

# Appropriate Diagnostic Approach in Patients with Suspicious Bone Metastasis from Low FDG-Avid Primary site in Thyroid gland: Case report

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## ABSTRACT

Metastatic bone tumors are the most common malignant tumor involving bone. Bone metastases from primary tumors of unknown origin are commonly attributed to prostate, breast, lung, and thyroid. <sup>18</sup>F-fluorodeoxyglucose (FDG) Positron Emission Tomography-Computed Tomography (PET-CT) has a very useful imaging modality to identify primary site in patients with suspicious bone metastasis. However, it remained unclear whether PET-CT have clinical value to identify primary site because some cancer types have low FDG-avidity. We report a case of 84-year-old female patient presenting with metastatic bone tumor in skull without showing any metabolic activity in primary site of her thyroid gland on FDG PET-CT and we discussed how to use other clinical information in this patient.

**Keywords:** PET-CT, metastatic bone tumor, thyroid, thyroglobulin.

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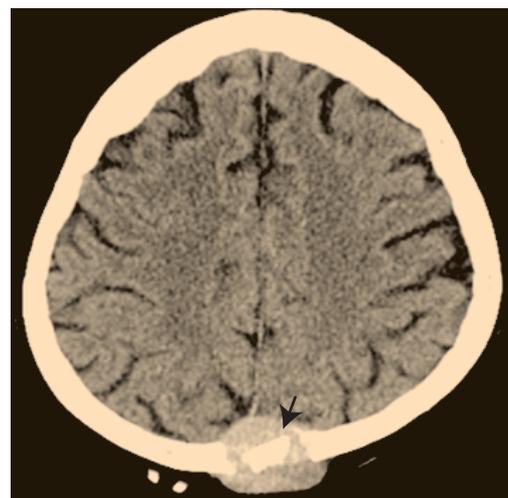
## INTRODUCTION

<sup>18</sup>F-fluorodeoxyglucose (FDG) Positron Emission Tomography-Computed Tomography (PET-CT) has a well-established role in cancer diagnosis, staging and treatment response monitoring (1). FDG PET-CT shows a high sensitivity and specificity to localize the potential primary malignancies as well as it provides important information for differential diagnosis in patients with suspicious bone metastasis (2). Shimada et al. reported that FDG PET-CT detected the primary cancer in 43.6% (17/39) of patients with bone metastasis (3). Yanagawa et al. showed that FDG PET/CT identified the primary in 50% (12/24) of patients with bone and soft-tissue metastasis from an unknown primary (4). In thyroid cancer, bone is the second most common site for distant metastasis after lung. Osteolytic metastases seem to be more FDG-avid

than osteoblastic or sclerotic metastases due to their aggressive nature with higher glycolytic rate (5). Diagnostic approach to find out the primary lesion with a suspicious bone metastasis from thyroid cancer includes combination of different imaging modalities, biochemical marker including serum thyroglobulin (Tg) level and clinical history. We report a thyroid cancer case who had suspicious bone metastasis but no abnormal FDG uptake in primary site.

## CASE REPORT

An 84-year-old female presenting with scalp swelling was admitted in CNUHH hospital for a suspected skull bone metastasis. We found a solitary osteolytic lesion along with enhancing soft tissue mass in parieto-occipital skull on CT (Figure 1).



**Figure 1 :** CT scan shows solitary osteolytic lesion with enhancing soft tissue mass in parieto-occipital region of skull (arrow).

To identify the primary lesion, FDG PET-CT was done (Figure 2). We found two bone uptakes, one in left iliac bone (maximum standardized uptake value, SUVmax:6.9) and another one in right 5th rib with mild hypermetabolic activity (SUVmax: 1.5).

