cervical lymph nodes, pleura, liver, and lung TB simultaneously, which are more confusing and easily misdiagnosed in clinical practice.

Case Presentation: A HIV-negative 56-year-old male was hospitalized for chest disease with main symptoms of chest tightness, chest pain, fatigue, anorexia, and weight loss. Heart rate 109 times/min, the computed tomography (CT) scans of the neck, chest, and abdomen revealed multiple nodules in the right pleura, right pleural encapsulated effusion, and limited, incomplete expansion of the middle and lower lobes of the right lung, enlarged lymph nodes in the right hilar and mediastinal and diaphragm groups, and multiple slightly low-density nodules in the liver, bone destruction in the 2nd thoracic vertebra, raising the possibility of multiple liver metastases of right lung cancer and malignant pleural fluid. The lymph nodes in the neck, mediastinum, abdomen, and pelvis were enlarged bilaterally. After comprehensive analysis, the patient was diagnosed with atypical systemic HDTB. After three months of conventional anti-TB treatment, the patient refused our hospital follow-up, and his symptoms improved significantly during the telephone follow-up.

Conclusion: Most previous TB misdiagnoses involved a single organ, and this case enriches the clinical experience of diagnosing atypical HDTB. We encourage clinicians to establish a dynamic diagnostic and therapeutic mindset, emphasizing the value of biopsy and pathology.

Keywords: tuberculosis, hepatic tuberculosis, pulmonary dysplasia, lung cancer, pathological diagnosis

Introduction

Tuberculosis (TB) is a common respiratory infection caused by *Mycobacterium tuberculosis* (MTB). According to the World Health Organization's global TB report, 9.87 million new cases of TB will occur worldwide in 2020. China has the second highest incidence and death rate of TB among infectious diseases and is one of 30 countries with a high TB burden.[1] TB affects middle-aged and older people with poor hygiene, poor nutritional status, and low immune function, posing a severe threat to patients' life and health.

With the rapid development of imaging and biotechnology, the number of middle-aged and elderly TB patients has increased substantially; newer detection and diagnostic techniques have provided more opportunities to detect atypical TB cases. Early detection, diagnosis, and treatment of TB patients is one of the key factors in halting the epidemic. The sputum smear antacid staining method—commonly used in clinical practice—is simple and economical, but false negatives and poor results are expected. The sputum or pleural fluid culture test takes 4–8 weeks to obtain results, which is not conducive to early diagnosis and treatment of TB and can easily lead to widespread transmission.[2] Some medical diagnostic techniques for TB have been developed: the peripheral blood T-cell spot test for TB infection, serum TB antibody (TB-Ab), and real-time fluorescence nucleic acid-fast bacilli thermostatic amplification detection technology. Quantitative diagnostic techniques, such as simultaneous amplification and testing (SAT) and histopathological

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examination, are crucial in diagnosing pulmonary TB (PTB) based on molecular and immunologic techniques.[3,4] The common TB foci occur in the apical part of the lung. With the increasing rate of TB, TB foci are also found in non-good sites, validated using atypical imaging X-rays and spiral CT images. Furthermore, the clinical symptoms and morbidity characteristics of lung cancer and TB are very similar[5] and often misdiagnosed. The main methods of differential diagnosis between lung cancer and TB patients in clinical practice are puncture biopsy and imaging. Another study[6] reported that guanylate binding protein 1 (GBP1) could be an essential marker to differentiate lung cancer from TB patients. Myxovirus 1 (MX1), interferon-stimulated Gene 15 (ISG15), interferon induced with helicase C domain 1 (IFIH1), Oligoadenylate Synthetase Like Protein (OASL), interferon-induced protein with tetratricopeptide repeats 3 (IFIT3), interferon-inducible-protein 44 (IFI44) and interferon-induced protein with tetratricopetide repeats 1 (IFIT1) are interferon (IFN)-responsive gene targets with the potential to differentiate TB from lung cancer. Machine learning combined with bioinformatics methods has been increasingly used in disease diagnosis research with high accuracy. Recent studies[7] have demonstrated that colorectal cancer diagnostic models can be established through gene expression databases, and some studies have explored the use of machine learning algorithms combined with bioinformatics methods to establish early differential diagnostic models between lung cancer and TB. With the continuous development of ultrasound interventional technology, ultrasound-guided percutaneous needle lung biopsy (PNCB) helps guide clinical diagnosis and is gradually becoming one of the necessary methods to clarify the pathological nature of organ lesions under current non-surgical conditions, which has the advantages of wide adaptability, convenient operation, low trauma, low cost, and high accuracy. Multiple diagnostic techniques will compete with and complement each other in the future.

