

Case Report

18F-FES PET-CT Scan Turns out a Problem Solving Modality in an ER Positive Metastatic Breast Cancer Patient

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Abstract

Introduction: Two of three breast cancer patients are estrogen receptor positive. Metastasis can present upfront or developed later. Accurate delineation of all metastatic sites and ruling out a concurrent primary is of prime importance. We present a breast cancer case with multiple unusual sites of potential metastatic involvement, wherein 18F-FES PET-CT played a crucial role in resolving the diagnostic dilemma.

Case Presentation: Treated case of strongly ER positive 52 year old female breast cancer patient presented with chest wall nodule and contralateral axillary lymphnode. FDG PET-CT showed many uncommon sites (scalp nodules, periampullary mass and lung infiltrates) and unsure about metastasis or inflammatory. FES PET-CT was positive in all these sites thus resolve the diagnostic uncertainty.

Conclusion: FES PET-CT scan can be of immense use as a problem solving modality in ER positive breast cancer. This case highlights the spectrum of metastatic sites potentially be evaluated by FES PET-CT scan which can play a crucial role in decision making and personalized medicine. However, it is important to remember the occurrence of triple negative cases and ER receptor heterogeneity in metastatic sites.

Keywords: Estrogen receptor; Metastatic breast cancer; ¹⁸F-FES PET-CT; Scalp nodules; periampullary mass

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Introduction

Breast cancer has taken the lead over cervical cancer in India in many cities in population based cancer registry and has been projected as the number one cancer in future [1]. Estrogen receptor-positive (ER+) breast cancer is the most common type diagnosed today [2]. According to the American Cancer Society, about two out of every three cases of breast cancer are hormone receptor positive. Hormone positivity has an impact on both treatment planning and prognosis [3]. Cancer metastasis is devastating. It can be present upfront at the time of diagnosis and may develop later-on in the natural course of the disease. Accurate delineation of all metastatic sites and ruling out a concurrent primary is of prime importance in the management. We present the case of a breast cancer patient with multiple unusual sites of potential metastatic involvement, wherein $^{16}\alpha\text{-}^{18}\text{F}$ -Fluoro- $^{17}\beta$ -Estradiol Positron Emission Tomography-Computed Tomography (^{18}F -FES PET-CT) played a crucial role in resolving the diagnostic dilemma.

Case presentation

A 52 year old female presented with right chest wall swelling since 2 months. She was also complaining of loss of appetite, backache and lethargy. In the past, she had been treated for locally advanced carcinoma of the right breast, for which she underwent neo-adjuvant chemotherapy, right modified radical mastectomy (MRM), adjuvant chemotherapy and radiotherapy. She also received hormone therapy for 3 years. Her original pathology report stated infiltrating ductal carcinoma (IDC) grade 2 with ER 100%, PR 50% and Her2 neu 0. Now, on examination she had a right chest wall nodule (1.5 x 1.2 cm) at the scar site and a left axillary lymphnode. She also had multiple sub-centimeter to centimeter sized nodular scalp swellings. FNAC of the chest wall nodule was reported as positive for metastatic cells, favoring local recurrence. On various blood tests she was found to have high serum bilirubin (7.6 mg/dl) and abnormal liver enzymes (SGOT: 91 U/L, SGPT: 85 U/L). ^{18}F - Fluorodeoxyglucose (FDG) PET-CT was advised to assess disease burden and to rule out the possibility of second malignancy. FDG PET-CT revealed an FDG avid right chest wall nodule with hypermetabolic left axillary and mediastinal lymph-nodes (Figure 1). PET scan also revealed FDG avid peribronchial interstitial parenchymal infiltrates in the right lung (Figure 2), left pleural deposit, left adrenal lesion and multiple lytic bony lesions. Scalp nodules were also FDG avid (Figure 3). There was an FDG avid periampullary soft tissue mass lesion with extra and intra hepatic biliary dilatation (Figure 4). With so many findings on the FDG PET-CT scan, multiple questions needed to be addressed. Was the periampullary mass metastatic in origin or a new primary? FDG PET-CT scan is also positive in inflammatory conditions [4], hence the possibility of FDG avid scalp nodules being inflammatory or metastatic needed to be clarified. Lung infiltrates which could be inflammatory in origin or secondary to lymphangitis carcinomatosa, are often difficult to characterize purely on the basis of CT pattern or FDG uptake. The same dilemma applied to contralateral axillary and mediastinal lymphnodes as well. Performing multiple biopsies is neither ethically correct nor feasible. The patient was advised upper gastrointestinal endoscopy (UGIE) for evaluation of the periampullary mass lesion but the procedure was refused by her. So, to characterize the FDG avid lesions, she was advised an FES PET-CT scan.

