

A Rare Case of Adrenal Gland Metastasis from Parotid Adenocarcinoma: Unveiling the Potential Augmented Utility of FAPI PET/CT

Abstract

Conventional imaging techniques, while essential, occasionally fall short in identifying elusive metastatic lesions, leading to delayed diagnoses and compromised patient outcomes. Gallium-68 fibroblast activating protein inhibitor (^{68}Ga -FAPI) positron emission tomography/computed tomography (PET/CT), leveraging the distinct affinity of fibroblast activation protein for cancer-associated fibroblasts, emerges as a promising solution to bridge this diagnostic gap. Parotid gland adenocarcinoma is a relatively rare malignancy with metastasis typically occurring in regional lymph nodes and distant sites such as the lungs and bones. However, there have been limited reported cases of rare metastatic sites such as the adrenal gland. This exceptional case report details the clinical presentation, diagnostic workup, and management steps of a rare case of a 47-year-old female patient diagnosed with parotid gland adenocarcinoma with confusing metastasis to the ipsilateral adrenal gland which was confirmed later with a follow-up ^{68}Ga -FAPI PET/CT scan. We aim to highlight FAPI unique ability to illuminate metastatic foci in challenging anatomical locations.

Keywords: Adrenal gland metastases, fibroblast activating protein inhibitor, fluorodeoxyglucose, fluorine-18 fluorodeoxyglucose, parotid gland adenocarcinoma, positron emission tomography/computed tomography

Introduction

Parotid gland adenocarcinoma is extremely rare and metastasis to distant sites is much scarcer.^[1] Fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) excels in detecting increased glucose metabolism, its application in cancer detection has proven to be particularly efficacious. However, it falls short in certain challenging anatomical sites such as the adrenal glands.^[2,3] Hence, a novel fibroblast activating protein inhibitor (FAPI) PET/CT imaging modality can be used to overcome this limitation.

Herein, we present a rare metastatic pattern to the bone and adrenal gland of a 47-year-old woman with parotid gland adenocarcinoma that was detected by initial FDG PET/CT and later confirmed by FAPI PET/CT.

Case Report

A 47-year-old female patient, with a well-controlled history of type II diabetes mellitus and hypertension, yet a negative

family history of malignancies, complained from a sudden onset of left parotid gland enlargement following upper respiratory tract infection that was unresponsive to self-administration of multiple over-the-counter medication trials including nonsteroidal anti-inflammatory medications. Afterward, the patient sought medical help, in which histopathological examination through fine-needle aspiration biopsy revealed typical features of high-grade adenocarcinoma. The patient underwent a series of diagnostic investigations to elucidate the nature and extent of the pathology. This included but was not limited to FDG PET/CT scan which advocated the malignant conduct of the tumor based on its hypermetabolic features with the maximum standardized uptake value (SUV_{max}) of 16. Interestingly, this case exhibited an uncommon metastatic pattern to the overlying skin of the parotid region, cervical lymph nodes, left humeral intramedullary lesion, and ipsilateral adrenal gland with SUV_{max} as high as 9.4 in the latter [Figure 1]. Consequently,

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Received: 25-01-2024

Revised: 30-04-2024

Accepted: 03-05-2024

Published: 18-11-2024

Access this article online

Website:

<https://journals.lww.com/ijnm>

DOI: 10.4103/ijnm.ijnm_13_24

Quick Response Code:



How to cite this article: Al-Ibraheem A, Abdulrahman M, Alrousan M, Haidar M. A rare case of adrenal gland metastasis from parotid adenocarcinoma: Unveiling the potential augmented utility of FAPI PET/CT. Indian J Nucl Med 2024;39:309-12.

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the patient underwent surgical excision of the cutaneous metastasis and cervical lymph node dissection for both therapeutic intervention and histopathological characterization. Metastatic to these sites was deemed through histopathological study as the tumor cells were positive for androgen receptors (AR), cytokeratin 7 protein, gross cystic disease fluid protein 15, and P63 but negative for caudal type homeobox 2, mucin 4-a glycoprotein, and transcription intermediary factor 1. Meanwhile, the decision was made to initiate chemotherapy as cisplatin, doxorubicin, and cyclophosphamide protocol with five cycles. To assist the diagnosis of left adrenal gland metastasis and to mitigate the necessity for invasive diagnostic procedures in the patient, gallium-68 FAPI (^{68}Ga -FAPI) was requested.