However, it is rare for PTB to spread to multiple organs with atypical clinical symptoms. The present report details a case of disseminated TB involving the lungs, lymph node, liver, and pleura admitted to our hospital to prevent missed diagnosis and misdiagnosis.

Case Information

A 56-year-old male patient was admitted to our hospital on 2022-09-19 with "chest tightness and chest pain for more than 2 months, aggravated for 20 days", The patient have mild cough and expectoration, and had a weight loss of 10 kilogram (KG) in the past 2 months. The patient had a history of afternoon low fever before 1 week and the Physical examination revealed body temperature 36.5 °C, respiratory rate 25/min, pulse rate 96 beats/min, oxygen saturation 93%, 24-hour urine output about 600 mL, Performance status (PS) 3 points, he had a clear consciousness, poor mental health, anemia, enlarged superficial lymph nodes, barrel-shaped chest, swollen skin on the right side of the chest and the right side of the upper abdomen, solid percussion sounds on the right side of the chest with mixed turbid sounds, enlarged liver on the right side, no edema in the extremities, and deep yellow urine. Past medical history: mitral valvuloplasty and aortic valve replacement for mitral valve and aortic valve insufficiency at the Second Affiliated Hospital of Nanchang University under general anesthesia on 2021-08-11, long-term oral treatment with warfarin anticoagulation and metoprolol. Personal history: smoker for 40 years, 10 cigarettes per day, and no alcoholic habits, have no history of contact with a chronically coughing person suspected of or treated for TB.

Admission biochemical examination: neuronal enolase 35.97 ng/mL, fibrin degradation products 10.86 mg/L, prothrombin time 141.2 seconds, prothrombin normalized ratio 11.87 INR, activated partial thromboplastin time 121.7 seconds, fibrinogen 4.72 g/L, leukocytes 11.94×10^9/L, hemoglobin 36 g/L, albumin 22.3 g/L, white/sphere 0.5, glutamate transaminase 114 IU/L, glutathione transaminase 288 IU/L, glutamyl transferase 92 IU/L, lactate dehydrogenase 492 IU/L, coagulation factor VIII activity 239.2%, coagulation factor IX activity 10.1%, coagulation factor XII activity 34.4%, Procalcitonin (PCT) 0.43 ng/mL, ultrasensitive C-reactive protein (gold standard) 124.00 mg/L, TSPOT negative, sputum negative for antacid bacilli, anti-TB antibody Weakly positive, fecal occult blood negative, EBV test was negative, and HIV was negative. The CT examination report (Figures 1a–i): multiple wall nodules in the right pleura, right pleural encapsulated effusion with limited swelling insufficiency in the middle and lower lobes of the right lung, enlarged lymph nodes in the right hilar and mediastinal diaphragm groups, bone destruction in the 2nd thoracic vertebra, multiple slightly hypodense nodules in the liver. The possibility of multiple metastases of right lung cancer with malignant pleural fluid and possible infection in the upper lobes of both lungs was considered. Finally, a Ultrasonic guided needle biopsy of the lymph node, pleural, liver was performed and the histopathology showed coagulative necrosis combining with

