

¹⁸F-FDG PET/CT in the Evaluation of Solitary Extramedullary Plasmacytoma: A Case Series

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ABSTRACT

The role of fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) in patients with multiple myeloma (MM) and other plasma cell disorders is well-known. Solitary plasmacytoma (SP), an extremely rare form within this entity accounting for approximately 4% of plasma cell malignancies, can be classified as solitary bone plasmacytoma (SBP) or solitary extramedullary plasmacytoma (SEMP). Extramedullary plasmacytoma (EMP) is a rare neoplasm characterized by the monoclonal proliferation of plasma cells outside the bone marrow. Breast and craniocerebral regions are the uncommon sites of the presentations of EMP, rarely reported in the literature. The most frequent site of presentation is the upper airways. The EMPs have similar pathogenesis as MM; however, they differ in management as they are radiosensitive in nature, and radiotherapy is the preferred treatment modality. As SEMP has a better prognosis than SPB with a lower conversion rate to MM, accurate staging is essential to plan for the treatment. The ¹⁸F-FDG PET/CT has higher sensitivity for the evaluation of treatment response. In the present case series, it was aimed to depict the role of ¹⁸F-FDG PET/CT in newly diagnosed SEMP with different sites of origin to exclude further lesions leading to changes in the treatment plan and treatment response assessment.

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Introduction

Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) is a valuable imaging modality in patients diagnosed with multiple myeloma (MM) and other disorders of plasma cells based on the recent recommendations by the International Myeloma Working Group (1). Sometimes, a solitary accumulation of clonal plasma cells either in the bone or soft tissue without the signs of systemic disease precedes MM. The presentations of solitary plasmacytoma (SP) can be either solitary bone plasmacytoma (SBP) or extra-medullary plasmacytoma (EMP); however, 3-5% of all plasma cell neoplasms can present as solitary extramedullary plasmacytoma (SEMP), a percentage lower than that reported for SBP.

The ¹⁸F-FDG PET/CT is the preferred imaging modality for the exclusion of further lesions and assessment of treatment response in newly diagnosed SEMP (1, 2). Nevertheless, EMP has a better prognosis in comparison to SBP as the rate of conversion to MM is lower in EMP, compared to that reported for SBP (3). Important steps in the management of EMP patients are to accurately stage patients and exclude the possibility of systemic involvement due to the poor prognosis of MM.

The present case series represents different sites of the presentations of SEMP with the incremental role of ¹⁸F-FDG PET/CT in the management of suspected SEMP and assessment of treatment response.

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Case 1

A 50-year-old postmenopausal female patient presented to the research institute with a history of a lump in her left breast since 1.5 months ago. The patient had no associated pain, nipple discharge, weight loss, systemic symptoms, and history of trauma or breast surgery. There was no familial history of breast carcinoma. On examination, a 3×2 cm well-defined, soft to firm, slightly mobile, non-tender mass was observed in the upper inner quadrant (UIQ) of the left breast with no palpable axillary/supraclavicular nodes or overlying skin fixation. Sonomammography conducted at the peripheral center demonstrated a lesion with Breast Imaging-Reporting and Data System-IVA and possible giant fibroadenoma with surrounding inflammatory changes .

Furthermore, fine-needle aspiration cytology revealed a malignant round cell tumor with the possibility of Non-Hodgkin's lymphoma plasmacytoid type. Trucut biopsy and immunohistochemistry (IHC) at the study

institute objectified a plasmacytoma. Serum kappa and lambda light chains increased with a kappa/lambda ratio of 1.45 on serum protein electrophoresis (SPEP) with raised serum immunoglobulin G (IgG) levels. Bone marrow biopsy, whole-body skeletal survey, liver function test, electrolytes, urea, creatinine, and abdominopelvic ultrasound were normal. The patient had normal chromosome analysis.

The case was subjected to FDG PET/CT for staging. The whole-body PET maximum intensity projection (MIP) images revealed a metabolically active well-defined enhanced soft tissue density lesion involving the UIQ of the left breast with no abnormal FDG avid lesion elsewhere to suggest a distant lesion (Figures 1 [A] and [B]). The FDG PET/CT and contrast-enhanced computed tomography (CECT) images showed the lesion measured approximately 2.9×2.3 cm in the transaxial plane (Figures 1 [C] and [D]) and craniocaudal extension of 3.2 cm (Figures 1 [E] and [F]) (SUV_{Max}=4.4).

