Case Report

Ureteral carcinoma metastasizing to the testicle: Can misdiagnosis of orchiepididymitis be avoided?

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Abstract

Testicular metastases from ureteral carcinoma are rare and they are generally mimic orchiepididymitis. For this reason, these are associated to misleading diagnoses and cancer treatment delay. We believe that both timing and knowledge of genital blood and lymph reverse flow routes may represent two important parameters for avoiding misleading diagnoses and speed proper anticancer treatment. We describe a case and discuss pathophysiological data and relevant literature.

Keywords: Metastasis, orchiepididymitis, testicular, upper tract urothelial carcinoma, ureter, vas deferens

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Submitted: 04.08.2020, Revised: 21.09.2020, **Accepted:** 02.11.2020, **Published:** 19.01.2021.

INTRODUCTION

Primary carcinomas of the ureter, most often rise in its distal end, occurring half as often as carcinomas the renal pyelocaliceal cavities.[1,2] Upper tract urothelial carcinomas (UTUCs) are generally discovered at an advanced stage, due to the thin wall of the ureter and renal pelvis, leading to a more dismal prognosis, compared to bladder cancer,[2] and being lethal in 65% of the cases.[3]

Data regarding the metastatic pattern of the UTUCs are scarce. In a study of 52 patients with UTUC, among whom 14 (27%) had ureteral cancer, metastatic sites were lymph nodes (75%), lungs (65%), liver (54%), bones (39%), and peritoneum (19%).[4]

Hereby, we present a case of a male patient, with ureteral transitional carcinoma with metastatic disease to the collateral testicle, mimicking orchiepididymitis.

CASE REPORT

A 67-year-old Caucasian male, former smoker, presented at our center, after being diagnosed with urothelial cancer of the lower left ureter, treated by robotic left ureteral nephrectomy and iliac lymph nodes resection in April 2019. The primary neoplasm was located at a distance of 0.4 cm from the ureterovesical junction, measuring 2.6 cm × 1.2 cm × 0.8 cm, and extending through the bladder cuff area. The histologic examination revealed a poorly differentiated, papillary, nodular and compact, and urothelial carcinoma,

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/UA.UA_124_20

How to cite this article: Gazouli I, Tsampalas S, Tsimaris I, Zarkavelis G, Grivas N, Kampletsas E, *et al*. Ureteral carcinoma metastasizing to the testicle: Can misdiagnosis of orchiepididymitis be avoided? Urol Ann 2021;13:86-8.

with focal necrosis and lymphovascular invasion. Immunohistochemistry was compatible with a mixed p-53-like and basal-like molecular subtype and Ki67 expression reached 30%–40%. The neoplasm infiltrated the muscular layer and the periureteral adipose tissue, while surgical limits were focally infiltrated. Eight out of the nine common iliac lymph nodes were infiltrated; the neoplasm was staged as pT3N2M0.

The patient received adjuvant chemotherapy with carboplatin and gemcitabine, from May to July 2019, and in August 2019, the patient underwent radiotherapy.

In October 2019, the patient was lamenting a painful and warm left testicular enlargement. Scrotal US and Urological examination were performed, orchiepididymitis was diagnosed and the patient was put on treatment with ciprofloxacin with a transient clinical benefit and pain reduction. in parallel, abdominal computed tomography scans [see Figures 1,2] evidenced local cancer progression, with malignant infiltration of the bladder, left sperm cyst, and inner iliac blood vessels. Immunotherapy with pembrolizumab was thereafter administered. In December 2019, testicular pain and enlargement of the left scrotum notably worsened, while swelling and discomfort appeared. Scrotal ultrasound revealed a cystic lesion in the center of the left testicle. Differential diagnosis between resistant orchiepididymitis or abscess was set and intravenous antibiotic treatment was again provided. Nonetheless, no improvement was noted, pain was unrelenting, and a left orchiepididymectomy was performed in January 2020. Both the left testis and epididymis were found infiltrated by the original urothelial carcinoma with a clean spermatic tone upper limit.

The patient's clinical condition ameliorated after the surgery, with significant pain reduction. Immunotherapy was continued, but in May 2019, disease progression was observed, and the patient was set in third-line treatment with vinflunine.

DISCUSSION

We report the case of an urothelial carcinoma of the left lower ureter, with metastasis to the collateral testicle, as the first manifestation of distant metastatic disease. Since its clinical presentation was mimicking an acute orchiepididymitis, it misled physicians with consequent delay in antineoplastic treatment provision.

