

Oncology

Metastatic-directed therapy using PSMA-PET/CT at PSA relapse

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ABSTRACT

The side effects of androgen deprivation therapy (ADT) as general treatment against prostate cancer are known to impair quality of life. However, the optimal onset of ADT at PSA relapse is unknown, especially in patients with normal testosterone. In our case a limited PSMA avid lymph node was detected on PET/CT. Our case highlights the importance of metastasis-directed therapy balancing general versus tailored treatment in the decision making in the era of advanced molecular imaging. By using PSMA-PET/CT and radiation we were able to pinpoint the metastasis prolonging the ADT-free survival, thus sparing the patient the side-effects of continuous ADT.

Introduction

Despite more than seven decades of knowledge about the effect of testosterone suppression on prostate cancer there is still a treatment dilemma of when to expose seemingly healthy men to the downsides of castration in the event of rising PSA rise after curative intent therapy. Our case highlights the challenges in this scenario and stresses never to forget the individual needs when performing medicine. The role of prostate-specific membrane antigen (PSMA)-PET/CT in metastatic prostate cancer lymph-node detection has been established, although the role of metastasis-directed therapies (MDT) is currently investigated.¹ Modern technology can be useful to adjust to the needs of the patient. In our case the novel introduction of PSMA-PET/CT at our department in staging patients with PSA relapse to tailor a locally applied radiation field, thereby trying to postpone continuously systemic treatment. Moreover, “nihil nocere” counseling survived as one of the most important guidelines in medicine and MDT as chosen in our case could be a valuable strategy applying modern imaging thereby avoiding the side effects of continuous androgen deprivation therapy (ADT).

Case history

Initial staging and imaging at biochemical failure

At the age of 60 years the patient was diagnosed with locally

advanced prostate cancer cT3aN1M0, Gleason score 3 + 4 and initial PSA 82 ng/mL. He received curative intent radiotherapy (RT) covering the pelvic lymph nodes to 46 Gy and a boost volume to 74 Gy applied to the prostate. He started with ADT 6 months prior to conformal radiation. He had two years planned ADT scheduled with LHRH-analogue but changed to antiandrogen bicalutamide shortly at the end of radiation. After 12 months he stopped ADT due to severe side effects including physical issues and sexual performance.

Seven years later a PSA relapse using the Phoenix definition was confirmed.

Magnetic resonance imaging protocol was performed with morphological sequences, T2W for skeletal metastasis detection, 3D T2W and diffusion weighing for local tumor and/or lymph node assessment according with the internationally recommended technical guidelines. No imaging-based tumor correlation was found, and the patient was monitored regularly with serum PSA values. He consented to start with intermittently applied bicalutamide 150 mg daily at a PSA rise to 21 ng/mL and the PSA declined to a nadir of 0.5 ng/mL over the following years saving normal testosterone levels and sexual performance.

In May 2018 the PSA value increased to 5.8 ng/mL and a PSMA-PET/CT was added to investigate the pattern of failure.² The radiotracer showed high avidity in a lymph node located anterior to the right common iliac and inferior caval vein divergence, closely to the upper border of the former pelvic radiation field (Fig. 1).

The patient received stereotactic radiation including the para-aortic lymph node chain to 46 Gy and a simultaneous boost to the visible lesion

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to 50 Gy planned with 6 months ADT.

The PSA dropped from 5.8 ng/mL to 0.7 ng/mL at 6 months follow-up. He reported no relevant toxicity with special emphasis on radiation induced morbidity. However, he discontinued bicalutamide three months after end of radiation due to fatigue and physical deterioration.

At relapse in May 2018 testosterone level was 21.3 nmol/L and PSA 5.8 ng/mL and at one year follow-up testosterone level was 26 nmol/L with a corresponding PSA 1.4 ng/mL achieved without ongoing systemic therapy.

The follow-up PSMA PET/CT in April 19 showed no detectable lymph node metastasis (Fig. 2).

