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CASE REPORT

Initial Misdiagnosis of Lung Cancer due to Elevated Carcinoembryonic Antigen in a Patient with Tuberculosis

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SUMMARY

Background: **Tuberculosis often presents on imaging in the form of a solitary nodule, sometimes accompanied by elevated CEA, which is clinically difficult to differentiate from lung cancer and prone to misdiagnosis.**
Methods: **Lung tissue taken by lung biopsy and sent for NGS and Xpert MTB/RIF finally led to the definitive diagnosis of nodular foci in the upper lobe of the left lung caused by tuberculosis.**
Results: **Enhanced CT of the chest showed nodular foci in the upper lobe of the left lung. Initially the nodules were thought to be malignant, but after a series of tests, were finally confirmed to be tuberculosis.**
Conclusions: **In patients with lung disease, when chest imaging reveals a space-occupying lesion accompanied by an elevated CEA level, a comprehensive analysis of the type of lung disease, the patient's age, and comorbidities should be performed before final diagnosis to avoid misdiagnosis and delay in appropriate treatment.**
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KEYWORDS

tuberculosis, carcinoembryonic antigen, bronchoscopy, Xpert MTB/RIF, next-generation sequencing, pathogenic microbial macro genomes

CASE REPORT

Tuberculosis (TB) is a major public health challenge. The most common form of TB is pulmonary tuberculosis (PTB) [1]. PTB sometimes may exhibit atypical or unusual radiological patterns, leading to a diagnostic quagmire and ultimately to a diagnosis with possible treatment delays. Therefore, when imaging suggests the presence of a space-occupying lesion, the diagnosis should be further confirmed with the help of appropriate laboratory tests.

A 46-year-old middle-aged male with a 40-year history of smoking presented to our respiratory clinic with a nodule in the upper lobe of the left lung found on physical examination 10 days earlier. Five days before admission, PET/CT was performed in other hospitals, suggesting "solid nodules in the upper lingual segment of the upper lobe of the left lung, metabolism increased, consider the possibility of peripheral lung cancer", with

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A

Mycobacterium tuberculosis complex						
Genus			Species			
Latin name	Number of sequences detected	Relative abundance (%)	Chinese name	Latin name	Number of sequences detected	Genomic coverage
Mycobacterium tuberculosis complex	1305	22.27	Mycobacterium tuberculosis	Mycobacterium tuberculosis	71	0.49%

B

Test items	Test method	Test results	Results prompt
Mycobacterium tuberculosis and rifampin resistance testing (Xpert MTB/RIF Assay)			
Nucleic acid detection in Mycobacterium tuberculosis	real-time fluorescence PCR	detection, low concentration	positive
Detection of mutations in rifampin resistance genes	real-time fluorescence PCR	not detected	sensitive

Table 1. High-throughput sequencing report of DNA-pathogenic microorganism nucleic acids.

A - suggestive of positivity, with 71 Mycobacterium tuberculosis detected, Mycobacterium tuberculosis and rifampicin resistance assay.
B - suggestive of positivity of Mycobacterium tuberculosis nucleic acid assay, and non-detection of rifampicin-resistant gene mutation assay.