FES PET-CT Scan was positive for all the lesions seen on the FDG PET-CT scan, hence demonstrating good ER expression on all metastatic sites. Thus, without doing any further biopsy and invasive investigations, it was ascertained that all sites of high tracer uptake were metastatic in origin from the breast primary.

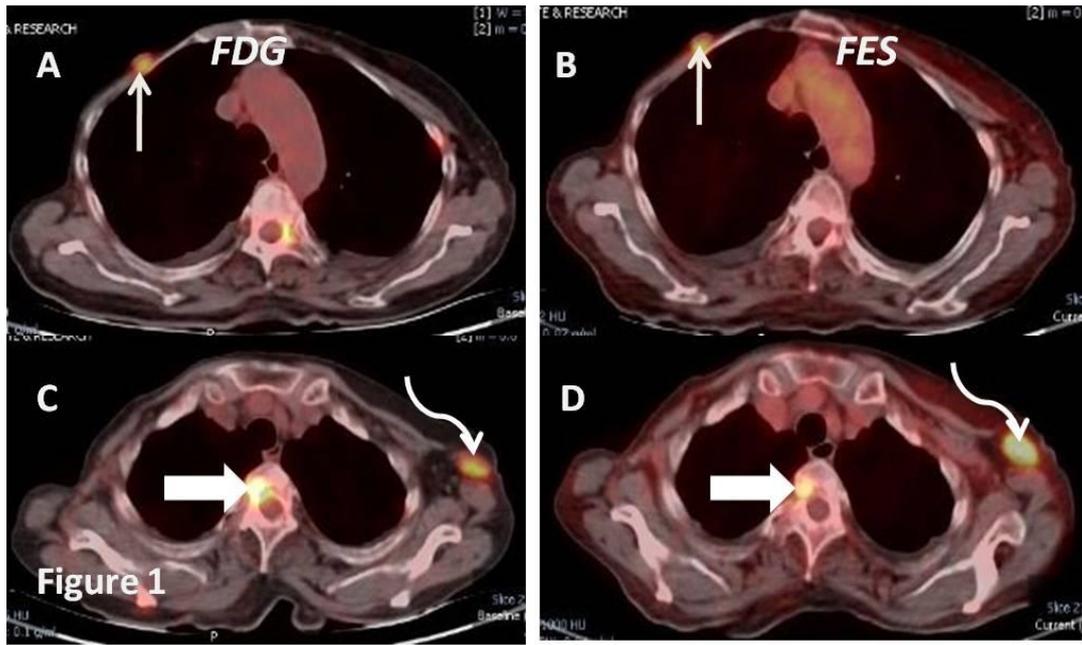


Figure 1 Right chest wall nodule (white arrow) with left axillary lymphnode (white curved arrow) suggestive of recurrence. Axial co-registered FDG (A& C)& FES (B & D) PET-CT images. A dorsal vertebral lesion can also be seen in both FDG (C) and FES(D) images (white block arrow).

