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Pancreatic Adenocarcinomas Detected on PSMA-PET Misreported as Benign Lesions

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Abstract

This paper explores the clinical implications of incidental PSMA ligand avidity in the pancreas. We present two cases referred to an author in Brisbane where PSMA-PET scans identified pancreatic lesions in patients undergoing preoperative evaluation for prostatectomy. In both cases, the radiology report misdiagnosed the pathology and falsely reassured the urologic surgeon. Subsequent resection with histopathological evaluation confirmed pancreatic ductal adenocarcinoma (PDAC) in both patients. These cases remind clinicians that PSMA avidity in the pancreas should warrant further investigation. There may also be potential value in evaluating pancreatic lesions of uncertain etiology.

Keywords

PSMA PET; pancreatic adenocarcinoma; diagnostic imaging; prostate-specific membrane antigen

1. Introduction

Prostate-specific membrane antigen (PSMA) is expressed in multiple solid organ malignancies. This surface membrane protein is found on prostatic and extraprostatic epithelium and is associated with tumor cell neo-vascularization [1].

The PSMA PET protocol utilizes a combination of PSMA ligand and Gallium-68 in positron emission tomography and computed tomography (PET/CT) for staging and assessing prostate carcinoma [1–3]. However, PSMA avidity has been observed in various extraprostatic malignancies such as renal cell, hepatocellular, lung, and breast carcinomas [3,4]. Physiological PSMA uptake is also noted in lacrimal, parotid, and submandibular glands, liver, spleen, bowel, kidney, ureter, urinary bladder, and urethral tissues [1]. Given the novelty of this biological tracer, the standard expected uptake in tissues is not yet fully understood.

We have recently treated two patients with early pancreatic ductal adenocarcinoma (PDAC) detected on PSMA scans. In both cases the initial radiology reports were misleading.

2. Case One

A 63-year-old male underwent a PSMA PET/CT scan for staging of newly diagnosed prostate cancer. PSMA Uptake was observed in a 2 cm lesion in the distal pancreas. This was initially reported as *"irregular cystic change which may represent intraductal papillary mucinous neoplasm"* **(Figure 1)**. Six weeks later, the patient underwent a robotic prostatectomy. Day two following the surgery, a CT scan revealed the tail lesion once more, which was reported as *"focal pancreatitis."* A follow-up MRI six weeks later showed interval growth, prompting a referral for an HPB opinion. FDG PET indicated some avidity in the lesion with no other abnormal uptake **(Figure 2)**. The Ca19-9 level was elevated at 109 U/mL (NR: <37 U/mL).

The patient underwent a laparoscopic distal pancreatectomy and splenectomy. Pathology results showed a moderately differentiated pancreatic ductal adenocarcinoma, measuring 27mm in maximal dimension with perineural and lymphovascular invasion. All margins were clear, and no evidence of malignancy in four lymph nodes. Surgery was complicated by a collection requiring EUS drainage, and the patient was referred for adjuvant chemotherapy.

