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A challenging diagnosis of prostate cancer seeding in the perineal needle-tract after transperineal biopsy: is PET-CT the imaging of choice?

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ABSTRACT

Perineal seeding is an extremely rare complication after prostate biopsy. We found a perineal localization of prostatic adenocarcinoma 5 years after the transperineal biopsy in a patient with metastatic castration resistant prostate cancer. The tumor was identified by a ^{18}F-Fluorocholin positron emission tomography-computed tomography (^{18}F-FCH PET-CT) performed after a sudden rise of PSA levels during androgen deprivation therapy and after a negative CT scan. This case report underscores the challenge one may encounter in detecting perineal prostate cancer metastasis after a biopsy when using traditional imaging with CT scan alone or MRI, and the added diagnostic value of PET-CT imaging.

1. Introduction

Ultrasound (US) guided prostate biopsy is considered the gold standard technique to diagnose prostate cancer and can be performed by either a transrectal or transperineal (TP) approach.[1] It has been estimated that at least two million procedures are performed every year in Europe and the United States of America alone.[2] The procedure is usually well tolerated, with a low risk of major complications. Post-procedural bleeding, voiding dysfunctions, and pain are the most common reported complications, which are typically not clinically significant and only seldomly troublesome.[3] Cancer seeding along the biopsy needle tract is a very rare but well documented hazard after any kind of percutaneous penetration of neoplasm.[4] In the specific case of prostate cancer, the reported incidence of needle track seeding seems extremely low, without any particular difference between transrectal or transperineal approach. Indeed, an extensive literature review has identified 42 reports describing needle-tract seeding of prostate cancer between 1953 and 2010, of these nine were reported after a transrectal biopsy while the remaining ones after a transperineal one.[5] This data can be primarily attributed to the fact that most of the cases described were published in the mid to late-20th century, when the transperineal approach was already widespread and predominantly used.[6]

In keeping with the rarity of needle-tract seeding of prostate cancer, there are no guidelines about its prevention, best detection method or management.

Hereinafter, we report a case of prostate cancer perineal seeding diagnosed using a ^{18}F-Fluorocholin positron emission tomography-computed tomography (^{18}F-FCH PET-CT) 5 years after a transperineal prostate biopsy and after a negative traditional imaging.

2. Case presentation

In 2013, a 75 years old patient, with a history of hypertension, heart failure, diabetes, atrial fibrillation, prostatic hypertrophy and with a Charlson comorbidity index of 7, underwent a TP prostate biopsy for raised PSA levels (11,2 ng/ml) and positive digital rectal examination (cT3). The histopathology confirmed the presence of bilateral adenocarcinoma of the prostate, Grade Group IV, Gleason score 8 (4 + 4). During the subsequent radiological staging exams, MRI revealed a locally advanced prostate cancer with a suspected invasion of the anterior rectal wall. Bone scan was negative, while CT showed a one-sided obturator lymphadenopathy deemed suspicious for harboring a secondary lesion (cN1M0). The patient was initially addressed to androgen deprivation therapy (ADT) with leuprorelin, while radiotherapy was not offered due to patient's several comorbidities.

PSA initially dropped to a nadir of 0,5 ng/ml. During the following 5

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years, PSA levels were regularly monitored and proven to be stable and follow-up with CT-scans and bone scans never revealed a disease progression.

Due to a sudden rising PSA to 6,2 ng/ml with serum testosterone at castration level, a ^{18}F-FCH PET-CT was performed, revealing secondary lesion to pelvic lymph nodes, L3 and a pathological hyperfixation of the tracer on a pseudo-nodular area in the cutaneous and subcutaneous tissues of the right paramedian perineum (Fig. 1).

At subsequent physical examination, the tumor appeared as a 3 cm hard, fixed, well defined and painless subcutaneous nodule located in the right perianal area, at 10–11 o'clock, 1 cm above the anal sphincter.

Upon interviewing the patient about any symptom or complain, he referred that he had been able to feel a very small perianal lump for almost 2 years and that it grew rapidly over the last 6 months while remaining painless.

Due to its location and radiologic characteristics, after multidisciplinary assessment the nodule was suspected to be the result of needle-tract seeding from the prostate biopsy performed in 2013, although the possibility of a secondary synchronous malignancy could not be definitively excluded. Consequently, Enzalutamide was added to ADT and surgical excision of the nodule was recommended to provide histological characterisation. After local anesthesia, a longitudinal incision on the perineal raphe was performed and extended to the right of the perineum. The nodule was exposed, separated along a surgical plane from the anal sphincter fibers which was firmly connected to and excised "en bloc" (Fig. 2). The intraoperative pathology consultation indicated the presence of adenocarcinoma; the complete examination including immunohistochemical methods with specific antigen reactions confirmed the nodule represented a metastasis from prostatic carcinoma, Gleason score 7 (4 + 3). No complications occurred as a result of the procedure. Subsequent follow-up visits with clinical examination and imaging were scheduled.

