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A Rare Case: Pulmonary Tuberculosis with Skeletal and Lymphatic Tuberculosis

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Abstract

Introduction: Tuboculosis is an infectious disease commonly in China especially in immunodeficiency patients. But multiple sites tuberculosis infection stays rare. We let's report A rare case: pulmonary tuberculosis with skeletal and lymphatic tuberculosis and successfully treated.

Observation: A 70-year-old male with a weight of 46 KG coughed and expectorated without obvious inducement 2 months ago.He had Diabetes history of 10 years.There were no obvious dry-wet rales or other positive signs in the lungs. A soybean sized lymph node was palpable in the right side of neck and the left hand wrist joint was characterized by multiple masses, with hard texture, partial fusion and poor mobility.The ultimate diagnosis of pulmonary tuberculosis with skeletal and lymphatic tuberculosis was accurately made through histopathology by needle biopsy samples. Throughout the long-term treatment course, clinical abnormalities of oral administration of antitubercular drugs were not observed and there were no significant alterations in serum parameters of liver and kidney.

Conclusion: This case underscores the importance of accurate diagnosis of multiple sites tuberculosis and provides an effective and useful experience for future clinical practice.

Keywords: Histopathology; needle biopsy; multi-focal tuberculosis; long-term chemotherapy of anti-tuberculosis

Introduction

Tuberculosis (TB) infects about one-third of the world's population and remains in the leading cause of death worldwide [1, 2]. China has success in controlling TB, including diagnostic, highest levels of treatment coverage and prevention services. However, China is still one of the 30 high TB burden countries and ranked the third of all estimated incident cases [2]. Tuberculosis is caused by different species of Mycobacteria, commonly known as Mycobacterium tuberculosis [3]. In general, a relatively small proportion (5%-15%) of people infected with M. tuberculosis develops tuberculosis disease during their lifetime. People who have risk factors, such as undernourishment, HIV infection, alcohol use disorders, smoking (especially among men) and diabetes, are much more likely to develop tuberculosis [2, 4]. Importantly, most people who develop active TB do not have one of these associated conditions [4]. Chest imaging [5] and microbiologic specimens are still the principal methods for diagnosing pulmonary TB [4]. CT scans of the chest show the extent of disease in greater detail than plain radiographs and may be beneficial when respiratory specimens are initially negative or other diagnoses are considered likely [4-6]. PET scans have also been suggested as a tool for diagnosing TB and monitoring response to therapy [7, 8]. They are not able to differentiate TB from malignancy very well but could be helpful in identifying active lesions for biopsy [5, 8]. Microbiologic specimens for active tuberculosis are sputum analysis, including smear, culture, and nucleic acid amplification testing [4, 6].

Although TB most commonly affects the lungs, it also can affect other sites, tissues and organs outside the pulmonary parenchyma, a form known as extrapulmonary TB. It accounts for 20% to 25% of all tuberculosis cases worldwide [2]. Extrapulmonary TB incidence may be increasing [9, 10]. The most common anatomic sites affected by extrapulmonary TB are lymph nodes, pleura, bones, and joints, although any organ can be involved [2, 9]. Diagnosis of extrapulmonary TB can be elusive, necessitating a combination of clinical suspicion, imaging, histopathology, and microbiology [11, 12]. Treatment of extrapulmonary TB generally follows similar principles to pulmonary TB, but the duration of treatment depends on the site of involvement and the extent of the disease [11].

Here, we report a rare case of pulmonary tuberculosis with skeletal and lymphatic tuberculosis in an elderly patient.

Case Presentation

Chief Complaints

Repeated cough and sputum, swelling and deformation of left wrist joint for 2 months.

History of Present Illness

A 70-year-old male with a weight of 46 KG coughed and expectorated without obvious inducement 2 months ago. Sputum was white and sticky, and not easy to be coughed up. Pain, swelling and difficulty in movement of the left wrist joint. He had weight loss of 16KG in the past 2 months.

History of Past Illness

Diabetes history of 10 years, oral metformin, blood glucose control is unknown. He got several local pain relief treatments for the left wrist joint as further examinations were not performed; however, the effect was unsatisfactory.

Physical Examination upon Admission

There were no obvious dry-wet rales or other positive signs in the lungs. A soybean sized lymph node was palpable in the right side of neck. The wrist joint of the left hand was characterized by multiple masses, with hard texture, partial fusion and poor

mobility (Figure 4 A, B and C).

