

⁶⁸Gallium-prostate-specific membrane antigen ligand positron-emission tomography or computed tomography in biochemical failure after radical prostatectomy: A case report

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Biochemical failure after radical treatment for prostate cancer occurs in up to 30% – 50% of cases. Localisation of clinical disease is challenging because clinical symptoms often manifest long after the initial rise in prostate-specific antigen. The detection rates of imaging modalities such as contrasted computed tomography (CT), bone scan, magnetic resonance imaging and choline positron-emission tomography (PET) or CT, are limited. Prostate-specific membrane antigen (PSMA) ligand PET or CT is a novel imaging modality under investigation for various diagnostic and therapeutic indications in the management of prostate cancer. We present a case report illustrating how ⁶⁸Gallium-PSMA ligand PET or CT was used to guide management in a patient presenting with biochemical failure after radical prostatectomy.

Introduction

Biochemical failure in prostate cancer is defined as a rise in prostate-specific antigen (PSA) by ≥ 2 ng/mL above nadir after external beam radiotherapy (EBRT) or two consecutive serum levels ≥ 0.2 ng/mL after radical prostatectomy (RP).^{1,2} This is reported to occur in up to 30% – 50% of cases at 10 years.³

Case summary

A 70-year-old man was referred to our uro-oncology multidisciplinary team (MDT) with a 2-year history of worsening lower urinary tract symptoms, hesitancy and interrupted stream. He had well-controlled hypertension and was a non-smoker.

The patient's PSA was 18.4 ng/mL, and the digital rectal examination (DRE) revealed a cT2b right lobe nodule. The transrectal ultrasound (TRUS)-guided biopsy confirmed an adenocarcinoma Gleason score (GS) 3 + 4 (Table 1). His Eastern Cooperative Oncology Group (ECOG) performance status score was 1.⁴

The full blood count, renal function tests and chest radiograph were normal. A bone scan was not done. This is reserved for high-risk disease or symptomatic patients because of resource constraints. He was classified as having high-tier intermediate risk prostate cancer with a life expectancy estimated to be ≥ 10 years. His nomogram probability of seminal vesicle involvement was 23% as estimated by the updated Partin tables.⁵ The patient was offered an RP or an EBRT. He opted for RP with bilateral pelvic lymph node dissection (BPLND). Brief courses of androgen deprivation therapy (ADT) are only offered in high-risk or metastatic patients.

The surgical pathology findings were bilateral adenocarcinoma, acinar NOS, GS 4 + 5, positive lympho-vascular and perineural involvement (PNI) with diffusely positive resection margins. None of the 13 lymph nodes were positive for metastatic adenocarcinoma, and there was no demonstrable extracapsular extension, pT2cN0. Unfortunately, no seminal vesicles were submitted for evaluation because of anatomical distortion at the time of surgery.

He presented with back pain and a persistently detectable serum PSA of 6.21 ng/mL 6 weeks after surgery. The bone scan showed no metastases. His symptoms had resolved 6 weeks later but PSA was still detectable, 6.71 ng/mL.

Because of the high PSA, the MDT was concerned that he had distant rather than local failure. To assess the site of relapse and thus the benefit of salvage radiotherapy, a ⁶⁸Gallium (Ga)-prostate-specific

membrane antigen (PSMA) positron-emission tomography or computed tomography (PET or CT) was performed.

This confirmed persistent localised disease in the right seminal vesicle with no distant metastases (Figure 1). He was offered salvage EBRT plus ADT.

Ethical considerations

The Human Research Ethics Committee under University of Cape Town Faculty of Health Sciences. HREC Ref: 229/2017.

Discussion

Prostate-specific membrane antigen is a transmembrane glycoprotein thought to be associated with angiogenesis in prostate cancer. The level of expression correlates with disease aggression.^{6,7,8,9,10,11}

TABLE 1: Summary of transrectal ultrasound prostate biopsy.

| Specimen | Cores | Percentage of tumour | Gleason score | PNI |
|----------------|-------|----------------------|---------------|---------|
| A (left lobe) | 4 | No malignancy | - | - |
| B (right lobe) | 1 | 100 | 3 + 4 | Absent |
| | 2 | 100 | 3 + 4 | Absent |
| | 3 | 50 | 3 + 4 | Present |
| | 4-6 | Nil | | Nil |

