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Resection of a singular metachronous testicular metastasis of prostate cancer: A case report

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ABSTRACT

We present the case of a 66-year-old patient with a biochemical recurrence of prostate cancer manifesting as an asymptomatic testicular metastasis. Two years after radical prostatectomy and salvage radiation, the prostate-specific antigen (PSA) level rose to 1.07ng/ml. PSMA PET/CT scan showed tracer accumulation in the left testicle. Inguinal orchiectomy confirmed the metastasis. After being non-detectable, the PSA level increased five months after orchiectomy, with PSMA PET/CT revealing positive iliac lymph nodes. In summary, the presented case illustrates orchiectomy as a metastasectomy. However, apart from a transient decrease in PSA, no medium-term oncological advantage could be seen.

1. Introduction

Prostate cancer is the most common form of cancer in men. It usually affects patients at an older age. In 2018, the average age of onset was about 66 years (Rawla, 2019). On the contrary, malignant germ cell tumor of the testis is a rather rare form of cancer and mainly affects younger patients. However, it is one of the most common forms of cancer in young men aged 15 to 45 (Gaddam et al., 2025). Young men account for >90 % of testicular germ cell tumors (Rajpert-De Meyts et al., 2025). In an older patient with a suspicious testicular mass, malignant germ cell cancer is rarely the cause. Here, potential differential diagnoses are an epididymitis or epididymorchitis, a scrotal hernia, a hydrocele, a varicocele, an epididymal (head) cyst or a metastasis.

Secondary neoplasms in the testis in general are very rare with an incidence from only 0.02 % to 2.5 % in autopsy (Dutt et al., 2000; Tiltman, 1979). Prostate cancer is the number one primary tumor for testicular metastasis with 15 % to almost 20 %, followed by lung, skin (malign melanomas), colon and kidney as well as stomach and liver cancer (Dutt et al., 2000; Kusaka et al., 2014). However, systematically analysed data of secondary neoplasms in the testis is limited.

Given that most detected cases of testicular metastasis from prostate cancer are discovered incidentally at autopsy or after bilateral orchiectomy (Gibas et al., 2015; Tu et al., 2002), the fraction of patients with testicular metastases in prostate cancer patients is inconsistent in the literature but appears to be in the low single digits at most. Few autopsy studies yielded results ranging from 0.06 % (Pienkos and Jablokow, 1972) to 0.5 % (Bubendorf et al., 2000). In patients who underwent bilateral orchiectomy for surgical castration instead of medical androgen deprivation therapy, the incidence of testicular metastasis was 4 % (Tu et al., 2002; Johansson and Lannes, 1983; Baykal et al., 1997).

We report the case of a 66-year-old patient with a biochemical recurrence of prostate cancer after radical prostatectomy and radiotherapy due to an isolated metachronous testicular metastasis. The left testicular mass showed tracer accumulation on PSMA PET/CT, which was otherwise unremarkable. After inguinal radical orchiectomy the PSA level of the patient dropped below the detection level but rose back up to 0.19ng/ml after 5 months, and 1.18ng/ml after 8 months. In the further course, a PSMA PET/CT was performed showing PSMA positive iliac lymph nodes.

2. Case presentation

In July 2023, a 66-year-old patient was referred to the outpatient clinic of our department due to a biochemical recurrence of prostate cancer after radical prostatectomy and salvage radiotherapy with a PSA level of 1.07 ng/ml.

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Initially, in March 2021 a biopsy of the prostate was performed at a PSA-value of 40,1ng/ml, revealing a cribriform adenocarcinoma of the prostate (Gleason 4 + 4 = 8) infiltrating 17 out of 18 tissue cylinders. 39 mm of in total 88 mm of the cylinders were infiltrated.

In the beginning of April 2021, a PSMA PET/CT as well as a whole-body skeletal scintigraphy were performed. The PSMA PET/CT revealed a locally advanced prostate carcinoma with markedly increased PSMA expression. Bilateral infiltration of the seminal vesicles was present, with tumor expression adjacent to the rectal wall. No pelvic or extrapelvic lymph node or distant metastases were detected. The skeletal scintigraphy showed no evidence of bone metastases.

The patient presented at our institution and underwent radical prostatectomy and regional lymphadenectomy in April 2021. The histological specimen of the prostatectomy showed a poorly differentiated acinar adenocarcinoma with a Gleason score of 4 + 4 = 8 in 30 % of the parenchyma. The final histopathological result was pT3b, pN0 (0/14), L0, V0, Pn1, Gleason score 8, R1.

