Case Report

Ga68-FAPI Imaging and Lu177-FAPI Therapy in a Case of Metastatic Solitary Fibrous Tumor

Abstract

Solitary fibrous tumor (SFT) of the central nervous system (previously called hemangiopericytoma) is a rare mesenchymal tumor. Malignant SFT has a tendency to recur after surgery and can metastasize to distant organs. Treatment options for metastatic disease are limited. This case demonstrated high expression of FAP (fibroblast activating protein) in all metastatic sites with Ga-FAPI positron emission tomography–computed tomography imaging. Subsequently, the patient was treated with Lu177-FAPI-targeted radionuclide therapy. There was significant clinical response. There was mild partial morphological response seen on follow-up imaging.

Keywords: *Fibroblast activation protein, Ga68-FAPI, hemangiopericytoma, Lu177-FAPI, solitary fibrous tumor, targeted radionuclide therapy*

Karuna Luthra, Vikram Lele, Kallur Kumar[1]

Department of Nuclear Medicine, Jaslok Hospital and Research Centre, Mumbai, Maharashtra, [1]Department of Nuclear Medicine, HCG Comprehensive Cancer Care Hospital, Bengaluru, Karnataka, India

Introduction

Hemangiopericytoma was first described by Murray and Stout in 1942[1] as a soft-tissue neoplasm, presumably originating from pericytes of small blood vessels with a typical feature that was a peripheral branching pattern of tumor growth. It consisted of predominant collagen-forming cells in typical "patternless" distribution. This rare tumor of mesenchymal origin is now categorized under the common name of solitary fibrous tumors (SFT).[2] SFT can arise in any part of the body – in adults, they are in three major locations – arising from pleura, in meninges, and in extrathoracic soft tissues. The SFTs arising in meninges were referred to as hemangiopericytoma by neuropathologists. However, as per the 2021 WHO Classification of the Central Nervous System (CNS) Tumors, these are now named as SFTs of the nervous system.[3] They are graded as 1, 2, and 3 as per the WHO classification. They can be benign or malignant – differentiation between benign and malignant is based on mitotic rate >4/hpf, presence of necrosis, higher cellularity, and cellular polymorphism. SFT is known to have typical genetic alterations related to NAB2-STAT6 gene fusion. 85%–95% of SFTs are positive for CD34 staining, other markers being CD99 and BCL2.[4]

The clinical presentation of SFTs depends on their site of origin. CNS SFTs are usually dural-based masses, and clinically present similar to meningiomas usually due to their mass effect. The malignant and anaplastic types have a metastatic potential, and the common sites of metastases are liver, lungs, and bones. Metastases can often occur late after the presentation of the original tumor.

Imaging of CNS SFTs is typically by means of magnetic resonance imaging (MRI) brain or computed tomography (CT) brain. Imaging of metastases is usually done with CT chest for lung metastases and CT or MRI for abdominal/bone metastases. Benign SFTs do not show significantly increased fluorodeoxyglucose (FDG) uptake. There have been some reports of malignant or metastatic SFTs detected on FDG positron emission tomography-CT (PET-CT).[5,6] FDG PET-CT may have some role to help distinguish benign from malignant SFT with higher SUVmax seen in malignant tumors.[7] Recently, it has been reported that SFTs can show somatostatin receptor (SSTR) expression and hence may be imaged using Ga68-DOTATOC PET-CT.[8,9]

Treatment of CNS SFT is based on surgery. Due to the basic pathology of peripheral infiltrative margins, these tumors often grow into the sinuses, and are hence difficult

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Address for correspondence:
Dr. Karuna Luthra, C 1202, Chaitanya Towers, A.S. Marathe Marg, Prabhadevi, Mumbai - 400 025, Maharashtra, India.
E-mail: karunaluthra@yahoo.com

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to completely remove surgically.[2] Adjuvant radiotherapy is known to improve the progression-free outcomes after surgery.[10] For metastatic disease, the treatment options are local radiotherapy. There is no definite systemic chemotherapy regimen known for metastatic disease, and the drugs tried so far do not show promising results.[2]