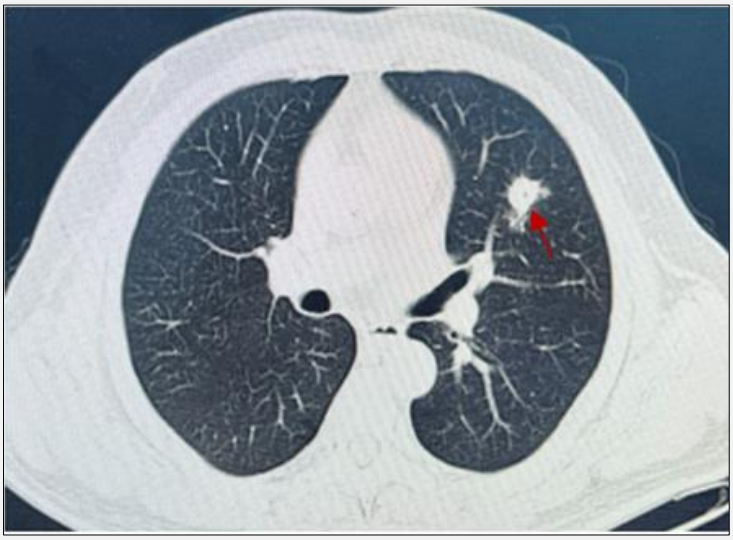

Figure 1. July 4, 2023 Enhanced CT chest suggests 1. nodular foci in the upper lobe of the left lung, with a high likelihood of a neoplastic lesion. 2. multiple nodules in the upper lobe of the right lung, the lower lobe of the right lung, and the upper lobe of the left lung.

occasional cough and sputum, but no fever, fatigue, night sweats, and other symptoms. In order to confirm diagnosis and treatment, he was admitted to the Department of Respiratory Medicine of the hospital on July 03, 2023. Examination results on admission: sputum culture: negative (-); tumor screen suggests carcinoembryonic antigen (CEA) was elevated; enhanced CT of the chest (Figure 1) suggests: 1. nodular foci in the up-

per lobe of the left lung, possibility of a neoplastic lesion, 2. multiple nodules in the upper lobe of the right lung, the lower lobe of the right lung, and the upper lobe of the left lung. Combining the patient's elevated CEA, imaging findings, and the patient's 40-year smoking history, we highly suspected that the patient had lung cancer. Therefore, we performed bronchoalveolar lavage in the lingual lobe of the left lung based on lung CT, and the lavage fluid was sent for pathogenic microorganism macro genome next-generation sequencing (mNGS) to further clarify the nature of the lesion. Radial-endobronchial ultrasound (r-EBUS) did not detect inhomogeneous hypoechoic echoes in the upper lingual lobe of the left lung, and the lavage fluid sent for mNGS still failed to clarify the nature of the left lung nodule. We decided to further perform CT-guided percutaneous lung puncture and remove the lung tissue to send it for relevant pathologic examination. Pathology results were returned: (left lung puncture material) chronic granulomatous inflammation with necrosis, positive mycobacteria were found by special staining, and tuberculosis was considered. In conjunction with the pathologic findings, we further performed histologic mNGS combined with Mycobacterium tuberculosis and rifampicin resistance testing (Xpert MTB/RIF) for antacid staining (+), silver hexamine (-), and PAS (-). Mycobacterium tuberculosis (MTB) was detected by mNGS in the tissue of the left lung puncture material with 71 MTB. The MTB nucleic acid test was positive and the rifampicin resistance gene mutation test was negative (Table 1 A, B). Therefore, the patient was definitively diagnosed with pulmonary tuberculosis Initial treatment Tuberculosis negative (-). The patient's condition improved after a combination of anti-tuberculosis drugs was given.

DISCUSSION

The patient was a middle-aged male in good health with a long history of heavy smoking and no specific occupational or past medical history. A nodule in the upper lobe of the left lung was detected on physical examination in the absence of obvious symptoms and other specific investigations. Based on suggestive chest CT as well as elevated CEA, we presumed the nature of this ill-defined nodule to be malignant. However, after lung puncture biopsy and histologic delivery of puncture material for mNGS combined with XpertMTB/RIF, proliferative tuberculosis due to infection with Mycobacterium tuberculosis was finally confirmed.