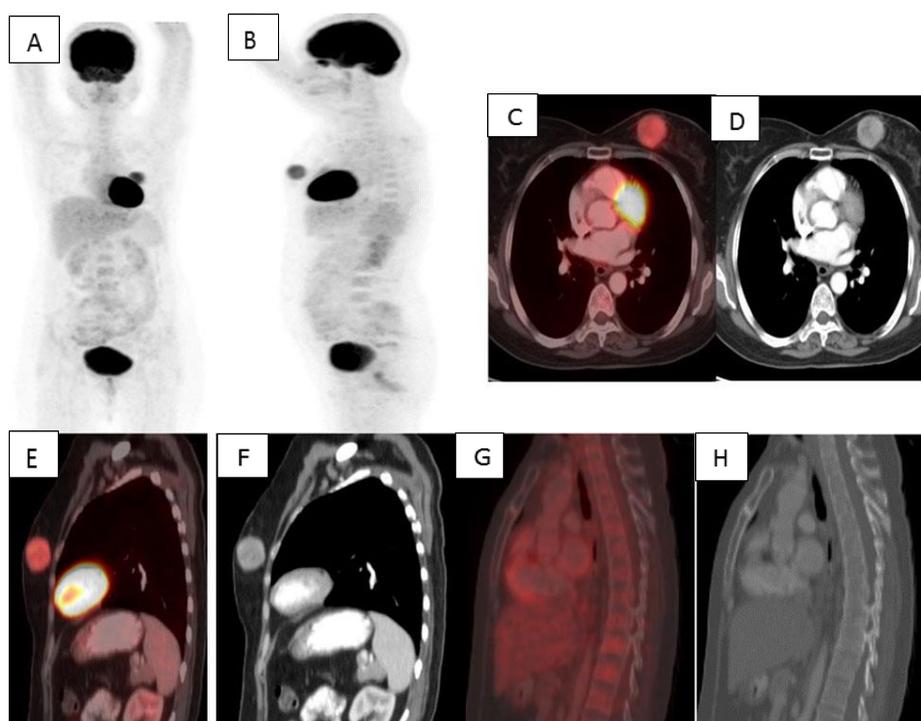


Figure 1. Whole-body fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) maximum intensity projection images illustrating metabolically active primary breast lesion with no evidence of any other bony/soft tissue lesions elsewhere (A) and (B); fused FDG PET/CT and contrast-enhanced computed tomography (CECT) transaxial[(C) and (D)] and sagittal [(E) and (F)] images depicting well-defined lesion involving upper inner quadrant of left breast region; fused FDG PET/CT (G) and CECT (H) sagittal images showing no evidence of bone marrow involvement in the visualized skeleton

There was no evidence of bone marrow involvement on FDG PET/CT and CECT images on sagittal images (Figures 1 [G] and [H]). The diagnosis of SP of the breast was confirmed by whole-body FDG PET/CT. The patient was scheduled for external beam radiation therapy

(EBRT) (200 cGy/fraction for a total of 20 fractions; 5 fractions per week) on a linear accelerator with tangential fields by three-dimensional conformal radiation therapy with proper immobilization over the left breast region.

Case 2

A 42-year-old male patient had symptoms of frontal headache and swelling for 2 months. The patient underwent bilateral frontal craniotomy and extradural tumor removal for suspected large frontal meningioma with compression over frontal lobes and bone erosion on a preoperative

computed tomography (CT) scan conducted at the study institute. However, postoperative histopathology and IHC objectified a plasmacytoma. Skeletal survey, serum creatinine, and bone marrow biopsy were normal. The SPEP showed M band on the gamma region.

