Letter to the Editor

Diffuse lymphadenopathy with significantly elevated standardized uptake values on positron emission tomography-computed tomography: a case description of lymph node tuberculosis without lung lesions

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Introduction

Tuberculosis (TB) is a preventable and curable disease. In 2023, it was the second leading cause of death from a single infectious agent worldwide, causing almost twice as many deaths as human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS). More than 10 million people contract TB every year (1,2). TB lymphadenitis is observed in nearly 35% of the cases of extrapulmonary tuberculosis (EPTB), which constitute approximately 15% to 20% of all cases of TB. EPTB accounts for approximately 15–20% of the cases of TB and is the type in which involvement of the peripheral lymph nodes is most common (3). However, most adult patients with lymph node TB have pulmonary TB, and simple lymph node TB is rare. This report describes a case of TB in which the patient had generalized and diffuse enlargement of lymph nodes that exhibited significantly elevated standardized uptake values (SUVs) but who had no lung lesions. The diagnosis and follow-up in this case were facilitated by positron emission tomography-computed tomography (PET-CT).

Case presentation

All procedures performed in this case were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this article and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

A 52-year-old woman who had been experiencing abdominal discomfort for more than 3 months and fever for more than 2 months was admitted to Nanjing Second Hospital. She had no underlying disease or smoking history. Chest computed tomography (CT) showed no active lesions (*Figure 1*). The laboratory findings, including the results for infection indices, serum tumor markers, serum autoantibodies, blood cultures, and viral serological markers, were within the normal limits. Sputum samples showed negative results for bacteria, mycobacteria, and fungi. The HIV test and lymphocyte subpopulation count of the patients at the beginning of the disease were normal. B-mode ultrasonography of the axillary, groin, and neck lymph nodes showed enlargement in multiple lymph nodes, especially in the left cervical root lymph node. PET-CT was performed since lymphoma could not be ruled out, and it showed multiple enlarged lymph nodes posterior to the right sternocleidomastoid muscle, bilateral posterior cervical triangle, bilateral clavicular region, bilateral axilla, anterior mediastinum, the region anterior to the right

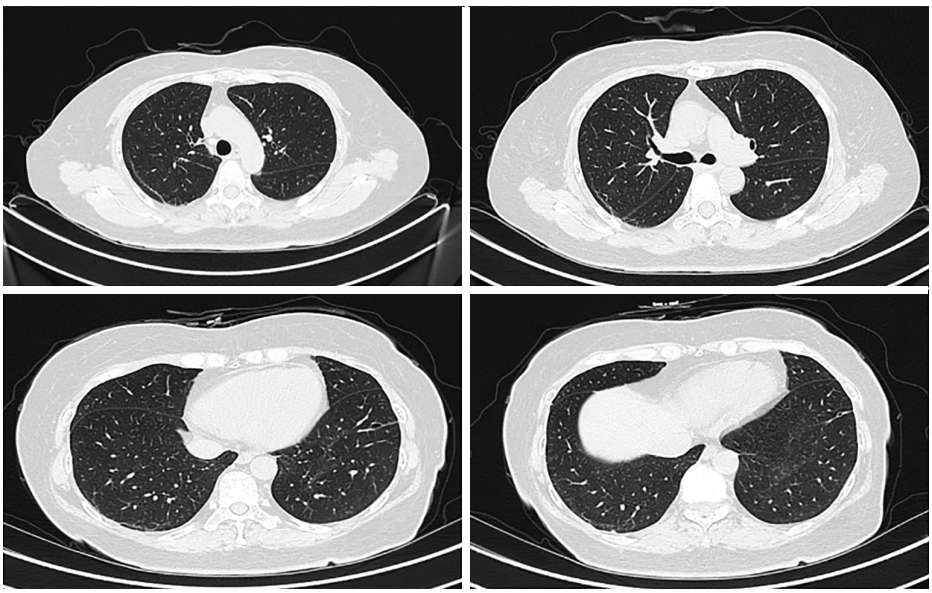

Figure 1 Results of the patient's chest CT examination. Chest CT showed no active lesions. CT, computed tomography.

