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CASE REPORT

False-positive [^{18}F]FDG PET/CT findings in breast cancer staging: Coexistence of tuberculosis, Warthin's tumor and a thyroid nodule

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ABSTRACT

Mediastinal lymphadenopathy is often a diagnostic challenge while evaluating metastasis, since it is commonly encountered in granulomatous disease or because of reactive hyperplasia due to pulmonary inflammation. In this breast cancer case, [^{18}F]fluorodeoxyglucose positron emission tomography/computed tomography ([^{18}F]FDG PET/CT) revealed a metastatic axillary lymph node with faint uptake and no detectable ipsilateral supraclavicular lymph node. However, hypermetabolic lymphadenopathies in the contralateral supraclavicular area and mediastinum were observed. Biopsy for these nodes demonstrated chronic necrotizing granulomatous lymphadenitis and the latent tuberculosis infection test was positive. Tuberculous lymphadenitis coexisting with breast cancer was diagnosed. [^{18}F]FDG uptake mimicking metastasis in benign lesions may be observed in cancer patients. Understanding the typical spread pattern of the disease is helpful in preventing misdiagnosis.

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INTRODUCTION

Mediastinal lymphadenopathy is a common finding that can be caused by both benign and malignant diseases. Common benign causes include granulomatous diseases such as sarcoidosis and tuberculosis, while common malignant causes include lung cancer, lymphoma and metastasis from extrathoracic cancers [1]. Early differential diagnosis in either cause is crucial for appropriate treatment and better outcomes.

[^{18}F]fluorodeoxyglucose positron emission tomography/computed tomography ([^{18}F]FDG PET/CT) is a widely used imaging modality for cancer staging. However, [^{18}F]FDG uptake is not cancer-specific, making interpretation difficult in some cases. This report presents the case of a stage II breast cancer patient with synchronous benign uptakes in different sites, including mediastinal lymph nodes.

CASE PRESENTATION

This case study was approved by the Institutional Review Board of Ilsan Paik Hospital on January 16, 2025 (IRB file No. ISPAIK 2024-12-029), and the need for informed consent was waived. A 76-year-old woman was referred to our institution with a palpable breast mass for three months. Mammography showed an irregular hyperdense mass in the left breast. Ultrasonography (USG) revealed an irregular hypoechoic mass with increased vascularity, hard elasticity and an echogenic halo at the same site, which was highly indicative of malignancy. An indeterminate lymph node with mild cortical thickening was also seen in the left axilla.

USG-guided core needle biopsy confirmed the diagnosis of invasive ductal carcinoma and lymph node metastasis.

On [^{18}F]FDG PET/CT scan for staging work-up (Figure 1), a 27mm-sized hypermetabolic tumor with a maximum standardized uptake value (SUVmax) of 9.0 was observed in the left lower outer breast (Figure 2A). A known metastatic lymph node in the left axilla showed faint uptake with a SUVmax of 1.1 (Figure 2C). In contrast, multiple enlarged lymph nodes with high [^{18}F]FDG uptake (SUVmax of 10.8) were observed in the right paratracheal and supraclavicular areas (Figure 3). Intense hypermetabolic parotid incidentalomas (SUVmax of 73.3) and a hypermetabolic left thyroid nodule (SUVmax of 5.2) were also detected (Figure 4).

Because the contralateral lymph node is considered to be a distant metastasis, biopsy of the right supraclavicular lymph node was requested and confirmed to be chronic necrotizing granulomatous lymphadenitis. The following polymerase chain reaction test for Mycobacterium was negative, but the interferon-gamma release assay was positive, indicating tuberculous lymphadenitis. Additionally, the parotid lesions were considered as Warthin's tumors based on neck CT and fine needle aspiration, which revealed syncytial clusters of oncocytic epithelial cells and scattered lymphocytes.

The thyroid nodule was evaluated as a mainly cystic lesion with low suspicion on USG. Follow-up observations were decided for the parotid and thyroid gland lesions.

