Case report

A Case of Well-differentiated Hepatocellular Carcinoma Identified on Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography/Computed Tomography

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Abstract

Prostate-specific membrane antigen (PSMA) is a glycosylated type-II transmembrane protein highly expressed in certain tumor cells. To the best of our knowledge, this is the first case reported of an isolated well-differentiated hepatocellular carcinoma (HCC) strongly suspected on gallium-68 (^{68}Ga)-PSMA positron emission tomography/computed tomography (PET/CT), which was not well characterized both on magnetic resonance imaging (MRI) liver with Primovist as well as fluorine-18 (^{18}F)-choline PET/CT. Our patient had previous prostate cancer and previously was imaged using ^{18}F-choline PET/CT. The last scan showed an indeterminate segment VII hypodensity which was not significantly choline-avid. The lesion was initially stable on serial MRI scans but then showed growth from 1.0 to 1.5 cm. ^{68}Ga-PSMA PET/CT was performed. The lesion was intensely tracer-avid. This was surgically excised and histology confirmed the presence of well-differentiated HCC. Well-differentiated HCC can be optimally imaged using ^{68}Ga-PSMA PET/CT and further prospective studies are needed to look into the potential of this imaging modality.

Keywords: Ga-68 PSMA PET/CT, HCC, well-differentiated

Introduction

Prostate-specific membrane antigen (PSMA) is a glycosylated type-II transmembrane protein highly expressed in prostate cancer cells.[1] Antibodies targeting the PSMA molecule were developed,[2] and gallium-68-labeled PSMA (^{68}Ga-PSMA) positron emission tomography/computed tomography (PET/CT) has recently generated significant interest.[3]

There are three previous reports of incidental findings of metastatic hepatocellular carcinoma (HCC) on ^{68}Ga-PSMA PET/CT performed in patients with suspicion for liver metastases from prostate cancer.[4-6]

To the best of our knowledge, this is the first report of an isolated well-differentiated HCC strongly suspected on ^{68}Ga-PSMA PET/CT, not well characterized both on MRI liver with Primovist and ^{18}F-choline PET/CT.

Case Report

We report a case of a 66-year-old Filipino male patient. Informed consent was obtained for publication. He is an

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ex-smoker and nondrinker. The patient had a previous history of thyroid nodular hyperplasia treated with total thyroidectomy, prostate cancer treated with robotic prostatectomy and external beam radiotherapy 5 years previously, cholecystectomy for cholecystitis, diabetes mellitus, and hyperlipidemia. He was also incidentally found to be positive for hepatitis B core antigen but had never received treatment for hepatitis B.

He had previously been imaged using fluorine-18 (^{18}F)-choline PET/CT for follow-up of his prostate cancer. The last scan done 11 months previously had shown an indeterminate hypodensity in segment VII but was not significantly choline-avid to be considered suspicious [Figure 1]. However, given the history of prostate cancer and that prostate cancer may metastasize to the liver, albeit rarely, the patient then underwent MRI of the liver with Primovist for further characterization. This showed a T2-hyperintense nodule with signal drop out on the out of phase sequence and suggestive of arterial enhancement and delayed washout corresponding to the lesion seen on PET/CT, with differentials of hepatic adenoma, HCC, and angiomyolipoma [Figures 2-5]. Follow-up MRI scans done over the next 10 months showed that the lesion remained stable and did not show any restricted diffusion, leading to the impression of a benign lesion. Interestingly, the patient's prostate-specific antigen (PSA) and alpha-fetoprotein (AFP) both remained within normal limits throughout the period of follow-up. The final MRI scan then showed an increase in size from 1.0 to 1.5 cm [Figure 6]. We therefore performed a whole body PET/CT using an integrated scanner (GE 690) 60 min after intravenous injection of 140.6 MBq of ^{68}Ga-labeled Glu-urea-Lys(Ahx)-HBED-CC (^{68}Ga-PSMA). The scan showed an intensely tracer-avid nodule corresponding to the lesion seen on MRI [Figures 7 and 8], without any suspicious lesion seen elsewhere in the body, particularly the prostate bed [Figure 9].

