Case Report

Combined ^{18}F-FDG and ^{11}C-Methionine PET/CT scans in a case of metastatic hepatocellular carcinoma

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ABSTRACT

A 37-year-old male who underwent a central hepatectomy of the liver for hepatocellular carcinoma (HCC) was referred for an ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) study to rule out tumor recurrence or metastases. The scan showed a recurrent hepatic mass at the operative site, along with low-grade uptake in bilateral pulmonary metastases, mediastinal and hilar lymph nodes, and few skeletal sites. A non-FDG avid intracranial extradural mass was visualized in the right frontal lobe. The ^{11}C-methionine PET/CT scan performed subsequently revealed a larger area of involvement at the primary site, along with widespread metastases to the lungs, mediastinal, hilar, and abdominal lymph nodes, and multiple skeletal sites. Further, dural metastasis with high tracer uptake was noted in the frontal region. To the best of our knowledge, this is the first case documented in the literature, wherein ^{11}C-methionine PET/CT played a significant role in delineating the widespread dissemination, including the extremely rare dural involvement in a case of HCC. This report highlights the potential value of ^{11}C-methionine PET/CT in assessing the hepatic and extrahepatic tumor burden in cases of HCC, especially in clinically unexpected locations.

Keywords: ^{11}C-methionine positron emission tomography/computed tomography, extrahepatic metastases, hepatocellular carcinoma

INTRODUCTION

Hepatocellular carcinoma (HCC) ranks as the sixth most common cause of cancer worldwide.[1] With longer survival of patients and enhanced imaging techniques, the reported incidence of extrahepatic metastases in HCC is increasing.[2] Dual-tracer positron emission tomography/computed tomography (PET/CT) scans using fluorodeoxyglucose (FDG) and ^{11}C-acetate have been extensively undertaken owing to their complementary role in detection of HCC, both well- and poorly differentiated forms.[3] The role of ^{11}C-methionine PET/CT in detecting tumor lesions in patients with HCC is less well defined. The present report depicts an unusual case of HCC, wherein ^{11}C-methionine PET/CT played a significant role in delineating the widespread dissemination, including the extremely rare dural involvement.

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CASE REPORT

A 37-year-old male who underwent a central hepatectomy of the liver for HCC presented 2 years later with progressive headache, gait unsteadiness, and altered behavior. Magnetic resonance imaging (MRI) revealed a dural-based mass lesion causing pressure effect on the right frontal lobe, which was suspected to be dural metastasis. He then underwent an ^{18}F-FDG PET/CT scan on a whole-body Full Ring PET camera (Discovery STE16-GE) after administration of 370 Mbq (10 mci) ^{18}F-FDG intravenously followed by a 60-min rest period, subsequent to a 6-h fast. After the CT scan, an emission scan was performed from head to thigh for 2 min per frame. Images were reconstructed by three-dimensional (3D) VUE algorithm (GE Healthcare) and viewed on a Xeleris workstation (GE Healthcare) using the volumetric protocol. An ^{11}C-methionine PET/CT scan was performed the next day on the same scanner 20 min after intravenous injection of 760 Mbq (20.5 mci) of ^{11}C-methionine. Both studies revealed a hypermetabolic recurrent hepatic mass at the operative site [Figure 1]. Although the tumor to background ratio was higher on the FDG scan, the ^{11}C-methionine scan could define a larger area of involvement at the operative site. Further, the ^{11}C-methionine study revealed hypermetabolic lymph nodes in the paraaortic, precaval, portal, peripancreatic, and mesenteric

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region, none of which showed significantly increased FDG avidity. Additionally, metastatic nodules were noted in both lung fields, showing low-grade FDG avidity, but significant ^{11}C-methionine uptake [Figure 2]. High ^{11}C-methionine uptake was also noted in the paratracheal, hilar, subcarinal, and left internal mammary nodes, with no significant hypermetabolism noted at any of these sites on the corresponding FDG PET images.

Metastases to multiple skeletal sites including vertebrae, ribs, pelvis, and right femur were also visualized. These lesions were better delineated on the ^{11}C-methionine scan and several lesions were picked up solely on this scan. An FDG avid hypermetabolic lesion was noted at C3 vertebra with more intense uptake on the corresponding ^{11}C-methionine image, which also showed evidence of encasement of the thecal sac [Figure 3]. In a similar manner, metastasis to D2 vertebra with intraspinal extension was noted on the ^{11}C-methionine scan, which was not visualized on the FDG image [Figure 4]. These findings were confirmed on subsequent MRI of the spine, which additionally showed spinal cord impingement and edema at this level. A subtle calvarial erosion was noted in the right frontal bone with an associated extra-axial mass [Figure 4]. The mass showed reduced FDG avidity but demonstrated increased ^{11}C-methionine uptake. The ^{11}C-methionine scan also showed additional sites of uptake in the bony calvarium, which appeared normal both on CT and the FDG image.

