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# $^{18}$FDG PET/CT IS SENSITIVE BUT NOT SPECIFIC FOR MALIGNANCY: TWO CASES OF DISSEMINATED TUBERCULOSIS MIMICKING METASTATIC CANCER ON IMAGING AND CLINICAL PRESENTATION

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## ABSTRACT

*Introduction:* $^{18}$Fluorodeoxyglucose positron emission tomography/computed tomography ($^{18}$FDG PET/CT) scan is widely used in the evaluation of suspected tumoral processes. In addition to its oncological applications, it is also employed in the diagnosis and follow-up of various conditions, including multiorgan tuberculosis.

*Case description:* We report a case series of two young patients with exclusive extrapulmonary disseminated tuberculosis that mimicked a neoplastic process both clinically and on $^{18}$FDG PET/CT imaging. Initially, both patients were admitted to the oncology unit with a presumed diagnosis of cancer. However, following an exhaustive work-up, a definitive diagnosis of tuberculosis was established via histopathological and microbiological analysis.

*Conclusion:* These cases underscore the importance of considering disseminated tuberculosis as a differential diagnosis during oncologic evaluations, especially in patients from endemic regions, and highlight the potential psychological impact of prematurely labelling a condition as cancer.

## KEYWORDS

Metastases, tuberculosis, $^{18}$FDG PET/CT, misleading diagnosis, case series

## LEARNING POINTS

- Extrapulmonary tuberculosis can mimic metastatic malignancies.
- Imaging does not replace pathology, which remains the gold standard for accurately diagnosing multiorgan involvement.
- Prematurely announcing a diagnosis of cancer before final confirmation can have significant psychological consequences.

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## INTRODUCTION/BACKGROUND

$^{18}$Fluorodeoxyglucose positron emission tomography/computed tomography ($^{18}$FDG PET/CT) scan is commonly used in the initial assessment of tumoral processes due to its high sensitivity, although its limited specificity can pose diagnostic challenges. Malignant lesions typically exhibit high $^{18}$FDG avidity, yet various benign conditions—particularly infections—may produce similar imaging findings. Therefore, histopathological analysis is essential for a definitive diagnosis. Tuberculosis may present as a disseminated disease with a metabolic pattern on PET/CT that mimics neoplasia, in this report, we describe two cases where the imaging features strongly suggested a metastatic process.

## CASE DESCRIPTION

*Case 1:* A 22-year-old Eritrean man, residing in Belgium for 2 years, was admitted to the oncology unit via the emergency department for evaluation of a painful left-sided mass at the base of the chest that had been progressively enlarging over 3 months. The patient reported an unintentional weight loss of 5 kg (8% of his body weight) and intermittent fever. Physical examination revealed a 10-cm, indurated, fixed thoracic mass without signs of local inflammation, as well as small, indurated bilateral inguinal lymph nodes. Laboratory investigations demonstrated an inflammatory syndrome (C-reactive protein of 85 mg/l) with a normal complete blood count. Serological tests for hepatitis A, B, and C, human immunodeficiency virus (HIV), cytomegalovirus (CMV), and Epstein-Barr virus (EBV) were negative, and tumour markers (carcinoembryonic antigen - CEA, carbohydrate antigen - CA 19-9, alpha-fetoprotein - AFP, beta-human chorionic gonadotropin - β-HCG) were within normal limits, although lactate dehydrogenase levels were at the upper range of normal.

A computed tomography (CT) scan of the chest confirmed a large, heterogeneous subcutaneous mass measuring 80 × 36 × 68 mm, with associated osteolysis of the left fifth rib. A subsequent $^{18}$FDG PET/CT scan revealed disseminated disease with both supra- and infradiaphragmatic lymphadenopathy, and involvement of the liver, spleen, muscles, peritoneum, and bone *(Fig. 1)*. These findings initially supported a diagnosis of metastatic malignancy.