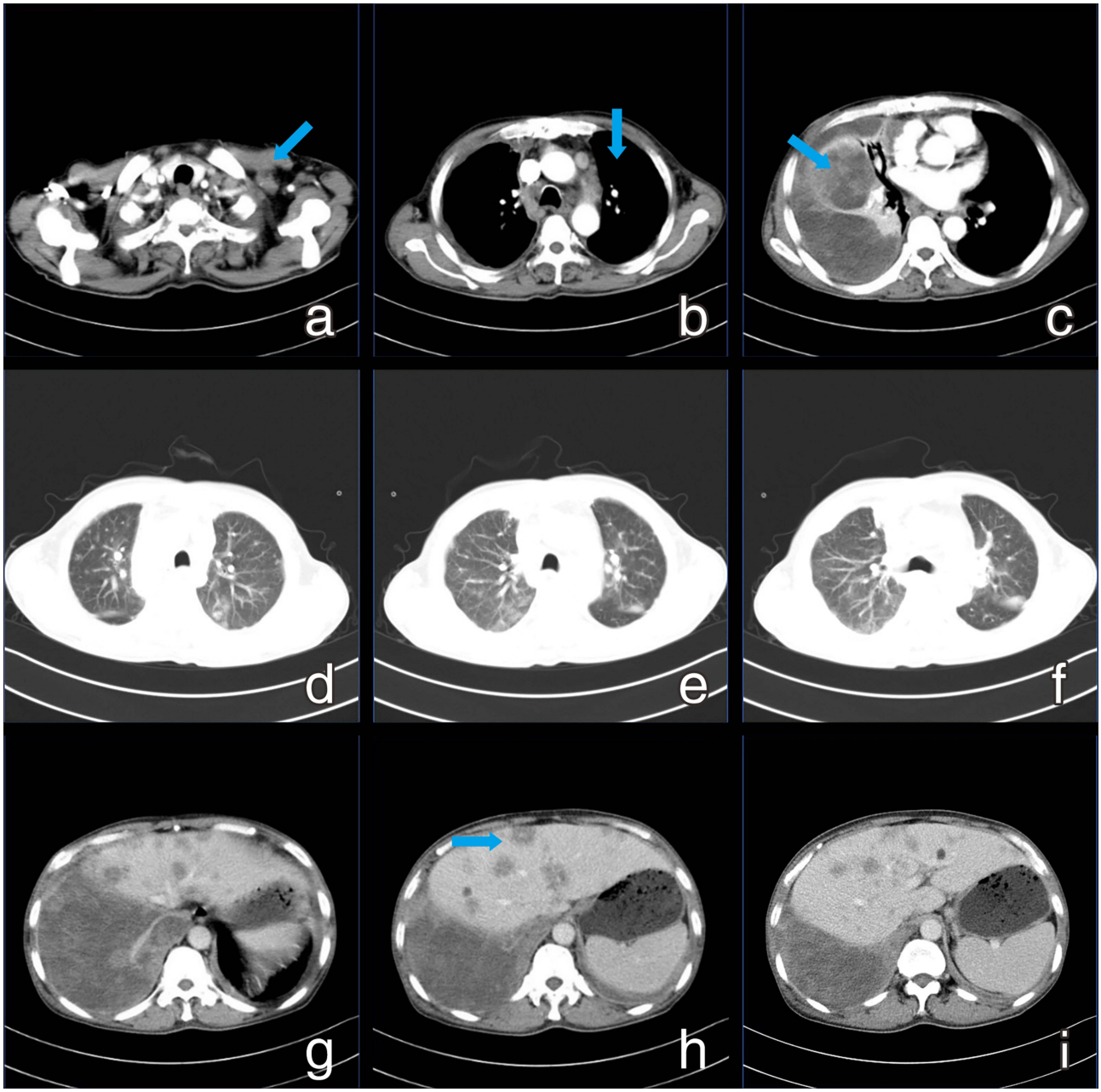

Figure 1 (**a**) enlarged supraclavicular lymph nodes (blue arrows); (**b**) enlarged lymph nodes in the hilar and mediastinal diaphragm groups (blue arrows); (**c**) Multiple wall nodules in the right pleura and right pleural encapsulated effusion, right pleural encapsulated effusion and restrictive expansion insufficiency in the middle and lower lobes of the right lung (blue arrows); (**d–f**) multiple nodules in both lungs with infection; (**g–i**) multiple slightly hypodense nodules in the liver (blue arrows).

granulomatous inflammation (Figure 2a–d) (acid-fast bacilli staining was positive). Research shows Tuberculosis (TB) in humans is characterized by formation of immune-rich granulomas in infected tissues,[8] And confirmative diagnosis is based on liver biopsy where demonstration of acid-fast bacilli on acid-fast bacilli staining and caseous necrosis is a very useful histopathological sign.[9] Thus, the diag-nosis of TB infection was definite.