Given the history of hepatitis B and prostate cancer as well as the absence of other suspicious lesions, the patient then underwent a robotic-assisted laparoscopic resection of the segment VII lesion.

Microscopic examination of the specimen showed a cirrhotic liver with a well-circumscribed, unencapsulated hepatocellular lesion [Figure 10] which showed macrovesicular steatosis [Figure 11]. Portal tract invasion was noted near the edges of the lesion on hematoxylin and eosin stained sections. Immunohistochemical (IHC) staining for CD34 showed capillarization of the sinusoids in the lesion. There was also focal positivity on IHC staining for glypican-3 and a raised Ki-67 index in the lesion. Overall, the features were consistent with a well-differentiated HCC.

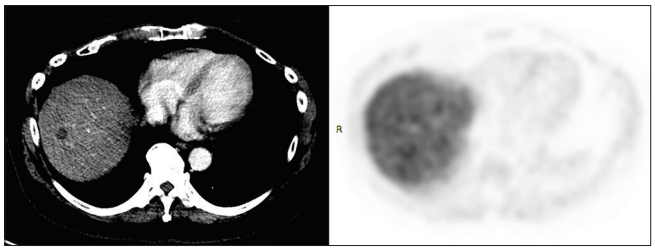

Figure 1: Axial computed tomography and attenuation-corrected positron emission tomography images of the latest fluorine-18 choline positron emission tomography/computed tomography

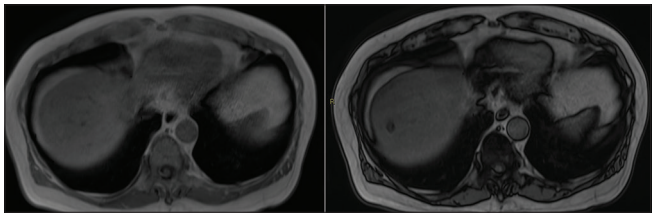

Figure 3: Axial in- and opposed-phase images of initial magnetic resonance imaging liver

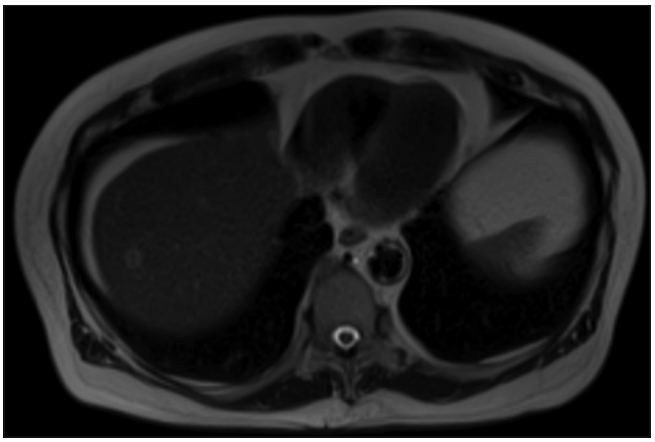

Figure 2: Axial T2 half-Fourier acquisition single-shot turbo spin-echo image of the initial magnetic resonance imaging liver

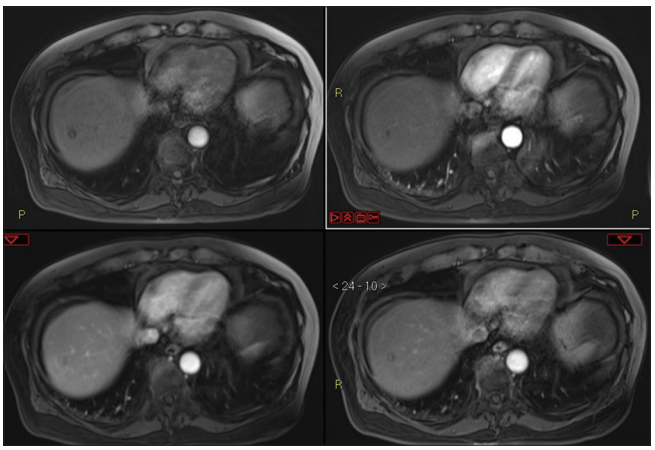

Figure 4: Axial contrast-enhanced images of initial magnetic resonance imaging liver

