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*Case Report*

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# PSMA PET/CT imaging: Unveiling potential incidental Hepatocellular Carcinoma (HCC) with portal vein thrombosis

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## Abstract

The radiopharmaceutical tracer [68Ga] Ga-Prostate-Specific Membrane Antigen (PSMA) has gained recognition for its efficacy in prostate cancer staging and detection, primarily via PSMA Positron Emission Tomography/Computed Tomography (PET/CT). Research has shown that despite its name, PSMA PET/CT is effective in diagnosing and potentially treating various solid tumors other than prostate cancer. These tumors include breast cancer, renal cell carcinoma, glioblastoma multiforme, thyroid cancer, colorectal carcinoma, lung cancer, and follicular lymphoma. HCC, which accounts for the vast majority of primary liver cancer cases, poses diagnostic challenges because it is frequently asymptomatic until advanced stages. Traditional imaging methods, such as Computerized Tomography (CT) or MRI, are important in diagnosis, with PSMA PET/CT demonstrating a high detection rate for HCC. This case report describes an 87-year-old man who was found to have on PSMA PET/CT prostate cancer and HCC. This case emphasizes the role of PSMA PET/CT in detecting primary liver lesions.

***Keywords:*** [68Ga] Ga-Prostate-specific membrane antigen; PSMA PET/CT; Hepatocellular carcinoma; Prostate cancer; Portal vein thrombosis; Medical imaging.

## Introduction

The radiopharmaceutical tracer [68Ga] Ga-Prostate-Specific Membrane Antigen (PSMA) has shown increasing promise in its application for prostate cancer detection and staging [1]. PSMA PET/CT is now the optimal imaging technique for staging prostate cancer, detecting biochemical recurrence, and eligibility for radioligand therapy [2]. While its name may no longer fully represent its potential applications, research has shown that it is effective in the detection of a variety of solid tumors including Hepatocellular Carcinoma (HCC) [3,4].

HCC accounts for almost 90% of all occurrences of primary liver cancer. HCC is usually asymptomatic, and clinical markers are rarely used to diagnose the condition. Consequently, the radiologic diagnosis of HCC depends heavily on medical imaging such as Multi-phase Computerized Tomography (CT) or Magnetic Resonance Imaging (MRI) [5]. The emergence of PSMA PET/CT as a promising imaging technique in the detection of HCC represents a significant improvement in medical imaging. For instance, when a hepatic lesion is found on Ultrasound (US) or CT scan, PSMA PET/CT has been shown to detect

HCC metastasis with higher accuracy than a CT scan [3,6,7]. In HCC, PSMA PET/CT and MRI were similar in terms of sensitivity (91% vs 87%), specificity (70% vs 73%), positive predictive values (71% vs 76%), and negative predictive values (90% vs 85%). Both of these imaging modalities were superior to multiphasic contrast-enhanced computed tomography [8]. Moreover, compared to F-18-Fluorodeoxy Glucose (FDG) PET/CT, PSMA PET/CT demonstrates superiority in the detection and staging of HCC [7,9,10]. Finally, PSMA PET/CT importance in detecting HCC was also linked to a change in treatment in roughly 50% of the patient population, indicating its high impact on management of HCC [7].

## Case report

This is the case of an 87-year-old male patient, previously healthy, who presented to urology division for acute lower urinary tract symptoms. His physical exam was normal except for a right prostate nodule on Digital Rectal Examination (DRE). The urine analysis and culture results were negative ruling out a possible urinary tract infection. In the setting of a right prostate nodule, Prostate-Specific Antigen (PSA) levels in serum were taken and showed a value of 10.9 ng/mL.

An ultrasound of the pelvis was done revealing a nodular hypertrophic prostate gland with mild ascites. In addition to that, a multiparametric Magnetic Resonance Imaging (mpMRI) was conducted to further analyze the prostate. The results showed a lesion with a Prostate Imaging Reporting and Data System version four (PIRADS IV) score on the right side. Thus, a prostate biopsy was recommended but refused by the patient. In this setting, the decision was taken to perform a PSMA PET/CT for a better assessment of the prostate lesion. The PSMA PET/CT revealed a large intense uptake in the right prostate lobe with a Standardized Uptake Value (SUV) of 15.2. The prostate lesion in question has a PRIMARY score of 5, indicating a high suspicion of malignancy [11]. It has also received a PSMA Reporting and Data System (PSMA RADS) score of 5, which emphasizes the high possibility of malignant activity in the prostate region [12,13]. Findings are indicative of prostate cancer with no locoregional metastasis (Figure 1).

Besides the prostate region, PSMA PET/CT showed multiple foci of increased uptake within the left liver lobe with an SUV up to 15.16, corresponding to hypodense lesions on nonenhanced CT scan (Figure 2). Furthermore, a diffuse linear uptake at the level of the main portal vein extending to its right and left main branches was observed raising the possibility of malignant thrombosis (Figure 3).

Further investigations were strongly advised including an MRI of the liver and a biopsy. However, the patient refused to undergo these tests but agreed to take an alpha-fetoprotein (AFP) test which showed a level of 1009 ng/mL, further raising the possibility of HCC.