Case Report and Discussion

We present the case of a 49-year-old female who was diagnosed with left parasagittal meningioma in 2014. She underwent surgery followed by stereotactic radiosurgery for the recurrence of the same lesion. She again developed recurrence in 2019, for which she underwent left parietal craniotomy with excision of lesion. Histopathology showed SFT/hemangiopericytoma with CD34 and CD99 positive. She received postoperative radiation to tumor bed. In May 2021, she developed local recurrence and excision of recurrent lesion was done. Biopsy showed hemangiopericytoma/SFT. In June 2022, she developed difficulty in passing urine and lower limb pain. MRI revealed an expansile lesion in sacrum S1-S3 compressing cauda equina. CT scan of the abdomen and pelvis showed arterially enhancing liver lesions suggestive of metastases. She received radiotherapy to sacral lesion. There was no significant improvement in her symptoms, and she was unable to walk independently.

A Ga68-DOTATATE PET-CT was planned to assess SSTR in disease for potential PRRT (Peptide receptor radionuclide therapy) in view of multiple metastatic sites. Ga68-DOTATATE PET-CT [Figure 1] revealed moderate-to-high SSTR expression in a metastatic lesion in the sacrum. However, the multiple metastatic liver lesions showed no significant SSTR expression. There were also multiple metastatic lung nodules and masses seen – few of these showed low-grade SSTR expression while some showed no significant SSTR expression. In view of poor SSTR expression in the liver and lung metastases, poorly differentiated disease was concluded and further evaluation with FDG PET-CT was planned.

FDG PET-CT [Figure 2] showed low-grade metabolic activity in the sacral lesion; there was minimally increased metabolic activity in the liver lesions and variable low-to-high glycolytic activity in the lung masses.

Overall, there was significant heterogeneity in tumor characteristics found in different metastatic regions. In view of the low SSTR expression in liver metastases and most of the lung metastases, the patient was not considered suitable for SSTR-targeted PRRT.

The patient was then imaged with Ga68-FAPI (fibroblast activation protein inhibitor) PET-CT. Ga68-FAPI PET