The patient underwent left partial mastectomy with axillary lymph node dissection, and one lymph node out of 11 was confirmed as metastasis (T2N1M0). She successfully completed postoperative radiotherapy and is currently on hormonal therapy without recurrence. Chemotherapy was omitted due to old age and impaired cardiac function. For latent tuberculosis management, she was treated with antitubercular drugs (isoniazid, ethambutol, rifampin and pyrazinamide) during 6 months after completing radiotherapy, and no respiratory symptoms were noted.

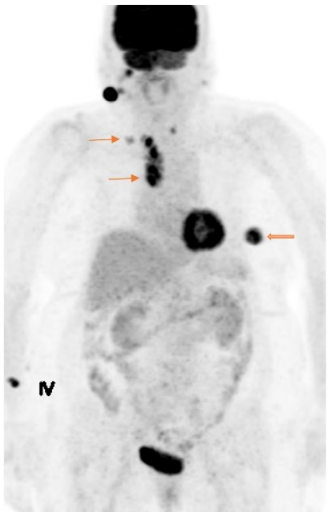

Figure 1. The maximum intensity projection (MIP) image of [^{18}F]FDG PET/CT. A hypermetabolic left breast tumor is observed (thick arrow), and the uptake in the left axillary lymph node is barely noticeable. In contrast, hypermetabolic lymph nodes are observed in the right supraclavicular area and mediastinum (thin arrow). Hypermetabolic lesions are also found in both the parotid areas and the left thyroid lobe

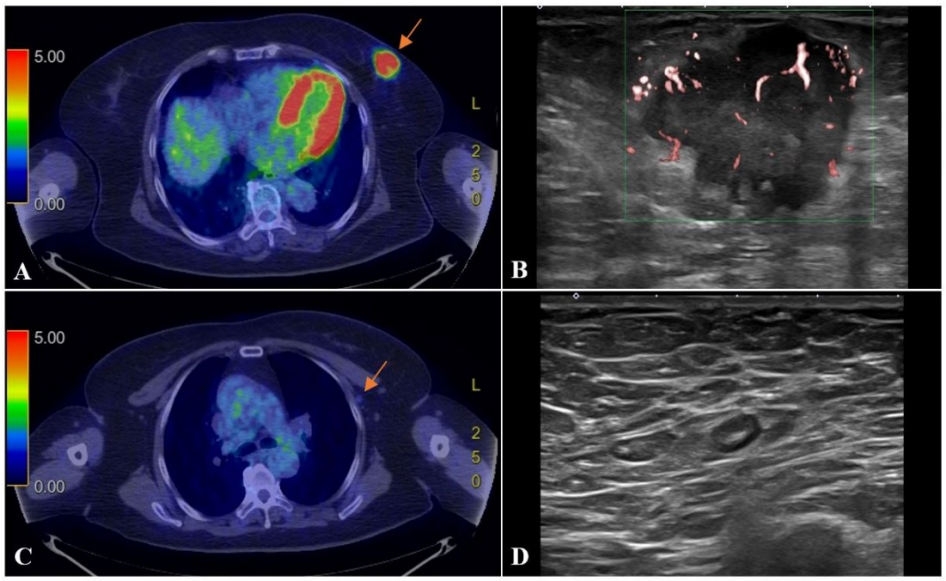

Figure 2. [^{18}F]FDG PET/CT reveals a hypermetabolic tumor (SUVmax of 9.0) in the left lower outer breast (A), along with a lymph node showing faint uptake (SUVmax of 1.1) in the left axilla (C). USG shows a breast tumor with malignant features (B) and an indeterminate axillary lymph node with mild cortical thickening (D)