Clinical Considerations and Diagnostic and Treatment Measures

The patient was admitted to our hospital with chest tightness, right-sided chest pain, and generalized weakness. The preliminary clinical diagnosis considered extensive metastasis of right lung cancer including liver metastasis, pleural metastasis with malignant pleural effusion. After discontinuing the oral anticoagulant warfarin for 5–7 days, the

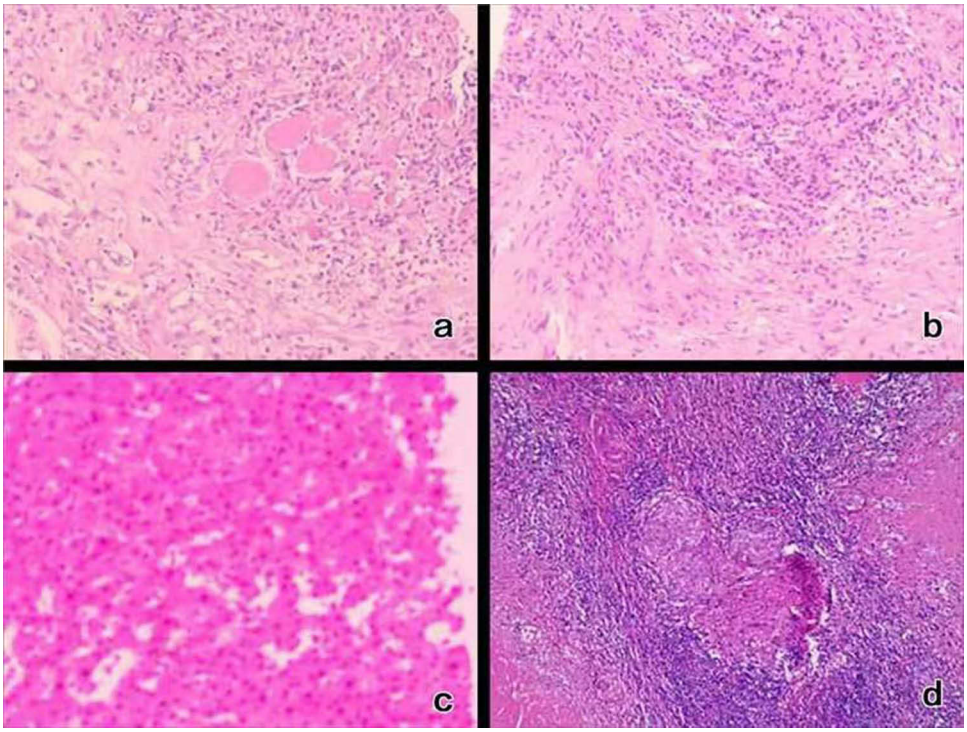

Figure 2 Pathological findings:((**a**) supraclavicular lymph node biopsy; (**b**) pleural biopsy) granulomatous inflammation; (**c**) (liver biopsy) necrotizing granulomatous inflammation (acid-fast bacilli staining was positive); (**d**) cervical lymph node excisional biopsy: necrotizing granulomatous inflammation, consistent with TB (HES staining ((**a**) ×200. (**b**) ×200. (**c**) ×200. (**d**) ×100)).