diaphragm, the lesser omental sac, splenic hilum, abdominal aorta, and mesenteric region (some of the lymph nodes showed uneven density); other results included an abnormal increase in ^{18}F-fluorodeoxyglucose (FDG) metabolism (*Figure 2A*); abdominal pelvic effusion; thickening of the peritoneum, mesangium, and omental membrane; and increased abdominal fat density. These findings were accompanied by diffuse nodular thickened shadows, increased FDG metabolism in many bones of the body, and no obvious bone destruction (*Figure 2B*). Although the possibility of malignant lesions was first considered, TB could not be completely excluded. Therefore, biopsy of the high-metabolism lymph nodes (left cervical lymph nodes showing increased metabolism) was performed to determine the pathology. The results for purified protein derivative (PPD) were positive. The results of the TSPOT. TB (TSPOT) were negative. A puncture biopsy of the left cervical lymph node was performed on December 19, 2023. Pathological examination showed granulomatous inflammation with necrosis (*Figure 3*). Targeted next-generation sequencing (tNGS) of cervical lymph node puncture tissue showed *Mycobacterium tuberculosis* (sequence number 5262). Contrast-enhanced magnetic resonance imaging (CE-MRI) showed foci in the subfrontal cortex and right paraventricular stem along with thickened and strengthened meninges. Therefore, lumbar puncture was performed, and no obvious abnormalities were found in the routine or biochemical analysis of the cerebrospinal fluid, although tNGS of the cerebrospinal fluid detected *M. tuberculosis*. Therefore, the patient was diagnosed with lymph node TB and craniocerebral TB and received anti-TB treatment (treatment regimen: isoniazid, 300 mg/day; rifampicin, 600 mg/day; pyrazinamide, 1,000 mg/day; ethambutol, 750 mg/day; and linezolid, 600 mg/day). Six months later, B-ultrasonography of the patient's neck, axillary, and inguinal lymph node showed no significant abnormalities. Since there was no obvious enlargement of superficial lymph nodes, the etiology could not be determined. However, measuring the size of the superficial lymph nodes was considerably more effective significant effect. The patient also underwent a second PET-CT examination, which indicated that multiple lymph nodes in the whole body had reduced significantly or had even disappeared (*Figure 2B*).

Discussion

Enlarged lymph nodes are a common symptom of a variety of conditions, including infections (4,5), tumors (6), and immune diseases. Lymph node enlargement accompanied by fever of unknown origin without obvious infectious signs usually indicates a diagnosis of lymphoma.

PET-CT is helpful in the diagnosis and staging of tumor-associated lymphoma (7). However, studies on tuberculous lesions and tuberculous lymphadenectasis are relatively limited. PET-CT has demonstrated value in aiding cancer

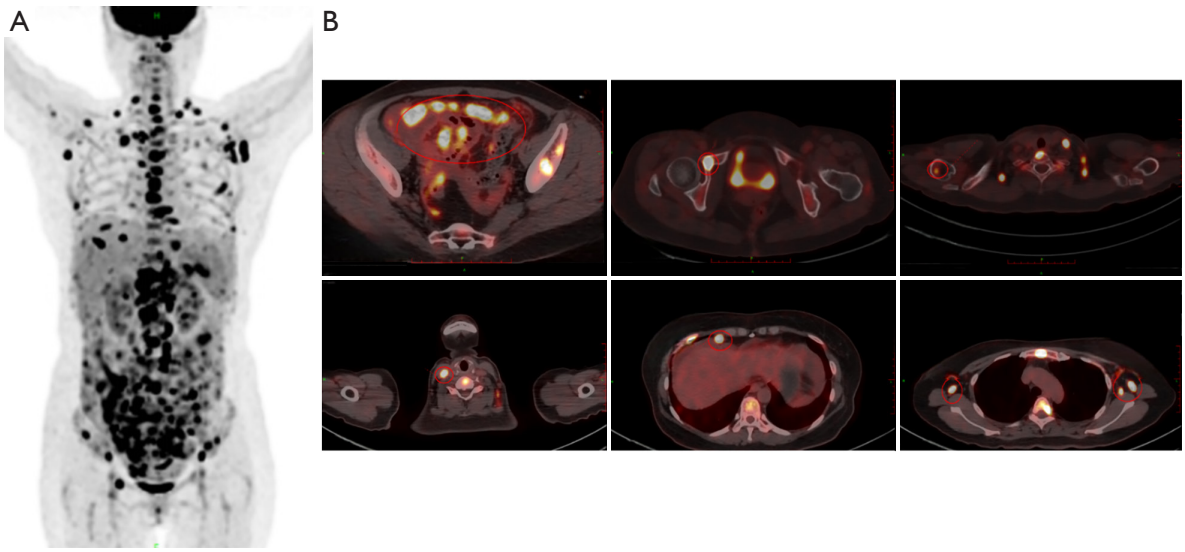

Figure 2 Results of the patient's whole-body PET-CT examination. (A) PET-CT showed multiple enlarged lymph nodes posterior to the right sternocleidomastoid muscle, bilateral posterior cervical triangle, bilateral clavicular region, bilateral axilla, anterior mediastinum, the region anterior to the right diaphragm, the lesser omental sac, splenic hilum, abdominal aorta, and mesenteric region; some of the enlarged lymph nodes had uneven density, indicating an abnormal increase in FDG metabolism. (B) Abdominal pelvic effusion, as well as thickening of the peritoneum, mesangium, and omental membrane and increased abdominal fat density, was accompanied by a diffuse nodular thickened shadow and increased FDG metabolism in many bones of the body but no obvious bone destruction. PET-CT, positron emission tomography-computed tomography; FDG, ^{18}F-fluorodeoxyglucose.