After radical prostatectomy, the PSA level dropped to a nadir of 0.60ng/ml six weeks after surgery. A PSMA PET/CT showed local tracer accumulation in August 2021 and thus a salvage radiation was performed. In addition, the patient started treatment with bicalutamide 150 mg per day at the beginning of April 2021. Hereafter, the PSA level dropped below the detection level.

Due to an increase of the PSA value, starting in April 2022 at a level of 0.13ng/ml, a PSMA PET/CT was performed in July 2023 at a PSA level of 1.07ng/ml. The PSA doubling time was calculated using the Memorial Sloan Kettering Cancer Center's PSA Doubling Time Calculator and resulted in a PSA doubling time of 6.0 months (Memorial Sloan Kettering Cancer Center 2025). In the PSMA PET/CT a scrotal tracer accumulation on the left side was detected (Fig. 1). The scan was otherwise unremarkable. The patient was asymptomatic. Primarily, a benign cause was assumed to be most likely. In an ultrasound examination of the testicle a suspicious cystic testicular mass was detected. Testicular tumor markers (hCG, AFP, LDH) were unremarkable. The initial external recommendation after interdisciplinary discussion was to stop the androgen deprivation therapy, to reassess PSA levels after 3 months, and to repeat the PSMA PET/CT.

Thereafter, the patient presented at our institution. In the physical examination in our department the scrotum showed no evidence of inflammation. Both testicles and epididymides were not painful on palpation. The left testis was slightly enlarged compared to the right testis with a volume of 16 ml. However, the patient did not notice any change in size. In the ultrasound examination the left testicle displayed a cystic mass that took up approximately 2/3 of the parenchyma with peripheral perfusion (Fig. 2). The right testis as well as both epididymides showed no pathological findings. Due to the patient's personal psychological distress regarding a possible testicular metastasis or a secondary testicular malignancy, a shared decision was made for inguinal exploration of the testis.

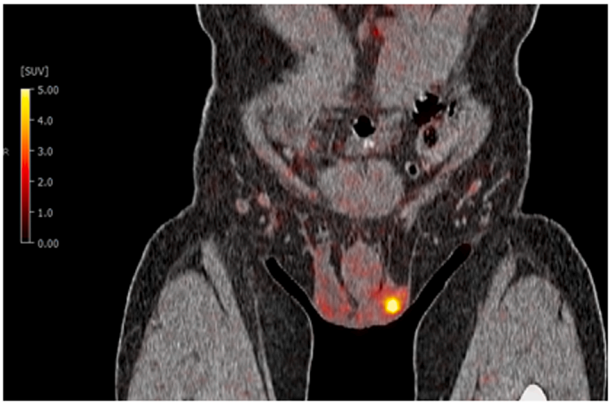

Fig. 1. Scrotal tracer enhancement in the PSMA PET/CT.

In August 2023, an inguinal exploration of the left testicle was performed. During surgery, the testicular tissue was found to be largely cystically disintegrating, including several hard encapsulated cysts containing brownish viscous tissue. The rapid frozen section revealed a glandular growing carcinoma with cribriform growth pattern, compatible with a metastasis of the prostate cancer. Therefore, high inguinal orchiectomy of the left testis was performed. In the final histopathological assessment (Fig. 3), the testicular parenchyma was found infiltrated with the known low-differentiated acinar prostate carcinoma (Gleason 4 + 4 = 8) in terms of a metastasis. The rete testis was infiltrated as well. The surgical margins were negative.

The postoperative course was without problems. The follow-up after 6 weeks was without any irregularities, the control of the PSA value after 6 weeks (without ADT) showed a PSA value below the detection level. After five months, the PSA level rose to 0.19ng/ml. After a steady rise up to 1.18ng/ml in April 2024 another PSMA PET/CT was performed showing PSMA positive external iliac lymph nodes on both sides and positive internal iliac lymph nodes on the right side up to 9 mm. The patient was still in a good physical condition. Therefore, after a tumor board meeting, the shared decision was made in favour of a triple therapy consisting of Darolutamide, Docetaxel and an GnRH analogue.

3. Discussion

Symptomatic testicular masses in elderly patients are rare. Although disseminated prostate cancer metastasizes regularly into testicular tissue, cases of isolated metachronous testicular metastases are seldom. Here we report a case of biochemical recurrence in a 66-year-old patient two years after radical prostatectomy of a locally advanced prostate carcinoma, followed by salvage radiation. In the PSMA PET/CT only a scrotal tracer accumulation was evident. Histopathologically, a testicular metastasis of the known prostate cancer was confirmed, and after inguinal orchiectomy the PSA level dropped below the detection level. After five months, the PSA level rose back up and multiple lymphatic metastases were detected by PSMA PET/CT.