A liver biopsy did not demonstrate carcinoma but revealed a necrotizing inflammatory granulomatous process *(Fig. 2)*. Special stains did not reveal any infectious agents in the tissue. Aspiration of the subcutaneous mass yielded purulent fluid containing necrotizing granulomas; although acid-fast bacilli were not observed, polymerase chain reaction (PCR) and subsequent culture confirmed the presence of *Mycobacterium tuberculosis*. Notably, bronchoalveolar lavage was negative for mycobacterial organisms. These findings led to the diagnosis of extrapulmonary tuberculosis with no lung involvement. The patient was transferred to the infectious diseases department, started on a full course of antitubercular therapy, and showed progressive clinical improvement. Follow-up imaging demonstrated complete resolution of the multiorgan involvement after a few months.

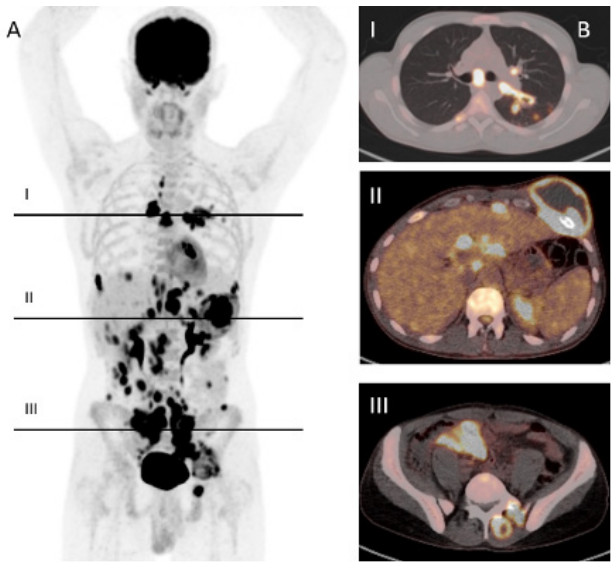



*Figure 1. Case 1. A) The maximal intensity projection image and B) the corresponding fused $^{18}$FDG-PET/CT scan axial slices, demonstrated a distribution pattern highly suggestive of an advanced, aggressive neoplastic process with extensive involvement of supra- and infradiaphragmatic lymph nodes, as well as the liver, spleen, peritoneum, bone, muscle, and gastrointestinal tract. Additionally, imaging reveals findings consistent with left Nelson's bronchopneumopathy.*

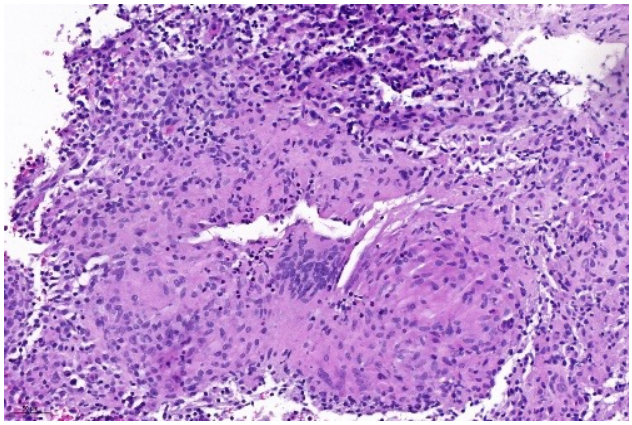


*Figure 2. Case 1. Liver biopsy revealed granulomatous inflammation, composed of nodular arrangement of epithelioid histiocytes with multinucleated giant cells and lymphocytes. The necrotic central zone was quite limited (hemalum–eosin staining, magnification 10×).*

*Case 2:* A 31-year-old woman from Angola, who had been living in Belgium for 2 years, presented to her general practitioner with a 6-month history of progressively worsening lumbar back pain. She also experienced an unintentional weight loss of 10 kg (12% of her body weight) and significant disability due to the pain. Physical examination was unremarkable. Spinal CT scan and magnetic resonance imaging revealed an infiltrative, osteolytic mass measuring 52 × 45 × 33 mm involving the L5 vertebra, prompting urgent referral to our oncology clinic.