Laboratory testing

Blood routine showed the percentage of lymphocytes was 17.02%, which was slightly decreased and mild hypochromic anemia, hemoglobin was 125 g/l. Liver function, renal function tests and serum sodium, potassium, creatinine, magnesium, calcium were all within normal limits. Twelve items of blood tumor biomarker test including carbohydrate antigen (CA) 199, CA 242, CA 153, CA 125, neuron specific enolase, carcinoembryonic antigen, -Human chorionic gonadotropin, ferritin, alpha fetoprotein, prostate specific antigen (PSA), free-PSA, and growth hormone were negative except for CA 125. CA125 was 131.77 KU/L and reference value was less than 35 KU/L. Fasting blood glucose was 15 mmol/l, which was apparently increased. Further detection demonstrated that glycosylated hemoglobin was markedly increased to 11.6% and reference value was between 4% and 6%. Fasting blood glucose was 15 mmol/l, and monitoring blood glucose showed 2-hour postprandial blood glucose fluctuated between 8 to 16 mmol/l. Erythrocyte sedimentation rate increased to 33mm/h. Tuberculin skin test, sputum stains for acid fast bacilli at least three times were all negative. Arterial blood gas analysis at room air revealed pH 7.43, PaO_2 80.2 mmHg and $PaCO_2$ 31.4 mmHg, no obvious abnormality was found in other parameters. The patient refused the puncture of the increased lymph node in the right side of neck. Needle aspiration cytology of left wrist mass and CT guided percutaneous pulmonary punctures were performed.

Examinations

The patient's first chest CT (Figure 1) showed increased markings, scattered mass like and nodular high-density shadows in both lungs. Patchy shadows were seen in both lower lungs, the edges were irregular and the boundaries are fuzzy. Mediastinum was in the middle, and no obvious enlarged lymph node shadow was found in it. Chest CT showed bilateral pleural thickening, pleural effusion and pneumatosis on the left side, no effusion in pericardial cavity, multiple enlarged lymph nodes in bilateral armpits, mainly on the left side. Two radiologists gave the report that tuberculosis may be considered for the polymorphic lesions of both lungs.

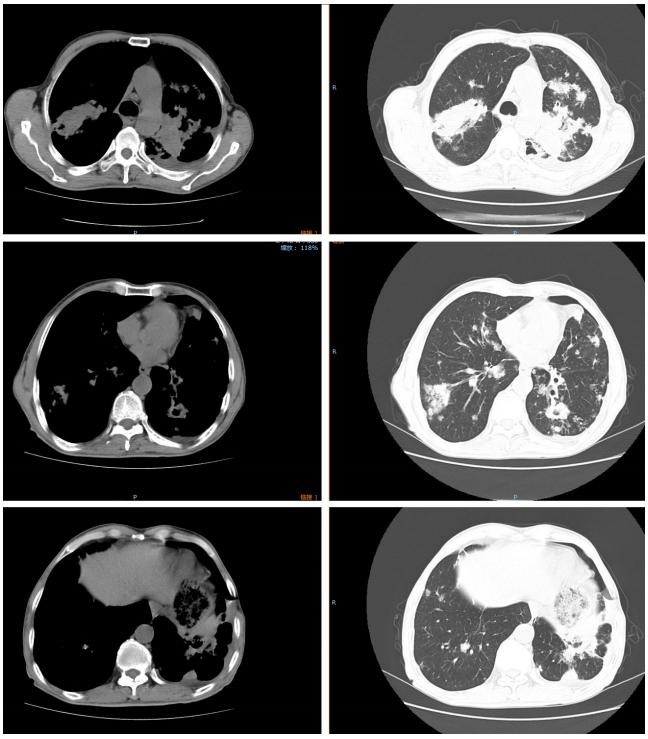

Figure 1: Typical images of upper, middle and lower lung from the patient's first chest CT done at Outpatient Department, 3 days before admission