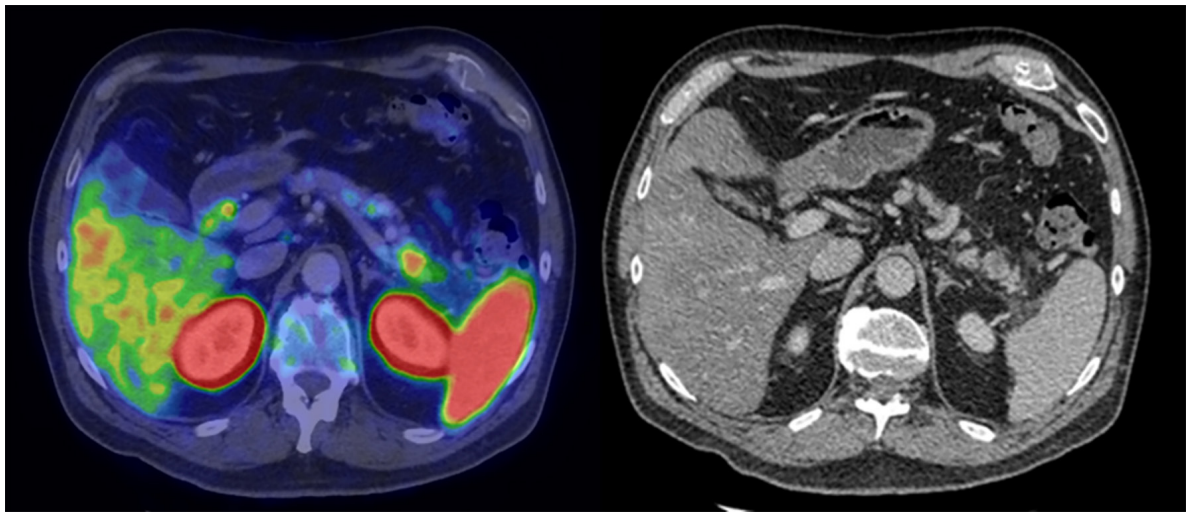

Figure 1: PSMA PET (left) and computed tomography (right) of tail of pancreas mass showing a 21 × 20mm reported as irregular cystic change.

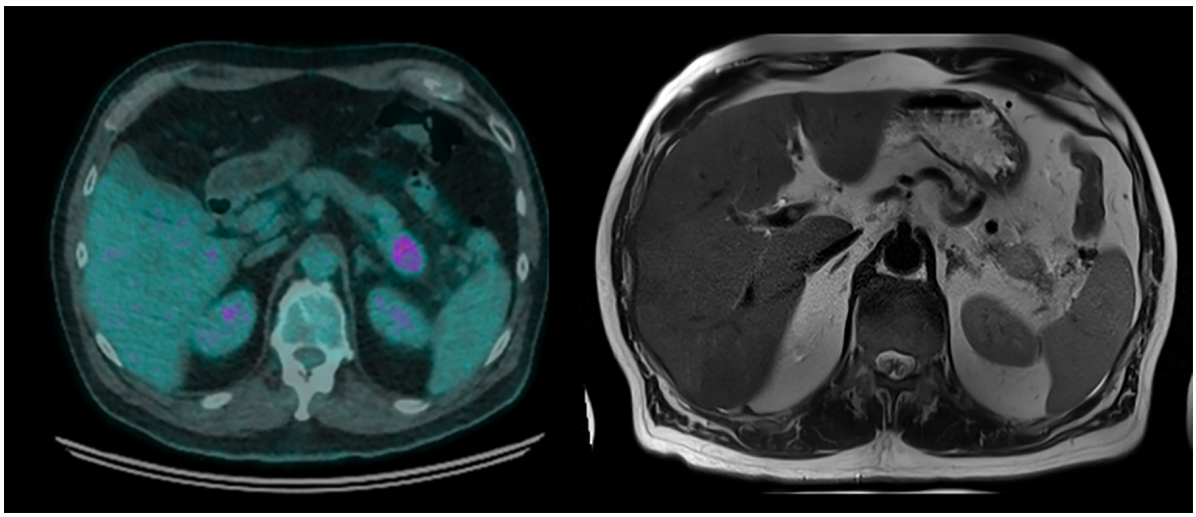

Figure 2: FDG PET (left) and MRI (right) of tail of pancreas mass measuring 29 × 26 mm with SUVmax 7.34 and photopenia centrally suggesting central necrosis.

3. Case Two

A 62-year-old man underwent a PSMA PET/CT for staging early prostate cancer, revealing prominent avidity within the pancreatic tail, initially reported as *"relating to physiological prominent islet cells"* **(Figure 3)**. The urologist, noting this finding, referred the patient for HPB opinion. Upon review, the original CT scan demonstrated pancreatic duct dilatation in the tail.