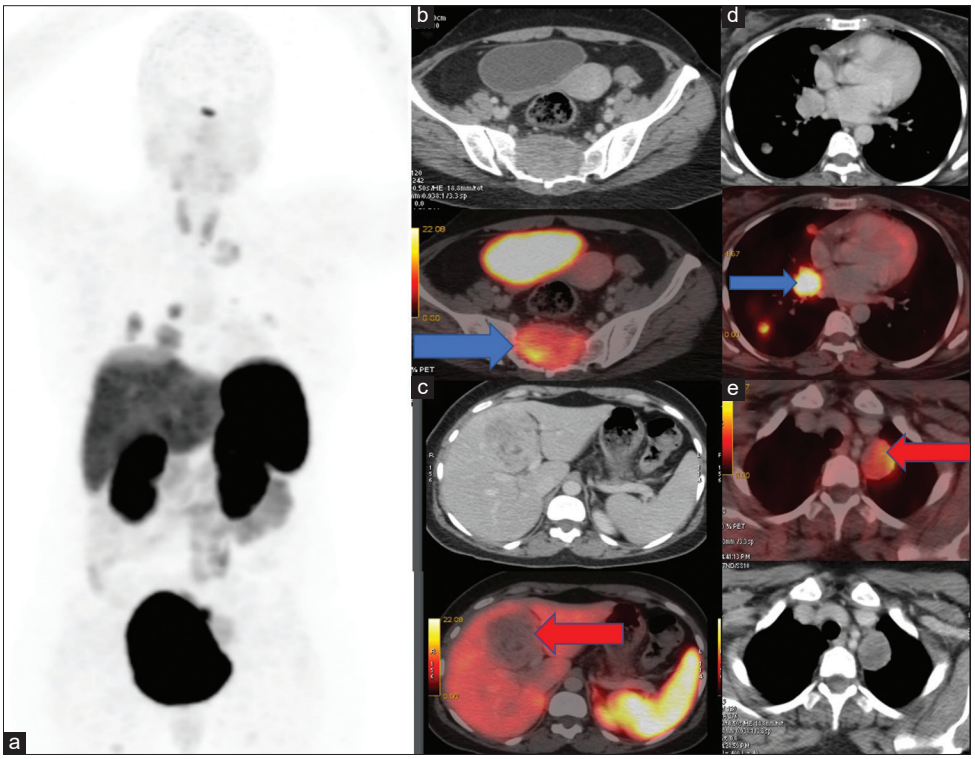

Figure 1: Ga68-DOTATATE PET-CT whole-body MIP (maximum intensity projection) image (a). There was moderate-to-high SSTR expression (Krenning's score 3) in an osteolytic lesion in the sacrum involving the body with associated soft-tissue component (b), with extension of lesion to the spinal canal and along presacral soft tissue alongside the sacral nerve roots. However, the multiple metastatic liver lesions (c) showed no significant SSTR expression (Krenning's score 0). There were also multiple metastatic lung nodules and masses seen (d and e) – few of these showed low-grade SSTR expression (Krenning's score 2) while some showed no significant SSTR expression (Krenning's score 0). PET-CT: Positron emission tomography–computed tomography, SSTR: Somatostatin receptor

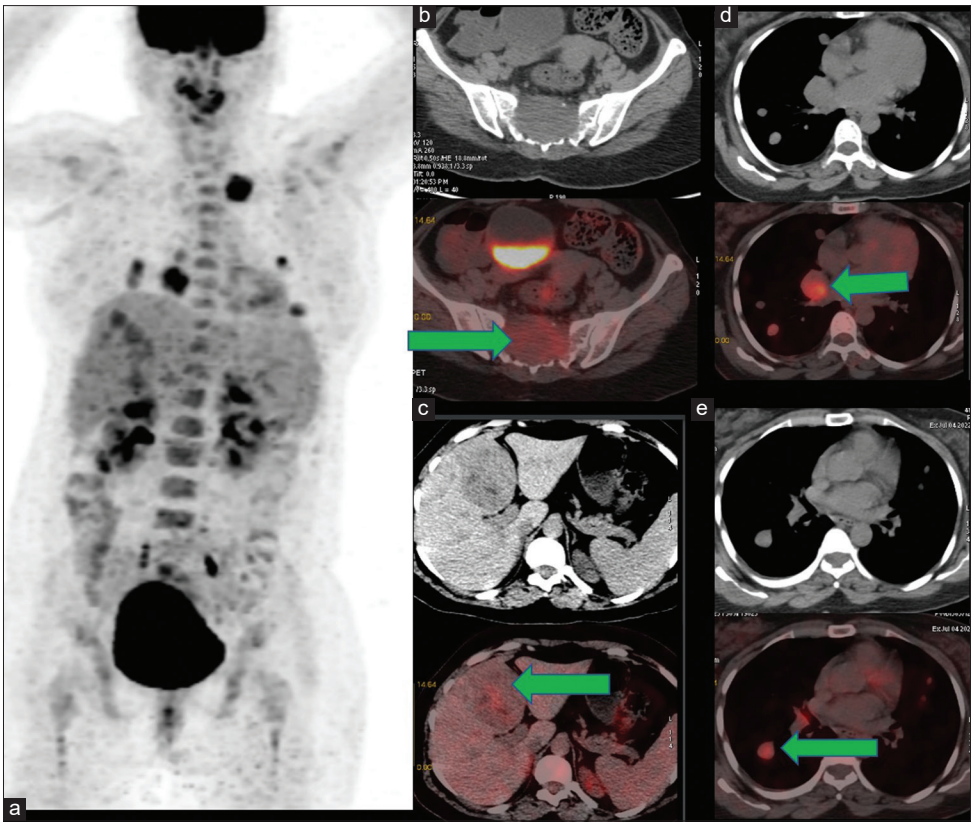

Figure 2: FDG PET-CT whole-body mip image (a) showed low-grade FDG uptake in the sacral lesion (b), there was mild FDG uptake in the liver lesions (c) – SUVmax ranging from 3.1 to 4.0, and there was variable low-to-high FDG avidity in the lung masses (d and e) – SUVmax ranging from 1.5 to 8. FDG: Fluorodeoxyglucose, PET-CT: Positron emission tomography–computed tomography