After few months, Enzalutamide was forcedly stopped due to a novel diagnosis of QT interval prolongation as a probable result of drug interaction between anti-coagulants and hormonal therapy. After this event the patient started a second line treatment for mCRPC with abiraterone acetate for 2.5 years but spread of nodal involvement and widespread bony metastases were found at follow-up imaging. Thus the patient started chemotherapy with Docetaxel until a general clinical worsening occurred. While recovering in a hospice care service, the patient ultimately died after a major adverse cardiovascular event.

3. Discussion

We described the clinical history of a rare case of perineal prostate cancer metastasis after transperineal prostate biopsy and negative traditional imaging, discussing the role of PET-CT in augmenting diagnostic accuracy.

Needle-tract seeding metastases of prostate cancer seems to be extremely rare. The true incidence of tumor seeding is difficult to estimate due to the poor quality of data available on this topic, as only case reports and retrospective reviews are available.[5] In the described cases, the local recurrence has been often identified through physical examination; and the imaging technique, when performed, was mostly represented by traditional imaging (CT or MRI).[5,7,8] Interestingly, in a significant number of these case reports, seeding occurred after TP biopsy. This predominance can likely be explained by the fact that most reports were published between the 1950s and the 1980s, when the TP approach was the most commonly used. Recently, the TRexit movement has been driving a resurgence in the adoption of the TP approach due to its favorable complication profile compared to the transrectal approach.[9] Future and contemporary evidence on TP biopsy complications may help investigate its role in needle tract seeding of prostate cancer.

The difficulties encountered in diagnosing this type of prostatic cancer recurrence can be attributed primarily to its extreme rarity. Additionally, men affected by prostate cancer are usually in their 70s, and the time needed for this clinical condition to present may be highly variable and potentially very long, ranging from 1 months up to 14 years.[5] This variability means that men may die from other causes first or that this diagnosis may be overshadowed by more serious comorbidities. In view of these considerations we might assume that the real incidence of perineal seeding is higher than currently reported.

Large tumor volume, high Gleason score and presence of castration-resistant cells have all been indicated to represent independent risk factors for needle-tract seeding.[7] However, the lack of an adequate volume of data hinders the design of guidelines to prevent, detect and manage this kind of recurrence. Likewise, the prognostic value of perineal seeding in prostate cancer is still unclear.

No straightforward diagnostic path has been established for this type of recurrence. Traditional imaging with CT scan is commonly used in case of prostate cancer recurrence but insufficient attention is often given to scanning the perineum, as no relevant prostate cancer-related findings are typically expected in this area. On the other hand, MRI might help in better defining perineal soft tissues but it is rarely requested in case of PSA recurrence; moreover, it needs expertise and does not provide clear information about the possible origin of the mass.

This is likely why a PET-CT scan (choline or PSMA as the tracer) might represent a valid diagnostic technique, as it makes it easier to identify high metabolic turnover tissues of prostatic origin.

The use of choline PET/CT in this scenario was already described in three cases. In 2014 Garcia-Bennett et al. described a needle-tract recurrence detected by ^{18}F-FCH PET-CT five years after a transrectal prostate biopsy.[10] However, in this case the images obtained from the

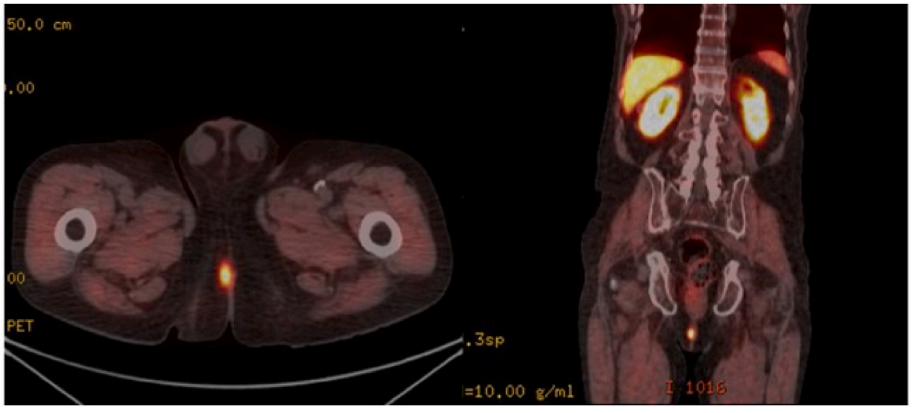

Fig. 1. Fused 18^{F}-FCH PET-CT cross sectional imaging of in axial and coronal plane, showing hyper fixation of the tracer on a pseudo-nodular area in the cutaneous and subcutaneous tissues of the right paramedian perineum.