Regarding the scheme of manifestation, testicular metastases from prostate cancer mostly occur metachronously in patients with known metastatic prostate cancer elsewhere (Kusaka et al., 2014; Hermi et al., 2023; Turk et al., 2019). Solitary metachronous testicular metastases from prostate cancer after radical prostatectomy are very rare (Gibas et al., 2015; Kwon et al., 2011; Janssen et al., 2010).

Concerning clinical presentation, patients present mostly with testicular swelling, scrotal induration or testicular pain (Kusaka et al., 2014; Gibas et al., 2015; Hermi et al., 2023; Turk et al., 2019; Kwon et al., 2011; Menchini-Fabris et al., 2007; Manikandan et al., 2006). Cases of asymptomatic testicular metastasis such as the case presented herein are rare (Janssen et al., 2010).

In terms of diagnostics, testicular metastases of prostate cancer present in different ways on ultrasound. Studies report heterogenous testes with areas described as hypoechoic, liquid formations, sometimes solid, sometimes containing hyperechoic spots. In most cases multiple masses can be seen, with a variation of the given aspects. An increased vascularisation is described in Doppler ultrasound. In our case, the sonographic examination showed an inhomogeneous cystic formation with peripheral perfusion. On CT scan heterogenous or hyperdense heterogenous masses are described (Kusaka et al., 2014; Turk et al., 2019).

In most cases of testicular metastasis of prostate cancer, PSA levels are extremely high due to the disseminated stage of cancer (Kusaka et al., 2014; Hermi et al., 2023; Turk et al., 2019). On the other hand, there are also cases where the PSA level was low, indicating a dedifferentiated form of prostate cancer (Menchini-Fabris et al., 2007). In our case, once the PSA elevation was detected in April 2022 after prostatectomy and radiotherapy, it showed a rather steep increase until July 2023, with a PSA doubling time of 6 months. Similar cases of solitary

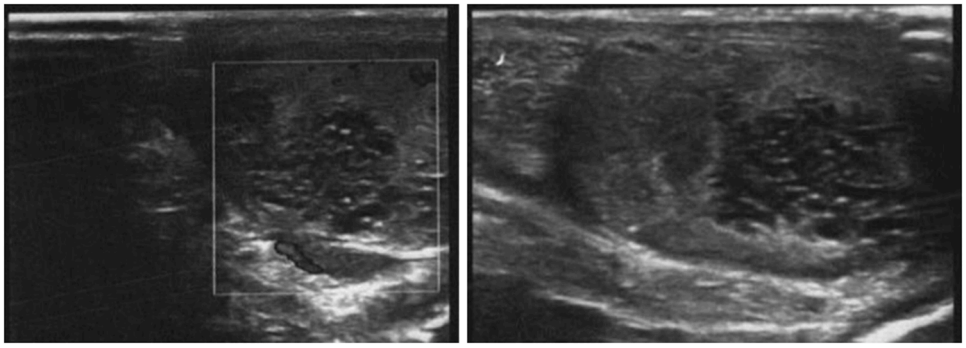

Fig. 2. Cystic mass in the ultrasound examination.

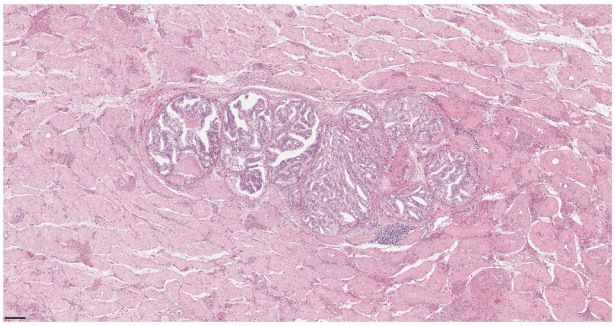

Fig. 3. A representative microphotograph (H&E, 5x lens, scale bar 200 μm) shows atrophic testicular tissue with nodular infiltrates of a gland-forming and cribriform malignant neoplasm, matching the metastasis of the previously recognized prostate carcinoma.

metachronous metastasis showed levels of 3,1ng/ml (Gibas et al., 2015), 0,347ng/ml (Kwon et al., 2011) and 3,08ng/ml at detection (Janssen et al., 2010). In our case, the PSA level was 1,07ng/ml (under concurrent ADT) when the solitary testicular metastasis was diagnosed, which therefore can be well classified in this range.