Subsequently, ^{18}F-fluorodeoxyglucose (FDG) PET-CT (Figure 2) showed: 1. Multiple nodular, lumpy, and patchy density increasing shadows with different sizes were scattered in both lungs, some lesions contained cavities, and some lesions showed high-density shadows. FDG metabolism was increased, with a maximum value of 12. Among them, the size of lumpy lesion in the upper lung was 54 × 46mm left, 72 × 38mm right. A small amount of pleural effusion was observed. 2. Multiple swollen lymph nodes can be observed in the right side of neck, bilateral supraclavicular and subclavicular area, axillas, hilus, mediastinum, abdominal cavity and retroperitoneum, at the bifurcation of iliac blood vessels, beside the left iliac blood vessels and subcutaneously in the left upper arm. The maximum value of increased FDG metabolism of lymph nodes was 12. 3. Bone destruction can be found in the left ulna and radius, carpus and 2-4 metacarpal bones. The surrounding tissue was obviously swollen and the maximum value of increased FDG metabolism was 13.9. The report confirmed by nuclear medicine specialists showed that tuberculosis may be considered, and metastatic tumor should be excluded.

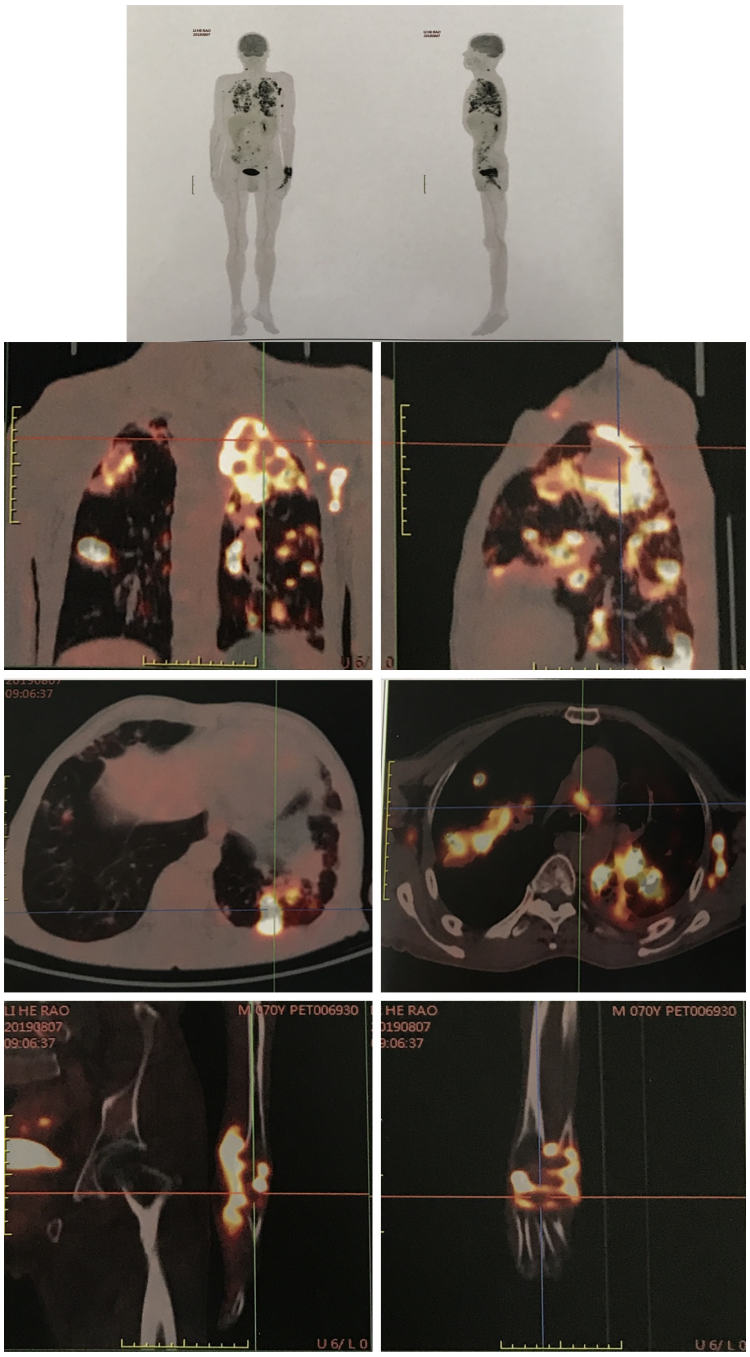

Figure 2: 2 days before admission, 18F-fluorodeoxyglucose (FDG) PET showed: multiple nodules and mass shadows in both lungs, multiple swollen lymph nodes in the whole body, multiple bone destruction (left ulnar bone, carpal bone and 2-4 meta-

carpal bone), and abnormal increase of 18F-FDG metabolism. Tuberculosis should be considered first, metastatic tumor should be discharged, and further examination was recommended; A small amount of fluid accumulated in the left thoracic cavity.