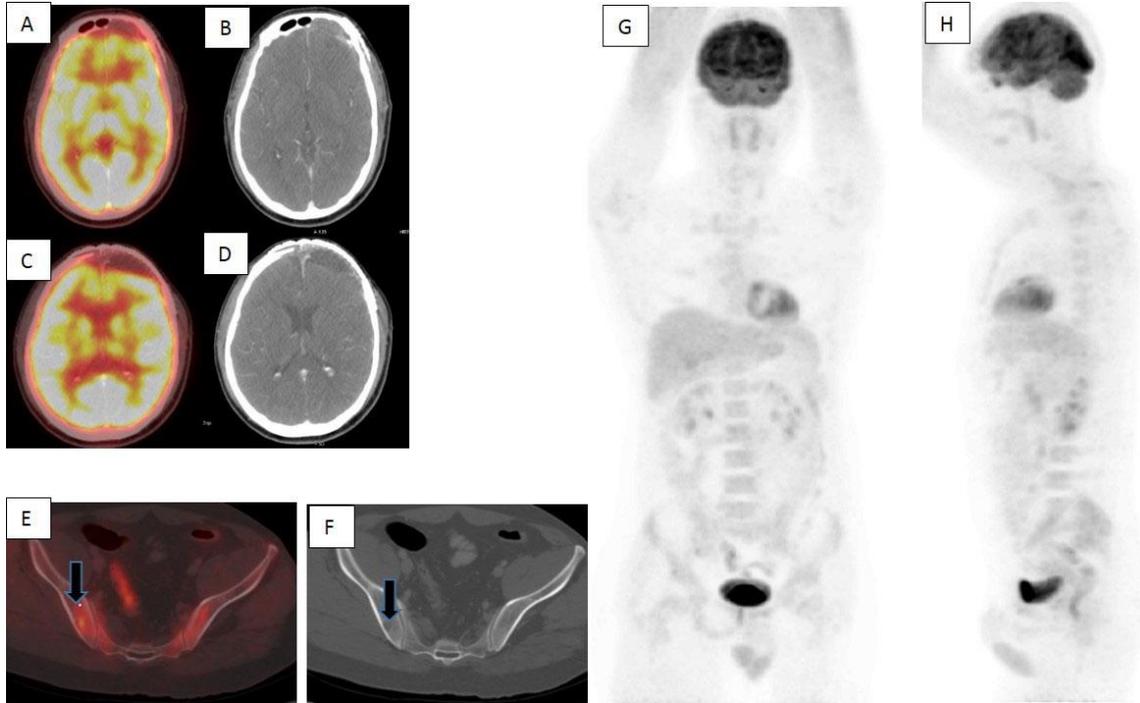


Figure 2. Fused FDG PET/CT (A) and (C); CECT transaxial images of brain illustrating postoperative changes at frontal region (B) and (D); fused FDG PET/CT (E) and CECT transaxial images of pelvis (F) showing a metabolically active lytic lesion in right iliac bone (arrow); whole-body FDG PET/CT maximum intensity projection images illustrating low-grade diffuse homogenous marrow uptake (G) and (H)

The patient was subjected to FDG PET/CT scan to exclude other lesions. The FDG PET/CT and CECT revealed postoperative changes at the operated site in the frontal region of the brain (Figure 2 [A-D]) and a focal FDG avid lytic lesion measured approximately 9 × 8 mm involving the right iliac bone adjacent to the inferior aspect of the right sacroiliac joint ($SUV_{max}=5.6$) (Figures 2 [E] and [F]). The patient was scheduled for chemotherapy instead of radiotherapy due to a distant lesion. The patient completed chemotherapy (nine cycles of bortezomib, thalidomide, and dexamethasone in addition to five cycles of melphalan and prednisolone), received maintenance thalidomide therapy for 2 years, and is kept under observation at present.

Case 3

A 25-year-old male patient with a mass lesion in the right maxillary sinus extending into the right nasal cavity was referred to the study institute post right rhinotomy, mass excision and further management. Preoperative CT scan revealed a mass lesion in the right maxillary sinus extending

into the right nasal cavity, ethmoid sinus, and frontal sinus with adjacent bony thinning. The biopsy objectified a plasma cell-rich neoplasm. The diagnosis of plasmacytoma was confirmed on IHC. The patient's bone marrow biopsy revealed marrow uninvolved by plasma cell dyscrasia.

The patient had a slightly raised kappa/lambda ratio of 1.63 and raised IgG level on SPEP. Due to a solitary lesion, the patient was scheduled for definitive EBRT (200 cGy per fraction up to a total dose of 46 Gy in 23 fractions; 5 fractions per week) on a linear accelerator by intensity-modulated radiation therapy with proper immobilization, 95 percentage of isodose covering, and 95 percentage of PTV of local disease status. The CT scan of the patient 5 months following the radiotherapy demonstrated a residual lesion.

The case was subjected to FDG PET/CT scan to differentiate the residual lesion from posttreatment changes. The FDG PET/CT and CECT transaxial images showed a metabolically active ill-defined soft tissue density lesion

(SUV_{max}=6.2) involving the right maxillary sinus with the erosion of the anterior wall, extension into the right premaxilar fat space (Figures 3 [A]

and [B]), erosion of the medial wall of the right maxillary sinus, and erosion of right-sided nasal turbinates (Figure 3 [C-F]).

