CASE REPORT

UROLOGICAL ONCOLOGY

PSMA PET-directed surgical metastasis-directed therapy in metachronous prostate cancer

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We present the case of a patient who underwent an open radical prostatectomy with pelvic lymph node dissection (Gleason 4+3, pT3a pN1 R0) in March 2017. In November 2020, prostate-specific membrane antigen (PSMA)-radioguided salvage lymph node dissection was planned due to a single left para-rectal lymph node at a [^{68}Ga] Ga-PSMA-I&T PET.
In January 2022, the [^{68}Ga] Ga-PSMA-I&T PET showed an isolated liver lesion. Biopsy confirmed prostate adenocarcinoma. A liver segmentectomy was performed. A complete biochemical response was reported until the last follow-up (December 2022). Prostate-specific membrane antigen positron emission tomography (PSMA PET)-directed metastasis-directed therapy may be an effective treatment in selected cases, allowing a benefit in the oncological outcome.

Key Words: prostate cancer ‹› prostate-specific membrane antigen ‹› liver ‹› radioguided surgery

CASE PRESENTATION

Recent evidence suggests a potential benefit of metastasis-directed therapy (MDT) in oligometastatic hormone-sensitive prostate cancer (omHSPC) in terms of progression-free survival (PFS) compared to observation alone [1, 2].
Furthermore, with the spread of more accurate imaging modalities such as radiotracer-labeled prostate-specific membrane antigen (PSMA) targeting positron emission tomography (PET), patients with omHSPC are likely to be detected earlier, with a reasonable impact on management [3, 4]. There is an unmet need to determine the optimal treatment strategy for omHSPC [5].
We describe the case of a patient with metachronous omHSPC who underwent an exclusively PSMA PET-directed surgical MDT.
In March 2017, a 55-year-old was referred to our institution for intermediate-risk prostate cancer (PCa). He was scheduled for open radical prostatectomy with pelvic lymph node dissection, after negative staging with conventional imaging.
The pathological report revealed a pT3a pN1 (1 positive node along the left internal iliac artery and 1 positive node in the left obturator fossa out of 9 nodes)

R0 L1 V0, Gleason 4+3 PCa with postoperative undetectable prostate-specific antigen (PSA).

In September 2017, the patient underwent salvage radiotherapy to the prostatic fossa including the pelvic lymphatic template, at an early PSA recurrence of 0.1 ng/mL with a complete PSA response. Within three following years the PSA increased to 1.05 ng/ml. Subsequent [^{68}Ga] Ga-PSMA-I&T PET showed tracer uptake within a single left pararectal lymph node (SUV_{max} 14.7) (miT0 miN1 miM0) (Figure 1.A). After extensive counseling of the patient on the individual treatment approach, a left-sided pararectal and presacral PSMA-radioguided salvage lymph node dissection was performed in November 2020 after injection of [^{99m}Tc] Tc-PSMA-I&S and preoperative SPECT/CT imaging (Figure 1.B) as previously described [6]. The pathological analysis revealed one positive left pararectal node out of 14 retrieved.

The PSA level remained undetectable until January 2022, when it increased to 1.58 ng/mL. [^{68}Ga] Ga-PSMA-I&T PET showed an isolated liver lesion (SUV max 9.4; miT0 miN0 miM1c; Figure 2), which was confirmed by MRI (Figure 1.C). Biopsy demonstrated PCa. Considering the single metastasis and the excellent general condition of the now 60-year-old patient, minimally invasive laparoscopic liver segmentectomy was performed in March 2022, after multidisciplinary consultation and detailed discussion with the patient. Resection was complete (liver segment VI, pM1c [unifocal], R0), and no postoperative complications occurred. The postoperative PSA level was undetectable and remained stable until the last follow-up in December 2022. A CT scan in December 2022 revealed no evidence of disease.

DISCUSSION

Based on the hypothesis that local ablative treatments of metastases might halt the development of new lesions and thus delay systemic therapy, some retrospective and few prospective studies investigated the role of MDT, with promising results [2, 7, 8, 9]. Ost et al. reported the first prospective randomized phase II trial (STOMP trial) assessing the role of MDT versus surveillance in patients with ≤3 extracranial metastases. After a median follow-up of 3 years, 39% of patients who received MDT were ADT-free versus 19% in the surveillance arm [2].

The main shortcomings of most studies are the concurrent ADT use and the heterogeneity of imaging techniques. Our patient underwent PSMA-radioguided salvage lymph node dissection due to the detection of a single positive pararectal spot at [^{68}Ga] Ga-PSMA-I&T PET. Recent evidence suggested that PSMA-targeted radioguided surgery leads to favorable outcomes (biochemical recurrence-free survival and therapy-free survival) in oligorecurrent patients with a low preoperative PSA and a low number of pelvic PSMA PET-avid lesions [10].