A subsequent MRI revealed a 20 mm mass at the junction of the pancreatic neck and body with upstream duct dilatation **(Figure 4)**. FDG-PET also showed avidity in the lesion **(Figure 4)**. Endoscopic ultrasound confirmed a 14 mm mass with upstream pancreatic ductal dilatation, and biopsy showed PDAC. The patient received neoadjuvant *FOLFIRINOX* for three months and then underwent a laparoscopic distal pancreatectomy with a partial splenectomy, as recently described [5]. Then, he was discharged on day four without complications.

Pathology results confirmed a moderately differentiated 12mm pancreatic adenocarcinoma with perineural invasion but no lymphovascular invasion. There was evidence of tumor regression. Follow up imaging showed a vascularized remnant spleen one quarter of its normal size with no Howell-Jolly bodies on peripheral blood smear.

4. Discussion

PSMA PET avidity is not exclusive to the prostate. PSMA becomes overexpressed in the context of neo-vascularization in a range of tumors [4]. In the presented two cases, pancreatic avidity was initially misreported as non-neoplastic lesions. In one case, there was definite PSMA avidity in the primary PDAC and the second demonstrated PSMA avidity adjacent to the lesion.

At the cellular level, prior immunohistochemistry studies have demonstrated PSMA expression on pancreatic cancer

cells [3,6,7]. A recent publication in Nature exploring theranostic possibilities found that while PSMA expression was high in the primary tumor, metastases did not share this expression [6]. Clinically, the evidence of PSMA avidity on imaging is significant.

Several isolated case reports have identified PSMA avidity on PET scans leading to a subsequent PDAC diagnosis [8–11]. A recent Dutch pilot study, prospectively enrolled 15 patients with clinically suspicious PDAC, without histologic confirmation, 12 of which had significant uptake on PSMA PET [12]. How does this compare to FDG-PET scans which have some demonstrated utility in the assessment of PDAC? [13,14] A larger prospective study from India recruited 40 patients with suspected primary pancreatic malignancy to undergo both PSMA PET scan and FDG PET scans. They demonstrated that PSMA PET had better sensitivity and specificity than FDG PET scans, which was reported as 95% and 90% respectively [15]. Notably, a difference in specificity was recorded, with 57% for FDG PET and 90% for PSMA PET. This is possibly because FDG PET avidity increases due to inflammation whereas PSMA is theorized to be specific to neo-angiogenesis of tumor cells [15–18].

Other pancreatic malignancies may be avid of PSMA PET scans. There are three case reports of neuroendocrine tumors diagnosed incidentally in patients receiving a PSMA PET scan for prostate work up [19,20]. Additionally, one case reported PSMA avidity in an intraductal papillary mucinous neoplasm and another in a metastatic pancreatic acinar cell carcinoma [21,22].

5. Conclusion

The presented cases illustrate the potential for PSMA PET scans in identifying pancreatic lesions for critical early intervention. Given the evidence demonstrating PSMA avidity in PDAC, surgeons and radiologists should maintain a high index of suspicion for malignancy when interpreting PSMA PET scans with pancreatic uptake. Ultimately, PSMA PET scans may have a role in the diagnosis of pancreatic malignancies with early studies demonstrating impressive sensitivity and specificity.