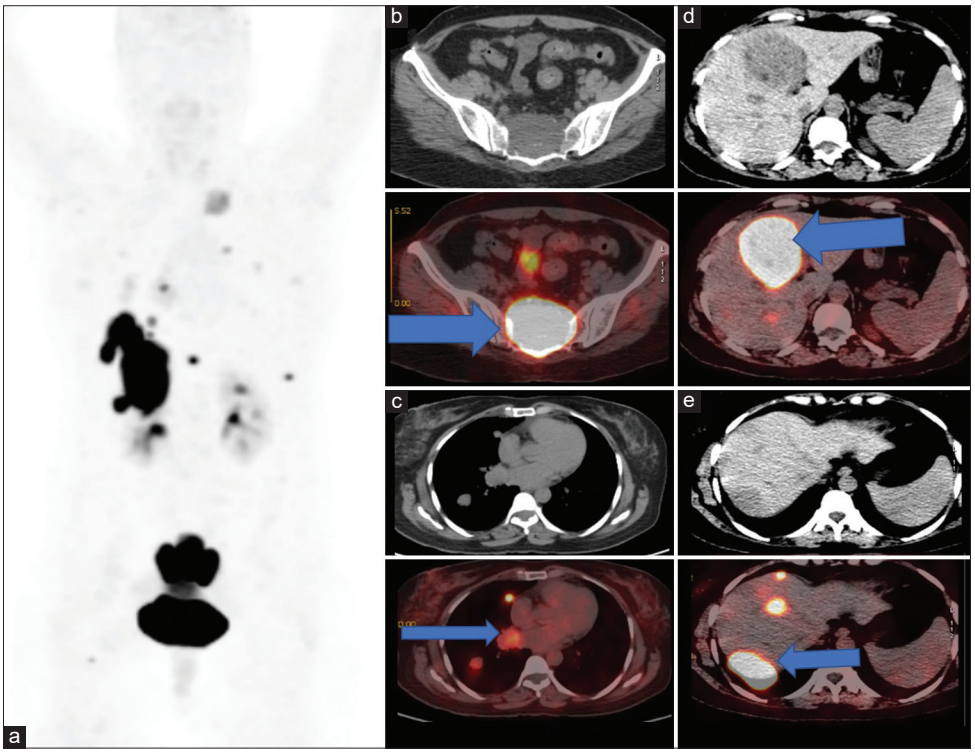

Figure 3: Ga68-FAPI (04) PET-CT revealed intensely increased tracer uptake in all the metastatic lesions (a) including sacral (b), variable moderate-to-high FAPI uptake in lung lesions (c) and intense uptake in multiple liver metastases (d and e). In addition, few other smaller bone metastases were also seen. PET-CT: Positron emission tomography–computed tomography

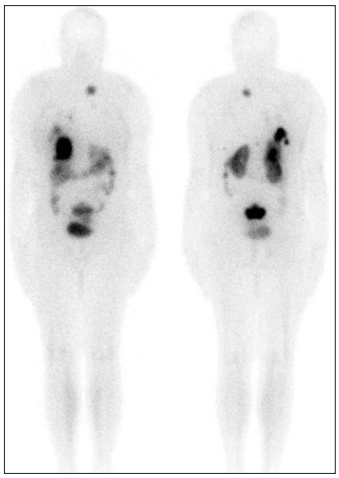

Figure 4: Whole-body images of Lu-177-FAPI acquired on gamma camera with medium energy collimator 5 days postintravenous injection of 200 mCi Lu177-FAPI (09) showed high retention of radiopharmaceutical in the multiple metastatic lesions similar to that seen on the imaging PET-CT. PET-CT: Positron emission tomography–computed tomography

