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^{68}Ga–Prostate-Specific Membrane Antigen, A Potential Radiopharmaceutical in PET/CT To detect primary Cholangiocarcinoma

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ABSTRACT

^{68}Ga Prostate-specific membrane antigen (PSMA) is an increasingly popular radiopharmaceutical tracer in prostate cancer and is becoming increasingly researched in other cancers such as breast cancer, renal cell carcinoma, glioblastoma multiforme, among others. Cholangiocarcinoma is the second most common primary hepatic malignant tumor; it is an aggressive tumor with a 5-year survival rate of less than 5 %. We herein report a case of primary cholangiocarcinoma detected on ^{68}Ga-PSMA PET-CT conducted as part of follow up for prostate cancer and confirmed by biopsy and immunohistochemistry.

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Introduction

^{68}Ga-Prostate-specific membrane antigen (PSMA) is a radiopharmaceutical tracer that has become increasingly promising in the staging and detection of recurrence in prostate cancer (1). Indeed, ^{68}GA-PSMA positron emission tomography-computed tomography (PET-CT) has been established as the preferred imaging modality in the diagnosis of recurrent prostate cancer (1). While other uses for ^{68}Ga-PSMA are being evaluated, potentially rendering its name a misnomer, its avidity to other solid tumors has been reported in the literature, including breast cancer(2), renal cell carcinoma (3), glioblastoma multiforme(4), differentiated thyroid cancer(5), colorectal carcinoma(6), non-small cell lung cancer(7)and follicular lymphoma (8). Recently, its avidity to hepatocellular carcinoma (HCC) has also been reported (9).Finally, and to a lesser extent, ^{68}Ga-PSMA accumulation in cholangiocarcinoma with skeletal metastasis has been reported (10, 11). We report a case of a primary cholangiocarcinoma detected on ^{68}Ga-PSMA PET-CT conducted as a follow up of prostate carcinoma.

Case Report

A 79-year-old male with a history of non-Hodgkin lymphoma and prostate cancer who had

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undergone radical prostatectomy presented with rising PSA and consequently underwent ^{68}Ga-PSMA PET-CT that revealed focal radiotracer uptake in segments VI and VII (Figure 1) in the right lobe of the liver and a decrease in physiological uptake in the rest of the liver.

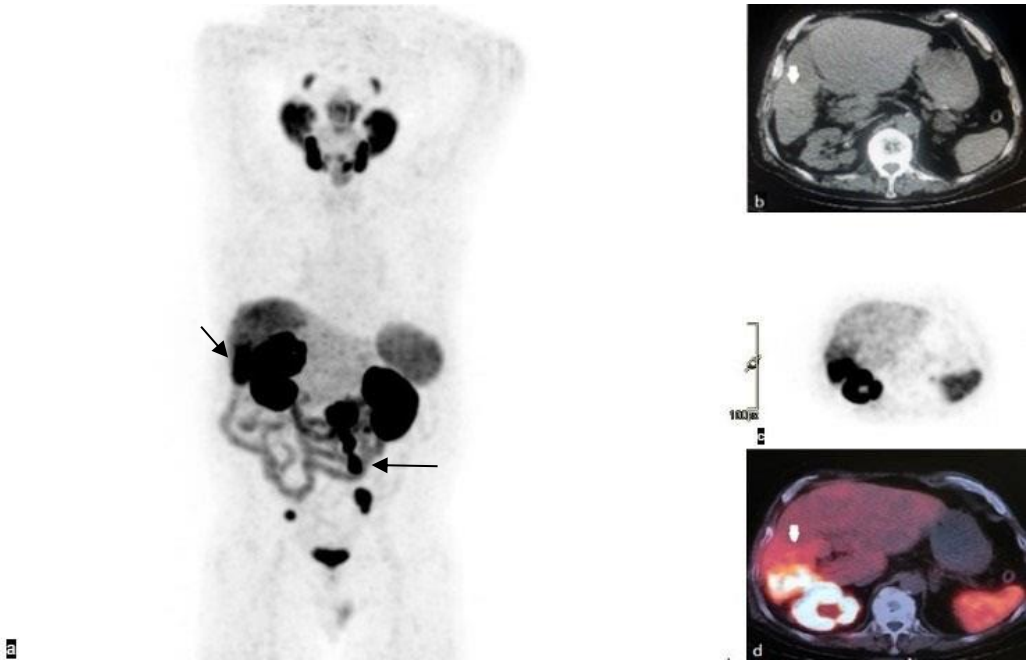
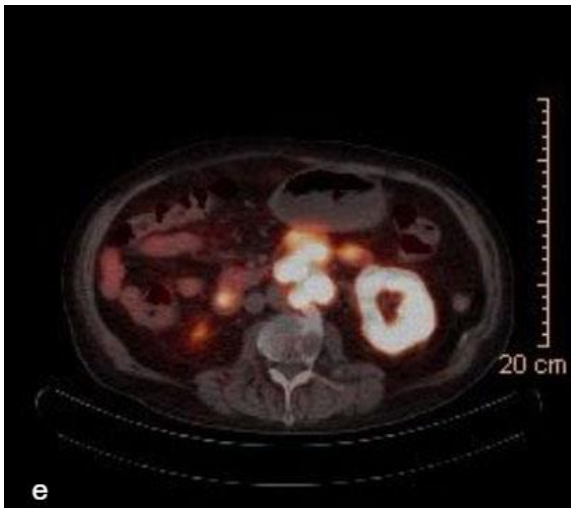