Fourteen months later, the patient experienced another PSA increase, and a single liver metastasis was diagnosed. The surgical MDT strategy avoided the initiation of a systemic treatment which should be the standard of care according to the current guidelines of the European Association of Urology.

The efficacy of PSMA PET-directed surgical MDT for recurrent omHSPC with a single liver metastasis is assessed only in a few case reports, all of which point to a potential oncological benefit of MDT in terms of PFS [11].

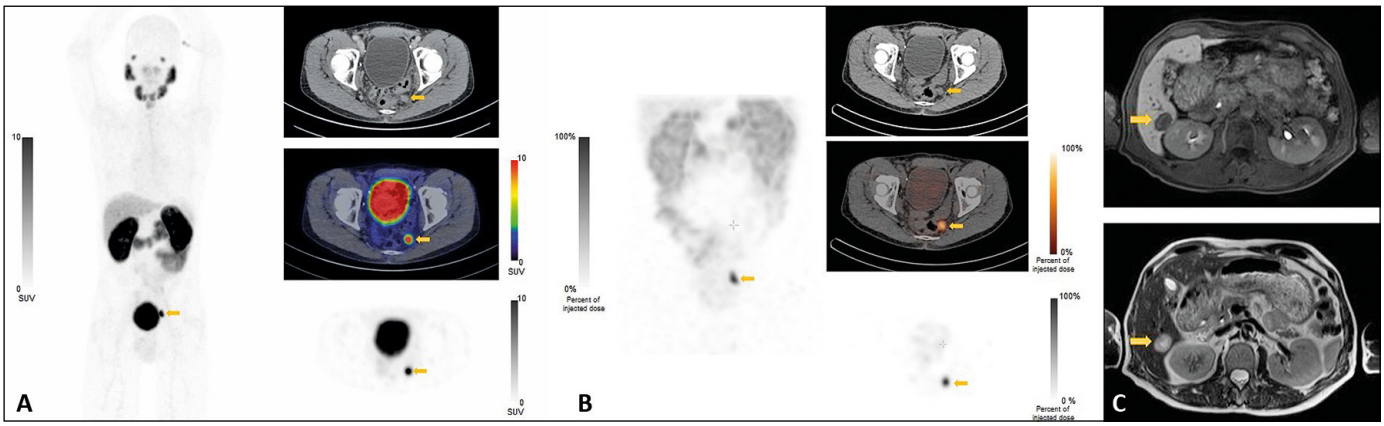

Figure 1. A. *[^{68}Ga] Ga-PSMA-I&T PET/CT showing radioligand uptake within a single left para-rectal lymph node (SUV_{max} 14.7; miT0 miN1 miM0) three years after radical prostatectomy.* **B.** *[^{99m}Tc] Tc-PSMA-I&S SPECT/CT obtained prior to PSMA-radioguided salvage surgery.* **C.** *MRI confirming the isolated liver lesion (T1w 20 min. after the injection of gadoxetate disodium [Primovist®] and T2w sequences).*

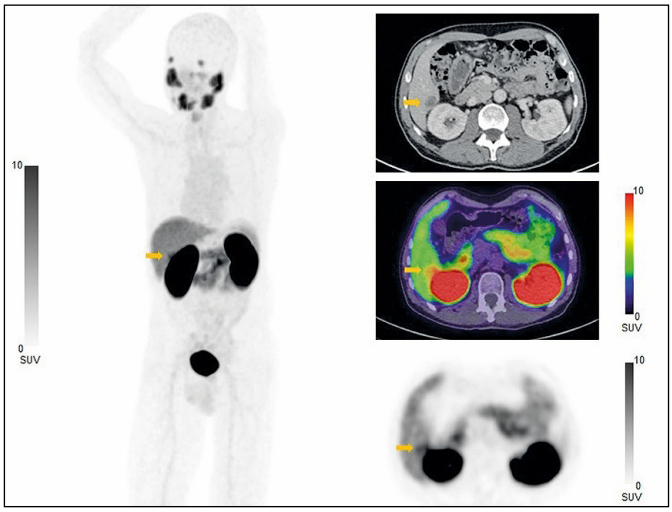

Figure 2. *[^{68}Ga] Ga-PSMA-I&T PET/CT showing an isolated liver lesion with moderate uptake (SUV max 9.4; miT0 miN0 miM1c).*

Although it remains unclear how MDT might alter the natural history of omHSPC, it should be considered only on the basis of PSMA-targeted PET/CT findings in our opinion, as early detection of metastases could have a significant impact on management and outcomes. In the ORIOLE trial which evaluated the role of stereotactic ablative radiotherapy in men with oligometastatic PCa compared with surveillance, complete consolidation of PSMA radiotracer-avid disease significantly reduced the risk of new lesions at 6 months (16% vs 63%; p = 0.006) [7].

