Prostate-specific Membrane Antigen-expressing Hepatic Lesion: Metastatic or Hepatocellular Carcinoma

Abstract

Prostate-specific membrane antigen (PSMA) is a glycosylated type-II transmembrane protein highly expressed in certain tumor cells. It has emerged as a novel radiotracer for evaluation of prostate cancer. Increased PSMA expression in isolated liver lesion is a diagnostic challenge. Solitary liver metastasis from prostate cancer is rare. On the other hand, PSMA avid primary hepatocellular carcinoma (HCC) has been reported in literature. We report a case of PSMA expressing atypical HCC with normal alphafeto protein (AFP) and raised prostate specific antigen (PSA).

Keywords: *Hepatocellular carcinoma, prostate cancer, prostate-specific membrane antigen, solitary liver lesion*

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Introduction

Prostate-specific membrane antigen (PSMA) is a glutamate carboxypeptidase II transmembrane glycoprotein. It is a novel target for prostate-specific imaging. ^{68}Ga-PSMA positron emission tomography–computed tomography (PET-CT) scan has already established the superiority over other imaging in the diagnosis of recurrent disease in prostate cancer (PCa).[1] The other applications of PSMA in PCa are under evaluation. However, affinity of PSMA for other malignancies with nonprostatic cell line was reported in literature. Metastatic renal cell carcinoma, metastatic breast cancer, and primary glioma are few examples.[2-4] PSMA accumulation in hepatocellular carcinoma (HCC) has recently been reported in literature.[5] We report a case of atypical HCC detected as only PSMA-expressing lesion in a follow-up case of carcinoma prostate with biochemical failure.

Case Report

A 69-year-old male patient with markedly raised prostate-specific antigen (PSA) (256 ng/ml) was diagnosed as adenocarcinoma prostate by transrectal ultrasonography (USG)-guided fine-needle aspiration cytology biopsy 4 years back. Magnetic resonance imaging evaluation showed locally advanced disease. Bone scan was normal. The patient was treated with 60 Gy/20 Fr of radiotherapy (intensity-modulated radiation therapy) for 4 weeks. Androgen deprivation therapy was continued for 2 years. The patient was on follow-up since then.

Biochemical recurrence was detected in January 2018. Detected PSA value at that time was 2.14 ng/ml, which was significantly raised from the postradiotherapy nadir value of 0.28 ng/ml. Subsequently, we performed a whole body ^{68}Ga-PSMA PET/CT scan using an integrated scanner (GE Discovery STE) 60 min after intravenous injection of 140.6 MBq of 68Ga-labeled PSMA-11 (Ga-PSMA). The scan showed a large encapsulated heterogeneously enhancing hypodense mass lesion in liver with increased PSMA expression with SUV_{max} of 8.66 at the periphery of the lesion. No other PSMA-expressing disease is seen in the scan [Figure 1].

USG-guided biopsy from the liver lesion was performed. Microscopic examination showed cores of liver tissue infiltrated by tumor cells in trabecular pattern. The tumor cells are highly pleomorphic and mitotically active with increased nuclear-to-cytoplasmic ratio, dense eosinophilic cytoplasm, hyperchromatic nuclei, and variably prominent nucleoli. A battery of immunohistochemistry tests

How to cite this article: Das J, Ray S, Tapadia R, Midha D, Mallick I. Prostate-specific membrane antigen-expressing hepatic lesion: Metastatic or hepatocellular carcinoma. Indian J Nucl Med 2020;35:58-60.

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Received: 10-08-2019,
Revised: 09-09-2019,
Accepted: 15-09-2019,
Published: 31-12-2019.

Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.IJNM_145_19

Quick Response Code:

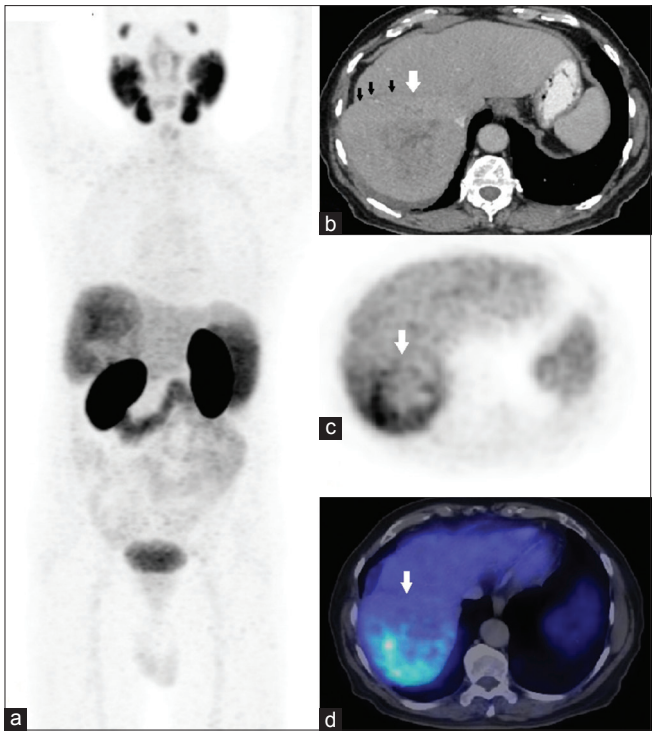

Figure 1: Prostate-specific membrane antigen positron emission tomography–computed tomography scan: (a) Maximum intensity projection image of the whole body prostate-specific membrane antigen scan shows heterogeneously increased radiotracer uptake in the right lobe of the liver. No other abnormal prostate-specific membrane antigen-expressing disease is seen. Contrast-enhanced computed tomography (b), positron emission tomography (c), and fused positron emission tomography–computed tomography (d) images of axial sections through liver show prostate-specific membrane antigen-expressing focal lesion in the right lobe (white arrows). The lesion shows well-defined capsule (black arrows) and heterogeneous enhancement with necrosis consistent with radiological features of hepatocellular carcinoma

aimed at identifying primaries other than prostate was performed. Immunohistochemistry showed the tumour cells to be strongly and diffusely positive for Glypican 3, patchy strong positive for Arginase and SALL4, focally positive for CK7 and negative for CK20, Hep Par1, AFP, MOC31, TTF1, PSA, PAX8 and OCT3/4. CD30 was non-contributory. CD10 showed focal canalicular pattern in the tumour cells. The tumour cells were negative for ERG and Synaptophysin. Immunohistochemistry result confirmed the diagnosis of primary hepatocellular carcinoma. [Figure 2]. However alpha-fetoprotein (AFP) was normal.

In multidisciplinary team meeting, the patient was referred for nonsurgical intervention like transarterial chemoembolization/transarterial radioembolization.

Discussion

Most common locations of metastasis from PCa are lymph nodes and bone. Less common sites are lung, liver, and brain. Isolated liver metastasis from PCa is rare.[6]

On the other hand, in a cell line study of effect of PSMA in microenvironment of various solid tumors, PSMA

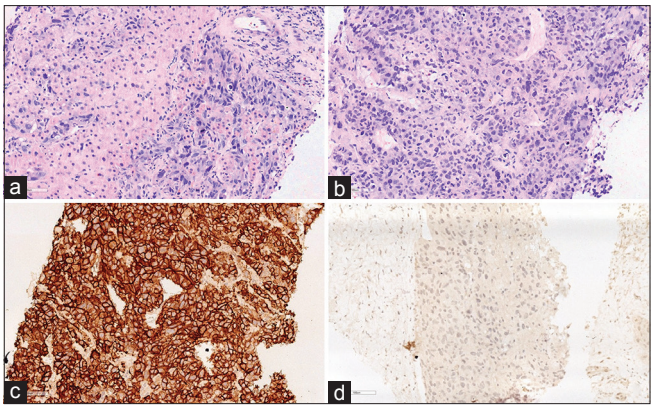

Figure 2: Histopathological features of liver lesion: (a) H and E image (×200) – Cores of liver tissue showing tumor cells in trabecular pattern, surrounded by a layer of flattened endothelial cells. (b) H and E image (×200). The tumor cells are highly pleomorphic and mitotically active with increased nuclear-to-cytoplasmic ratio, dense eosinophilic cytoplasm, hyperchromatic nuclei, and variably prominent nucleoli. Gland formation is not seen. (c) Strongly and diffusely positive for Glypican 3 on immunohistochemistry (×200). (d) Negative for prostate-specific antigen on immunohistochemistry (×200)

expression was detected in neovasculature of HCC cell line.[7] PSMA-expressing HCC was very infrequently reported in literature. In a prospective pilot study on ^{68}Ga-PSMA PET-CT scan for imaging of HCC, 36 out of 37 HCC lesions showed raised ^{68}Ga-PSMA uptake with mean SUV_{max} of 13.2.[8] In the case described by Huang *et al*., both AFP and PSA were within normal range and biopsy showed an encapsulated hepatocellular lesion in a cirrhotic liver.[9]

In our case, the patient had raised PSA and normal AFP level in the blood. No PSMA-expressing lesion attributable to prostatic cancer was demonstrated in our case. False-negative PSMA scan in case of biochemical failure may result because of number of factors such as very small lesion size below the threshold of PET resolution, low level of PSMA uptake, and adjacent uptake in the urinary bladder.[10,11]

The only PSMA-expressing lesion in our case is seen in the liver. With normal background liver parenchyma, PSMA-expressing focal lesion in a follow-up case of carcinoma prostate makes HCC an extremely unusual presentation.

Conclusion

PSMA-expressing isolated focal lesion in liver is a diagnostic challenge. On the one hand, isolated liver metastasis from PCa is rare. On the other hand, PSMA expression has been reported in primary HCC. In a patient who has isolated liver lesion with PSMA uptake on follow up with prostate cancer, a differential of HCC must be kept in mind, and a biopsy confirmation should be considered.

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

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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