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Case Report

Testicular metastasis of prostate adenocarcinoma: the other side of orchiepididymitis

Gianluca Di Rienzo[1]*, Alessandro Tafuni[1]*, Umberto Maestroni[2], Livia Ruffini[3], Enrico Maria Silini[1], Donatello Gasparro[4], Francesco Paolo Pilato[1], Letizia Gnetti[1]

[1] Anatomic Pathology Unit, University Hospital of Parma, Parma, Italy; [2] Urology Division, University Hospital of Parma, Parma, Italy; [3] Nuclear Medicine Division, University Hospital of Parma, Parma, Italy; [4] Oncology Division, University Hospital of Parma, Parma, Italy
**Authors contributed equally*

Summary

Background. Metastatic prostate adenocarcinoma is a rare event and there are few references to this topic. We report an unusual case of prostate cancer metastasis and review of contemporary literature. Moreover, we discuss the pathogenesis and the clinical aspects of this event.

Case presentation. A 70-year-old patient was admitted to the hospital for right scrotal pain. The ultrasound examination described an increase in testicular size, suggesting the possibility of orchiepididymitis. Past medical history reported a previous prostate adenocarcinoma. Inflammatory blood tests were normal. Importantly, PSA was 3.3 ng/ml. PET scan positivity in the scrotum raised suspicion of a relapse. Therefore, he underwent right orchiectomy.

Conclusion. Although metastatic prostate adenocarcinoma is rare, a correct diagnosis is of paramount importance because the therapy changes accordingly. Patients who complain of scrotal pain need to be examined accurately. Although the most common cause behind this symptom is infectious, the patient's past medical history should be reviewed to exclude previous malignancies.

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Correspondence
Letizia Gnetti
E-mail: letizia.gnetti@gmail.com

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Background

Scrotal pain is a common reason for visits to the emergency room in adults. This symptom may be due to orchiepididymitis, testicular torsion, inguinal hernia or testicular neoplasm [1].

Metastases to the testis are rare events. The most common metastatic neoplasm is leukemia; reported solid neoplasms are less frequent and include melanoma, prostate, lung and kidney adenocarcinomas. However, the incidence of this latter group is below 1% [2,3].

We report the case of a man who was admitted to the hospital for scrotal pain; ultrasound examination showed an increase in testis size, and thus the patient underwent right orchiectomy. Surprisingly, the histology report revealed the presence of prostate adenocarcinoma.

Case presentation

A 70-year-old patient was admitted to the emergency room of our hospital for right scrotal pain. He had no significant past medical history ex-