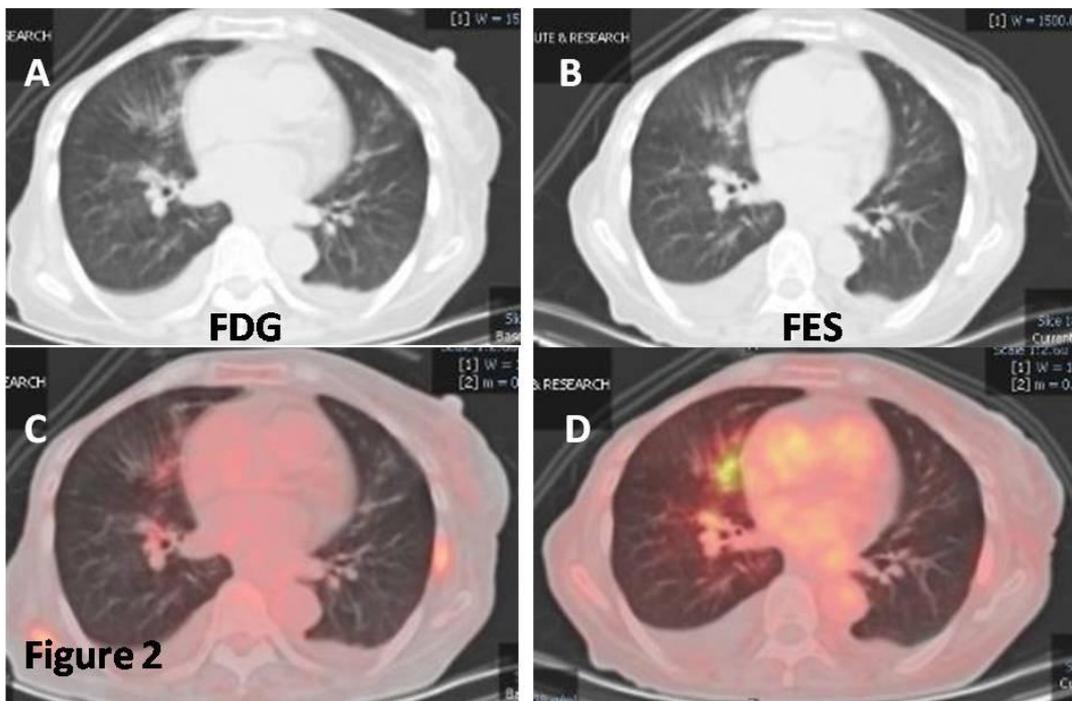


Figure 2 Lung window CT and fused FDG (A,C) and FES (B,D) PET-CT axial images: FDG avid prominent bronchial markings with peri-bronchial infiltrates in right middle lobe which show good FES uptake.

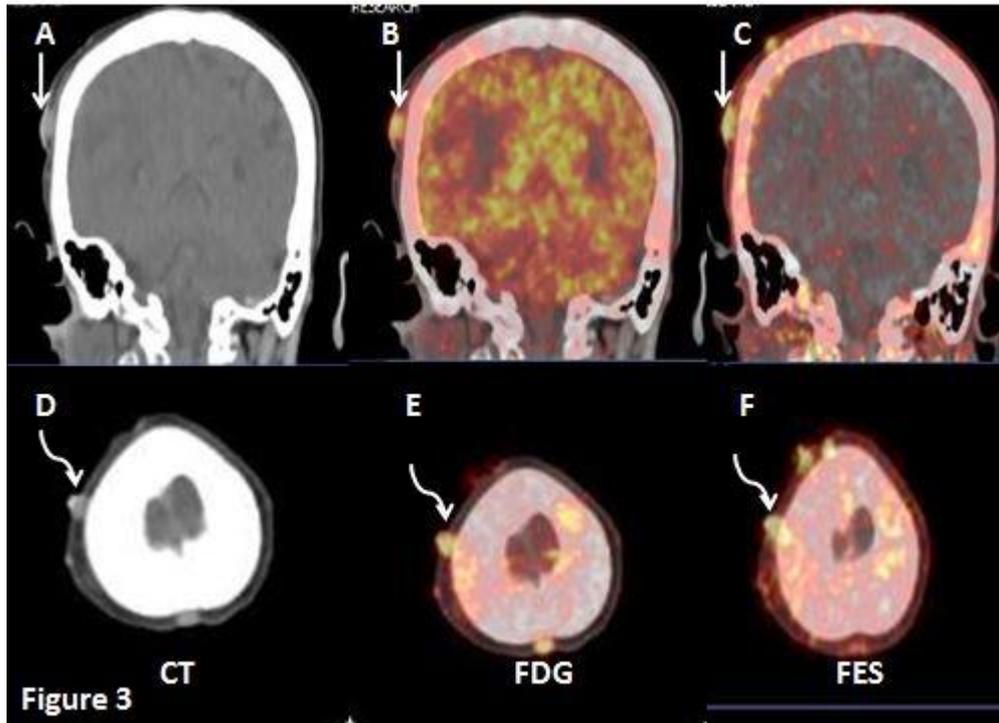


Figure 3 Coronal and axial CT (A,D), fused FDG (B,E) and fused FES (C,F) PET-CT images. Images show multiple scalp nodules with good FDG and FES uptake. Findings suggest ER expressing scalp metastases.