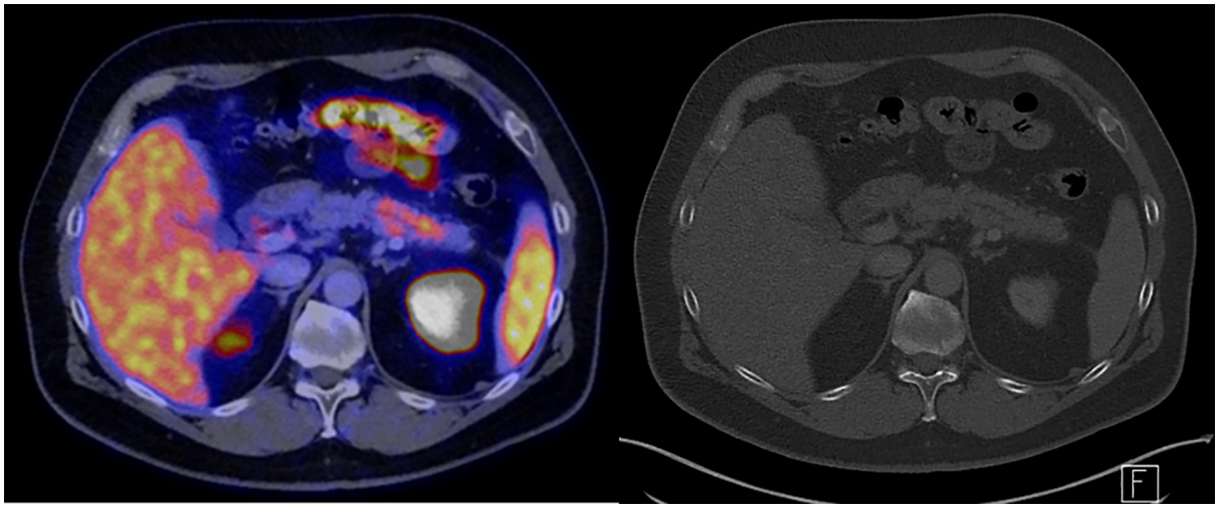

Figure 3: PSMA PET (left) and computed tomography (right) reported as increased avidity in the pancreatic tail.

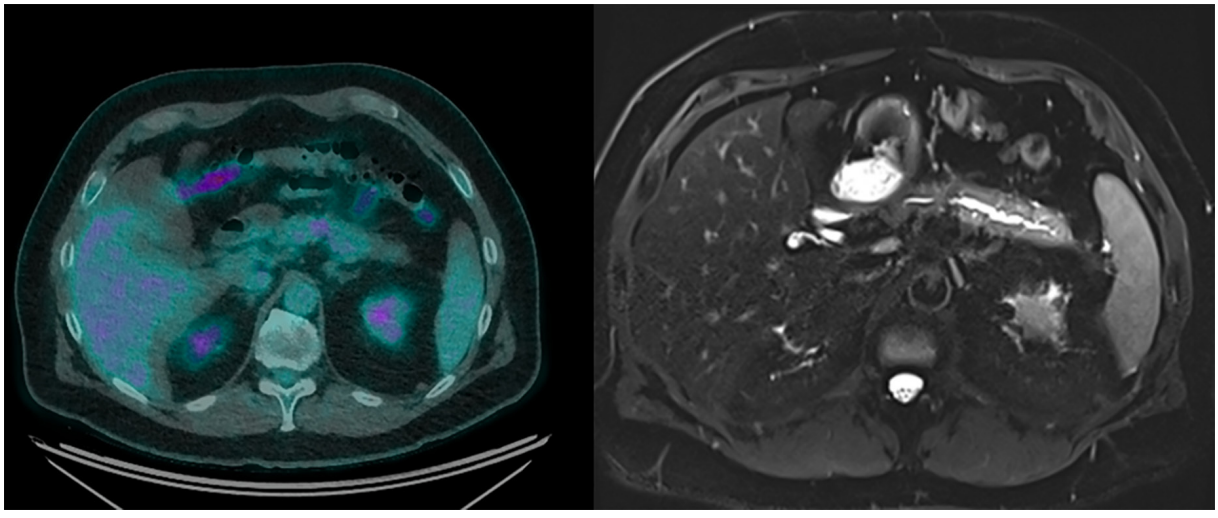

Figure 4: FDG PET (left) with avidity and MRI (right) showing 25mm mass at junction of pancreatic neck and body with distal duct dilation.

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This research has not received any funding.

Conflicts of Interest

There are no conflicts of interest to disclose.

Ethical Approval

This case report adheres to the ethical standards of the institutional research committee and the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from each patient for the publication of this report and accompanying images.

Informed Consent

All patients' informed consents were obtained prior to the beginning of the study.

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