Case Report

Metabolic flare phenomenon on 18 fluoride-fluorodeoxy glucose positron emission tomography-computed tomography scans in a patient with bilateral breast cancer treated with second-line chemotherapy and bevacizumab

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ABSTRACT

Increase in radiopharmaceutical uptake is an indicator of progression of disease. Paradoxical increase in the radiopharmaceutical uptake also occurs during favorable response to therapy, which is designated as flare phenomenon. Flare phenomenon is well documented on bone scinitgraphy when initially noted lesions show increased radiotracer uptake after therapy is instituted. This happens despite favorable response to the treatment. The osteoblastic activity associated with healing response of bone tumors is the cause of flare phenomenon. Recently, metabolic flare phenomenon has been described in patients with breast cancer who undergo hormonal therapy. Changes in the hormonal level during initial part of the treatment is the cause of metabolic flare. We describe a patient with bilateral breast cancer who underwent second line chemotherapy along with bevacizumab. Serial positron emission tomography scans done showed interesting phenomenon of metabolic flare.

Keywords: Breast cancer, fluorodeoxy glucose positron emission tomography, metabolic flare, response assessment

INTRODUCTION

Breast cancer is a typical example of multi-modality management of cancer. It is treated with surgery, chemotherapy, radiation therapy, hormonal therapy, and newer biologicals. Assessing the response to newer therapies is of paramount importance, not only to identify candidates who are not responding to therapy, but also to avoid unnecessary delay in institution of definite treatment and to reduce potential adverse effects. 18-fluoride fluorodeoxy glucose (^{18}F-FDG) positron emission tomography (PET)-computed tomography (CT) is being increasingly utilized in evaluating early response to therapy. Potential pitfalls exist even in this modality and the phenomenon of metabolic flare phenomenon is elucidated in this case report.

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CASE REPORT

A 53-year-old female, a case of bilateral breast cancer, presented to the oncologist with back pain of recent onset. She was a known case of bilateral breast cancer and was treated with bilateral mastectomy 6 months before. She has previous history of six cycles of chemotherapy after her initial surgery. She also had a breast implant on the right side. She was referred for a whole body ^{18}F-FDG PET-CT to our center following the end of chemotherapy. She underwent whole body FDG-PET-CT scan as per standard institution protocol. The initial whole body ^{18}F-FDG PET scan (Figure 1; a-maximum intensity projection [MIP], e-CT axial, i-axial fused PET-CT) showed a metabolically active lesion in the D9 vertebra with evidence of

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lytic changes in the corresponding vertebra on CT. Another focus of FDG uptake was also noted in the posterior elements of D7 vertebra. The maximum standardized uptake value normalized to the lean body mass (standardized uptake values [SUVmax]) was 3.6. She underwent three cycles of chemotherapy based on (paclitaxel, adriamycin and bevacizumab). The whole body ^{18}F-FDG PET scan performed 12 days after three cycles of chemotherapy (b-MIP, f-CT axial, j-axial fused PET-CT) showed increase in the FDG uptake and the SUVmax (from 3.6 to 4.5). The injected activity and the imaging time were not significantly different between the two scans. However, sclerotic changes were noted on CT. A diagnosis of favorable response was made despite the increase in metabolic activity.

The patient underwent a ^{18}F-FDG PET scan (c-MIP), at completion of six cycles of chemotherapy. There was complete suppression of FDG avidity in the previously noted lesion. Dense sclerotic changes were noted on CT indicating healing response (g-CT axial, k-axial fused PET-CT). Patient underwent end of treatment PET scan 6 weeks after completion of nine cycles of chemotherapy (d-MIP, h-CT axial, l-Axial fused PET-CT) which didn't reveal any other new abnormality. Patient is on follow-up without any evidence of active disease. The paradoxical increase in the FDG uptake was attributed to metabolic flare response.

DISCUSSION

Flare phenomenon is a paradoxical increase in the tracer avidity in a previously diseased site during the course of treatment. Flare phenomenon is a well-known process noted in bone scintigraphy during the course of treatment of osseous metastases.[1-3] Flare response has also been described with ^{18}F bone PET scanning.[4] This process occurs when bone metastases respond to chemotherapy and osteoblastic activity sets in. Flare phenomenon has also been proposed as an indicator of treatment efficacy. However, flare phenomenon is rare in ^{18}F-FDG PET scans in patients with breast cancer on conventional therapy. This is because, ^{18}F-FDG uptake reduces when there is a favorable response to chemotherapy which is evidenced by fall in SUV. ^{18}F-FDG PET scan serves as an excellent tool in evaluating the response of tumor to chemotherapy.[5,6]

In patients with breast cancer, metabolic flare phenomenon is known to occur during endocrine treatment (hormonal therapy).[7,8] This is explained by the initial estrogen-like agonist