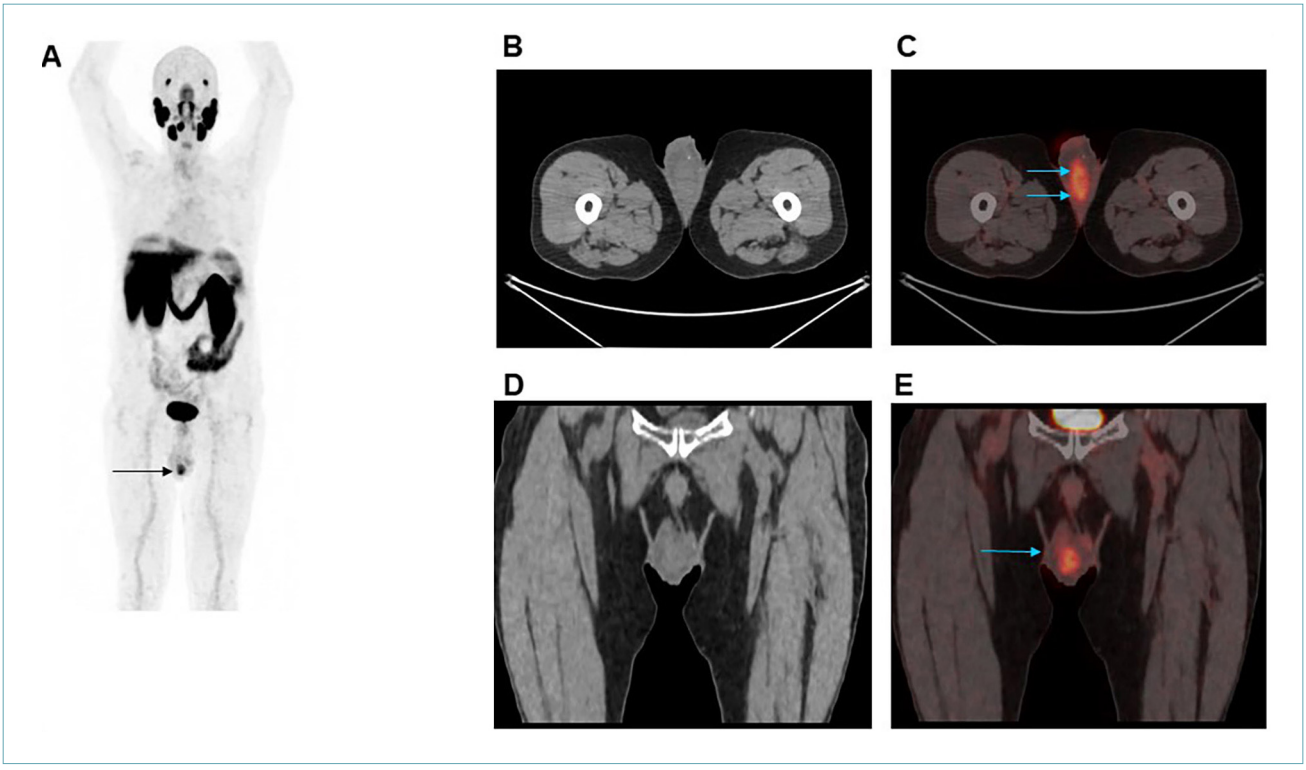

Figure 1.68Ga-PSMA PET/CT in the restaging of prostate adenocarcinoma. MIP images (A); CT and fused PET/CT axial sections (B, C); CT and fused PET/CT coronal sections (D, E). PSMA PET/CT showed increased uptake in the right scrotum (black and light blue arrows) with SUVmax value of 5.6.

cept for a previous transurethral resection of the prostate (TURP) that led to the diagnosis of prostate adenocarcinoma (Gleason Score 9, Grade Group 5) six years earlier. The patient was treated with androgen deprivation therapy (leuprorelin) and radiotherapy.

After hospital admission an ultrasound examination of the pelvic region was performed. It reported an increase in right testis size (46 x 22 mm), hydrocele, heterogenous echotexture and enhanced vascularity. Physical examination of the right testis showed swelling, hardness and soreness. Abdominal examination was unremarkable. The clinical presentation was suggestive of orchiepididimitis.

Blood tests were normal, except for PSA which was 3.3 ng/ml. Therefore, disease restaging was performed using positron emission tomography/computed tomography (PET/CT) with 68Ga-PSMA. The radiopharmaceutical was prepared in the local radiopharmacy as previously described [4].

PSMA PET/CT revealed increased tracer accumulation in the right scrotum (SUVmax = 5.6) suggesting prostate cancer recurrence (Fig. 1).

The patient underwent right orchiectomy. The gross description reported that the testis measured 5 x 3 x 2 cm, featured an area of induration and was diffusely gray on cut sections (Fig. 2A). The histology report described that most testis and epididymis were replaced by a glandular neoplasm with nests of plasmacytoid cells (Fig. 2B). Previous prostate adenocarcinoma was comparable to the testicular neoplasm (Fig. 2C). Immunohistochemistry showed that the tumor in the biopsy was positive to ERG (Fig. 2D), PSA (Fig. 2E) and AR (Fig. 2F), negative to inhibin, p63 and ER. The lesion in the testis was positive to PSMA (Fig. 2G), thereby suggesting metastatic prostate adenocarcinoma in the testis. To confirm the primary site, NKX3.1 was performed on the metastasis because it is considered both a sensitive and specific marker for prostate adenocarcinoma [5]. Figure 2H shows positivity in tumor cells.

Discussion

A metastasis in the testis is a rare event. The incidence is below 1% except for leukemia and lympho-