To clarify the nature of intrapulmonary lesions, CT guided percutaneous pulmonary puncture of left lower lung (Figure 3A) was performed. For poor absorption of intrapulmonary and extrapulmonary lesions, CT guided percutaneous pulmonary puncture of right upper lung (Figure 3B) and needle aspiration cytology of left wrist mass were performed more than a month later. The pathological results were confirmed by two pathology experts.

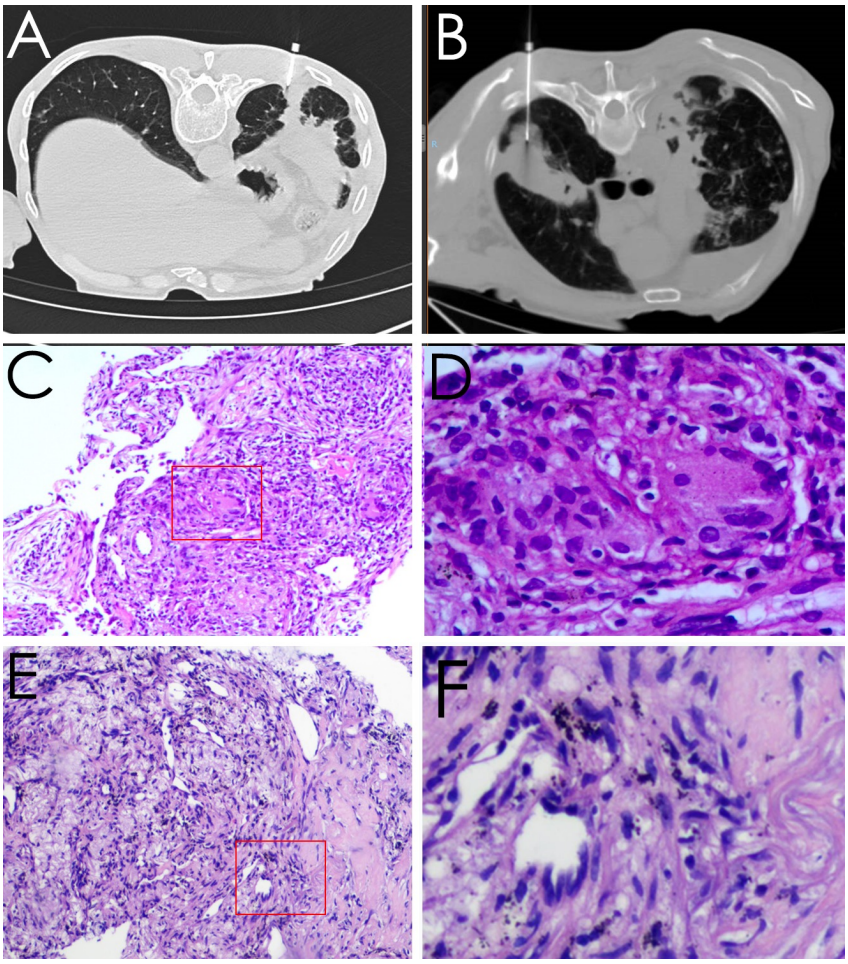

Figure 3: CT guided percutaneous pulmonary punctures of left lower lung (A) and right upper lung (B) and pathological results (C, D, E and F). The pathological result of left lower lung by CT guided percutaneous pulmonary puncture (C and D): granulomatous inflammation with caseous necrosis was found, but positive acid-fast staining was not found. Tuberculosis could not be excluded. The pathological result of right upper lung by CT guided percutaneous pulmonary puncture (E and F): fibrous tissue hyperplasia with necrosis, no obvious granuloma.

Multidisciplinary Expert Consultation

The pathological results were confirmed by Yongping Cai and Hao Li, Pathologists, Department of Pathology.

