Solitary castrate-resistant prostate cancer metastasis to adrenal gland with concordant intense avidity on PSMA and FDG PET

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\textbf{A B S T R A C T}

Isolated prostate cancer metastasis to the adrenal gland is rare. We report a case of concordant high uptake in a solitary adrenal metastasis on both prostate-specific membrane antigen and fluorodeoxyglucose positron-emission tomography in a patient with castrate-resistant prostate cancer. Good initial biochemical response was achieved with laparoscopic adrenalectomy. The patient developed lymph node recurrence 12 months later, although remains asymptomatic on hormonal treatment 22 months post-operatively, in keeping with prior results for metastasis-directed therapy which can delay time to additional treatment. Application of dual tracer PET can be valuable for prostate cancer staging and guidance of metastasis-directed treatment.

\textbf{Introduction}

Only 0.3\% of solitary PCa metastases involve kidney or adrenal gland.\textsuperscript{1} To our knowledge, this is the first reported case showing concordant high uptake in a solitary adrenal metastasis on both PSMA and FDG PET in a patient with CRPC. Application of dual tracer PET can be valuable for PCa staging and guidance of MDT.

\textbf{Case presentation}

A 79-year-old man had received EBRT for Gleason 4 + 5 = 9 prostate cancer seven years prior. Two years ago, he was re-staged with PSMA PET/CT due to biochemical recurrence, with serum PSA of 5.2 ng/mL, which showed a mildly PSMA-avid 6mm pulmonary nodule in the left lower lobe and intense uptake in a 22mm right adrenal nodule with SUV\textsubscript{max} of 16.2. He was started on ADT with goserelin.

Serum PSA began to rise from 2.1 to 3.9 to 5.5 ng/mL over eight months despite castration (serum testosterone <0.3 nmol/L), confirming a diagnosis of castrate-resistance. Subsequent PSMA PET/CT showed intense uptake in a solitary right adrenal lesion, now measuring 33mm, with SUV\textsubscript{max} of 15.7. The previously seen lung nodule was no longer visible. The PSA rose further to 18 ng/mL with a PSA-DT of 2.4 months. Functional adrenal testing was normal. MRI of the adrenal glands showed a 43 × 33 × 35mm heterogeneous right adrenal mass on T2-weighted imaging, with markedly reduced apparent diffusion coefficient values as low as 295, considered consistent with malignancy of either metastatic or primary adrenal origin.

Given his good performance status, he was considered suitable for MDT so was referred for adrenalectomy. FDG PET/CT was performed to rule out sites of metastatic disease of adrenal (if primary adrenal malignancy) or colorectal (given prior history of colorectal cancer) origin in the context of atypical PCa metastasis. This showed intense FDG uptake in the right adrenal gland (SUV\textsubscript{max} 15.06) and no other suspicious lesions. Imaging comparison is shown in Fig. 1.

He underwent uneventful laparoscopic right adrenalectomy and was discharged two days post-operatively. Histology of the adrenal gland showed metastatic prostate carcinoma. A good postoperative PSA response was observed (0.09 ng/mL). However, his PSA continued to slowly rise over 12 months to 1.6 ng/mL and PSMA PET/CT showed moderate to intense uptake in one para-aortic and one inferior mediastinal lymph node. At 17 months, the PSA reached 5.6 ng/mL with PSA-DT of 2.8 months and bicalutamide was added for maximal androgen blockade. He remains asymptomatic at 22 months post-adrenalectomy with a PSA of 7.8 ng/mL on ADT with a PSA-DT of 18.7 months.

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https://doi.org/10.1016/j.eucr.2021.101696
Received 1 April 2021; Received in revised form 20 April 2021; Accepted 24 April 2021
Available online 27 April 2021
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Discussion

Prostate cancer metastasis is most commonly to regional pelvic lymph nodes or bone, although up to 15–20% of men can have atypical locations of metastatic disease. In a United States population-based study of metastatic PCa, 1% of patients had metastasis to kidney or adrenal gland, and only 0.3% of solitary metastases were to kidney or adrenal gland. MDT is an emerging approach to metastatic PCa, supported by clinical trials such as the STOMP trial, which reported an improvement in ADT-free survival with radiotherapy-based MDT compared to surveillance (34% versus 8%; p = 0.06) at 5 years. Thus, there are very few reports of adrenalectomy as MDT.

Dual tracer imaging may assist in appropriate selection for MDT, as has been utilised for assessment of patient eligibility for radioligand therapy (RLT) in advanced CRPC. While traditionally used to exclude other sites or sources of metastatic disease, FDGPET has improved disease characterisation in hormone-naïve PC and CRPC. For CRPC, the addition of FDG PET after PSMA PET increased the detection of nodal or distant metastases from 65% to 73% in men with high risk CRPC and no metastasis on conventional imaging with CT and bone scan. Furthermore, patterns of PSMA and FDG PET uptake may inform eligibility for RLT, so FDG PET uptake may further assist with patient selection for MDT. PSMA-negative FDG-positive disease is more likely to occur in CRPC than hormone-naïve PC with a subsequently worse prognosis, and vice versa. Given the likelihood of PCa due to PSMA uptake, the concordant FDG uptake informed disease characterisation and supported a MDT approach. This is the first CASE showing concordant high PSMA and FDG uptake in a solitary adrenal metastasis, with subsequent treatment showing a good initial PSA response, however with rapid progression.

While dual tracer concordance raised our confidence in an oligometastatic disease state, as would a negative FDG PET, the high FDG uptake (SUVmax 15.06) may have predicted the recently observed PSA progression. High FDG uptake has been reported as a negative prognostic indicator in patients who underwent 177-Lu PSMA RLT, with SUVmax >15 correlating with a worse 12-month progression free survival and poor response to RLT. As such, consideration should be made to use of FDG in addition to PSMA PET for patients with PSMA-negative biochemical recurrence or castration-resistant PCa. The presence of high FDG uptake in this CASE may be hypothesised as a negative prognostic indicator, although this has not been specifically examined in outcomes following surgical MDT.

Conclusion

Isolated PCa metastasis to the adrenal gland is rare. This case had concordant intense uptake on PSMA and FDG PET in CRPC. Good initial biochemical response was achieved with adrenalectomy. The patient subsequently developed nodal recurrence 12 months later, although remains asymptomatic on hormonal treatment 22 months post-operatively with a PSA of 7.8 ng/mL. This pattern is in keeping with reported MDT results, which can decrease time to additional therapies. PSMA PET can be used for optimal patient selection, with the addition of FDG in CRPC or PSMA-negative biochemical recurrence.

Conflicts of interest

None.

Consent

Informed consent for publication of this case was obtained from the patient.

Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. MJR is supported by a Clinician Research Fellowship from the Metro North Office of Research, Queensland Health, and a Doctor in Training Research Scholarship from Avant Mutual Group Pty Ltd.

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**Abbreviations**

- prostate cancer: (PCa)
- prostate-specific membrane antigen: (PSMA)
- fluorodeoxyglucose: (FDG)
- positron emission tomography: (PET)
- castrate-resistant PCa: (CRPC)
- metastasis-directed treatment: (MDT)
- external beam radiotherapy: (EBRT)
- androgen-deprivation therapy: (ADT)
- PSA doubling time: (PSA-DT)
- maximum standardised uptake value: (SUV_{max})