Compared with fluorine-18 FDG (^{18}F -FDG) and ^{68}Ga -FAPI PET/CT [Figure 2], the results conclusively verified the presence of a metastatic process within the left adrenal gland with an intense uptake up to 13.19, however, this activity is slightly suppressed in the conducted delayed images with SUV_{max} of 8.25. Therefore, the plan was to proceed with radiotherapy treatment.

Discussion

Parotid gland adenocarcinoma is extremely rare and metastasis to distant sites is much scarcer.^[1] FDG PET/CT excels in detecting increased glucose metabolism, and its application in cancer detection has proven to be particularly efficacious. However, it falls short in certain challenging anatomical sites such as the adrenal glands.^[2,3] Hence, a novel FAPI PET/CT imaging modality can be used to overcome this limitation.

An adrenal mass lesion can encompass various pathological conditions, both benign and neoplastic.^[4] The majority of these lesions are either straightforward adenomas or, to a lesser extent, primary malignancies or metastatic tumors of a secondary nature.^[5]

Although using the uptake of the liver as a threshold value, FDG-PET for differentiating malignant from benign adrenal gland lesions showed a sensitivity of 100%, a specificity of 94%, and an accuracy of 96%;^[2] a lot of cases of benign hyperfunctioning adenoma have been reported. This is due to the fact that FDG uptake is not exclusive to tumors; it may also occur in normal tissue or benign conditions such as inflammation or posttraumatic repair, leading to potential misinterpretation as cancer, adding challenges to the diagnostic paradigm.^[3] In addition, the adrenal glands naturally have some degree of FDG uptake under normal conditions with a signal close to the liver and an adrenal-to-liver maximum SUV ratio of 1.0 ± 0.3 on FDG PET/CT,^[6] yielding difficulties in differentiating between physiological and pathological uptake. FAPI PET/CT which is a relatively new imaging technique that utilizes radiotracers targeting fibroblast activation protein, a type II membrane-bound glycoprotein being a member of the dipeptidyl-peptidase 4 family, is highly expressed in around 90% of cancer-associated fibroblasts of many epithelial carcinomas.^[7] Furthermore, the reduced background activity in FAPI PET/CT contributes significant diagnostic value in the context of challenging metastatic sites.^[8]

FAPI imaging can also be useful in differentiating benign inflammatory and malignant lesions by semiquantitative analysis as stated in a study found that benign lesions

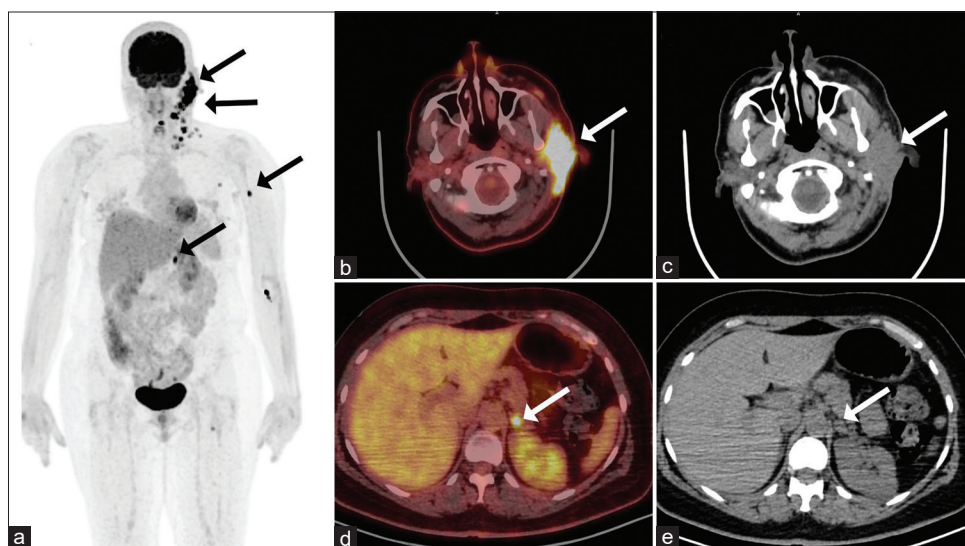


Figure 1: (a) The maximum intensity projection image of an fluorine-18 fluorodeoxyglucose (^{18}F -FDG), positron emission tomography/computed tomography (PET/CT) scan from vertex to knees standard protocol to a 47-year-old patient after 72 min postadministration of 267 MBq; 7.216 mCi of ^{18}F -FDG, illustrating a hypermetabolic malignant left parotid gland with eminent metastasis to the ipsilateral cervical lymph nodes, left humerus, and ipsilateral adrenal gland (black arrows). Initial fused ^{18}F -FDG PET/CT (b) along with CT images (c) axial section illustrating a huge left parotid gland exhibiting intensely heightened ^{18}F -FDG uptake with evidence of overlying skin infiltration. (white arrows). The measurements for this hypermetabolic parotid gland were as follows: 3.9 cm×3.4 cm in the maximal active component and the maximum standardized uptake value (SUV_{max}) was 16 (d) axial plane of the abdomen fused revealing an FDG avid left adrenal gland with SUV_{max} of 9.4. This adrenal gland appears thickened with 1.5 cm in the short axis in the corresponding CT scan (e) (white arrows)