The pathological result of left lower lung by CT guided percutaneous pulmonary puncture (Figure 3C and D) showed: granulomatous inflammation with caseous necrosis was found, but positive acid-fast staining was not found. Tuberculosis could not be excluded. The pathological result of right upper lung by CT guided percutaneous pulmonary puncture (Figure 3E and F) showed: fibrous tissue hyperplasia with necrosis, no obvious granuloma. Further immunohistochemical examination revealed

negative results of CK, EMA, CK7, CK5/6, Napsin-A, P63, TTF-1 and P40 (not shown). PAS staining was also negative (not shown). Besides, no tumor cells were found in the puncture fluid. At the same time, needle aspiration cytology of the left wrist mass (not shown): lymphocytes, spindle cells, fibrous cells and histiocytes, and reexamination was recommended after anti-infection treatment.

Final Diagnosis

Pulmonary tuberculosis with skeletal and lymphatic tuberculosis

Treatment

The patient was started with oral combined medication of isoniazid 300mg QD, rifampicin 450mg QD on an empty stomach in the morning, ethambutol 750 mg QD and pyrazinamide 1250mg QD for 2 months. Continued combined medication of isoniazid 300mg QD, rifampicin 450mg QD on an empty stomach in the morning, ethambutol 750g QD sustained for 10 months.Short-acting insulin aspartate before three meals combined with long-acting insulin glargine once a day was used to control blood sugar. Maintain fasting blood glucose between 6 to 8 mmol/l, and 2-hour postprandial blood glucose between 8 to 10 mmol/l by modulating insulin aspartate and glargine.

Outcome and Follow-Up

Ten months after the beginning of the treatment, multiple masses of the left wrist joint were disappeared and the left wrist joint recovered normal shape from back surface (Figure 4D), lateral surface (Figure 4E) and palm surface (Figure 4F). Function of the left wrist joint was recovered. Moreover, a soybean sized lymph node in the right side of neck was disappeared. The patient had no discomfort and weight gain of 10kg. Except for transient elevated transaminases and uric acid levels, severe side effects were not observed. Ultrasound examination for lymph nodes did not show obvious positive results, especially located in the right side of neck, bilateral supraclavicular and subclavicular area, axillas, abdominal cavity and retroperitoneum, at the bifurcation of iliac blood vessels, beside the left iliac blood vessels and subcutaneously in the left upper arm.

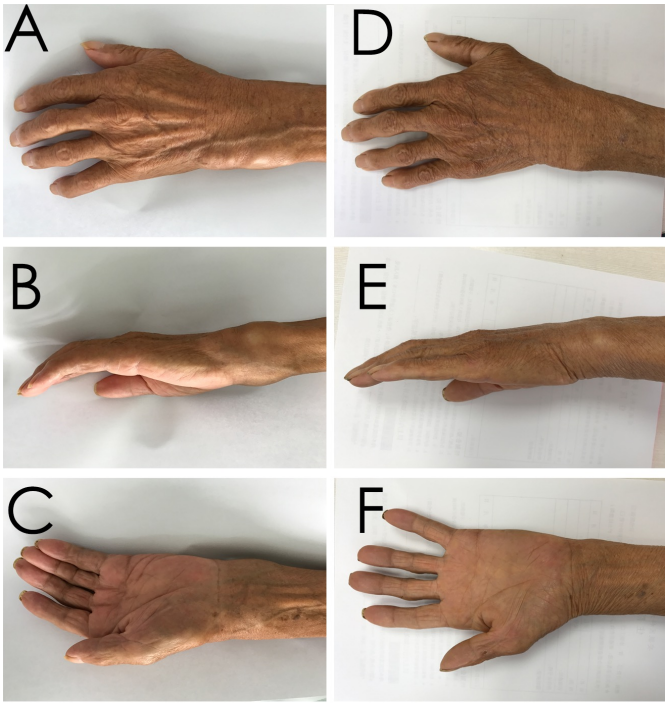

Figure 4: Swelling of the left wrist joint and its surroundings, multiple nodular protrusions before treatment (A, B and C). The left wrist joint returned to normal shape (D, E and F). Back surface of the left wrist joint (A and D), lateral surface of the left

wrist joint (B and E), palm surface of the left wrist joint (C and F).

