

CASE REPORT

Pulmonary Tuberculosis with Elevated CEA and Positive PET-CT

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SUMMARY

Background: Pulmonary tuberculosis presenting as solitary pulmonary nodules in imaging is sometimes difficult to differentiate from lung cancer and is more likely to be misdiagnosed when accompanied by elevated CEA and positive PET-CT findings.

Methods: By reporting a case of misdiagnosed lung cancer, which was confirmed to be pulmonary tuberculosis by lung biopsy, a joint literature analysis was performed to raise clinicians' awareness of isolated nodules in the lung.

Results: With a series of ancillary tests, we initially considered the nodule to be malignant, and the lung biopsy pathology eventually confirmed pulmonary tuberculosis.

Conclusions: When chest imaging suggests the presence of malignant features in solitary pulmonary nodules, invasive procedures can be performed appropriately to clarify the nature of the lesion. The diagnosis cannot be made blindly to ensure that no incorrect diagnosis is made nor wrong treatment given.

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KEYWORDS

solitary pulmonary nodule, lung cancer, pulmonary tuberculosis, CEA, PET-CT, lung biopsy, bronchoscopy

CASE REPORT

As the population becomes more health-conscious, lung nodules are increasingly detected in the population. Solitary pulmonary nodule (SPN) usually presents as a well-defined round-like hyperdense shadow less than 3 cm in diameter surrounded by inflated lung tissue without associated pulmonary atelectasis, hilar lymph node enlargement, or pleural effusion [1]. Proliferative pulmonary tuberculosis usually presents as a chronic granulomatous disease caused by Mycobacterium tuberculosis infection. It has long been assumed that proliferative pulmonary tuberculosis is a structure formed to protect the host to suppress infection. Its imaging presentation is most commonly of the nodular type with a focal distribution, which is sometimes difficult to distinguish from malignant nodules [2]. Early identification of benign and malignant pulmonary nodules and early intervention is of great significance for further treatment of pulmonary tuberculosis.

The patient was an elderly male, 63 years old, who had

smoked for 30 years. He was seen in the Department of Neurology of our hospital for headache, and a right upper lobe lung nodule with a diameter of about 1.0 cm was accidentally detected during chest CT (Figure 1A). It was accompanied by multiple mediastinal lymph nodes enlargement, the largest of which was about 1.7 cm in diameter (Figure 1B - C). Physical examination: T: 36.3°C, P: 78 beats/minute, R: 20 beats/minute, Bp: 123/74 mmHg, and no palpable enlargement of superficial lymph nodes. After admission, blood tests showed no significant abnormality, and superficial lymph node ultrasound showed multiple enlarged lymph nodes on the right side of the clavicle, the larger one measuring about 0.95 x 0.71 cm (Figure 2A), and no enlarged lymph nodes on the left side of the clavicle; tumor series suggested elevation of carcinoembryonic antigen (CEA); tuberculosis antibody was negative. PPD test was negative; whole-body bone imaging showed no significant abnormalities; positron emission tomography-computed tomography (PET-CT) was performed outside the hospital, suggesting that the nodule area exhibited increased uptake of ^{18}F -fluorodeoxyglucose (^{18}F -FDG) (no images were available). To further clarify the benign and malignant nature of the nodule, we performed a bronchoscopy under general anesthesia on the 6th day following admission, and, based on the chest CT findings, we found heterogeneous hypointense echoes in zone 7 and zone 4R. We performed endobronchial ultrasound-guided transbronchial needle aspiration in these two zones, respectively. Transbronchial needle aspiration (EBUS-TBNA) was performed in these two areas, and rapid on-site evaluation (ROSE) was performed in area 7, suggesting good sampling and visible nucleated macrophages. Then the tissues were examined pathologically. The results suggested that no tumor component was seen on lymph node biopsy in both regions, and no tumor component was seen on lymph node brush examination in region 4R. However, the possibility of lung cancer could still not be excluded at this time. So, we performed thoracoscopic right upper lung wedge resection and pleural adhesion branding on the 13th day after admission. During the procedure, we palpated the nodule in the apical segment of his right upper lung lobe, which was tough, with clear borders and poor mobility, then the lung nodule was completely resected and sent for intraoperative rapid pathology, which returned chronic granuloma caused by *Mycobacterium tuberculosis* (Figure 3A - C), but the special staining results returned were PAS (-), Hexamine silver staining (-), and antacid stain (-). The patient recovered well after surgery (Figure 4A - B) and was discharged after a total hospital stay of 29 days.