The main pathological process of PTB is proliferative lesions, which refer to secondary pulmonary tuberculosis lesions occurring in the lungs with proliferative nodules with clear or blurred borders. Proliferative TB is usually a chronic granulomatous disease caused by infection with MTB [2]. Lung cancer is the most common cancer and the leading cause of cancer-related deaths worldwide. Common signs of both tuberculosis and lung cancer include coughing, coughing up sputum, fever, hemoptysis, weight loss, and shortness of breath [3]. Diagnosis of PTB and lung cancer can be challenging due to similar symptoms and imaging presentations [4]. Imaging of primary tuberculosis is characterized by the concomitant presence of primary intrapulmonary lesions, lymphadenitis, and enlarged hilar and mediastinal lymph nodes, accompanied by homogeneous or circumferential enhancement of the lymph nodes on enhanced CT [5]. Imaging of secondary tuberculosis shows patchy, heterogeneous solid lesions involving the apical, posterior, and upper segments of the lung lobes with ill-defined borders [6]. Currently, lung cancer is mostly detected by imaging in the clinic, and the imaging manifestations of lung cancer are lobulated lung cancer masses with burrs and cuts [7]. According to the site of growth, both primary lung cancer and tuberculosis favor the upper lobes of the lungs. A determination can be made based on the appearance of the nodule. Malignant nodules usually have irregular, lobulated, or acicular margins, whereas benign nodules exhibit smooth, rounded borders and a benign growth pattern [8]. However, there is a significant overlap between nodules with irregular margins in inflammatory/infectious disease and the smooth, rounded margins observed in up to 20% of primary lung cancer nodules [9]. CEA is a nonspecific serum biomarker that is widely used as a marker for lung cancer. However, because CEA is associated with various types of malignant and nonmalignant diseases, elevated serum CEA is not a definitive marker for a specific site of origin of cancer [10]. It has been noted that serum CEA can be higher than normal in patients with PTB, mostly in active tuberculosis [11]. In this case, our judgment of this benign nodule was further misdirected by the fact that the patient's pulmonary nodule occurred in the upper lobe of the lungs, the shape of the nodule foci was indistinctly bordered, and the patient's serum CEA level was elevated.

Diagnosis of PTB relies on chest imaging and etiology; however, it is difficult to confirm the diagnosis by chest imaging alone, and bacteriological examination or tissue biopsy is still needed to detect MTB. The limited specificity of sputum smears and the inability of antacid staining to differentiate Mycobacterium tuberculosis from nontuberculous mycobacteria, as well as the fact that this method of culturing MTB is often time-consuming, make it less than optimal for the diagnosis of PTB [12]. Some studies have shown that mNGS combined with Xpert MTB/RIF plays an important role in the diagnosis and treatment of early PTB [13]. The mNGS technology is a high-throughput sequencing technology, which has the characteristics of fast detection, high accuracy, low cost, wide coverage, and huge output. It has become an important tool for clarifying the presence of MTB infection and its classification [14]. As a rapid, automated molecular testing tool, Xpert MTB/RIF has been reported to be potentially valuable in the diagnosis of PTB. This automated, single-card cassette-based nucleic acid amplification test

detects the presence of tuberculosis infection through the detection of specific gene sequences in the DNA of the MTB, and simultaneously detects resistance-associated genes, with results available within 2 to 3 hours [15]. This feature makes it more efficient and time-effective in detecting TB patients with low bacilli load, for the first time, enabling the diagnosis of TB patients as well as identifying drug-resistant TB patients.

The case was filled with many misleading factors, but after a series of tests, the patient was finally diagnosed with PTB caused by MTB infection. The Xpert MTB/RIF test showed that the patient was more sensitive to rifampicin, which helped us to accurately determine the patient's condition, and make timely decisions to improve the patient's prognosis.

CONCLUSION

The incidence of tuberculosis is increasing, and the disease is highly susceptible to misdiagnosis due to its lack of clinical symptoms and the fact that imaging can also resemble a malignant tumour. This case demonstrates that when imaging suggests that a patient has a large-diameter, ill-defined pulmonary nodule with elevated CEA, the etiology should be actively searched for. When it is difficult to determine the cause of the disease, differential diagnosis should be fully utilized with tests such as NGS and Xpert MTB/RIF, to guide the early diagnosis and treatment and to improve the prognosis.

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Ethical Approval:
This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest.

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