After PSMA-PET-directed MDT, our patient was ADT-free with undetectable PSA at the last follow-up suggesting the efficacy of MDT and even an indolent behavior of disease. It is worth noting that the spread of PCa to the pararectal lymph node and subsequent liver metastasis may suggest a similar spread pathway as compared to colorectal cancers. Liver metastases from PCa are not as common as bone metastases, and they occur late in the disease course as a result of hematogenous spread, leading to the poor median overall survival (13.5 months) [12]. We could assume that the single liver metastasis originated from hematogenous spread via the portal vein, as in the case with rectal cancer.

Perhaps, future research in genomic analysis will shed new light on the clinical features of omHSPS. A recent update of long-term MDT outcomes in omHSPS by pooling STOMP and ORIOLE demonstrated the ability of a high-risk mutation signature (pathogenic somatic mutations within ATM, BRCA1/2, Rb1, and TP53) to stratify outcomes after MDT [1].

Median PFS was longer in MDT compared with observation (pooled hazard ratio [HR], 0.44; 95% CI, 0.29 to 0.66; p <0.001), with the greatest benefit of MDT occurring in patients with a high-risk mutation (HR high-risk, 0.05; HR no high-risk, 0.42; p-value for interaction: 0.12). A high-risk mutational signature may thus be a valuable tool to identify the best candidate for MDT [1].

We acknowledge the limited strength of the evidence presented in this case report; nevertheless, we consider it a potential springboard for future research. Further studies are needed to define the role of isolated PSMA-PET-directed MDT in recurrent omHSPC and to determine the most appropriate criteria for patient selection, with the goal of deferring or avoiding systemic therapy and providing a potential survival benefit.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

References

1. Deek MP, Van der Eecken K, Sutera P, et al. Long-Term Outcomes and Genetic Predictors of Response to Metastasis-Directed Therapy Versus Observation in Oligometastatic Prostate Cancer: Analysis of STOMP and ORIOLE Trials. J Clin Oncol. 2022; 40: 3377-3382.
2. Ost P, Reynders D, Decaestecker K, et al. Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial. J Clin Oncol. 2018; 36: 446-453.
3. Bianchi L, Castellucci P, Farolfi A, et al. Multicenter External Validation of a Nomogram for Predicting Positive Prostate-specific Membrane Antigen/Positron Emission Tomography Scan in Patients with Prostate Cancer Recurrence. Eur Urol Oncol. 2023; 6: 41-48.
4. Bianchi L, Ceci F, Costa F, et al. The Impact of PSMA-PET on Oncologic Control in Prostate Cancer Patients Who Experienced PSA Persistence or Recurrence. Cancers. 2022; 15: 247.
5. Bianchi L, Ceci F, Balestrazzi E, et al. PSMA-PET Guided Treatment in Prostate Cancer Patients with Oligorecurrent Progression after Previous Salvage Treatment. Cancers. 2023; 15: 2027.
6. Maurer T, Robu S, Schottelius M, et al. 99mTechnetium-based Prostate-specific Membrane Antigen-radioguided Surgery in Recurrent Prostate Cancer. Eur Urol. 2019; 75: 659-666.
7. Phillips R, Shi WY, Deek M, et al. Outcomes of Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer: The ORIOLE Phase 2 Randomized Clinical Trial. JAMA Oncol. 2020; 6: 650-659.
8. Palma DA, Olson R, Harrow S, et al. Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Cancers: Long-Term Results of the SABR-COMET Phase II Randomized Trial. J Clin Oncol. 2020; 38: 2830-2838.

9. Steuber T, Jilg C, Tennstedt P, et al. Standard of Care Versus Metastases-directed Therapy for PET-detected Nodal Oligorecurrent Prostate Cancer Following Multimodality Treatment: A Multi-institutional Case-control Study. Eur Urol Focus. 2019; 5: 1007-1013.

10. Knipper S, Mehdi Irai M, Simon R, et al. Cohort Study of Oligorecurrent Prostate Cancer Patients: Oncological Outcomes of Patients Treated with Salvage Lymph Node Dissection via Prostate-specific Membrane Antigen-radioguided Surgery. Eur Urol. 2022; S0302-2838(22)02408-3.

11. Tilmans G, Navez J, Komuta M, Saussez T, Lerut J. Solitary prostate cancer liver metastasis: an exceptional indication for liver resection. Acta Chir Belg. 2021; 121: 427-431.

12. Halabi S, Kelly WK, Ma H, et al. Meta-Analysis Evaluating the Impact of Site of Metastasis on Overall Survival in Men With Castration-Resistant Prostate Cancer. J Clin Oncol. 2016; 34: 1652-1659. ■