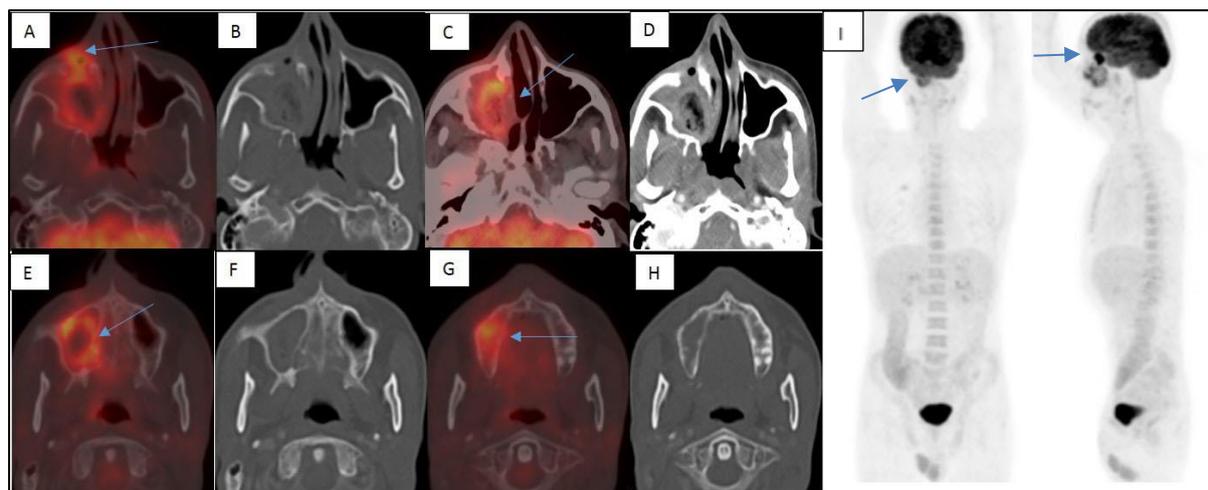


Figure 3. Fused FDG PET/CT and contrast-enhanced computed tomography transaxial images showing a metabolically active lesion involving right maxillary sinus with erosion of anterior wall and extension into right premaxilar fat space (arrow) (A) and (B); erosion of medial wall (arrow) (C), (D), (E), and (F); floor of right maxillary sinus (arrow) (G) and (H); whole-body FDG PET/CT maximum intensity projection images showing a metabolically active lesion in right maxillary sinus with no evidence of any other bony/soft tissue lesions elsewhere (arrow) (I)

There was cortical thinning of the posterolateral wall and floor of the right maxillary sinus (Figure 3 [G] and [H]). The whole-body FDG PET MIP images showed a metabolically active lesion in the right maxillary sinus with no evidence of other bony/soft tissue lesions elsewhere (Figure 3 [I]). The findings revealed residual active disease involving the right maxillary sinus. The patient was lost to follow-up after FDG PET/CT.

Discussion

The EMP firstly described by Schridde in 1905 is an extremely rare and discrete solitary mass of neoplastic monoclonal plasma cells (4). The staging system by Durie and Salmon has considered EMP as stage I myeloma. According to Wiltshaw, there are three clinical stages of EMP, namely stage I in patients presenting with a single extramedullary site, stage II in patients with regional lymph node involvement, and stage III in patients with a lesion at a distant site (i.e., multiple SP or metastasis); however, it is no longer an SP (5).

The plasma cells with reduced expression of adhesion molecules, such as VLA-4, CD44, and CD56, forming the appropriate microenvironment and being deposited as plasmacytomas in tissues, are the proposed pathogenesis of extramedullary involvement (6). Etiopathogenesis of EMP is similar to MM; however, the main difference compared to MM is in clinical presentations and management approach as EMP is radiosensitive in nature, and the treatment of choice for solitary lesions is local

radiation therapy (RT) (7, 8). Approximately 10-20% of EMP patients will progress to MM despite curative treatment worsening the overall survival (9). Therefore, it is essential to accurately stage the patient with the identification of all sites of lesions and implement the appropriate plan of treatment.

The EMP most frequently presents in the upper airways and oral cavity region; nevertheless, it may originate from soft tissues throughout the body (10). Other sites are the pulmonary system, digestive tract, spleen, pancreas, ovary, thyroid gland, rarely in the breast (11, 12), and craniocerebral region (13, 14).