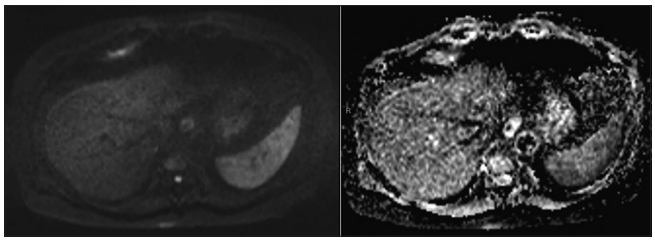

Figure 5: Axial diffusion-weighted imaging (B = 600) and apparent diffusion coefficient map of initial magnetic resonance imaging liver

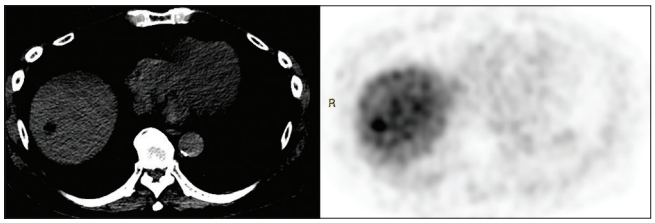

Figure 7: Axial computed tomography and attenuation-corrected positron emission tomography images of gallium-68 prostate-specific membrane antigen positron emission tomography/computed tomography

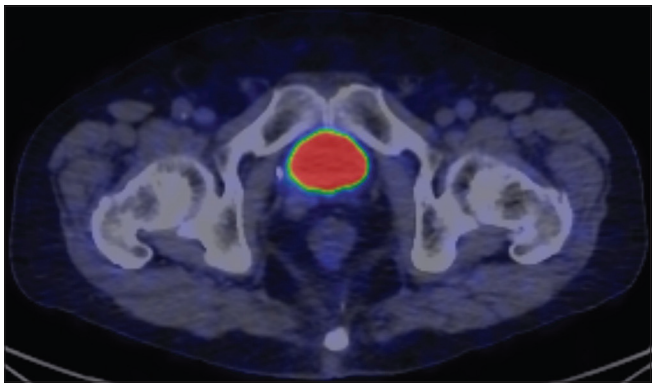

Figure 9: Fused axial image of the prostate bed on gallium-68 prostate-specific membrane antigen positron emission tomography/computed tomography

The patient recovered well from the operation and was discharged on the 3rd day postoperation.

Discussion

It has been shown that PSMA can be expressed not just on prostate cancer cells but also on cell lines of other cancers. In a recently published paper using cell lines, the expression of PSMA on HCC cells was reported to reach 95%.[7]

Interesting features, in this case, included the fact that both AFP and PSA were within normal limits throughout the duration of follow-up and that the lesion turned out to be a fairly slow-growing, well-differentiated HCC which would likely have a favorable patient outcome given surgical resection and lack of metastases. Furthermore, despite the fact that

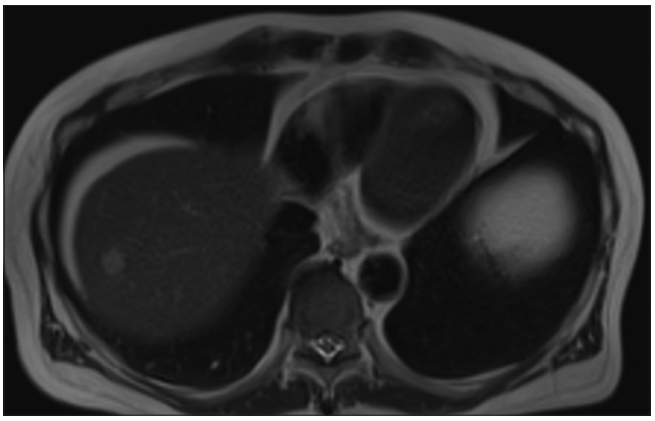

Figure 6: Axial T2 half-Fourier acquisition single-shot turbo spin-echo image of the latest magnetic resonance imaging liver showing interval increase in size