Figure 1. Prostate-specific membrane antigen positron emission tomography–computed tomography scan and non-contrast enhanced computed tomography:
(a) Maximum intensity projection image of the whole body prostate-specific membrane antigen scan shows a focal area of increased radiotracer uptake in the inferior segments of the right lobe of the liver (black arrow) and decreased physiological uptake in the rest of the liver. There are also foci of increased radiotracer uptake in the left aspect of the abdomen, which correspond to metastatic retroperitoneal lymph nodes from the known prostatic malignancy (horizontal black arrow). Non-contrast enhanced computed tomography axial images showing a hypodense area in segment VI of the liver (bold white arrow) (b), corresponding to the area of increased radiotracer uptake seen on the positron emission tomography (c), and fused positron emission tomography–computed tomography (bold white arrow) (d), suspicious for an underlying infiltrative mass, which drove us to recommend better assessment by MRI. Axial PET-CT fused images (e) showing that the foci of increased radiotracer uptake in the left hemiabdomen seen on the MIP image, correspond to enlarged retroperitoneal lymph nodes, related to the known metastases from the primary prostatic malignancy



This prompted us to conduct an enhanced magnetic resonance imaging (MRI) of the abdomen which revealed an ill-defined infiltrative process in the right hepatic lobe (Segment VII) with associated right portal vein thrombosis (Figures 1& 3). We followed this with a magnetic resonance cholangiopancreatography (MRCP) that revealed dilation of the right hepatic lobe ducts (Figure 2) secondary to an ill-defined mass (Figure 2) obliterating the right portal vein. Our differential diagnosis included metastatic tumor and cholangiocarcinoma.

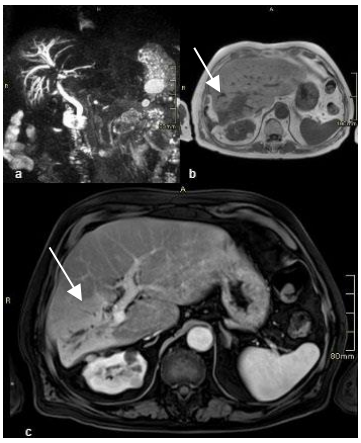


Figure 2. 3D reconstructed Magnetic resonance cholangiopancreatography (MRCP) images in the coronal plane showing dilated right hepatic ducts (a), secondary to an ill-defined infiltrative mass hypointense on T1 weighted images centered in segment VI (white arrow) (b). Ill-defined infiltrative mass extending from segment VI to VII, showing heterogeneous enhancement (white arrows), associated with obliteration of the right portal vein at that level, radiological features of suggestive of Cholangiocarcinoma (c)

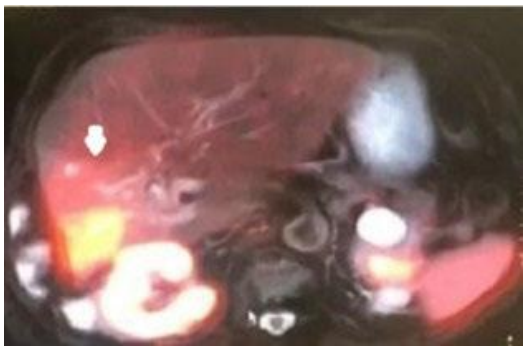


Figure 3. Fused PET and MRI- images showing that the area of the infiltrative mass corresponds to the increased uptake seen on PET images

Core-biopsy of the lesion in the liver was taken and histopathology revealed invasive glands with intestinal-type morphology with goblet cells. Non-invasive glands with intestinal metaplasia (Figure 4) were also seen in the portal tracts. The background consisted of mucinous metaplasia of bile duct epithelium. Immunohistochemistry was performed in order to differentiate primary cholangiocarcinoma from a metastatic gastrointestinal tumor. The tumor cells were found to be positive for Cytokeratin 7, focally positive for CDX-2 and negative for CK20, TTF-1, and prostate-specific antigen consistent with primary cholangiocarcinoma. The patient was subsequently started on stereotactic body radiotherapy for cholangiocarcinoma.