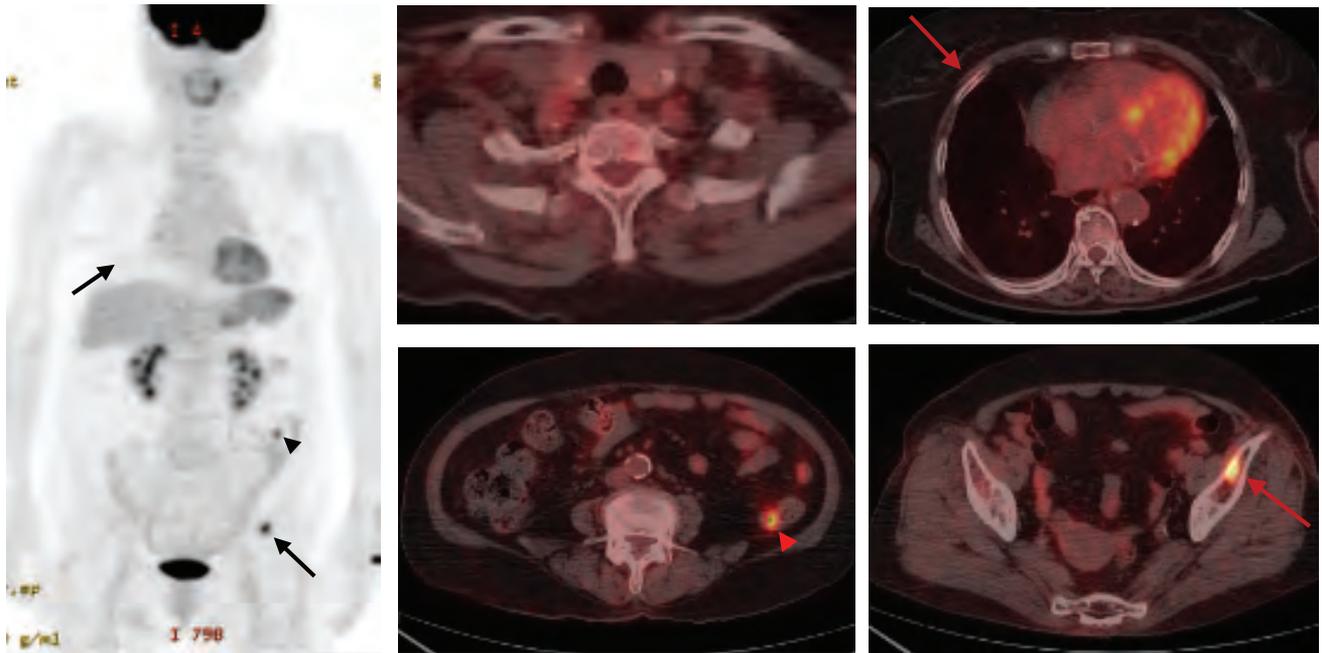


Figure 2: <sup>18</sup>F-FDG PET-CT shows two hypermetabolic lesions in left iliac bone (SUVmax: 6.9) and right 5th anterior rib (1.5) (arrows). Small focal hypermetabolic lesion is also noted in descending colon (SUVmax: 5.4, arrowhead). However, there is no abnormal FDG uptake in thyroid gland.