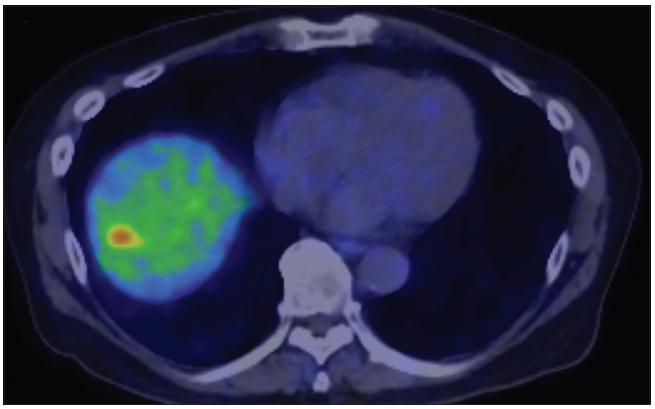

Figure 8: Fused axial image of the liver lesion seen on gallium-68 prostate-specific membrane antigen positron emission tomography/computed tomography

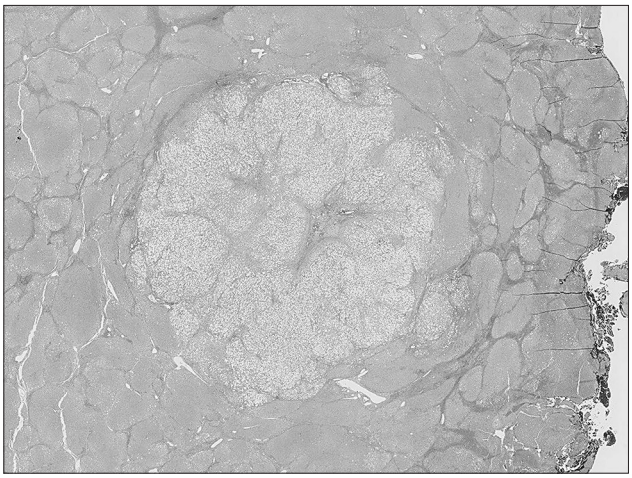

Figure 10: The lesion and the background liver at scanning magnification (H and E, ×40)

^{18}F-choline PET/CT has been shown in several studies to show uptake in well-differentiated HCC[8,9] in this case, the lesion was not confidently characterized on either ^{18}F-choline PET/CT or MRI liver with Primovist.

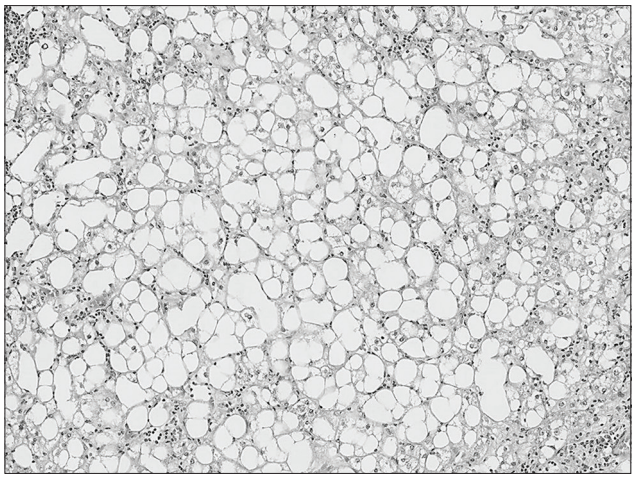

Figure 11: Macrovesicular steatosis within the lesion (H and E, ×100)

In summary, lesions detected on ^{68}Ga-PSMA PET/CT may in the proper clinical context turn out to be due to malignant tumors other than prostate cancer as mentioned above. It appears that well-differentiated HCC can be optimally imaged using ^{68}Ga-PSMA PET/CT and further prospective studies are needed to look into the potential of this imaging modality, both for initial characterization of indeterminate liver lesions and for staging purposes, especially before surgery.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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