DISCUSSION

HCC ranks as the sixth most common cause of cancer worldwide, with the highest incidence noted in east and south-east Asia and sub-Saharan Africa. The sensitivity of FDG-PET/CT does not exceed that of conventional imaging (50-70%),[4,5] largely owing

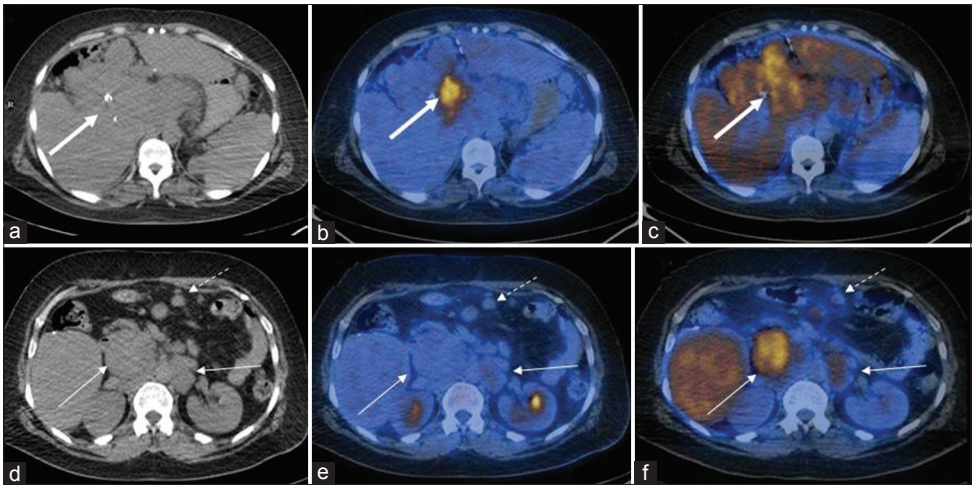

Figure 1: Transaxial CT (soft-tissue window) at the operative site (a), with corresponding FDG (b) and 11-C methionine (c) PET/CT fusion images showing recurrent hepatic mass (thick arrows). Transaxial CT (d) reveals retroperitoneal lymph nodes (thin arrows) and mesenteric (dotted arrows) lymph nodes, which do not show significantly increased FDG avidity (e), but show increased 11-C methionine uptake (f). CT = Computed tomography, FDG = Fluorodeoxyglucose, PET = Positron emission tomography.

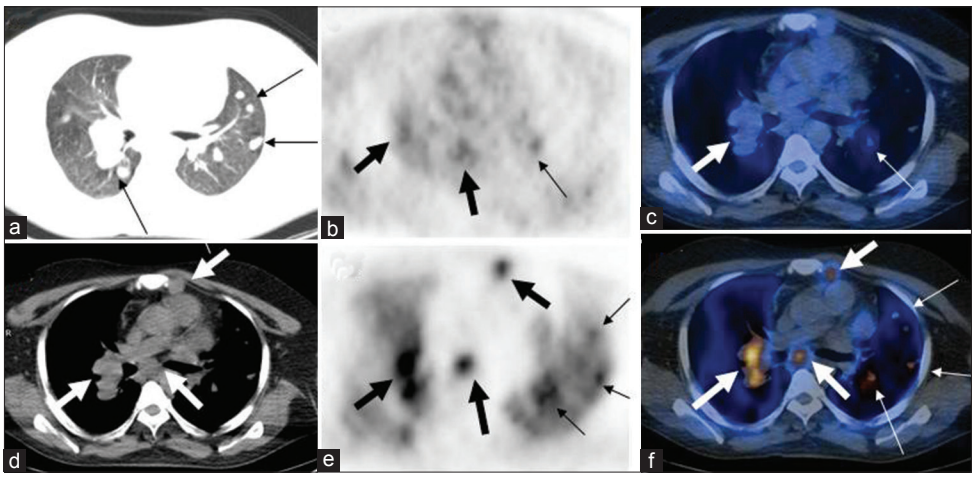

Figure 2: Transaxial CT in lung window (a) shows metastatic pulmonary nodules, which show low-grade FDG avidity but significant ^{11}C-methionine uptake on the transaxial PET (thin arrows in b and e) and fused PET/CT image (thin arrows in c and f), respectively. Transaxial CT (d) shows right hilar, subcarinal, and left internal mammary nodes (mediastinal window). Significant ^{11}C-methionine uptake also noted on the PET (e) and PET/CT fusion image (f) at these sites (thick arrows). The corresponding FDG PET and PET/CT fusion images (b and c) show low-grade uptake (thick arrows). CT = Computed tomography, FDG = Fluorodeoxyglucose, PET = Positron emission tomography.