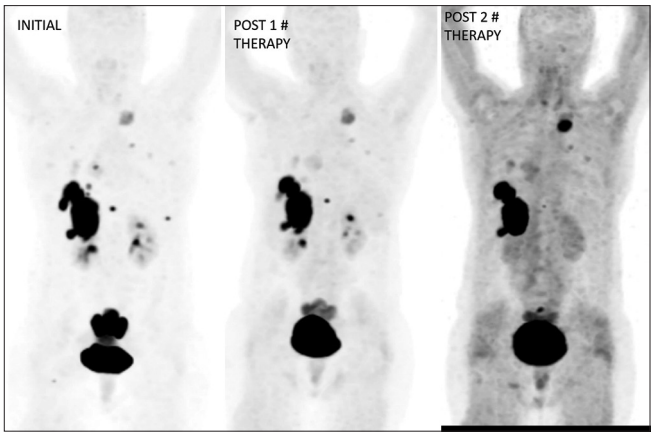

Figure 5: Ga68-FAPI PET-CT scan mip images of the initial scan done in July 2022, 8 weeks after the first cycle of Lu177-FAPI therapy (October 2022), and 8 weeks after the second cycle of Lu177-FAPI therapy (December 2022). There was a partial reduction in FAP expression seen in the sacral lesion. There was persistent high FAP expression in liver lesions though they showed reduction in number. Persistent moderate-to-high FAP expression seen in lung lesions. No new lesions were seen. PET-CT: Positron emission tomography–computed tomography

[Figure 3] revealed intensely increased tracer uptake in all the metastatic lesions including lung, liver, and sacral metastases. In addition, few other smaller bone metastases were also seen.

This led to multidisciplinary review, and in view of limited treatment options of chemotherapy, unsuccessful response with radiotherapy, and high FAPI expression seen in all the lesions, the patient was planned for targeted molecular radiation therapy with Lu177-FAPI.

She received the first dose of 200 mCi of Lu177-FAPI therapy in August 2022. Posttherapy Lu177-FAPI scans on day 1 showed high uptake of radiotracer, as well as high retention on day 5 [Figure 4].

Within a month after the first cycle of therapy, she obtained partial (70%) relief in pain score. A follow-up FAPI PET-CT 8 weeks posttherapy showed a mild partial reduction in FAPI expression in sacral lesion with largely stable extent of the lesion. She received the second dose of FAPI therapy after 8 weeks. After the second therapy, she developed a significant reduction in pain and improved mobility. She was able to resume her professional routine. There were no new symptoms. There was no significant hematological toxicity seen in intervening investigations between cycles. Follow-up Ga68-FAPI PET-CT in December 2022 2 months after the second cycle of Lu17-FAPI therapy showed a partial reduction in FAPI concentration in the sacral lesion with mild decrease in the extent of the lesion. There was a mild reduction in the extent of the liver lesions seen with persistent high FAPI expression [Figures 5-7].

The above case demonstrates the high expression of fibroblast activation protein in SFT metastases. Being a tumor of mesenchymal origin with predominant fibrous component, this observation was consistent with previous demonstrations of high FAP expression in primitive mesenchymal cells[11] other fibrous tumors and fibroblastic disease.[12] There have been few recent reports of the use of Ga68-FAPI imaging in SFTs.[13-15]

There are a variety of tumors, for which targeted radionuclide therapy using FAP ligands is being tried, including metastatic iodine-refractory thyroid cancer[16] and non-SSTR-expressing neuroendocrine tumors. We did not find any previous reports of Lu177FAPI targeted therapy used for treatment of metastatic Solitary Fibrous Tumor, and it is possibly the first case where it has been used and good clinical result demonstrated. It opens up the possibility of imaging more tumors of mesenchymal origin and possible theranostic applications for the same.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not