DISCUSSION

This patient was an elderly male, in good physical condition, with a long history of heavy smoking, no underlying disease, and no specific occupational or past med-

ical history. In the absence of symptoms and special tests, abnormal imaging was found incidentally. Based on the imaging findings, we were more inclined to the nature of this irregular nodule as a malignant nodule rather than a benign nodule. Moreover, this patient had an elevated CEA. However, the evidence supporting the nodule as benign was negative, which made us think even more that this pulmonary nodule might be lung cancer, but after invasive manipulation biopsy, this nodule was finally identified as proliferative pulmonary tuberculosis caused by *Mycobacterium tuberculosis*. Tuberculosis can be classified as exudative, proliferative, or caseous necrotic, with the proliferative form usually presenting as a granulomatous lesion. Granulomatous lung diseases are a heterogeneous group of diseases, which are general terms for lung diseases with granulomatous inflammation and granuloma formation as common pathological features [3]. Usually, its etiology can be classified as infectious (e.g., infectious diseases) and non-infectious (e.g., allergic diseases, inorganic dust or foreign body deposits, autoimmune granulomas, etc.) [4]. Once *Mycobacterium tuberculosis* enters the lung parenchyma, it causes a slow inflammatory response through infected macrophages, and then these infected macrophages recruit uninfected macrophages and eventually form granulomas [5]. The pathology of granuloma in this patient could see multinucleated giant cells and epithelioid cells typical of pulmonary tuberculosis. Although special staining did not reveal *Mycobacterium tuberculosis*, in the absence of bacteriological evidence of *Mycobacterium tuberculosis*, we consider the histological diagnosis of granuloma as a definitive diagnosis of pulmonary tuberculosis [6]. As one of the most common malignant tumors in the world, lung cancer is mostly asymptomatic in its early stages, yet most patients in clinical practice only seek medical attention when symptoms appear in late stages, resulting in a low overall survival rate of lung cancer. Early lung cancer screening can usually be achieved by low-dose computed tomography of the chest in people at high risk of lung cancer, but malignant lung nodules are less common than benign lung nodules, and even in people at high risk of lung cancer, the nodules are usually benign [7]. In terms of site of growth, many primary lung cancers are located in the right upper lobe of the lung; however, pulmonary tuberculosis is also commonly seen in the upper lobe of the lung; in terms of appearance, there is significant overlap between the malignant appearance (irregular margins) exhibited in inflammatory/infectious disease and the benign appearance (smooth, rounded margins) exhibited by up to 20% of lung cancer nodules [8]. CEA is a serum glycoprotein that is currently a more widely used marker for lung cancer. However, CEA is not only elevated in serum levels in patients with malignancies but the level of this substance can also be elevated in smokers or certain benign diseases (e.g., pancreatitis, cirrhosis, diabetes, hypothyroidism, etc.) [9]. One study found that CEA serum levels can also be higher than normal in patients with pulmonary tu-

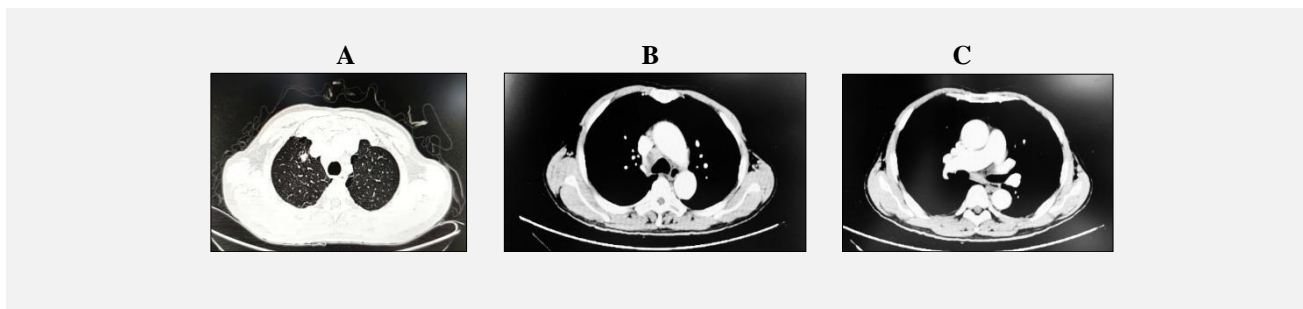


Figure 1. Chest CT showed irregular nodular foci in the upper lobe of the right lung and multiple enlarged lymph nodes in the mediastinum.