## Discussion

This case highlights the enhanced ability of PSMA PET/CT in detecting potential HCC, emphasizing its usefulness beyond its conventional boundaries. It reveals lesions outside the prostate region, demonstrating its capacity to fully assess disease burden.


**Figure 1: PSMA avid prostate and liver lesions:** (a-c) [68Ga] Ga-Prostate-Specific Membrane Antigen (PSMA) Positron Emission Tomography/Computed Tomography (PET/CT) Maximum Intensity Projection (MIP), coronal and axial fused images show a large radiotracer avid lesion at the right aspect of the prostate gland in keeping with the primary prostate lesion. Multiple lesions within the liver are seen on MIP image. Incidental findings are the multifocal radiotracer avid lesions in the liver.


**Figure 2: Multifocal liver lesions on CT :** (a-c) Multifocal radiotracer avid lesions in the left liver lobe corresponding to hypodense lesions on CT correlate

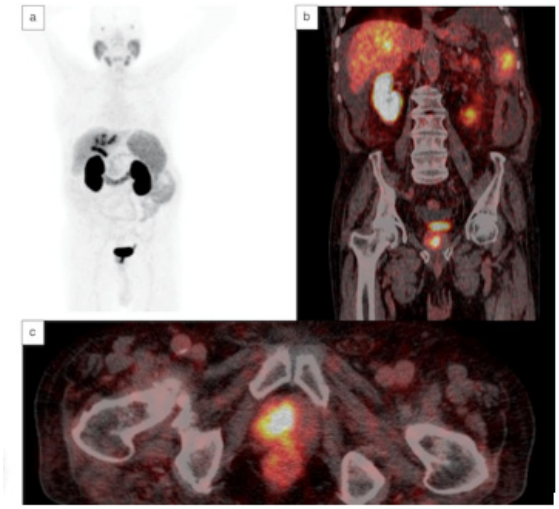


**Figure 3: Malignant portal vein thrombosis with ascites:** (a-c) Intensely radiotracer uptake in the main portal vein. Findings are suggestive of malignant portal vein thrombosis. There is also mild to moderate ascites

PSMA PET/CT detected HCC with comparable sensitivity and specificity to MRI and correlated well with clinical outcomes [8]. The increased accuracy of PSMA PET/CT was also highlighted in its lower false negative when compared to MRI and CT scan [8]. Furthermore, PSMA PET/CT supports MRI in tumor staging, particularly in demonstrating multicentric tumors, and can be superior to MRI in demonstrating extrahepatic involvement [9] and portal vein thrombosis as demonstrated by Shamim et al. (2023) who showed that portal vein thrombosis or invasion was found in two-thirds of the patients with HCC showing high PSMA uptake [14].

The importance of PSMA PET/CT in changing the management of patients was already demonstrated in the literature.

The ability of this imaging technique to detect metastasis reflects its usefulness in providing a valuable tool for clinicians to modify interventions based on a comprehensive disease understanding, increasing the precision of therapeutic management in patients with HCC [7]. The increased uptake of PSMA in HCC opens the door for the evaluation of the effectiveness of PSMA-targeted radionuclide treatment in HCC warranting further research in this field.

Radiolabeled PSMA has shown superior imaging capabilities for HCC in comparison to 18F-FDG. It has demonstrated sensitivity and accuracy that sometimes surpasses conventional CT and MRI, particularly in cases of metastatic illness. Although PSMA-directed Radioligand Therapy (RLT) has been proven safe and effective in prostate cancer treatment, clinical validation of its use in HCC is ongoing, and limited scientific evidence exists. Despite its limitations such as low uptake and quick tumor wash-out, RLT has potential benefits, including targeted therapy, individualized dose, and reduced toxicity. This makes it a promising option in the limited treatment options available for advanced-stage HCC patients [15].

It is important to note that there are limitations concerning the diagnosis of HCC in this patient such as the absence of a confirmatory biopsy. Moreover, studies have shown that 80% to 90% of HCC patients have cirrhosis [16]. However, in Non-Alcoholic Steatohepatitis (NASH) only around 20% of patients will develop cirrhosis in their lifetime [17]. The imaging of this patient shows no signs of cirrhosis, further questioning the HCC diagnosis. Despite these limitations, some factors strongly favor the diagnosis of HCC among these the lack of evidence for bone metastasis or metastatic lymph nodes and the relatively low PSA level (10.9 ng/mL) make these hepatic lesions unlikely to be metastases from the prostate gland, more likely to be a primary liver malignancy. Finally, the presence of ascites and increased AFP make HCC very likely.

## Conclusion

In conclusion, PSMA PET/CT, which was initially recognized for its ability to detect prostate cancer, has proven beneficial in the diagnosis of a potential HCC. This case study demonstrates its high sensitivity in detecting a highly probable HCC, prompting significant shifts in diagnostic strategies, and confirming its critical role in advancing precision medicine for HCC patients.

## Declarations

**Ethical standards:** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Availability of data and material:** Contact the corresponding authors for data requests.

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