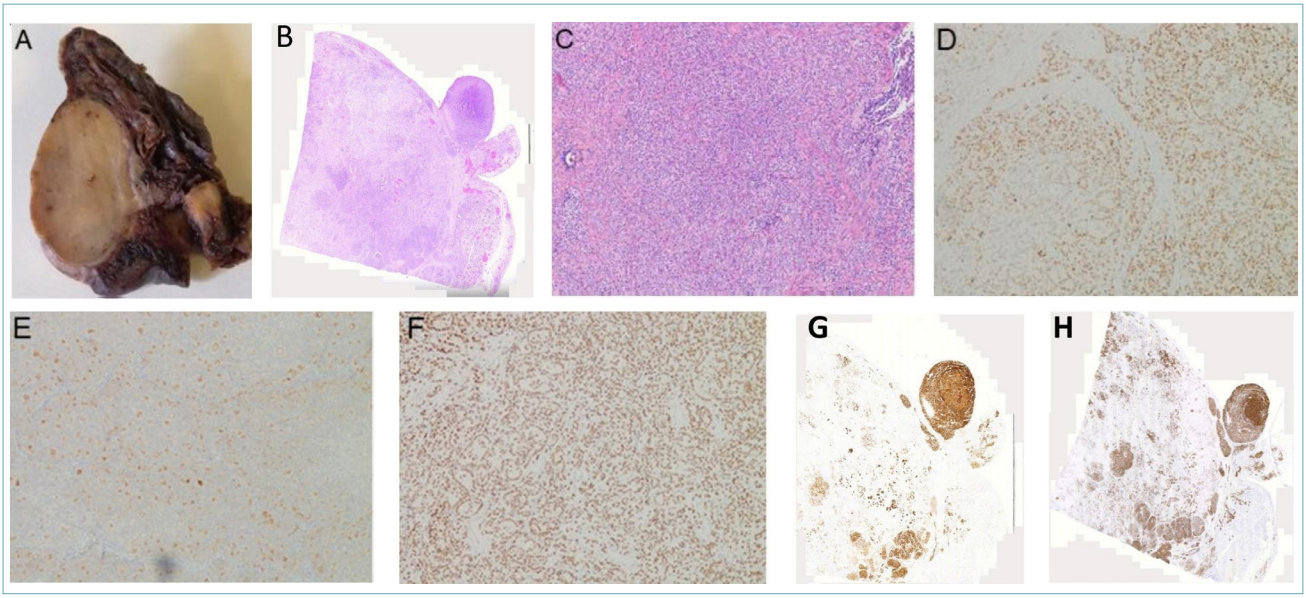

Figure 2. Transurethral resection of the prostate (TURP) specimen and testis with prostate adenocarcinoma. Gross photograph of the testis (A); whole slide image of testicular metastasis at 4x (B); TURP specimen with prostate adenocarcinoma at 10x (C); ERG expression in the TURP specimen at 10x (D); PSA expression in the TURP specimen at 10x (E); androgen receptor expression in the TURP specimen at 10x (F); PSMA expression in the testicular metastasis at 4x (G); NKX3.1 expression in the testicular metastasis at 4x (H).

ma [2]. The likely explanation is that scrotal temperature prevents tumor cell proliferation. The risk of metastasis might also be reduced by the presence of Sertoli cells tight junctions, which constitute the blood-testis barrier [6,7].

A palpable unilateral nodule is the clinical presentation of metastasis to the testis. However, testicular metastasis is often an incidental finding during specimen processing or autopsy. Both testes might be involved, but it is usually unilateral [6,8]. The interval between the event and the metastasis may range from six months to some years [9]. Metastatic prostate cancer usually has a high Gleason score which matches the primitive neoplasm [6]. Table I shows literature cases of prostate adenocarcinoma metastatic to the testis.

Metastatic high grade prostate adenocarcinoma should be differentiated from primary tumors of the testis. The International Society of Urological Pathology (ISUP) suggests performing the following antibodies: SALL4, OCT4 and EMA; alternatively, OCT4, Glypican 3, EMA and cytokeratin 7 might be used [10].

Patient survival is limited to one year, despite reports of longer periods. Prognostic significance is uncertain. Both increase in PSA levels and PSMA PET/CT positivity should improve surveillance in hormone-treated patients, especially to detect isolated metastases as in our patient [9].

The best treatment following surgery is still a matter of debate. A single testicular metastasis might have a low risk of spreading to other organs, but this cannot be excluded. Therefore, orchiectomy may be followed by adjuvant therapy, which is based on radiotherapy or hormone therapy [9]. The latter includes androgen pathway inhibitors such as abiraterone and androgen receptor antagonists such as apalutamide and enzalutamide [11].

Olaparib, a poly(adenosine diphosphate–ribose) polymerase (PARP) inhibitor, may be used in case of progression with hormonal agents on condition that patients have alterations in BRCA1 or BRCA2. For this reason, we suggest that metastatic prostate cancer be screened for these two mutations [12].

Conclusion

Patients who complain about scrotal pain need to be examined accurately. Although the most common cause behind this symptom is infectious, the patient's past medical history should be reviewed to exclude previous malignancies.