Laboratory tests were normal, and tumour markers were negative. Viral serologies—including hepatitis A, B, and C, CMV, EBV, and HIV—were all negative. A subsequent $^{18}$FDG

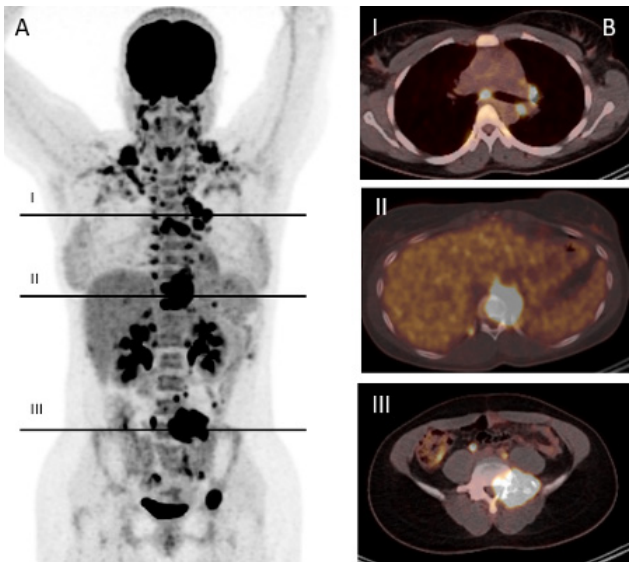



*Figure 3. Case 2. A) The maximal intensity projection image and B) the corresponding fused $^{18}$FDG-PET/CT scan axial slices, show supradiaphragmatic and infradiaphragmatic lymphadenopathies along with multiple lytic bone lesions.*

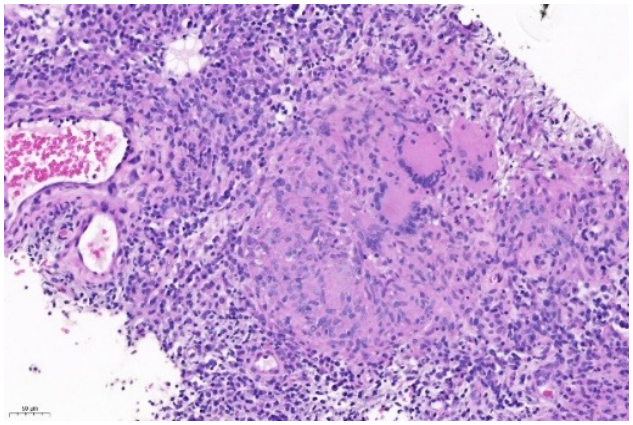


*Figure 4. Case 2. Tissue from the paraspinal mass revealed granulomas constituted by numerous epithelioid histiocytes, multinucleated giant cells and lymphocytes forming rather well-delimited nodules. Necrotic areas are scarce (hemalum–eosin staining, magnification 10×).*

PET/CT scan demonstrated a bulky hypermetabolic mass involving the L5 vertebra, in addition to other osteolytic lesions and supra- and infradiaphragmatic hypermetabolic lymphadenopathy, with no pulmonary abnormalities *(Fig. 3)*. An interferon-gamma release assay, performed given the history of Case 1, returned positive.

A biopsy of the vertebral lesion confirmed the presence of necrotizing granulomas *(Fig. 4)*. Both PCR and culture tests for *M. tuberculosis* were positive, while pulmonary evaluation remained negative. The diagnosis of disseminated extrapulmonary tuberculosis was established. The patient's pain gradually improved with antitubercular therapy, and follow-up imaging demonstrated complete resolution of the lesions after a few months.