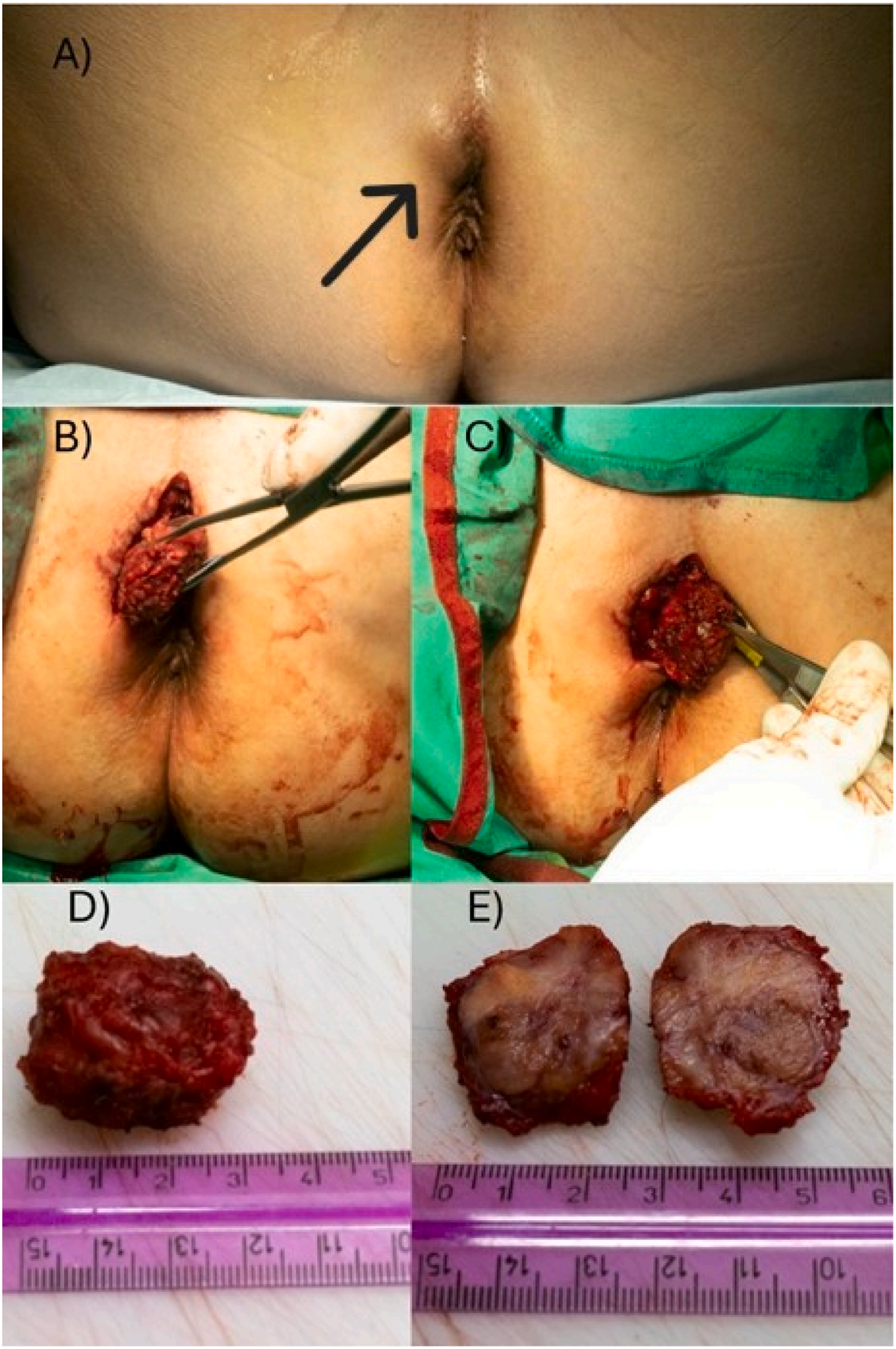

Fig. 2. Surgical steps of nodule excision and macroscopic findings: A) Identification of a right perineal lump; B,C) perineal median incision and nodule excision; D-E) gross anatomy of the nodule.