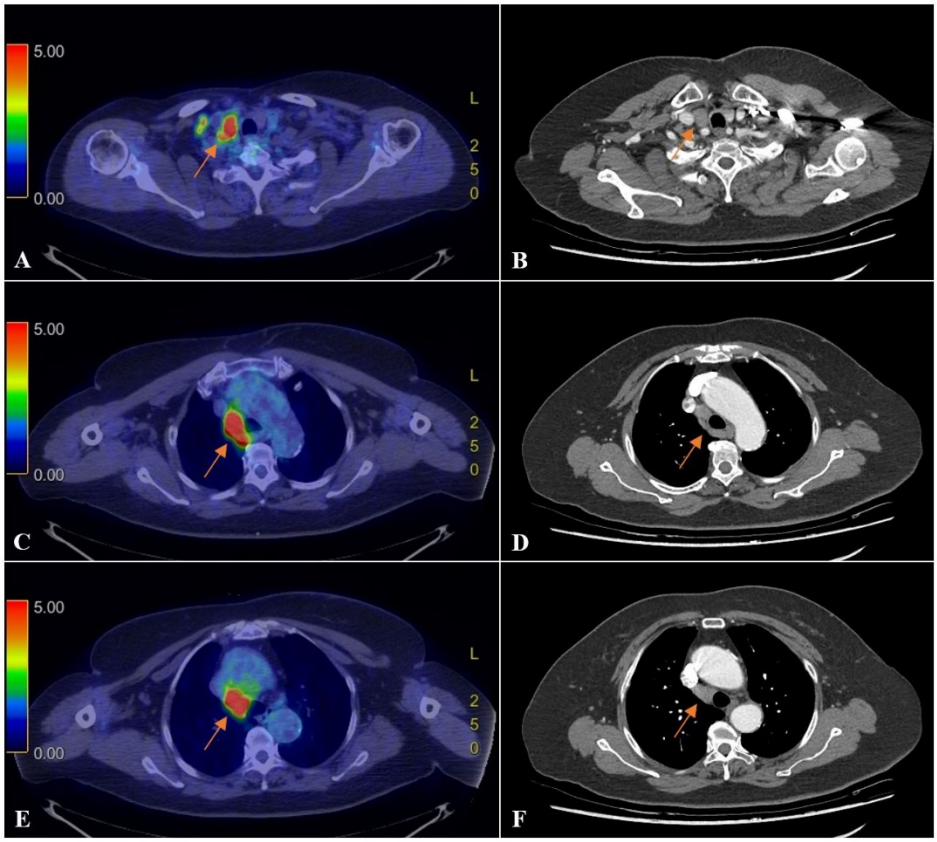

Figure 3. [^{18}F]FDG PET/CT reveals hypermetabolic lymphadenopathies (SUVmax of 10.8) in the right supraclavicular area (A), right upper paratracheal area (C) and right lower paratracheal area (E). Chest CT also demonstrates enlarged lymph nodes in the corresponding sites (B, D, F). These lesions were diagnosed as tuberculous lymphadenitis through biopsy and interferon-gamma release assay