The case we present herein aligns with the mentioned cases of metachronous singular testicular metastases regarding the initial histopathological aspects of the prostatectomy specimen. Especially a locally advanced stage of cancer, an infiltration of the seminal vesicle and a positive surgical margin appear to be relevant for the development of a singular metachronous testicular metastasis (Gibas et al., 2015; Kwon et al., 2011; Janssen et al., 2010).

Regarding the timeframe between radical prostatectomy and first diagnosis of singular testicular metastases, intervals range from 1.5 years (Kwon et al., 2011) to 7 years (Gibas et al., 2015), with our case lying in between with 2.3 years.

In patients with testicular metastases, in total only a small number of patients present with clinically manifested metastases to the testis. The majority of cases with testicular metastases of prostate cancer are only discovered via autopsy or bilateral orchiectomy for surgical castration (Kusaka et al., 2014). Studies show that 4 % of patients with bilateral orchiectomy exhibited testicular metastases (Tu et al., 2002). Hence, it could be assumed that in the group of patients requiring some form of ADT, numbers of testicular metastases are higher than the reported numbers of 0.06 %−0.5 % in autopsy studies (Pienkos and Jablokow, 1972; Bubendorf et al., 2000). These incidents were reported around 30–40 years ago and data on this issue considering recent changes in ADT are sparse.

Moreover, the mechanism of metastatic spread of prostate cancer to the testis is still unknown. Some assumptions exist for the metastatic pathway: especially if the prostatic urethra is affected by the cancer, a retrograde venous extension or arterial embolization may be a possibility (Kusaka et al., 2014; Kwon et al., 2011; Menchini-Fabris et al., 2007; Smelzo et al., 2022). Spreading via direct invasion into the lymphatics of the vas deferens, anatomically unique lymphatic connections, or endocanalicular spreading via the vas deferens could also be possible (Kusaka et al., 2014; Kwon et al., 2011; Menchini-Fabris et al., 2007; Smelzo et al., 2022). Since in the presented case the prostate cancer was already in a locally advanced stage and was also microscopically boarder-forming in the area of the seminal vesicles, invasion into the lymphatic vessels of the vas deferens and retrograde spread could be considered. However, although the rete testis showed infiltration in the pathological specimen of the orchiectomy, the tumor was confined to the testis and had been completely removed, pathological margins were negative. Therefore, a hematogenous spread should most likely be assumed.

Regarding the follow-up, our case highlights the importance of a complete physical examination as well as an ultrasonography including the testicles, especially when abnormalities are suspected, and therefore concurs with the recommendation of other authors to do so (Smelzo et al., 2022). Furthermore, once a singular testicular metastasis of prostate cancer is suspected, as a form of maximally non-morbid salvage therapy inguinal orchiectomy should be considered if tissue needs to be obtained for histopathological examination anyway, following the recommendation of other authors (Gibas et al., 2015; Janssen et al., 2010; Menchini-Fabris et al., 2007).

In the end, we present the case of inguinal orchiectomy as a form of secondary metastasectomy. Attempts of secondary metastasectomies have been made repeatedly as part of individual treatment trials, e.g. in the form of secondary PSMA- or PET/CT-guided lymphadenectomies (El-Malazi, 2022). However, the results in terms of long-term oncological benefit were modest. Although the orchiectomy is of low invasiveness and causes little surgical damage the procedure did not result in medium-term oncological benefit in our case either, apart from delaying the PSA-recurrence.

4. Conclusion

Singular metachronous testicular metastasis of the prostate is rare. In our case, we present a patient with an asymptomatic testicular metastasis. An inguinal exploration of the left testicle was performed to rule out a second malignancy and at the patient's request, showing a metastasis of prostatic cancer, thus resulting in a secondary metastasectomy. After a brief decline in PSA, it rose again after five months. Despite the uncomplicated operation, there was no significant change in the disease course. Due to the limited number of cases in the literature, this issue must still be decided on an individual basis in the future.

Patient consent statement

The authors declare that they have obtained consent from the patient.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Marie Semmler reports a relationship with Bristol-Myers Squibb GmbH und Co KGaA that includes: travel reimbursement. Marie Semmler reports a relationship with Janssen-Cilag GmbH that includes: travel reimbursement. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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