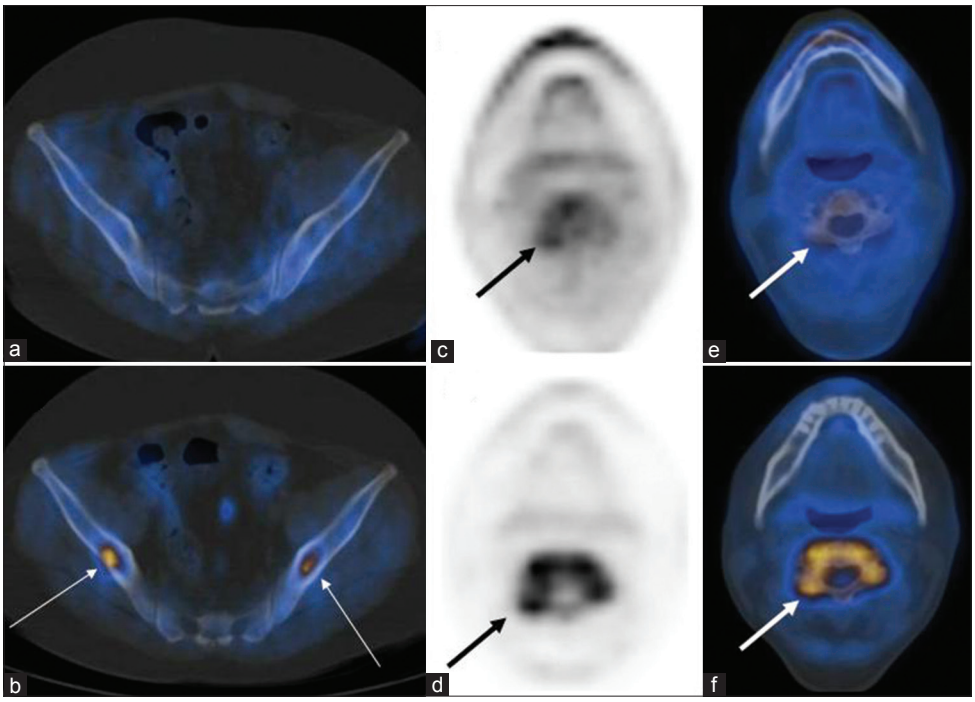

Figure 3: Transaxial fused FDG PET/CT image of the pelvis shows no abnormal uptake (a), whereas the corresponding ^{11}C-methionine scan (b) shows focal increased uptake in both iliac bones (thin arrows). Transaxial FDG PET (c) and fused PET/CT (e) image at C3 vertebra shows a hypermetabolic lesion (thick arrows). Corresponding ^{11}C-methionine image (d and f) shows more intense uptake with evidence of encasement of the thecal sac (thick arrows). CT = Computed tomography, FDG = Fluorodeoxyglucose, PET = Positron emission tomography