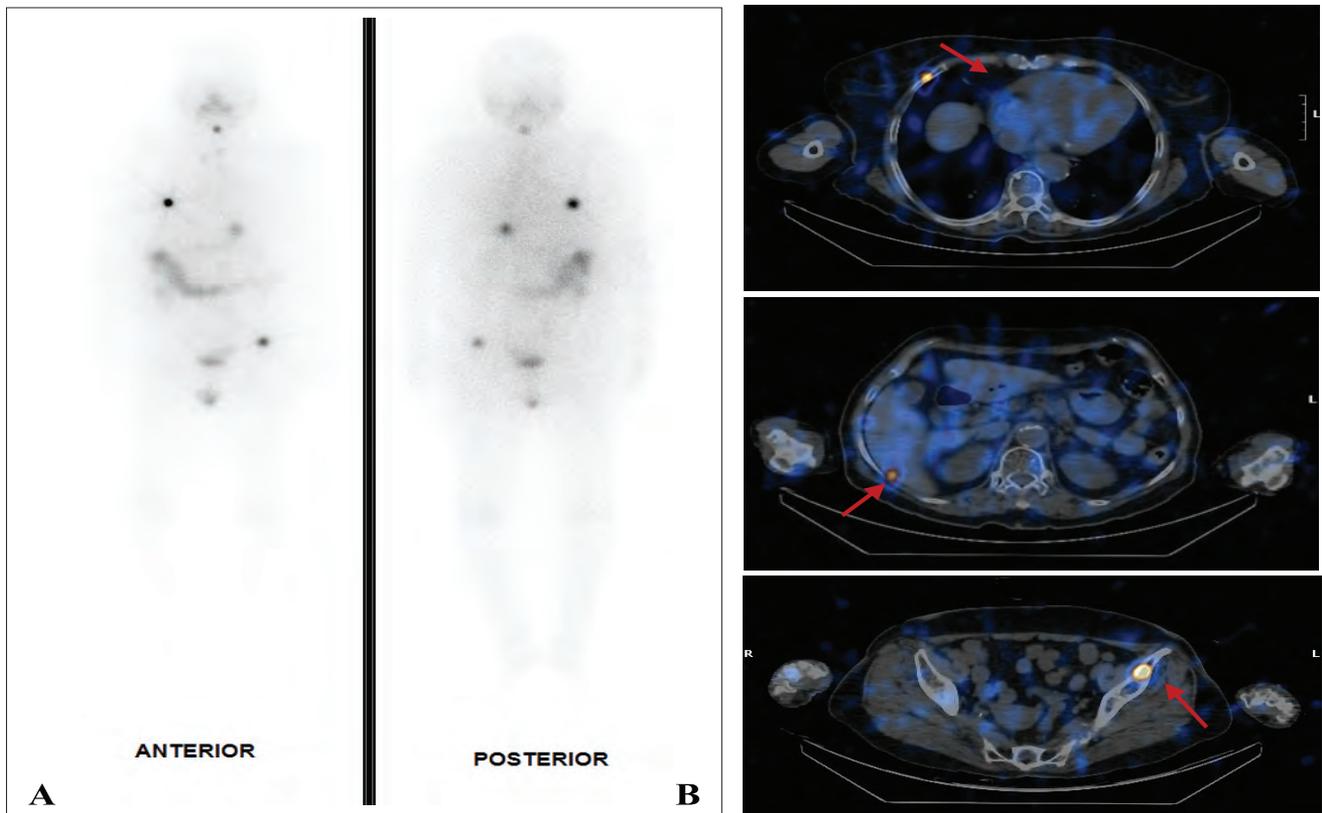


Fig. 3(A)Whole body scan after <sup>131</sup>I-ablation therapy shows iodine-avid lesions in right chest, left pelvic areas, as well as the anterior neck. (B) <sup>131</sup>I-SPECT-CT shows focal uptakes in right 5th anterior, 10th posterior ribs, and left iliac bone (yellow arrows).

There was also small focal hypermetabolic activity in descending colon (SUVmax: 5.4). Somewhat inhomogeneous hypermetabolism was noted in spleen which may be due to systemic inflammation or underlying hematologic disorders rather than malignancy. But there was no abnormal FDG uptake in thyroid gland, breast or lung. Patient was recommended for colonoscopy and biopsy revealed tubular adenoma with low grade dysplasia in the sigmoid-descending colon junction. Others tumor markers were within normal limit (CEA: 2.79 ng/ml, AFP: 1.67 IU/ml, CA19-9: < 2.00 U/ml and CA-125: 27.7 U/ml). Interestingly, serumTg level was markedly elevated (1672.00 ng/ml). Craniectomy with cranioplasty was performed and pathology report revealed metastatic follicular carcinoma of thyroid with positive results in immunohistochemical stains for TTF-1 (thyroid transcription factor-1), thyroglobulin and CD56. Neck ultrasonography (US) showed two calcified nodules in right thyroid lobe with multiple reactive lymph nodes in right neck level III-IV. However, fine needle aspiration cytology (FNAC) showed benign nodules. Then total thyroidectomy with lymph node dissection was done and pathology revealed both follicular carcinoma in right lobe and papillary carcinoma with follicular variant in left lobe. Patient was treated with high dose radioactive iodine ablation therapy with 150 mCi. Post-therapeutic whole-body scan showed iodine-avid metastatic lesions in right chest and left pelvic areas as well as remnant thyroid tissue uptake in the anterior neck (Fig. 3). Three iodine-avid metastatic lesions were detected in right 5th anterior, 10th posterior ribs, and left iliac bone in <sup>131</sup>I tumor SPECT-CT.