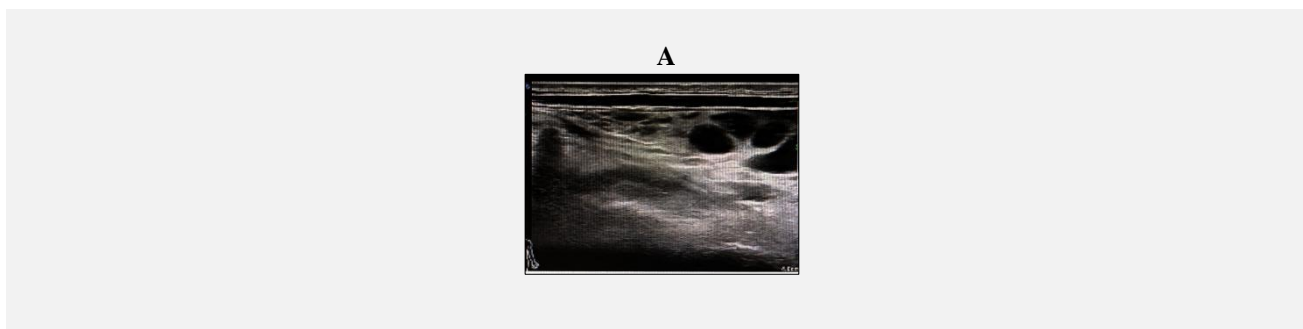


Figure 2. Superficial lymph node ultrasound showed multiple enlarged lymph nodes in the right supraclavicular region.

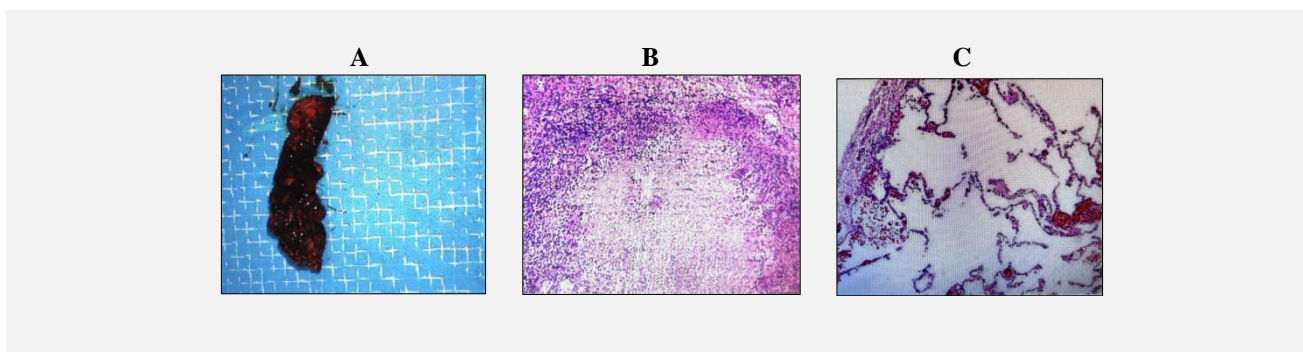


Figure 3. A wedge-shaped piece of lung tissue measuring 11.5 cm x 5 cm x 3.2 cm was surgically excised, and a solid gray-white nodule, approximately 1.0 cm, with a slightly hard texture was seen 0.4 cm from the lung membrane in the cut surface.

Pathological findings: granulomatous nodules composed of multinucleated giant cells and epithelioid cells were seen in the interstitium of the lung, and chronic inflammatory cell infiltration was seen.

berculosis [10]. The elevated CEA in this patient further misled our judgment of the benignity of this nodule. Because benign SPN usually does not require surgical resection, whereas timely surgical resection of malignant SPN ensures a better prognosis, early qualitative diagnosis of SPN is extremely important.

PET-CT is now largely accepted as a diagnostic tool for cancer. Other imaging modalities such as X-ray, CT, and MRI have different advantages in lung cancer screening and diagnosis, but the common disadvantage is that they do not directly reflect the metabolic activity of the tumor. PET-CT uses semi-quantitative param-