At the end of the treatment, the patient's chest CT (Figure 5) showed bilateral lung markings increase, multiple patchy and nodular high-density shadows were in both lungs. The mediastinum deviated to the left, and no obvious enlarged lymph node shadow was found in the mediastinum and bilateral armpits. Bilateral pleural thickening. Bilateral lung lesions were obviously absorbed compared with those in the chest CT before treatment (Figure 1). Sputum smear at least three times were negative, and half year after the treatment, the chest CT (not shown) did not show obvious changes compared to that at the end of the treatment.

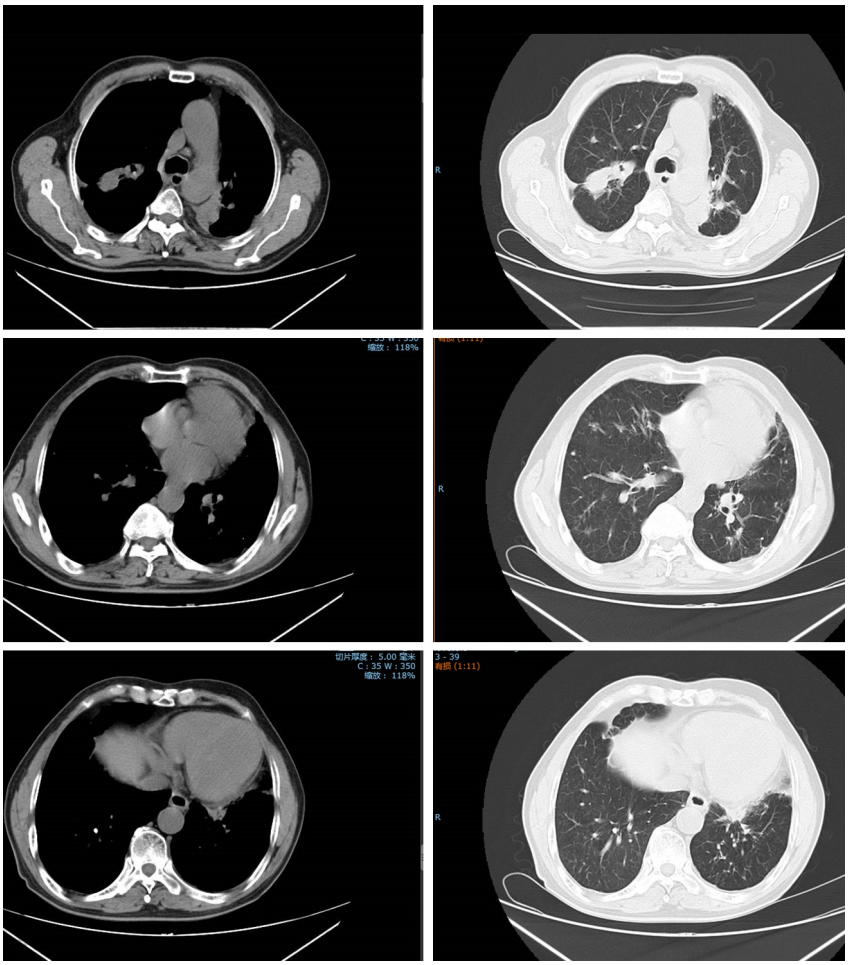

Figure 5: Typical images of upper, middle and lower lung from the patient's chest CT Nine months after treatment.

Discussion

Tuberculosis has been considered a global public health emergency for the past 25 years [1, 13]. In WHO Global Tuberculosis Report 2022, until the coronavirus (COVID-19) pandemic, TB was still the leading cause of death from a single infectious agent, ranking above HIV/AIDS [2]. Clinical characteristics of pulmonary tuberculosis are not specific, especially for respiratory tract specimen acid-fast bacilli negative patients. Subjects with primary tuberculosis are much more likely to be asymptomatic or minimally symptomatic [14].The most common symptoms include cough, fever, weight loss and hemoptysis [14]. This 70-year-old male patient showed repeated cough and sputum for 2 months. Cough and sputum were not severe and did not get his attention. Pain in the left wrist joint and weight loss of 16KG prompted him to undergo further examination, chest CT. The chest CT report suggested tuberculosis may be considered. The patient had cough and weight loss, consistent with part of pulmonary tuberculosis common symptoms. Negative tuberculin skin test and acid-fast bacilli stains on sputum smears cannot exclude pulmonary tuberculosis [1].Because the pulmonary lesion was located in the peripheral and FOB was inaccessible, we can-

not test sputum samples by NAAT besides and we found that more than fourfold increase in CA125, an enlarged lymph node in the right side of neck, and multiple masses in left wrist joint did not support pulmonary tuberculosis completely. Lung cancer or malignant tumors especially originating from abdominal organs may be distinguished first. This patient also had mild hypochromic anemia, which may be due to multiple reasons [15] and did not show any clear indication for the diagnosis.