The EMP of the breast is rare and has been observed at diagnosis in only 14% of cases. Most (75%) of breast plasmacytomas occur during the relapse of MM, and few cases are bilateral or synchronous with other lesions (11, 12). Breast EMP presents a similar fashion as other lumpy lesions of the breast and mimics adenocarcinoma or fibroadenoma on examination. However, trucut biopsy of breast lesion assisted with IHC lead to a diagnosis of breast plasmacytoma (11, 12).

On FDG PET, the breast lesion mimics adenocarcinoma, lymphoma, abscess, cystic disease, or metastatic disease if imaging is performed before the biopsy (15). Case 1 was reported with no history of MM and referred for staging after the confirmation of biopsy. The FDG PET/CT confirmed SEMP. Clinical experience for the treatment of this lesion is limited due to the rare occurrence of the disease; however, due to

solitary lesion, RT would be a better option for treatment (7, 8).

Intracranial EMPs as uncommon neoplasms are solitary or multiple, arising from the skull, meninges, or rarely brain (13, 14). Intracranial plasmacytomas are generally localized and noninvasive; however, aggressive features, such as local brain invasion, can rarely occur (13, 14). The clinical presentations of intracranial EMP depend on the tumor site and its extension. Bone or soft tissue lesions with different manifestations of mass effects, pain, and infiltration are the frequent presentations of these tumors (13).

Cranial nerve palsies and clinical manifestations of space-occupying lesions, such as headaches, visual problems, seizures, or paresis, are the frequent symptoms of intracranial plasmacytomas (13, 14). These tumors may present with deceptive clinical presentations and neuroradiological findings and resemble other most prevalent tumors, such as meningioma, requiring further evaluation. As in case 2, the patient had frontal headaches and swelling in the frontal region and extra-axial location with intense enhancement on CT scan suspected of meningioma. In addition, the patient underwent the excision of the lesion.

Systemic evaluations (i.e., bone marrow examination and skeletal survey) were normal, and no evidence of monoclonal gammopathy (M component) was observed in serum and urine protein electrophoresis. However, FDG PET/CT conducted for the postoperative staging of the disease revealed a small metabolically active lytic lesion in the right iliac bone. The FDG PET/CT changed the management plan of this patient from radiotherapy to chemotherapy.

Out of all head and neck EMPs, mucosa-associated lymphoid tissue (MALT) of the upper respiratory tract is affected in 80-90% of cases, out of which the nasal and paranasal areas are affected in 75% of patients (16). Out of all nonepithelial sinonasal tumors, 4% of them can present as EMP (17). It occurs frequently in males than in females (3:1 ratio), and the most frequent occurrence is in patients older than 50 years (10). RT is the preferred treatment modality for head and neck EMP. For tumors with a size of less than 5 cm, the radiation doses of 30-40 Gy in 20 fractions can achieve excellent local tumor control; however, tumors with a size of more than 5 cm require a dose increase up to 40-50 Gy (10).

Effective treatment for small lesions is surgical resection with no adjuvant RT unless the surgeon has a suspicion of residual tumor. Large and well-defined masses might be resected by surgery but requiring adjuvant radiotherapy (2). Patients

have better outcomes in case of EMP occurrence in the head and neck region, age of under 50 years, tumor size of less than 4 cm, and absence of monoclonal protein (M-protein-spike) in SPEP (18). Chemotherapy is indicated in tumor sizes of more than 5 cm, higher-grade tumors, relapsed and/or refractory disease, and in case of disease progression to MM (16).

PET/CT is more sensitive than MRI for the evaluation of treatment responses. Persistent high uptake on FDG PET/CT indicates residual disease (2). In case 3, the post radiotherapy CT scan was indicative of the suspicious residual lesion; therefore, the patient was subjected to FDG PET/CT. The FDG PET/CT revealed residual disease involving the right maxillary sinus with significant metabolic activity. Patients with persistent disease on FDG PET/CT after initial radiotherapy are subjected to chemotherapy (2). However, the patient was lost to follow-up after the scan. Although EMP has a rare occurrence, a thorough follow-up protocol is required due to the possibility of disease recurrence and progression of disease into a systemic disease, such as MM (17, 19).

Conclusion

The ¹⁸F-FDG PET/CT has an incremental role in the management of suspected SEMP for the staging of disease with the identification of new lesions leading to a change in treatment plan. In addition, it is helpful in the evaluation of treatment response.

Conflicts of interest

The authors declare that there is no conflict of interest.

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