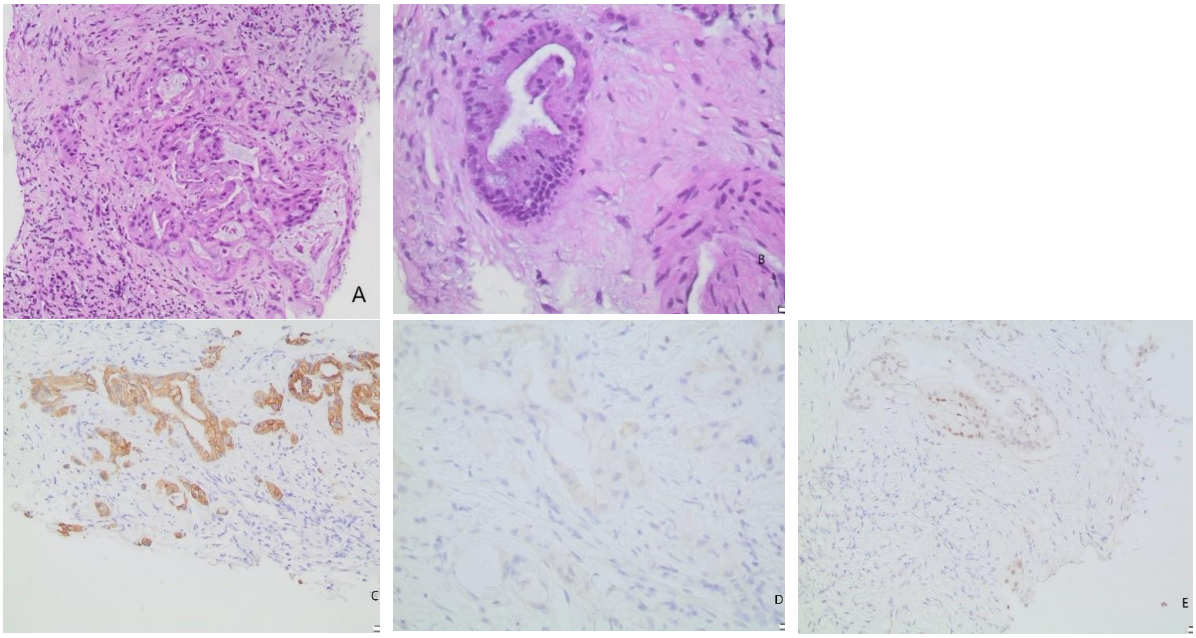


Figure 4. Histologic examination of the liver lesion. A: Core biopsy (H&E) showing Invasive glands with intestinal-type morphology. In the background, there is a ductular reaction. B: Higher power view (H&E) of a bile duct within a portal tract showing intestinal metaplasia with goblet cells. Part of the gland has a normal cuboidal epithelium (upper part of the gland). C: The cells lining the invasive glands show cytoplasmic and membranous expression for CK7. D: The malignant cells are negative for CK20. E: The tumor cells are only focally positive for CDX2

Discussion

Accounting for 10% of all primary hepatic malignancies, intrahepatic cholangiocarcinoma is the second most common primary hepatic malignant tumor (12). Prostate cancer most often metastasizes to lymph nodes and bone, and less commonly to the liver (13). Cholangiocarcinoma is an aggressive tumor with a 5-year survival rate of less than 5% (14). In our patient, initially diagnosed with metastatic prostate cancer, we usually see metastasis to bones and lymph nodes. ^{68}GA-PSMA PET-CT revealed uptake in the liver lesion.MIP showed increased uptake that corresponded on the fused PET-CT image to enlarged retroperitoneal lymph nodes, related to the known metastases from the primary prostatic malignancy. Later staining of the biopsied liver lesion was negative for PSA on immunohistochemistry.

Immunohistochemistry compounded our findings on PET-CT. The specimen was found positive for CK7 more than any other carcinoma of the pancreas or biliary tract 11. It also showed positive result focally for CDK2, shown to have prognostic value for intrahepatic cholangiocarcinoma (15).

As previously mentioned, ^{68}Ga-PSMA has been reported in a variety of solid tumors whereby it is expressed in the endothelium of associated neo-vasculature (16).

Of course, with such radiological findings, metastasis needs to be considered and ruled out. To the best of our knowledge, there is one case in the literature that reported intrahepatic cholangiocarcinoma (ICC) metastasize to the prostate (17). Tosev et al helpfully point out that in both ICC and prostate cancer (PCa) vascular endothelial growth factor C (VEGF-C) is overexpressed and that Ki-67 index is up-regulated in PCaand is a poor prognostic factor in ICC .

Finally, further investigation of the utility of ^{68}Ga-PSMA in cholangiocarcinoma is warranted. This could provide a promising therapeutic horizon in the currently limited treatment of cholangiocarcinoma, potentially allowing for radionuclide legend therapy with α/β-emitters.

Conclusion

Our case is one of the few published on the uptake of prostate-specific membrane antigen in confirmed cholangiocarcinoma cases, adding to the incentive to further investigate its potential use. Current available options for the treatment of cholangiocarcinoma, especially when metastatic, are currently limited and with low-survival rates. Prostate-specific membrane antigen uptake in cholangiocarcinoma opens the potential for employing radionuclide legend therapy, especially where the standard treatments fail.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed .

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Conflict of Interests

None.

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