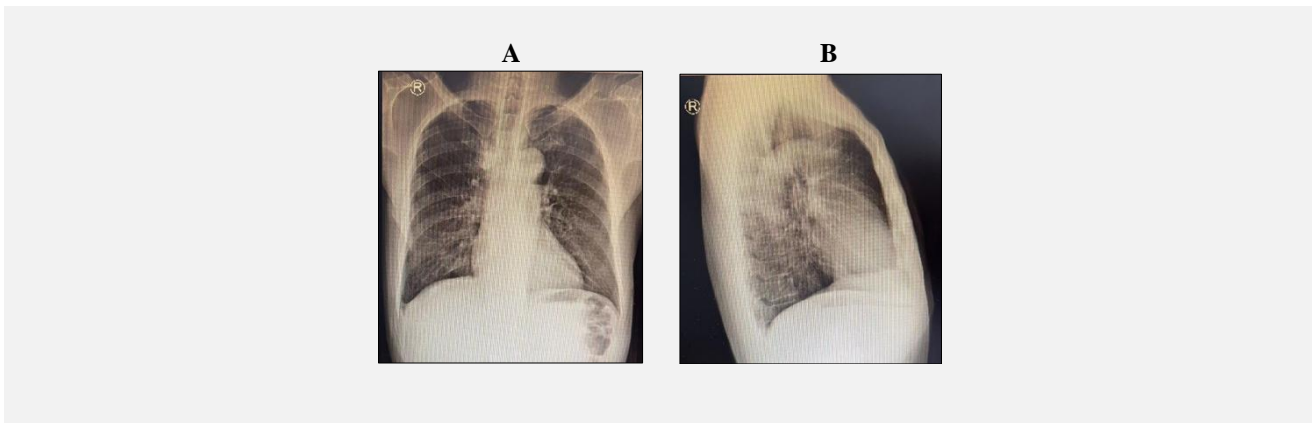


Figure 4. Chain suture shadow and round-like hyperdensity shadow were seen in the right hilar region, the right rib diaphragm angle was blunted, and the right lung exudative lesion was basically absorbed.

ters such as standardized uptake values to detect early metabolic changes in lung cancer. It has the unique advantage of both CT anatomical images and PET functional metabolic images, which are now widely used in clinical practice for diagnosis, staging, and efficacy evaluation of lung cancer, etc. [11]. Since malignant tumors mostly exhibit higher glucose metabolism than normal tissues, using this property, we can use ^{18}F -FDG PET-CT to detect whether the region presents high FDG metabolism, which has high sensitivity and specificity [12]. Although PET-CT is currently used as a more trusted tool for cancer diagnosis, it may also show false positives and false negatives. Because ^{18}F -FDG is a nonspecific imaging agent, certain benign lesions (e.g., tuberculosis, infection, granulomatous inflammation, etc.) can also show higher uptake of ^{18}F -FDG, which can lead to misdiagnosis [13]. However, some studies have shown that PET-CT can still be used as a screening tool to exclude mediastinal lymph node involvement in lung cancer in areas with a high prevalence of pulmonary tuberculosis, provided that a positive PET-CT result is needed to exclude the possibility of underlying pulmonary tuberculosis [14]. In the case we report, PET-CT was performed because of high suspicion of lung cancer, and the return confirmed a higher uptake of ^{18}F -FDG in the nodule, which reinforced our opinion that the nodule was malignant.

In this patient, the irregular imaging nodes, enlarged lymph nodes, elevated CEA, and positive PET-CT findings suggested to us in multiple ways that this node was malignant. Considering the enlarged mediastinal lymph nodes, we thought there might be metastatic lesions, so we first performed a bronchoscopy. EBUS-TBNA allows pathological diagnosis of mediastinal lymph nodes by real-time ultrasound localization and aspiration of mediastinal lymph nodes. During this time, ROSE can help the clinician to assess whether the sample taken meets the criteria, as well as determine whether additional samples are needed for other ancillary examina-

tions [15]. Therefore, we performed EBUS-TBNA and ROSE on this patient but did not find tumor cells. Such results swayed us from our initial diagnosis, and we recommended that the patient undergo a lung biopsy to clarify the nature of the nodule. Television-assisted thoracoscopic surgery (VATS) is becoming an important treatment modality for the biopsy of pulmonary nodules to clarify the pathogenic pathology with less perioperative risk, lower complication rate, and faster postoperative recovery than open lobectomy [16,17]. Therefore, we performed a thoracoscopic wedge resection of the upper right lobe of the lung and performed a biopsy of the nodule to determine its nature of the nodule. However, not all patients who cannot be evaluated preoperatively for the benignity or malignancy of a pulmonary nodule should undergo pulmonary wedge resection or segmental lung resection, which can be a biopsy for a definitive diagnosis but may affect the patient's future lung function [16]. Therefore, preoperative evaluation is particularly important at this time to minimize patient harm from invasive procedures.

The diagnosis and treatment of this case were fraught with too many misleading factors. While the evidence from the ancillary tests all pointed to malignancy, the pathological biopsy showed opposite results. The treatment options for pulmonary tuberculosis and lung cancer are very different. Therefore, identifying the two can not only reduce patient suffering from unnecessary treatment but also reduce the waste of medical resources and avoid misdiagnosis and overtreatment.

CONCLUSION

Given the high incidence of pulmonary tuberculosis, however, sometimes its clinical presentation is nonspecific or even asymptomatic, and imaging can show features of malignancy, which can easily lead to misdiagnosis. If patients with SPN accompanied by elevated

CEA and enlarged lymph nodes are encountered clinically, the possibility of malignancy should be considered, as well as the possibility of other diseases. Although PET-CT is currently used as a better test to diagnose malignant tumors, there are still certain false-negative results. Blind obedience to imaging results can greatly increase the probability of misdiagnosis. By reporting this case, we aim to remind clinicians to enhance their understanding of SPN and to remind clinicians to consider multiple factors when identifying benign and malignant nodules to make a more accurate judgment while minimizing harm to the patient.

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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 the studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:

No conflicts of interest.

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