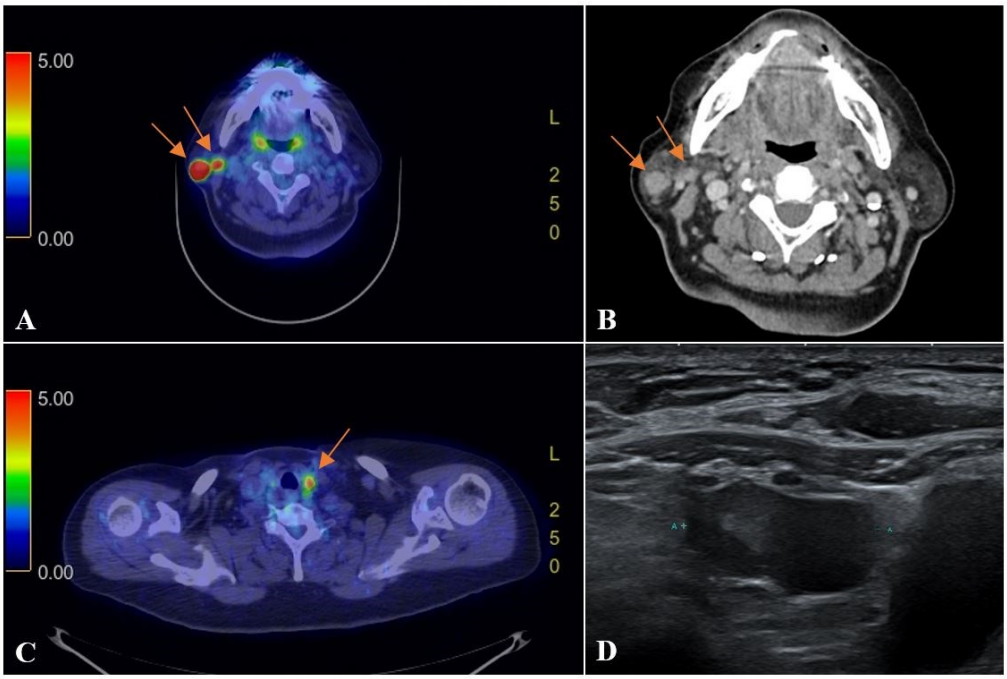

Figure 4. [18F]FDG PET/CT reveals incidental hypermetabolic parotid nodules (SUVmax of 73.3) (A) and a hypermetabolic left thyroid nodule (SUVmax of 5.2) (C). Neck CT shows well-defined enhancing nodules in the parotid gland (B), which were considered as Warthin's tumors by fine needle aspiration. USG shows a mainly cystic nodule with low suspicion in the left thyroid lobe (D)

DISCUSSION

[18F]FDG accumulates not only in malignant cells but also in inflammatory cells due to the increased glycolysis of cellular infiltrates composed of lymphocytes and macrophages [2]. This pathophysiology is advantageous in evaluating patients with inflammatory or infectious diseases but may be a pitfall in assessing disease extent or progression in patients with malignancies. In this case of breast cancer, no ipsilateral supraclavicular lymph node was detected whereas hypermetabolic lymphadenopathies were observed on the contralateral side. This unusual spread pattern implied the possibility of skip metastasis or another distinct pathology. The final diagnosis was tuberculosis-associated benign lymphadenopathies, which was unexpected since the patient had no lung parenchymal lesions or respiratory symptoms. There are several similar cases in which tuberculous lymphadenitis was simultaneously identified on [18F]FDG PET/CT in patients with various cancers [3, 4]. Hypermetabolic lesions in uncommon metastatic sites may suggest the coexistence of different pathologies from primary cancer.

The prevalence of tuberculous lymphadenitis among breast cancer patients is reported to be 0.034% to 6.8% [5, 6]. Despite its low incidence, tuberculosis should be included in the differential diagnosis of mediastinal lymphadenopathy in cancer patients when considering increased risk of tuberculosis in patients with malignancies, especially gastrointestinal, breast and hematologic cancers [7], tuberculous lymphadenitis being the most common manifestation of extrapulmonary tuberculosis and finally the fact that there are still several tuberculosis-endemic countries globally, including our own country, where the elderly population is predominantly affected [8]. Besides tuberculosis, chronic inflammatory diseases such as anthracofibrosis, sarcoidosis and silicone granuloma may also exhibit high [18F]FDG uptake, which can be mistaken for metastasis [9-11]. Therefore, more attention is required when evaluating inflammation-prone mediastinal lymph nodes.

On the other hand, this case showed incidental hypermetabolic lesions in the parotid and thyroid glands, which are rare metastatic sites from breast cancer. Warthin's tumor is a representative benign neoplasm showing high [18F]FDG uptake due to its abundant mitochondrial density in oncocytic cells [12]. Interestingly, the malignancy rate in parotid incidentalomas has been reported to be lower than that of non-incidental parotid tumors [13]. In cases of incidental focal thyroidal uptake, the possibility of double primary thyroid cancer is

known to be approximately 30% in patients with nonthyroidal cancer, but this risk seems to be unrelated to the intensity of [^{18}F]FDG uptake [14].

CONCLUSION

Benign [^{18}F]FDG uptake independent of primary cancer may mimic metastasis. Metastasis should not be diagnosed solely based on high [^{18}F]FDG uptake. It is essential to consider the characteristic pattern of the disease in terms of the probability of metastasis. Pathological confirmation may be necessary in some cases to differentiate between unusual metastasis from an unrelated coexisting pathology. When interpreted appropriately, [^{18}F]FDG PET/CT has a clinical significance in simultaneously detecting inflammatory conditions or benign lesions in cancer patients.

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