coagulation function improved, and ultrasound-guided percutaneous biopsy was selected to obtain biopsies of enlarged lymph nodes in the neck, liver tumor, and pleural tumor. The patient's thorax revealed many solid lung lesions combined with liquefied necrotic lesions and a small amount of pleural effusion, which was unsuitable for thoracentesis drainage to obtain pleural fluid for etiological diagnosis. The patient's serum was weakly positive for anti-TB antibody, negative for TSPOT, and negative for sputum MTB. Because the clinical diagnosis did not match the pathological diagnosis, a biopsy of the enlarged lymph nodes in the neck was suggested after the Multi-DisciplinaryTreatment (MDT) discussion in the hospital multidisciplinary room. The pathological result was consistent with TB, necrotizing granulomatous inflammation. The patient refused to undergo bronchoscopic biopsy and lavage for mycobacteria because of the high risk of bleeding. The histopathology of multiple organ tumors was granulomatous inflammation, consistent with TB. And the nonspecificity of Neuron specific enolase (NSE). The final diagnosis of multiple organ TB was confirmed, and specific drugs included: isoniazid (300 mg /qd), rifampicin capsules (450 mg/ qd), ethambutol hydrochloride (750 mg /qd), and pyrazinamide (500 mg/ Bid). A week later, the patient's chest tightness symptoms have improved, Anti-TB treatment was recommended for about 3–6 months, after which the patient was not admitted to the hospital for follow-up. The patient's symptoms improved substantially after the telephone follow-up for chest tightness and pain.

Discussion

In the present report, cases of PTB secondary to hepatic TB and lymph node TB infection were rare.[10] Because of the special anatomical findings and biological behavior of the liver, the liver is rich in blood flow, and TB bacilli mostly flow from the pathogenic bacilli of pulmonary infection into the liver via the bloodstream, which can easily cause hepatic TB infection; TB foci in the lymphatic system and adjacent organs and tissues can also cause hepatic infection.[11] There is no precise specification for the typology of hepatic TB. Luther et al[12] classified hepatic TB into plasmacytic and parenchymal types, with the latter subdivided into the cornu, tuberculoma, and intrahepatic tuberculous cholangitis types. The different stages of hepatic TB revealed caseous necrosis, liquefied necrosis, and fibrous tissue proliferation and calcification. The imaging of liver TB lacks specificity, so if the diagnosis and treatment are based solely on imaging features and clinical symptoms, it is easy to

misdiagnose liver TB as metastatic liver cancer. However, confirmative diagnosis is based on liver biopsy where demonstration of acid-fast bacilli on antacid staining and caseous necrosis is a very useful histopathological sign; but this may be absent in a majority of patients and can be used to a diagnosis of liver TB.[9]

The relationship between lung cancer and pulmonary tuberculosis is very complicated, and mutual identification is very important. Finally, histopathological findings are gold standard for intestinal tuberculosis (ITB) diagnosis and lung cancer.[13] This paper confirmed the presence of tuberculosis, not lung cancer. The value of positron emission tomography (PET)- CT in evaluating the efficacy of TB treatment, especially extrapulmonary tuberculosis(EPTB), has been widely recognized. Because of its high cost, it cannot be widely used in China. The patient also refused to accept re-examination using PET CT for this reason. Otherwise, the effect of an individualized chemotherapy regimen can be better evaluated through the changes in pathological metabolism. Unfortunately, the patient refused to enter our hospital to review the therapeutic effect, and only communicated through the phone, and the patient informed that the symptoms have improved significantly.

In our case, the pathological findings revealed that the initial diagnosis of liver metastasis from lung cancer was confirmed as multi-organ TB, tuberculosis involving liver, lymph nodes, lung, pleura is called multi-organ TB, a rare case. The relationship between lung cancer and pulmonary tuberculosis is very complicated, and mutual identification is very important, so it is crucial to combine imaging, clinical symptoms, biology, pathological cytology, and other comprehensive analysis and dynamic observation to arrive at a reasonable and accurate etiological diagnosis for lung diseases to avoid misdiagnosis and mistreatment.

Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethical Approval and Consent

The study was approved by the Institutional Research the First Affiliated Hospital of Nanchang Medical College, Nanchang, Ethics Review Committee Protocol No.2023-002 and Consent /assent were obtained from participant or their families/caregiver. Confidentiality was maintained throughout the study.

Informed Consent and Patient Perspective

The patient was satisfied with the medical procedure and the patient agreed with the publication of the article.

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Disclosure

The author declares no competing interests.

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