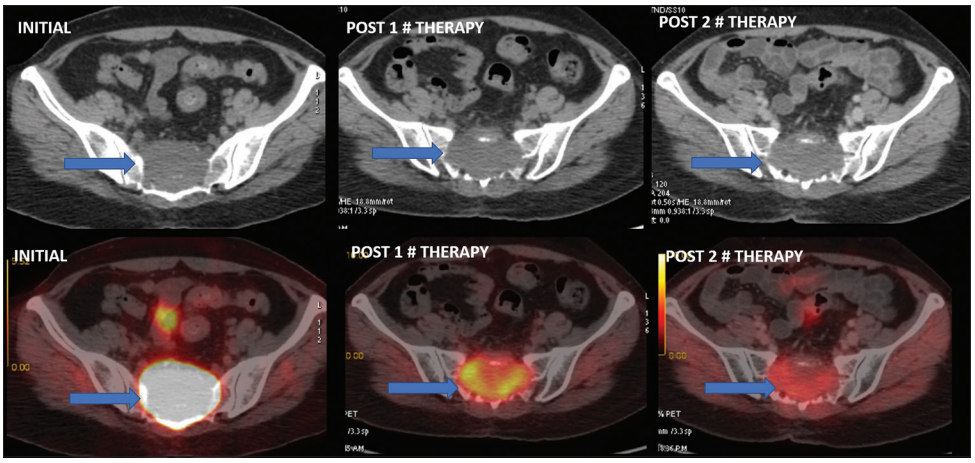

Figure 6: Ga68-FAPI PET-CT scan – cross-sectional CT and fused PET-CT images of the Sacrum of the initial scan done in July 2022, 8 weeks after the first cycle of Lu177-FAPI therapy (October 2022), and 8 weeks after the second cycle of Lu177-FAPI therapy (December 2022). There was a partial reduction in FAP expression seen in the sacral lesion. There were mild reduction seen in the extent of the soft-tissue component and reduction in the extent of the soft-tissue thickening along the exiting sacral nerve roots. PET-CT: Positron emission tomography–computed tomography, CT: Computed tomography

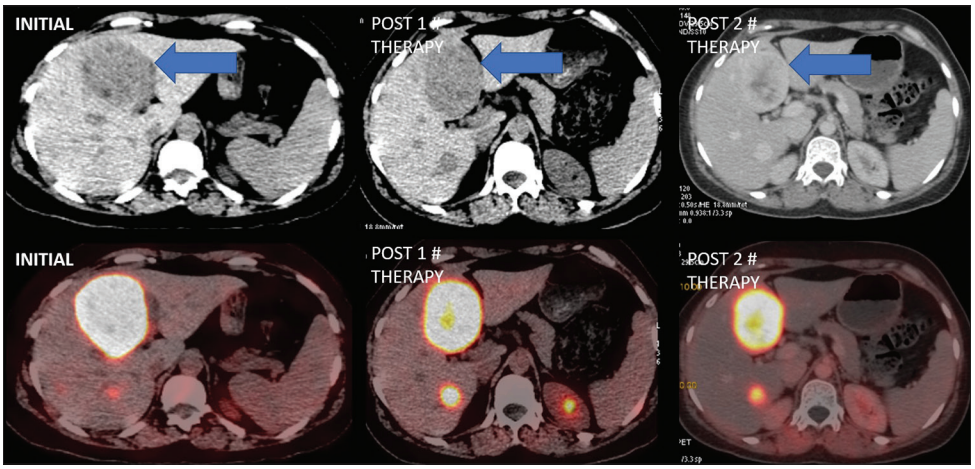

Figure 7: Ga68-FAPI PET-CT scan – cross-sectional CT and fused PET-CT images of the liver of the initial scan done in July 2022, 8 weeks after the first cycle of Lu177-FAPI therapy (October 2022), and 8 weeks after the second cycle of Lu177-FAPI therapy (December 2022). There was a mild reduction in size of the largest liver lesion with persistent high FAP expression. The other multiple liver lesions also showed a partial reduction in size. PET-CT: Positron emission tomography–computed tomography, CT: Computed tomography

be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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