Discussion

Depending on the stage of disease, patients with relapsed locally advanced prostate cancer (PCa) have a variable natural course but most men will develop metastatic disease. Since Huggins and Hodges demonstrated the androgen-dependent nature of PCa in the 1940s, ADT aiming to minimize testosterone levels either achieved by orchiectomy or chemically using LHRH-axis manipulation has become the mainstay for treatment of relapsed disease.

Despite the improvement in survival, quality of life (QoL) is often severely affected by ADT. QoL is a top preference in patients with advanced disease³ a finding in line with our case. The decision to initiate castration therapy in apparently healthy men has far reaching consequences regarding toxicity and issues of QoL. We have previously shown that high level of fatigue is seen in patients after curative radiation and long-term ADT.⁴

Here, we report the case of a patient with intolerance to ADT and the visualisation of metastatic deposit in the anterior right common iliac and inferior caval vein divergence on PSMA-PET/CT treated with radiation of the lesion and the drainage vicinity lymph nodes leading to prolonged ADT-free survival.

He preferred a delayed intermittent anti-androgen treatment approach, accepting the possible impact on longevity but preserving acceptable QoL including daily physical activities and conserved sexuality.

Additionally, in high-risk patients with PSA relapse the clinical outcome is highly variable depending on Gleason grades and tumor burden.⁵ Therefore, often clinicians are reluctant to intervene early in healthy but elderly men with a PSA rise after former curative intend therapy. But, if salvage ADT is used in these patients the disease nearly always re-emerges despite castrate levels of testosterone. However, biochemical progression usually occurs before the actual identification of metastases on conventional and advanced imaging. The use of modern imaging, PSMA-PET/CT, as applied in our case could become a cornerstone when dealing with PSA relapse.

Conclusion

The concept of MDT embedded in a comprehensive approach possibly adds to optimized solution in selected patients with limited disease after PSA relapse. MDT could be a valuable strategy in the clinic to delay the initiation of ADT and thus sustain QoL for the patient over a clinically relevant period.

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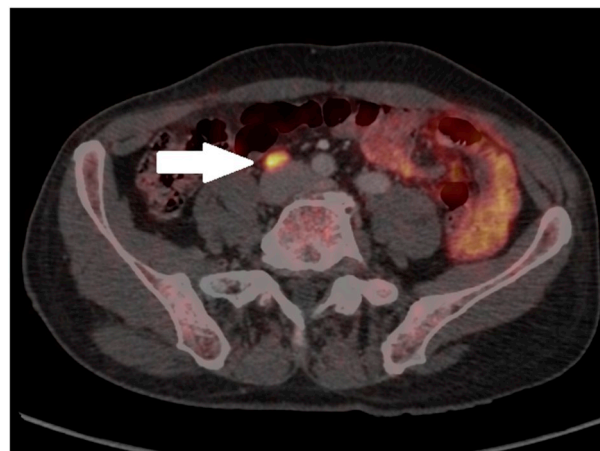


Fig. 1. PSMA PET/CT avidity in a metastatic lymph node, anterior to the right common iliac and inferior caval vein divergence white arrow.

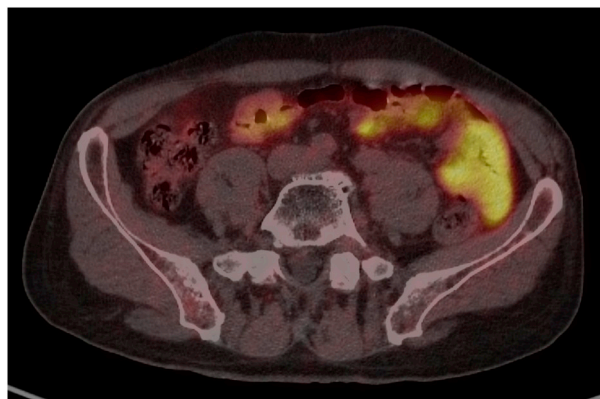


Fig. 2. Follow-up PSMA PET/CT without detectable metastatic lymph nodes.

Found (SP2519).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.eucr.2019.100992>.

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