Prostate cancer metastasis mimicking appendicitis—A rare but important differential diagnosis in PET/CT imaging

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Prostate cancer most commonly metastasizes to lymph nodes, bones, the liver, and the lungs. Prostate cancer carcinomatosis with an affinity for the appendix is not well described in current literature and is usually reported with acute appendicitis as the primary presentation. A 65-year-old male with a history of recurrent prostate cancer presented with an increase in PSA value. 18F-PSMA-1007 PET/CT showed nodular tissue growth and increased PSMA uptake in the prostate, on the appendix, in the umbilicus, and in several intra- and extra pelvic lymph nodes. The patient had no symptomatic complaints at time of referral. Imaging findings of the appendix resembling characteristic findings of acute appendicitis raised doubts about the interpretation of these as inflammatory disease or peritoneal carcinomatosis secondary to prostate cancer. This case demonstrates the importance of correct differentiation between the 2 conditions based on imaging, clinical symptomatology, and patient history to provide proper care in time.

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Introduction

Prostate cancer carcinomatosis in the abdominal cavity is rare, with an incidence of 1%-2% in patients with disseminated disease [1]. Carcinomatosis in relation to the appendix is even more uncommon and not well described in the literature. To the best of our knowledge, only 11 cases of prostate cancer with a metastatic affinity for the appendicular tissue have been reported worldwide, all located in the appendiceal lumen [2–11].

In Denmark, prostate cancer recurrence is diagnosed by biochemical measurement of prostate specific antigen (PSA) and imaged with a prostate-specific membrane anti-

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gen (PSMA) positron emission tomography–computed tomography (PET/CT) [12]. PSMA PET/CT has been shown to have superior sensitivity and specificity in imaging disease in the prostate, soft tissue and the bone compared to conventional CT and MR imaging [13]. However, PSMA expression is not solely seen in sites of prostatic cancer activity, as varying levels of expression can occur in normal tissue, inflammatory diseases, and non-prostatic benign and malignant tumors. Knowledge of physiologic distribution and potential pitfalls is essential to improve image interpretation [13,14].

This report describes the appearance of prostatic carcinomatosis near the appendix on a 18F-PSMA-1007 PET/CT scan and how it initially was interpreted as appendicitis due to the radiological characteristics. Appendiceal dilatation, wall thickening, peripancreatic fat stranding, and regional adenopathy are common CT findings both in patients with appendicitis and appendiceal tumors [15]. This case demonstrates imaging findings of carcinomatosis near the appendix and highlights the importance of multidisciplinary collaboration between clinicians, radiologists, and nuclear medicine specialists regarding image diagnostics in patients with risk of recurrent disseminated cancer.

Case report

Case presentation

A male in the early 60s with a history of recurrent prostate cancer was referred to the urology department and booked for a 18F-PSMA-1007 PET/CT scan due to an increased PSA value at 25 ng/mL.

Initial diagnosis of the patient’s prostate cancer was made in 2015 by biopsy and was staged T3N0M0 adenocarcinoma (Gleason score 9). The patient underwent radiation therapy (78.00 Gy in 39 fractions) followed by androgen deprivation therapy (ADT) with a Gonadotropin-releasing hormone (GnRH) analog (Leuprolrelin 45 mg subcutaneous injection, 1 injection every 6 months, for 3 years) with a curative intent. Castrate levels of testosterone were confirmed at 0.33 nmol/L after 1.5 years of ADT. PSA was routinely measured every 6 months. The patient’s first cancer relapse occurred in 2018 with an increase in PSA and local tumor recurrence confirmed by a 18F-PSMA-1007 PET/CT scan. The recurrence was treated with salvage cryotherapy and unaltered hormonal therapy with a GnRH analog, following national and European guidelines on treatment of biochemical recurrence after radiation therapy [12]. PSA levels persisted to drop subsequently. At sustained low PSA values, antiandrogenal treatment was discontinued in 2019. However, a year later, in 2020, a 2-fold increase in PSA levels was observed and a 18F-PSMA-1007 PET/CT scan showed local tumor progression and growth of lymph nodes near the left external iliac artery. This time, the patient was enrolled in a phase I/II, first-in-man study on immunotherapy with peptide-based vaccination which did not stop tumor progression. Antiandrogen therapy (Bicalutamide 150 mg tablet, 1 tablet daily) was applied, and the patient received prophylactic breast irradiation for prevention of gynecomastia. In 2021, PSA value increased significantly to 25 ng/mL despite continued antiandrogen therapy and the patient was referred to the urology department. Clinically, the patient had no complaints at the time of referral.