Table I. Literature cases of prostate adenocarcinoma metastatic to the testis.

Year	Authors	Age	PSA (ng/ml) at diagnosis	Histological type	GS	Time between diagnosis and metastasis in the testis (months)	Presentation in the testis	Involvement	Sides	PSA (ng/ml) at metastasis in the testis	Orchiectomy	ADT	RT	CT
2018	Su et al. [13]	72	129	Acinar	9	6	Swelling	Bilateral	Both	6.2	Yes	Yes	No	No
2016	Hsieh et al. [14]	62	NA	NA	NA	84	Induration	Unilateral	Right	NA	Yes	Yes	Yes	No
2021	Olorunsola et al. [6]	71	6.8	Acinar	10	0	None	Bilateral	Both	NA	Yes	Yes	No	No
2006	Manikandan et al. [15]	56	1100	Acinar	6	30	Swelling	Bilateral	Both	60	Yes	Yes	No	No
2017	Santos-Lopes et al. [16]	69	NA	Acinar	8	60	Nodule	Unilateral	Left	20	Yes	No	Yes	No
2015	Sampathrajan et al. [17]	63	225.5	Acinar	8	0	None	Unilateral	Right	NA	Yes	No	No	No
2019	Bilal et al. [18]	55	100	NA	NA	0	None	Unilateral	Left	NA	Yes	No	No	No
2019	Dahiru et al. [19]	82	25.8	Acinar	5	0	None	Unilateral	Left	NA	Yes	No	No	No
2023	Kato et al. [20]	73	4.3	Acinar	8	28	Swelling	Unilateral	Left	1.5	Yes	Yes	No	Yes
1997	Baykal et al. [21]	64	80	Acinar	5	0	None	Unilateral	Right	NA	Yes	No	No	No
2015	Aydogmus et al. [22]	69	33.1	Acinar	9	0	Swelling	Unilateral	Left	NA	Yes	No	No	No
2016	Campara et al. [23]	48	597	Acinar	7	108	Swelling	Unilateral	Left	23.1	Yes	Yes	Yes	No
2009	Haupt et al. [24]	71	NA	Acinar	9	48	Nodule	Unilateral	NA	NA	Yes	Yes	Yes	No
2022	DiMarco et al. [25]	67	3.3	Acinar	6	144	Swelling	Unilateral	Right	0.3	Yes	No	No	No
2023	Hermi et al. [26]	55	100	Acinar	10	6	Induration	Unilateral	Left	3.2	Yes	Yes	No	No
2018	Gao et al. [27]	69	100	Acinar	8	24	Swelling	Unilateral	Left	19.2	Yes	Yes	No	No
2011	Kim et al. [28]	73	10.8	Acinar	6	96	None	Bilateral	Both	9.3	Yes	Yes	No	No
2016	Zhang et al. [29]	69	100	Acinar	6	0	Swelling	Unilateral	Right	NA	Yes	Yes	Yes	No
2010	Janssen et al. [30]	71	7.7	Acinar	6	30	Swelling	Unilateral	Left	2.1	Yes	Yes	Yes	No
2013	Upchurch et al. [31]	78	1240	NA	NA	30	Swelling	Bilateral	Both	NA	Yes	Yes	No	No
2010	Rahardjo et al. [32]	66	40	NA	NA	0	Swelling	Unilateral	Left	NA	Yes	No	No	No
2007	Menchini-Fabris et al. [33]	67	15.5	Acinar	9	6	Pain	Unilateral	Left	NA	Yes	No	No	No
2014	Kusaka et al. [34]	56	137	Acinar	9	64	Swelling	Unilateral	Right	4.9	Yes	Yes	Yes	Yes
2022	Fortier et al. [35]	64	150	Ductal	8	264	Induration	Unilateral	Right	40	Yes	Yes	Yes	No

PSA = prostate specific antigen; GS = Gleason Score; ADT = androgen deprivation therapy; RT = radiotherapy; CT = chemotherapy; NA = not available.

Conflicting of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors' contribution

EMS, FPP and LG conceived the idea of this case report. UM, LR and DG provided clinical and radiological data. GDR and AT wrote the manuscript. LG, GDR and AT reviewed the manuscript. All authors contributed to the article and approved the submitted version.

Ethical consideration

We confirm that the local Ethics Committee has been consulted and that ethical approval is not necessary for the report of a single case.

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