## DISCUSSION

In oncology, $^{18}$FDG PET/CT scan is a standard tool for staging primary lesions and assessing disease progression. Despite its high sensitivity, its specificity is limited because increased uptake can occur in a variety of benign conditions, such as infections and inflammatory disorders. *Table 1*[1–3] lists the most common non-oncological causes of a strong metabolic pattern. Physiological uptake reflects the normal metabolic activity of tissues, whereas pathological uptake may be incidental (e.g., in thyroid or adrenal adenomas), medication-induced, or due to inflammatory processes. Both infectious and non-infectious conditions—whether granulomatous or non-granulomatous—can result in false-positive findings.

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|---|---|
| **Exam conditions** | Blood sugar<br>Temperature<br>Patient comfort<br>Patient stress |
| **Artifacts** | Misregistration artifact<br>Injected clot<br>Injection artifact |
| **Physiologic uptake** | Brown fat<br>Skeletal muscle<br>Renal collecting system<br>Liver<br>Spleen<br>Gastro-intestinal tract<br>Salivary glands<br>Adrenal activity<br>Thyroid activity<br>Uterus/ovaries |
| **Incidentalomas** | Gastrointestinal tract<br>Thyroid<br>Adrenal |
| **Post-therapeutics** | Post-chemotherapy<br>G-CSF<br>Post-radiotherapy<br>Metformin |
| **Infectious diseases** | Myocarditis<br>Abscess<br>Pneumonia<br>Osteitis<br>Endocarditis<br>Syphilis<br>Lyme disease |
| **Granulomatous diseases** | *Non-infectious:*<br>Sarcoidosis<br>Anthracosilicosis<br><br>*Infectious:*<br>Tuberculosis<br>Cryptococcosis<br>Histoplasmosis<br>Coccidioidomycosis<br>Blastomycosis<br>Aspergillosis |
| **Autoimmune diseases** | Crohn's disease<br>Ulcerative colitis<br>Thyroiditis<br>Vasculitis |

**Abbreviations:** G-CSF, granulocyte colony-stimulating factor.

*Table 1. Conditions associated with hypermetabolic lesions on $^{18}$FDG-PET/CT scan.*

In a review of 24 publications, Strauss et al. reported that $^{18}$FDG PET/CT scan has a sensitivity ranging from 72.7 to 100% and a specificity between 60 and 100% for tumour localization[4].

Tuberculosis, particularly in its extrapulmonary form, exhibits a wide range of clinical manifestations and can mimic malignancies as well as other granulomatous inflammatory and infectious diseases. For instance, distinguishing peritoneal tuberculosis from peritoneal carcinomatosis is challenging because the two conditions may present with similar clinical and radiological features and may even lead to elevated tumour markers such as CEA, CA 19-9, and CA 125, which are typically associated with gastrointestinal or gynaecological cancers[5]. Neither CT nor PET/CT scans can reliably differentiate between cancer and tuberculosis; definitive diagnosis requires tissue biopsy for histopathological examination and specific microbiological testing.

The literature provides limited data regarding the frequency and statistical details of misleading oncologic diagnoses, particularly concerning disseminated *Mycobacterium tuberculosis*, which is a common incidental finding on $^{18}$FDG PET/CT scan.

In both cases presented, the patients were referred to the oncology department with a high suspicion of metastatic malignancy. Patient 1 was admitted via the emergency department, and Patient 2 was referred by her general practitioner. These cases highlight the importance of considering tuberculosis in the differential diagnosis of disseminated lesions, especially in patients from endemic regions. They also serve as a reminder that a presentation highly suggestive of malignancy should not preclude the consideration of alternative diagnoses. In these instances, a presumptive diagnosis of cancer based on clinical and radiological findings was overturned by histopathological confirmation of tuberculosis.

Finally, the psychological impact of the diagnostic workup should not be underestimated. Informing patients of a high suspicion of cancer early can be extremely distressing, particularly for young individuals awaiting confirmatory tissue diagnosis. This case series emphasizes the need for clinicians to communicate the possibility of alternative diagnoses, including tuberculosis, rather than prematurely focusing solely on cancer. Histopathological and laboratory investigations remain the most accurate methods for establishing a definitive diagnosis in cases of disseminated cancer.

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