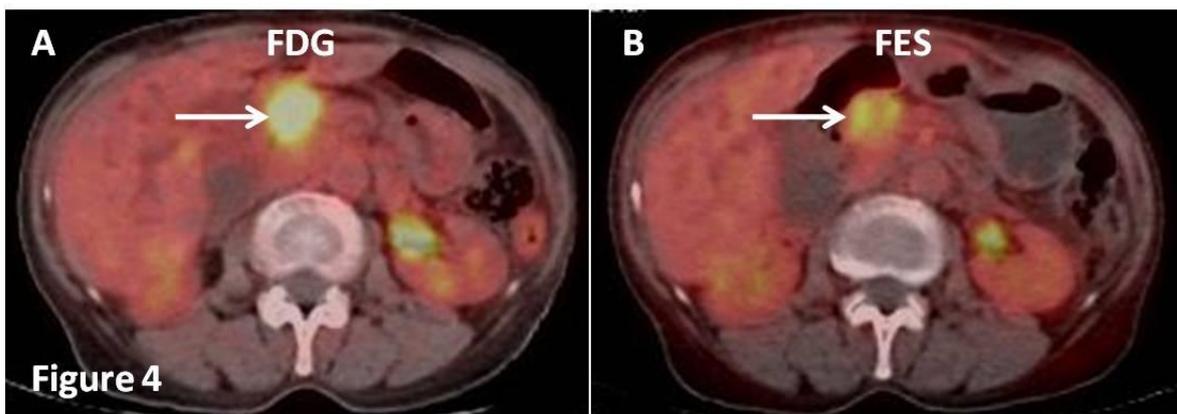


Figure 4 Fused axial FDG (A) and FES (B) PET-CT images showing periaampullary lesion (white arrow) with intra-hepatic biliary dilatation. Findings suggest ER expressing periaampullary lesion likely breast metastasis in this case.

Discussion

Estrogen is involved in the growth of both normal and cancerous breast tissues. Its activity is mediated by the estrogen receptor (ER). ER-positivity in breast cancer cells has a profound impact on treatment and patient outcome. Measurement of ER expression by biopsy at the time of primary diagnosis of breast cancer is part of standard care. 16- α -17- β -Estradiol is a synthetic estrogen and showed good affinity for ER receptor in in-vitro studies [5]. Available in-vivo data is also supporting good correlation between FES uptake and ER expression [6-10]. In a recent article, FES PET has been presented as a diagnostic

tool in breast cancer patients with clinical dilemma [11]. To our knowledge this is the first case highlighting FES uptake in unusual sites of metastasis (scalp nodule, periampullary mass and lymphangitis carcinomatosa) which played a crucial role in clinical decision making.

We have experienced a spectrum of different sites of metastasis from breast cancer diagnosed by commonly available FDG PET-CT scan which pose diagnostic uncertainty. Enlarged FDG avid contralateral axillary lymph nodes were easy to suspect in this clinical context, however still needed cytology for confirmation. Good FES concentration is almost signature of breast cancer metastasis in this case (Figure 1). Prominent bronchial markings with interstitial infiltrates and mediastinal lymph nodes are so commonly seen in this part of the world due to the high prevalence of tuberculosis, that it is often difficult to characterize them as inflammatory or neoplastic on the FDG PET-CT scan, which has a high propensity for both lesions. Good FES uptake in lung infiltrates and mediastinal lymph nodes helped in making the diagnosis of lymphangitis carcinomatosa with metastatic mediastinal lymphadenopathy easy. Breast carcinoma metastasis is the most common carcinoma with cutaneous infiltration encountered by the dermatologist and can present in various forms [12]. In our case, the patient had multiple scalp nodules. Differential diagnosis was furunculosis, fungal infection or metastasis. FDG avidity could not help in solving the query. However, FES uptake which simulates expression of ER in the scalp nodules (Figure 3), pointed towards metastasis from breast cancer.

The possibility of the periampullary mass causing common bile duct (CBD) obstruction, as being either metastatic or a second primary was a clinical problem that needed a definite answer for effective management. Being an uncommon site of metastasis and obstructive in nature, UGIE was advised, however, the procedure was refused by the patient. FES PET-CT scan was most helpful in solving this issue. FES uptake in the periampullary mass points towards breast origin in this setting (Figure 4). Bony lesions and adrenal lesion were also FES positive.

Cancer management is moving towards targeted treatment. Molecular radionuclide imaging has to play a significant role in making specific diagnosis and planning individualized treatment. Novel tracers for breast cancer i.e. FES, FENP (21- [¹⁸F]Fluoro-16 α -ethyle-19-norprogesterone), ⁸⁹Zr-transtuzumab, ⁸⁹Zr-bevacizumab etc. not only help in diagnosis, but also pave the way for specific treatment [13]. It is noteworthy to remember that these tracers have a high positive predictive value but a negative test cannot rule out metastasis (triple negative cases). Further it is important to note the occurrence of heterogeneous ER expression which may be different in metastatic sites in approximately 20% of patients [14].

Conclusion

FES PET-CT scan can be of immense use as a problem solving modality in ER positive breast cancer. This case highlights the spectrum of metastatic sites potentially evaluated by FES PET-CT scan which can play a crucial role in resolving a diagnostic dilemma. However, it is important to remember the occurrence of triple negative cases and ER receptor heterogeneity in metastatic sites.

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