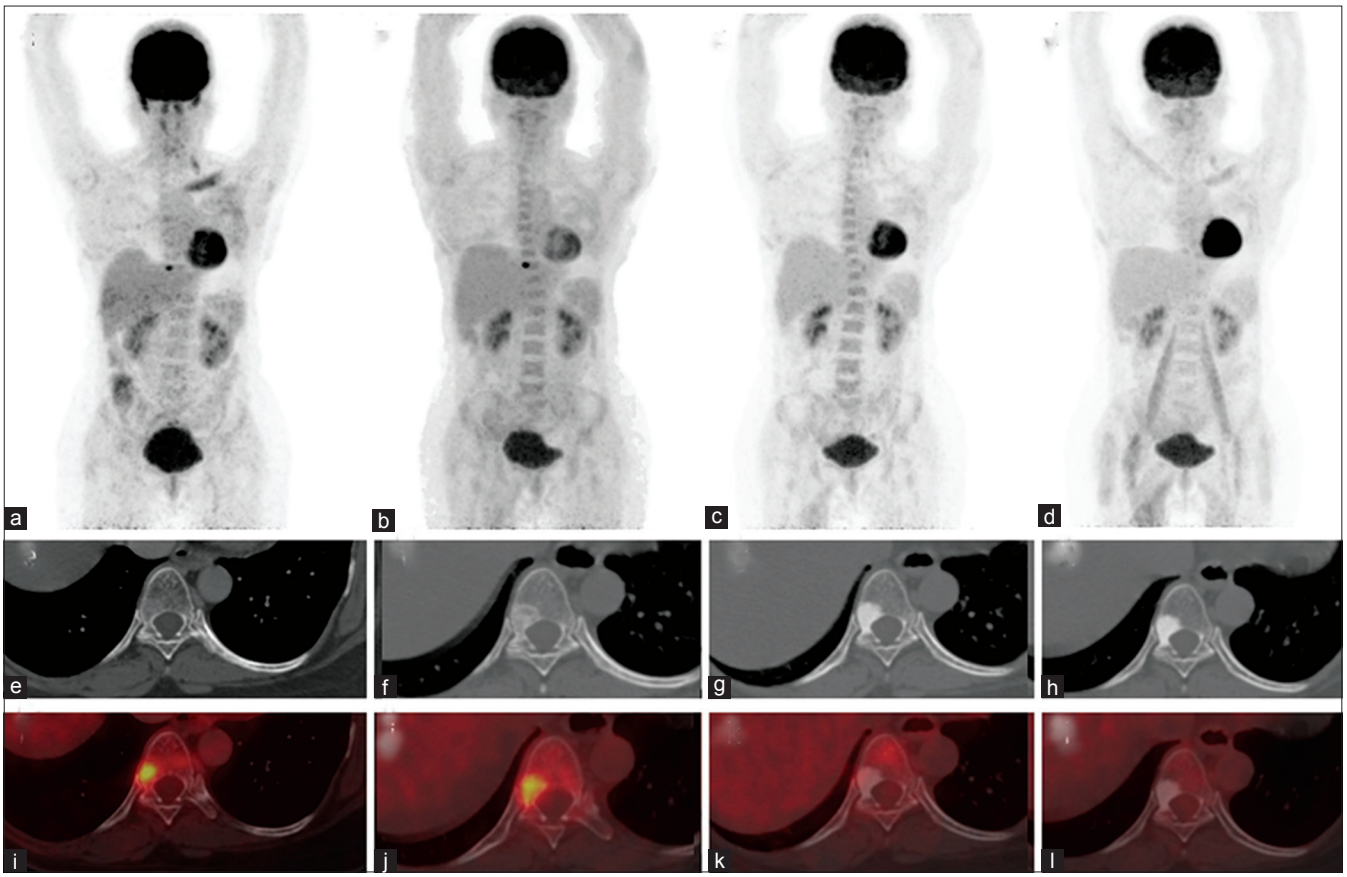

Figure 1: Serial maximum intensity projection images and the axial computed tomography (CT) and axial fused positron emission tomography (PET)-CT of the serial PET scans during the course of second line treatment of bilateral cancer breast are shown. Initial images (a, e, i-prechemotherapy; showing a focus of elevated fluorodeoxy glucose (FDG) uptake in a lytic lesion in the posterior body and right pedicle of the D9 vertebra. Follow-up scan (b, f, j-three cycles after chemotherapy) showed an increase in the FDG uptake (flare phenomenon) with sclerotic changes on CT; PET scan after six cycles of chemotherapy (c, g, k) and nine cycles of chemotherapy (d, h, l) show complete suppression of FDG uptake with dense sclerotic change in the involved vertebra

effect of these drugs. Flare phenomenon during conventional and second-line chemotherapy has never been described before. The index patient also received bevacizumab during the therapy. Flare phenomenon has been previously described in lung cancer patients receiving bevacizumab in addition to the standard treatment.[9] The flare phenomenon noted in the index case might be due to addition of bevacizumab to the second line chemotherapeutic drugs.

Paradoxical increase in the SUVmax on follow-up PET scan may also be due to variety of technical factors, the most important of which is significant variation in waiting period between the two scans (delay in imaging increases the SUV). Follow-up scans should ideally be acquired with the same delay as the initial PET scans.

Flare phenomenon is a potential indicator of responsiveness of the breast cancer to hormonal therapy.[7] It remains to be seen if flare phenomenon has got any significant prognostic information. Further studies are required to evaluate this.

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