Misleading testicular metastasis from urothelial carcinomas of the upper urinary tract, mimicking orchiepididymitis, have been already reported in literature, both for upper and lower ureteral locations [Table 1].[5-8]

Figure 1: Lower abdominal computed tomography scan, showing local disease regression within the left inguinal area, with infiltration of the left bladder wall

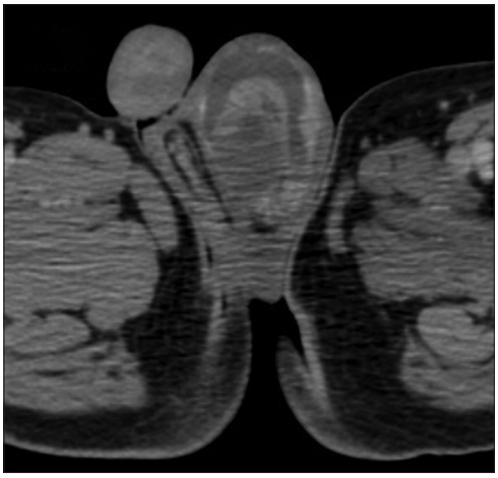

Figure 2: Lower abdominal computed tomography scan, showing metastatic spread to the left testicle, with prominent scrotum enlargement

Table 1: Table summarizing reported cases of ureteral carcinomas giving testicular metastases, initially misdiagnosed as orchiepididymitis

Case#	Primary location of urothelial carcinoma/stage	Time from the initial diagnosis to testicular involvement	Clinical manifestation	Reference
Present	Left distal ureter- T3N2M0	7 months	Scrotal pain, swelling	present
1	Left Renal pelvis - T3N1M0	7 months	Scrotal pain, discomfort	Wang *et al*., 2020
3	Left renal pelvis-pT3N0M0	2 years	Chronic left orchiepididymitis	Kubiak *et al*., 2016
2	Left proximal ureter-not known	0 (testicular metastasis at initial presentation)	Testicular swelling	Manav *et al*., 2014
4	Left ureter-not known	5 months	Testicular palpable mass	Wang *et al*., 1995

Hence, the question is how we can suspect and explain this unusual metastatic spread to provide a prompt and timely anticancer treatment. Genitourinary anatomy and timing are probably the two most important tools that can help physicians in differentiating diagnosis between testicular neoplastic metastatic spread and an orchiepididymitis.

With respect to anatomy, metastatic neoplastic disease generally occurs through vascular, lymphovascular, and direct spread of malignancies. Since reverse blood and lymph flow may be noted in various physiologic and pathological conditions, "reversal flow location metastasis" may develop. Testicular "reverse-flow" metastatic spread from lower, median, and upper ureteral and pelvic malignancies may follow two different blood/lymphatic reverse flow routes. Left ureteral and pelvic neoplasms may spread to the ipsilateral testicle through of lymphatic/vascular reticulum and through reverse blood flow from the left renal to the left testicular vein.[5,7,9,10] Similarly, and for both sides, a malignancy of the inferior part of the ureter (i.e., ureteral loop and ureteral bladder implant) may directly invade nearby organs, the seminal vesicle and last part of vas deferens, and afterward spread to the ipsilateral testicle through the deferens duct and its lymphatic/vascular domains. In our case, disease extended within the bladder cuff, compromising surgical limits, and subsequently spreading to the urogenital system through infiltration of the left seminal vesicle and the left vas deferens.

Timing is not a redundant issue. Although an orchiepididymitis may potentially affect any individual, such a diagnosis following soon after a surgery or a diagnosis of a locally advanced cancer of the ureter should raise clinical suspicion of a potential reverse flow metastatic spread, and the possibility of malignancy should be included in the differential diagnosis algorithm.

Of note, the immunophenotype of the primary neoplasm was compatible with p-53-like and basal-like urothelial carcinoma, two molecular subtypes associated with rapid disease dissemination and resistance to treatment as well as squamous histologic differentiation, also described in the testicular metastatic site.

In conclusion, time from oncological detection/management and knowledge in blood and lymph reverse flow routes may avoid misleading diagnoses and cancer treatment delays of testicular metastasis from ureteral carcinomas mimicking orchiepididymitis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgment

The authors have nothing to acknowledge.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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