Investigations

A 18F-PSMA-1007 PET/CT scan was performed to evaluate the extent of recurrence and dissemination. Local recurrence was found in the right side of the prostate gland with nodular tissue growth on CT and increased uptake on PET. A blind-ending tubular structure originating from the cecum was identified as the appendix, which appeared enlarged with multiple nodules and associated inflammatory fat stranding when compared to a previous CT scan from September 2020 (Fig. 1A and B). In addition, nodular growth in relation to the umbilicus was identified on CT. The PET modality showed increased uptake in the right side of the prostate, the external iliac lymph nodes bilaterally, lymph nodes in the mesentery, carcinomatosis near the posterior wall of the bladder, in the umbilicus, and on the appendix (Fig. 2).

Differential diagnosis

The findings in relation to the appendix on both the CT and the PET modality could resemble characteristic imaging findings of appendiceal tumors growth as well as appendicitis [14,15]. Due to the extreme rarity of appendiceal tumors, appendicitis was considered most likely from an epidemiological point of view by the radiologists. However, the patient had no symptoms supporting the suspicion. Keeping the history of the patient’s prostate cancer in mind, the diagnostic and nuclear radiology team changed their suspicion from inflammation to peritoneal carcinomatosis surrounding the appendix. The concurrent presence of carcinomatosis near the umbilicus and the posterior wall of the bladder strengthened this suspicion. They did, however, encourage the patient to be aware of abdominal pain, fever, and nausea, as imaging could not eliminate the possibility of appendicitis.

Treatment

The patient started androgen deprivation therapy (Triptorelin 22.5 mg, intramuscular injection, 1 injection every 24 months) immediately after the findings on the 18F-PSMA-1007 PET/CT indicating tumor recurrence and dissemination. The urologists did not find indication for surgical intervention of any kind. At follow-up 3 months later, a minor decrease in PSA and lactate dehydrogenase (LDH) was found, indicating slight regression in cancer activity. The patient continued androgen deprivation therapy and was scheduled for regular follow-up with PSA and a 18F-Sodium Flouride (NaF) PET/CT after 6 months of treatment.

Outcome and follow-up

In January 2022, a 18F-NaF PET/CT was performed. CT showed increased tissue growth in the prostate, in the external iliac lymph nodes bilaterally, and of the carcinomatosis behind
Fig. 1 – Transaxial CT images demonstrating appendiceal tumor growth with increasing wall thickening, periappendicular fat stranding and soft tissue nodules, developing from (A) no appendiceal involvement in September 2020, to (B) progressive involvement in August 2021.

Fig. 2 – Transaxial $^{18}$F-PSMA-1007 PET imaging with high intensity expression seen in nodules on the appendix and in the umbilicus.

the bladder, in the umbilicus, and on the appendix resembling peritoneal carcinomatosis. $^{18}$F-NaF PET bone scintigraphy showed no signs of malignant bone involvement. In addition, PSA value had increased from 25 to 30 ng/mL within the time period. These findings confirmed the suspicion of malignancy from the previous scan from August 2021 and indicated little or no effect of ADT since then. Based on the new image findings and increased PSA value, Enzalutamide was prescribed as a supplement to ongoing ADT. The patient continues regular PSA measurements and treatment follow-up 3 months later.

Discussion

Prostate cancer most commonly metastasizes to the lymph nodes, bones, the liver, and the lungs. Only a small percentage of disseminated prostate cancer shows metastasis in the digestive system or the peritoneum, [1] and even more uncommonly carcinomatosis in relation to the appendix. In all previously reported cases of prostatic metastasis in the appendix, the patients presented with acute appendicitis and had an appendectomy performed from which metastasis was confirmed through histopathological assessment of the surgical specimen [2-11]. Acute appendicitis is found to be the most frequent initial manifestation of appendiceal tumors, seen in 30%-50% of patients [15]. In contrast to previously reported cases, however, the patient in the present report did not have acute appendicitis since carcinomatosis was surrounding the appendiceal tissue and seemingly not obstructing the lumen. Hence, surgical intervention was not performed, and
no operation or biopsy specimen exists on the carcinomatosis in this patient. Therefore, the local recurrence and metastasis is not histopathologically verified. In patients with metastatic castration-resistant prostate cancer, biopsy and histopathological examination of localized metastases are not recommended in national guidelines on follow-up [12]. Tumor dissemination and bone involvement are recommended to be evaluated with CT imaging and bone scintigraphy. In cases of image-detected appendiceal tumor without concurrent symptomatic appendicitis demanding surgical treatment, biopsy is not routinely performed if findings substantiating the suspicion of tumor origin are considerable. Thus, when lacking definite diagnosis through histopathological assessment, reliable diagnostics must rely on clinical symptomatology, patient history and image findings, as well as evaluation of treatment response after targeted treatment [12].