Thyroid carcinoma comprises only about 1% of all malignant neoplasm, about 0.5% of cancers in men and 1.5% in women (6). Nearly 7%–23% of the patients with thyroid carcinomas may develop metastases during disease progression; however, only 1%–3% of patients present with distant metastatic lesions (7). Metastatic spread is most commonly seen in lymph nodes, lungs, and bones through lymphatics in well-differentiated papillary carcinomas whereas hematogenous spread in follicular carcinomas. In our case, patient was presented with suspected bone metastasis and diagnosed as

metastatic follicular carcinoma in biopsy of skull lesion. Although most of the solid tumors demonstrate high FDG uptake but for some cases false-negative result can be found if the primary site is located in kidney, prostate, colon, thyroid or even in breast. Reasons for low FDG uptake may include tumor with low cellularity or low-glucose-metabolizing factor. The ability to detect lesions at FDG PET-CT also depends on many factors, including lesion size, ability of the tumor to concentrate FDG, proper patient preparation, background FDG uptake in surrounding tissues and type of scanner used. In this patient, there was no FDG-avid lesion found in breast or lung. And we could exclude colonic malignancy by colonoscopy. We should try to find another way to identify primary site in this case. In this patient, serum Tg level and immunohistochemical stain can be very helpful to find the primary lesion. Neck US and FNAC can play important role for diagnosis of thyroid cancer. A microcarcinoma of < 3 mm in size having the potential to develop metastases, might not be detected under routine pathologic examination (8). FNAC from two small calcified nodules on US, was not informative in this case. Therefore, resection of the thyroid gland is needed to identify the primary tumor. Normal thyroid tissue takes up little FDG. Well-differentiated thyroid carcinomas (follicular and papillary) typically demonstrate high iodine uptake and low FDG uptake because of having heterogeneous and often poor GLUT-1 expression. GLUT-1 was shown to be expressed in 0–10 % of follicular adenoma, 52.9–100 % of PTC, 33.3–58.8 % of FTC, 80 % of PDTC, and almost all ATC cases. So FDG uptake follows GLUT-1 immunohistochemical expression with more avidity in dedifferentiated thyroid tumors. When thyroid cancers dedifferentiate, they typically lose the ability to accumulate iodine. Histologically, 2 to 5 % of well-differentiated thyroid tumors will lose their differentiation and become candidates for the “flip-flop” phenomenon (9). In this phenomenon well differentiated thyroid cancer having their originating follicular cell can take up iodine and cancer lesion can be visualized on radioiodine imaging but not on FDG PET. Conversely, poorly differentiated thyroid cancer does not have the characteristics of the originating thyroid

follicular cells and has cancer hallmarks, and therefore, the cancer can take up glucose, but not iodine. Therefore, the cancer lesions can be visualized on F-18 FDG PET imaging, but not on radioiodine imaging (10). This phenomenon could be represented in the same patient. Sodium-iodide symporter (NIS) expression could be different among primary and metastatic lesions as carcinogenesis disrupts the regulatory growth mechanism and follicular cells lose their ability to express the NIS. In this case, FDG avidity was higher in metastatic lesion than in primary lesion. Further study is necessary to understand this phenomenon in the same patient.

## CONCLUSION

Metastatic tumor without an identifiable primary lesion represents a diagnostic problem and a therapeutic challenge. If FDG PET-CT shows false negative result to identify primary site like this patient, we should consider other modalities like biochemical marker, pathologic examination as well as clinical history for appropriate management.

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