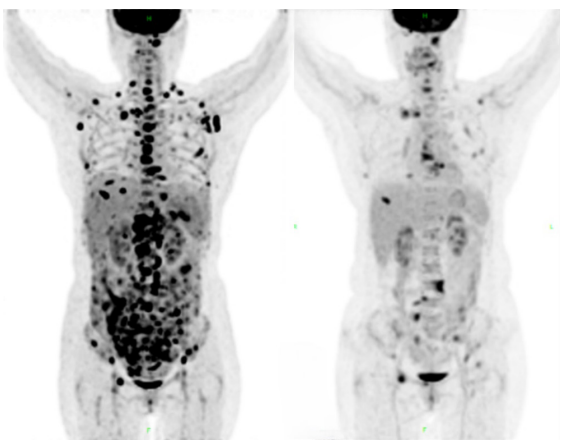

Figure 3 Reexamination with PET-CT after 6 months of treatment that multiple lymph nodes in the whole body had reduced significantly or had even disappeared (*Figure 2A*). PET-CT, positron emission tomography-computed tomography.

management and has been suggested to have the potential to revolutionize research in infectious diseases. More specifically, the capacity of PET-CT to provide functional data on changes in metabolism, drug penetration, and immune control of tuberculous lesions can facilitate drug development and regimen selection in TB (8).

The routine clinical use of FDG PET/CT imaging for the assessment of treatment response in patients with TB is hindered by cost and availability. PET-CT provides a unique noninvasive whole-body imaging approach for the diagnosis, staging, and evaluation of treatment response in many infectious and inflammatory diseases. Some PET tracers, such as ^{18}F-FDG, have been proven useful in various infectious diseases for detection, disease activity assessment, staging, and monitoring of response to therapy. TB can also be identified by this tracer. TB foci can absorb ^{18}F-FDG in large quantities, and thus ^{18}F-FDG PET is valuable for assessing the extent of active TB (9). However, the sensitivity of PET-CT to granulomatous diseases such as sarcoidosis and TB is not clear (10). Sánchez-Montalvá *et al.* reported that patients with TB show increased FDG uptake on PET-CT regardless of the organ involved (11). PET-CT can be particularly useful for diagnosing TB and EPTB and for evaluating early treatment response; however, it is costly and involves radiation exposure and

thus is not recommended for all patients with TB (12). However, there is no evidence that PET-CT can predict prognosis, and additional studies in this area are needed.

In our case, PET-CT was performed on the basis of these considerations. Although the PET-CT findings strongly indicated lymphoma, biopsy of the left cervical lymph node showed granulomatous inflammation. TB is the most common cause of granulomatous inflammation (13), and the two most common diseases associated with granulomatous inflammation are sarcoidosis and TN (14). However, the possibility of similar diseases could not be ruled out, especially since the patient's chest CT scans showed no obvious abnormalities. Sivaratnam *et al.* reported that Xpert MTB/RIF assay has high sensitivity and specificity (15). However, the Xpert results for the lymphatic tissue in this patient were negative. The observations from this case suggest the sensitivity of tNGS is stronger than that of Xpert (16). The current diagnostic techniques for TB remain inadequate for clinical needs, especially in patients with phlegm-free and EPTB. Therefore, tNGS was performed on lymph node puncture tissue. Murphy *et al.* reported that tNGS can help diagnose TB and drug resistance (17,18). Moreover, NGS has also demonstrated good sensitivity with other kinds of specimens, such as stool (19) and cerebrospinal fluid (20). In our case, tNGS facilitated the diagnosis of lymph node TB and craniocerebral TB. tNGS can also provide the clinical information required for precision medicine-guided therapy for multiple drug-resistant TB (18,21). tNGS may provide higher accuracy than other established diagnostic methods and can play a crucial role in the rapid and accurate diagnosis of TB, including drug-resistant TB (22).

Conclusions

Although pure generalized diffuse lymphadenopathy caused by TB is relatively rare, the possibility of TB should be considered. tNGS may be a viable option for the rapid diagnosis of tuberculous lymphadenitis. Lymph node TB is easy to misdiagnose, but timely ^{18}F-FDG PET-CT imaging combined with tNGS of lymph node biopsy tissue may reduce misdiagnosis and mistreatment and critically inform the assessment of the disease condition.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-1722/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this case were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this article and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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