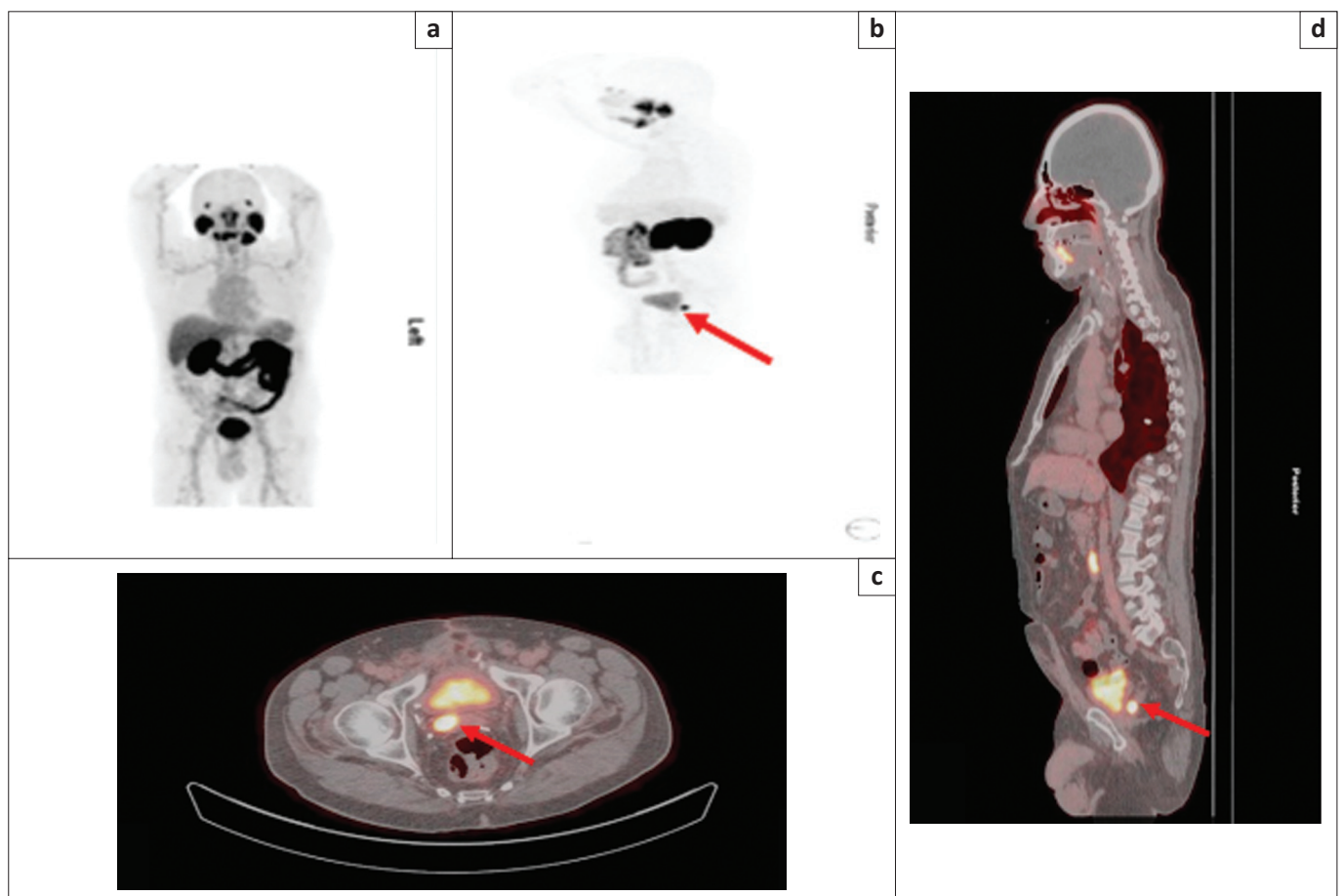
PNI, perineural involvement.

Normal tissues such as lacrimal and salivary glands, proximal small bowel and kidneys also express PSMA as demonstrated here. Other benign and malignant conditions may also show uptake.

Factors that predict treatment failure include high Gleason score, positive surgical margins, seminal vesicle invasion and extraprostatic extension as seen in this case.¹

An important clinical decision in patients with biochemical failure is distinguishing patients with local failure (who would thus benefit from salvage or adjuvant radiotherapy) versus those with distant spread. Another issue is the timing of salvage radiotherapy. The American Society for Radiation Oncology (ASTRO) guidelines recommend radiotherapy at the earliest sign of recurrence and warn that progression free survival (PFS) drops by 18% for 1 ng/mL increase in pre-RT PSA.¹

Current guidelines recommend investigating suspected treatment failure with a bone scan and whole body contrasted CT or multiparametric magnetic resonance imaging (MRI) or choline PET or CT to rule out both local and distant disease.^{12,13} However, morphologic or anatomic imaging after surgery is a challenge as it is often difficult to discriminate between post-surgical changes and new pathology. In our case, the reported intra-op findings of distorted anatomy may have further complicated local diagnostic accuracy.



⁶⁸Ga-PSMA, ⁶⁸Gallium-prostate-specific membrane antigen; PET, positron-emission tomography; CT, computed tomography.

FIGURE 1: ⁶⁸Ga-PSMA PET and CT showing (a), MIP image with normal bio-distribution of tracer in lacrimal and salivary glands, proximal small bowel, kidneys, bladder; (b), Sagittal MIP with focal uptake in the right seminal vesicle; (c), Fused sagittal PET or CT image with similar uptake; (d), MIP, maximum intensity projection.

The sensitivity of choline PET or CT is directly related to PSA kinetics, and the European Association of Urology (EAU) recommends it as a staging option in patients with a PSA > 1 ng/mL in the setting of biochemical failure after RP. We chose to use PSMA PET or CT as its sensitivity and specificity has been shown to superior to choline PET or CT.¹⁴

When functional imaging with choline PET or CT and PSMA ligand PET or CT was compared following biochemical recurrence, the detection rates were considerably higher for PSMA PET or CT than choline PET or CT even at PSA values of < 0.5 ng/mL (50% vs. 12.5%) and especially at values > 2 ng/mL (86% vs. 57%).¹¹ Overall, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) are higher for ⁶⁸Ga-PSMA PET.^{7,8}

The findings in our case were in keeping with persistent localised disease within the unresected seminal vesicles. Because the initial surgery was limited by anatomic distortion, biopsy of the suspicious area or re-resection was not possible.

A decision was made by the MDT to offer our patient salvage radiotherapy with ADT.

Conclusion

We have here reported a case highlighting not only the benefit of ⁶⁸Ga-PSMA PET or CT but also the invaluable role of a multidisciplinary approach in the management of prostate cancer. As more data emerge, PSMA PET or CT is gaining application in primary staging of disease, investigation of recurrence and targeted radioimmunotherapy (RIT). Full integration into clinical practice in a resource constrained setting will be limited by cost in favour of standard MRI, CT and bone scans.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

I.A.C. was responsible for research on information written in discussion regarding PSMA PET/CT's as well as led the whole write-up process, including determining structure. D.B.A. identified case, added information in discussion section and supervised all case details.

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