PET-CT is an appropriate imaging modality in most patients with suspected lung cancer and can rule out malignancy in most solitary pulmonary nodules due to high sensitivity [16]. Chinese Medical Association guideline for clinical diagnosis and treatment of lung cancer recommends eligible individuals to undergo PET-CT examination [17]. PET-CT examination of this patient showed multiple lesions in lungs, lymph nodes and left forearm with obvious increased FDG metabolism. Consistent with the character that ^{18}F-fluorodeoxyglucose (FDG) PET-CT cannot differentiate between TB and other diseases such as malignancy [18], this PET-CT showed that tuberculosis may be considered, and metastatic tumor should be excluded. CT-guided biopsy is one of the preferred methods to obtain tissue specimens for diagnosing peripheral lung cancer [16, 17]. To obtain tissue specimens as much as possible, biopsy of lymph node in the right side of neck, left wrist mass and lung was suggested. According to the patients' preference, needle aspiration cytology of the left wrist mass and CT guided percutaneous pulmonary punctures were performed. The pathological results of lung inclined towards pulmonary tuberculosis. The cytology of the left wrist mass only can confirm infection. For obtaining much more tissue samples, biopsy of the left wrist mass may be a better method than cytology by needle aspiration, but the latter might cause less trauma. Multi-focal bone tuberculosis can mimic many pathologies and is frequently confused with a malignant tumor, presenting a real challenging diagnosis [19]. For this patient, the cytology of the left wrist mass may exclude tumors and inclined towards tuberculosis considering the pathological results of lung. In our case, antituberculosis drug treatment was successful in curing the lesions including lungs, lymph nodes and bones. This patient was at good general health with recovery of shape and motion of the left wrist and regain of weight.

The diagnosis of bone and lymph nodes tuberculosis are a genuine challenge for the clinician because the clinical samples obtained are often from relatively inaccessible sites [20, 21]. The confirmatory diagnosis of tuberculosis requires the detection of Mycobacterium tuberculosis from the biological sample by at least one of the current microbiological techniques: microscopical analysis, isolation in culture or molecular methods such as the use of polymerase chain reaction on obtained tissue biopsies [22-24]. Histopathology is also a sensitive aid for diagnosis [25-26].Taken together, pulmonary lesions with bone and lymph nodes lesions were rare and lack of specificity, which is difficult to achieve diagnosis and increase the possibility of misdiagnosis[22, 27]. The presence of primary foci can orient the diagnosis. But the confirmatory diagnosis of pulmonary tuberculosis obtained samples via biopsy for pathological confirmation as a presumption diagnosis of other organs and tissues still involves a certain degree of misdiagnosis risk because of coexistence of other diseases[28-30]. Fortunately, in this case, we got the samples from the lesions of intrapulmonary and extrapulmonary that guaranteed the accuracy and sensitivity of tuberculosis diagnosis.

Duration of treatment, abnormalities of oral administration such as impaired gastric accommodation, visceral hypersensitivity, and gastric dysrhythmias were not observed. There were no significant alterations in serum parameters of liver and kidney. In particular, successful and complete treatment for multi-focal tuberculosis was associated with normalization of serum of liver and kidney parameters and clinical manifestations after administration of antitubercular agents [31, 32].

Conclusion

In summary, we accurately diagnosed a rare case of pulmonary tuberculosis with skeletal and lymphatic tuberculosis through histopathology by needle biopsy samples and successfully treated with long-term chemotherapy of antitubercular drugs.These findings also have general implications in the diagnosis and treatment of tuberculosis, thus provide an effective and useful experience for future clinical practice.

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Author Contributions

Xuebo Yan, Yukun Liu, Lei Fang, Peishan Ding and Jiong Wang collected clinical data; Xuebo Yan and Jiong Wang designed and wrote the paper.

Informed Consent Statement

Consent was obtained from the patient for publication of this report and any accompanying images.

Declaration of Interest

The authors declare no conflict of interest for this report.

CARE Checklist (2016)

The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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