^{18}F-FCH PET-CT, due to the lack of intravenous contrast, were also superimposed with the images obtained from a pelvic MRI in order to obtain a more accurate depiction of the perianal mass. Eppinga et al. instead reported a case of perineal recurrence of prostate cancer after transperineal brachytherapy.[11] Once again, the recurrence occurred after about five years from diagnosis of prostate cancer. Diagnosis was made using ^{11}C-choline PET/CT followed by a MRI of the pelvis that showed a perineal mass of 14 mm dorsally to the penile bulb; a subsequent biopsy confirmed it was a prostate cancer metastasis. In 2021, Sidibe et al. described a case of prostate cancer perineal recurrence almost eight years after brachytherapy, initially diagnosed using pelvic MRI and ^{18}F-FCH PET-CT.[12]

Additionally, with the diffusion of novel tracers, Zhuo et al. reported the first case of perineal prostate cancer seeding using a ^{68}Ga-PSMA PET-CT three years after the biopsy.[13] As shown by the proPSMA trial, PSMA PET-CT currently provides excellent diagnostic accuracy,[14] and the OSPREY trial demonstrated a spatial resolution limit of 2–4 mm for lymph node metastasis.[15] This encouraging data may promise an increase in the rates of diagnosis of metastatic PCa. Future evidence arising from the widespread adoption of PSMA PET-CT will determine whether this will also translate to a possible increase in the diagnosis of perineal needle tract metastases.

In our case the prostate cancer needle-tract recurrence occurred five years after transperineal biopsy and was revealed by staging ^{18}F-FCH PET-CT, while traditional imaging did not detect.

Indeed, in our case, at a retroactive reviews of CT scan images performed two years prior to the ^{18}F-FCH PET-CT, a small nodule located on the upper quarter of the right perineum could be identified, confirming the clinical findings referred by the patient as a small lump in the perianal area, even though it had not been reported by radiologist at the time (Fig. 3). An open question then arises from the case we are reporting: should the perineal needle tract be routinely investigated and reported by radiologists during follow-up imaging after a biopsy diagnosing high risk prostate cancer?

The paucity of available data prevents the establishment of guidelines on prevention of this type of cancer seeding. Nonetheless, some preventative technical modification to TP biopsy technique could be suggested. Firstly, the use of a perineal access cannula to support the biopsy, such as probe-tethered access cannulas,[16] would significantly decrease the contact of the biopsy needle with the perineal layers, probably reducing the chances of seeding. Additionally, washing the biopsy needle in saline solution after each biopsy core may help flush away any potential cancer cells present on the needle.

4. Conclusion

The real incidence of prostate tumor seeding is hard to quantify, and consequently its real impact in terms of prognosis and clinical significance are not clear. Advances in imaging, like PET-CT, during follow-up might support early detection of this rare occurrence.

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 scientific publications.

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CRediT authorship contribution statement

Claudia Fede Spicchiale: Writing – original draft, Data curation. **Federico De Leonardis:** Writing – review & editing, Data curation.

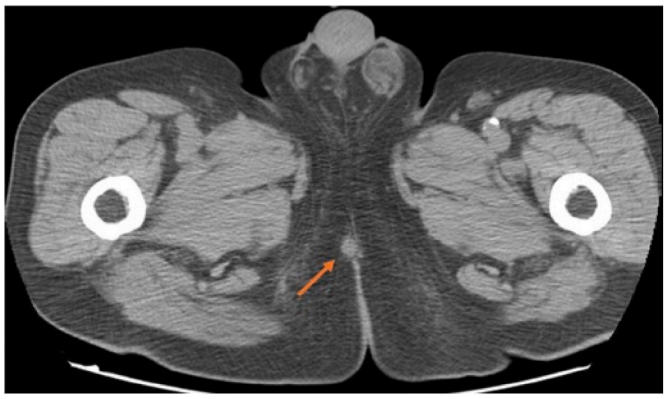

Fig. 3. Axial CT pelvis performed two years prior to ^{18}F-FCH PET-CT. A small perineal nodule is visible (arrow).

Luca Orecchia: Writing – original draft, Supervision. **Stefano Germani:** Data curation. **Anastasios D. Asimakopoulos:** Writing – review & editing. **Roberto Miano:** Writing – review & editing, Supervision, Project administration, Conceptualization.

Declaration of competing interest

There are no conflicts of interest.

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