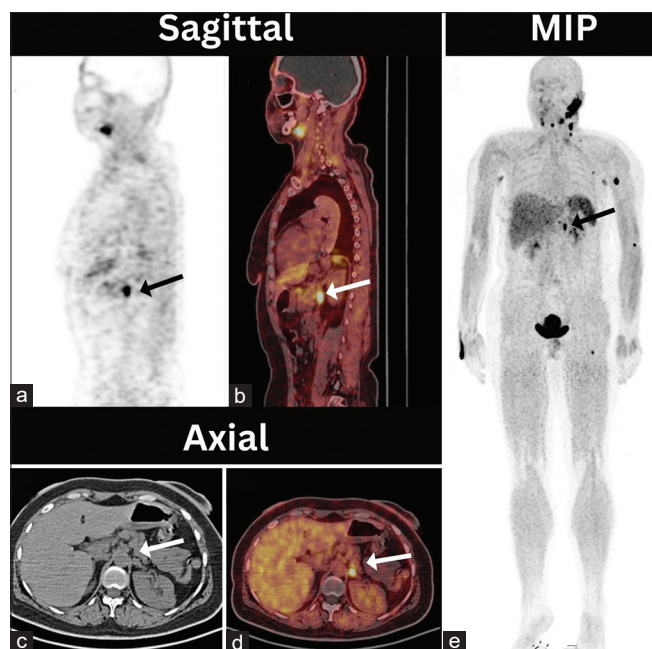


Figure 2: Gallium-68 fibroblast activating protein inhibitor (^{68}Ga -FAPI) positron emission tomography/computed tomography (PET/CT) scan, (a and b) sagittal PET and fused PET/CT images, respectively, showing increased FAPI uptake in the left adrenal gland. Axial CT (c) and fused image (d) showing a thickened left adrenal gland with increased ^{68}Ga -FAPI activity, measuring about 1.1 cm in maximum axial dimensions with maximum standardized uptake value: 8.25. (white arrows). Corresponding maximum intensity projection image illustrating primary parotid gland malignant tumor with metastatic sites involving cervical lymph nodes, left humerus, and left adrenal gland (e) (black arrows). LADs: Longest axial dimensions

showed significantly lower FAPI uptake compared to malignant lesions, with the SUV_{max} cutoff value for all lesions being 5.5, which in our case was 13.19. Therefore, FAPI PET/CT imaging may provide additional confirmatory diagnostic information in detecting metastatic sites.^[9]

Although there are currently recognized constraints related to its limited accessibility and nononcologic shortcomings,^[10] FAPI generally provides extensive understanding, enhancing, and potentially surpassing other radiotracers in the domain of nuclear oncology.^[11,12]

In cases where metastasis to distant sites is identified, a more aggressive treatment approach may be necessary because this reflects how advanced the stage is.^[13] Thus, the role of FDG scans in revealing these sites cannot be undervalued. In our specific case, there was an increased FDG activity in the overlying skin and left adrenal gland which was depicted only by FDG PET/CT scan during staging. These findings have prompted the urge to proceed with further imaging modalities such as FAPI PET/CT and histopathological examination, particularly with the AR-positive nature of the tumor by which metastatic process is typically maintained.^[14] All had corroborated the metastasis to the ipsilateral adrenal gland. The FAPI results guided further the treatment plan by providing additional information on the extent of metastatic disease based on FAPI uptake degree.

To the best of our knowledge, very few cases resembling this have been documented and reported to date. Therefore, it is important to report a case that is unique due to metastasis to unusual sites, such as the adrenal gland. This report will also emphasize the role of FAPI in this context.

In conclusion, this case report sheds light on the diagnostic challenges associated with uncommon metastatic sites such as the adrenal gland. The integration of ^{68}Ga -FAPI PET/CT into the diagnostic workup has played a remarkable role in identifying and characterizing the atypical metastatic pattern with the acknowledgment that ^{68}Ga -FAPI is still in the process of evolving.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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