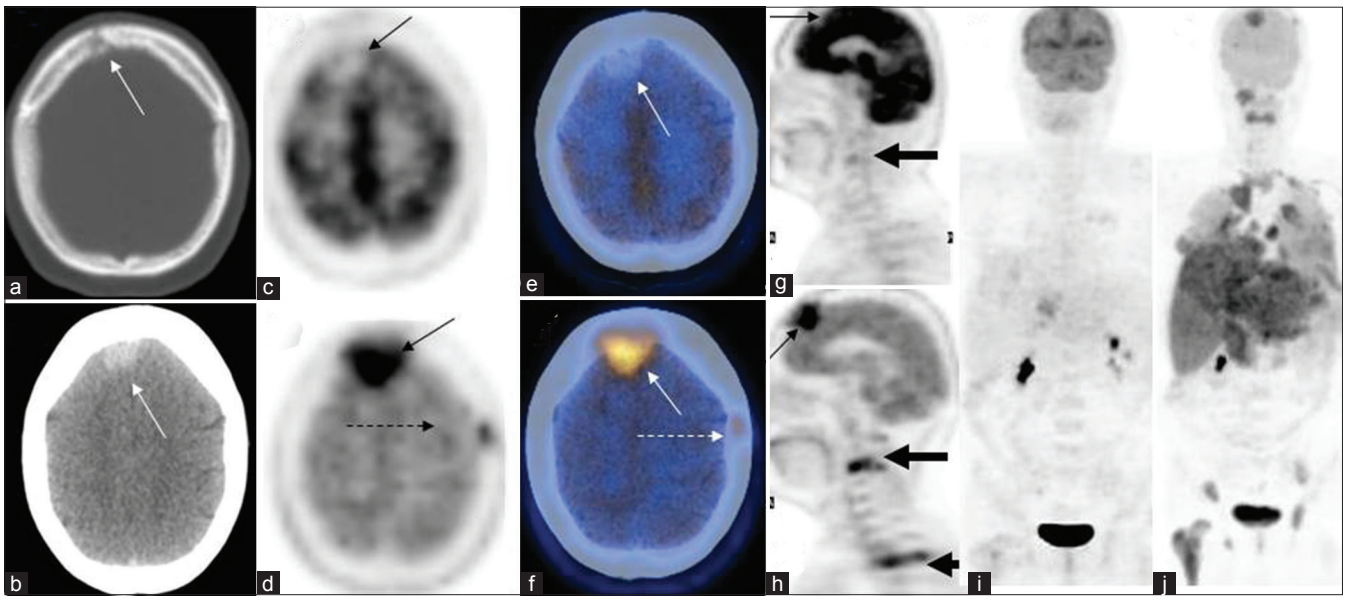

Figure 4: CT shows erosion in right frontal bone (bone window a) with an extra-axial mass (brain window b), with reduced FDG avidity on the axial FDG PET (c), PET/CT (e), and sagittal PET (g) image (thin arrows). Corresponding Met images show increased uptake (d,f,h), with additional calvarial sites of uptake (d,f–dotted arrows). Vertebral metastases with spinal canal extension noted on sagittal Met-PET image (h–thick arrows), whereas single lesion is seen on the FDG PET image (g). MIP image shows several additional sites of uptake on the Met scan (j) compared with the FDG scan (i). CT = Computed tomography, FDG = fluorodeoxyglucose, PET = Positron emission tomography, MIP = Maximum intensity projection

to the high rate of gluconeogenesis in well-differentiated HCC, resulting in uptake similar to that of normal liver parenchyma. Dual-tracer PET/CT scans using FDG and ^{11}C-acetate have been extensively undertaken owing to their complementary role in detection of HCC, both well- and poorly differentiated forms. The ^{11}C-methionine is also used to image a variety of tumors, including lymphomas and tumors of the brain, lung, and head or neck.[6] The ^{11}C-labeled methionine, the most widely studied novel radiotracer for brain tumors, has been found to be more efficacious than FDG for the primary detection of tumor, delineation of its extent, treatment planning, and assessment of therapeutic response.[7]

However, its role in detecting tumor lesions in patients with HCC is less well defined. This is probably owing to the high physiological uptake of ^{11}C-methionine in the liver.[8] It is important to bear in mind that one of the practical limitations in the use of this novel radiotracer is its short half-life of 20 min, which restricts its use to centers with an on-site cyclotron.[7]

With longer survival of patients and enhanced imaging techniques, the reported incidence of extrahepatic metastases in HCC is increasing. The most common sites for metastases are the lungs, followed by regional lymph nodes, bone, adrenal, and occasionally the peritoneum, pancreas, and kidney.[9] The present case also showed advanced disease, with metastatic nodules in both lung fields, mediastinal, hilar, and abdominal lymph nodes, showing low-grade or absent FDG avidity but significant ^{11}C-methionine uptake. Bone metastasis from HCC occurs with an incidence of 5.8%, with the vertebrae, followed by sternum and ribs being the most commonly involved sites.[10] Occasional cases of vertebral metastasis with extradural involvement and spinal cord compression have also been described.[11] Multiple skeletal metastases were visualized in the present case too. The ^{11}C-methionine scan picked up more skeletal lesions and also delineated the extradural involvement at two vertebral sites. These findings are concordant with a recent study on HCC, which showed that the overall detection rate of ^{11}C-methionine for extrahepatic lesions was superior (91%) to FDG (64%).[12] The authors have thereby proposed that ^{11}C-methionine could be a useful alternative to detect extrahepatic lesions and could provide additional information if distant metastases are suspected. Intracranial metastases from HCC is extremely rare, with a reported frequency ranging from 0.2 to 2.2% at autopsy.[13] Dural metastases can arise from direct skull involvement or hematogeneous spread.[14]

Dural involvement from calvarial metastasis is usually encountered in lung, prostate, and breast cancers. It may be clinically asymptomatic or may produce progressive neurological sequelae, as seen in our case. The ^{11}C-methionine scan showed multiple sites of calvarial metastases, several of which appeared normal on the CT and FDG PET images. The associated dural metastases in the right frontal region were also well delineated on the ^{11}C-methionine scan. This characteristic pattern of increased ^{11}C-methionine uptake, with poor FDG avidity in dural metastases has been described in the past.[15] In the present case, ^{11}C-methionine PET identified significantly more lesions than ^{18}F-FDG PET. This report highlights the potential value of ^{11}C-methionine PET/CT in assessing the hepatic and extrahepatic tumor burden in cases of HCC, especially in clinically unexpected locations.

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