Characteristic CT image findings of appendiceal tumors include focal or diffuse soft tissue mass infiltration of the appendix, enlarged appendiceal lumen, perappendiceal fat stranding, and diffuse wall thickening. These image findings could equally come as a result of the extension of the metastasis or from a superimposed appendicitis [15]. Preoperative CT scans from previously reported cases of acute appendicitis secondary to prostate cancer metastasis predominantly show dilated appendix, perappendiceal stranding and/or wall thickening [2,3,7,8]. Christou et al. present a patient with an identical initial staging and Gleason score to the patient in the present report [2]. Their patient had an elongated and dilated appendix on CT imaging as well but differed in symptomology by presenting with lower quadrant abdominal pain [2]. Ozuyazici et al. present a similar patient with abdominal pain, nausea, and vomiting, whose CT scan showed wall thickening and dilation of the appendix [7]. Since these patients had symptomatic acute appendicitis and focal metastasis concurrently, it is difficult to differ between the radiological findings being caused by one or another. The patient in the present report had similar image findings to the previous cases but no clinical symptoms of appendicitis (e.g., right lower quadrant pain, abdominal rigidity, periumbilical pain, fever etc. [16]) at time of CT-imaging or in the follow-up period. The absence of such symptoms may be explained by the carcinomatosis surrounding the appendix and seemingly not obstructing the lumen. As this is a case of peritoneal carcinomatosis merely in relation to the appendix, the findings should also be seen in the light of previous cases of peritoneal carcinomatosis from prostate cancer in general [17,18]. A common condition in such patients is ascites [17]. Achar et al. found that in 14 cases of peritoneal carcinomatosis following prostate cancer treated without surgery, all but one had malignant ascites and a Gleason score ≥ 8 [18]. The patient, in this case, did not present with ascites but did fit into the interval of Gleason scores, other metastatic sites, and time between initial diagnosis and peritoneal involvement described in some of the 14 cases [18]. This case demonstrates that radiological findings known to be associated with appendicitis can be seen in patients with peritoneal carcinomatosis near the appendix without a concurrent symptomatic appendicitis or symptoms of peritoneal involvement. The similarities of image findings emphasize the importance of including patient history and symptoms in clinical decision-making.

In the present report, there are several circumstances that strengthen the suspicion that this was indeed carcinomatosis from the patient’s prostate cancer. First, the patient had local prostate cancer recurrence and growth concurrently with the tissue growth in relation to the appendix. The previous CT scan performed one year earlier showed normal appearance of the appendix (Fig. 1A). Second, the patient had a history of disseminated cancer and present diffuse adenopathy as well as carcinomatosis in the umbilicus, indicating ongoing extrapelvic dissemination. Third, the PSMA PET modality showed high intensity PSMA uptake around the appendix. The applied PSMA ligand was a 18F-PSMA-1007, which equally to the other commonly applied 68Ga ligand has demonstrated the highest diagnostic value in imaging prostate cancer compared to other PET tracers [14]. The PSMA protein is highly expressed on the cell surface in prostate cancer cells. High uptake correlates with high tumor grade. However, expression is also seen in normal tissue, inflammatory diseases, and non-prostatic benign and malignant tumors [13]. Most non-prostate cancer conditions show low to moderate intensity or diffuse PSMA expression compared to prostate cancer. But along with additional studies being published on the use of PSMA, several examples of high-intensity uptake in non-prostate cancer tumors are being reported [13,14]. Thus, one condition is difficult to differentiate from the other based solely on the PSMA expression. The high-intensity PSMA expression in this case created suspicion of malignancy but could not be used to rule out inflammatory disease. CT imaging combined with the full patient history and symptomatology stands as the most important information on which the clinicians can base their decision on further course of treatment.

In patients with a history of disseminated prostate cancer and present imaging showing appendiceal wall thickening, nodular enhancements and perappendiceal fat stranding, it is important to consider the possibility of prostate cancer having spread to the appendix or surrounding peritoneal tissue regardless of symptomatology. Although the patient in the present report did not have appendicitis, previous published reports and studies amplify acute appendicitis as a frequent superimposed condition to appendiceal tumors obstructing the appendiceal lumen. Clinicians and radiologists should be aware of the overlapping image findings of appendicitis and peritoneal carcinomatosis near the appendix to ensure diagnostic accuracy and provide proper care.

**Patient’s perspective**

“After the scan (red. In August 2021), the hospital contacted me over the phone and made me aware of their interpretation of the scan and recommended me to be aware of symptoms such as pain, fever, and so on.

It was very comforting to me that the response from the hospital was quick and that I was directly involved.

All things considered, it is reassuring for me as a patient to get all the information on the course of my disease – also the bad news. Lack of information would leave a void that could be filled with speculation, concern, and a risk of worsening of the situation.”
Patient consent

Written informed consent for publication of this case (including images) was obtained from the patient and is available upon request. Prior to submission, the patient approved the final manuscript and provided a patient perspective, which has been included in the manuscript.

REFERENCES


