Case Report

Metastatic renal pelvis carcinoma to the testis: a case report and review of the literature

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Abstract: Metastasis from urothelial carcinoma to the testis is rare. This case report presented an extremely rare case of testicular metastasis from renal pelvis carcinoma in a 69 year old man who had experienced painless left testicular swelling, after he underwent radical nephroureterectomy and bladder cuff excision for the urothelial carcinoma of left renal pelvis ten years ago. Physical examination found a 2- to 3-cm mass in the left testicle and he was slightly tender on palpation. A scrotal ultrasound demonstrated a soft tissue mass, measuring 3.0×2.5×2.0 cm, within the left testicle. Left radical orchiectomy was performed. The pathologic diagnosis was metastatic urothelial carcinoma of the left testicle. We reviewed 12 cases of testicular metastasis from urothelial carcinoma in the existing literature in English. To our knowledge, our case is the first individual case report of testicular metastasis from renal pelvis urothelial carcinoma. We hypothesized that the most possible pathway for testicular metastasis from urothelial carcinoma is the lymphovascular system and transurethral surgery. Excision of local lesions in selected patients is suggested and may provide satisfactory management of the tumor.

Keywords: Renal pelvis carcinoma, urothelial carcinoma, metastasis, testicular neoplasm

Introduction

Urothelial carcinomas (UCs) are the fourth most common tumors [1]. Bladder tumors account for 90-95% of UCs and are the most common malignancy of the urinary tract. However, Upper tract urothelial carcinomas (UTUCs) are uncommon and account for only 5-10% of UCs [1]. The most common metastasis of UC is to the regional lymph nodes, although metastasis to the bone, lung, and liver is not rare [2]. A multitude of tumor types metastasizes to the testes, including some sarcomas, but most studies have found tumors from prostate, lung, skin (melanoma), colon and kidney in descending order of frequency, to be the more common ones [3]. Metastasis from UC to the testis is very rare. We searched the English medical literature using the MEDLINE/PUBMED database. Our search yielded 12 cases of testicular metastasis from UCs (Table 1) [4-15]. Only two case reports are available in the literature regarding UTUCs metastasizing to the testicle [6, 15]. This report presented an extremely rare case of metastatic renal pelvis carcinoma to the testis. To our knowledge, this is the first individual case report of testicular metastasis from renal pelvis urothelial carcinoma.

Case report

A 69-year-old man initially presented to a local hospital in October of 2005 with a symptomatic visible hematuria. His preoperative investigations revealed a left renal pelvis tumor. A cystoscopy at the time was normal. Open radical nephroureterectomy with bladder cuff excision was performed and the histology showed a moderately differentiated papillary urothelial carcinoma of the left renal pelvis with invasion to the muscularis. He presented again in November 2009 with gross, painless hematuria. Cystoscopy showed a small papillary tumor arising from the prostatic urethra and a 2-cm tumor to the left bladder wall. Transurethral resection of the tumor (TURBT) showed G3pT1 UCs of the bladder and prostatic urethra. After surgery, he was scheduled to start instillations
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**Table 1. Clinical characteristics of reported cases of testicular metastasis from urothelial carcinoma: a review of the literature**

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Author</th>
<th>Age, years</th>
<th>Clinical presentation of primary tumors</th>
<th>Treatment of primary tumors</th>
<th>Pathology of primary tumors</th>
<th>Time of testicular metastasis</th>
<th>Laterality and symptom of testicular metastasis</th>
<th>Other sites of metastatic presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Turo R et al</td>
<td>61</td>
<td>5-cm tumor from the base of the bladder</td>
<td>TURBT + radical cystoprostatectomy</td>
<td>G3pT4</td>
<td>2 years</td>
<td>Right, painless swelling</td>
<td>Not noted</td>
</tr>
<tr>
<td>2</td>
<td>Mahmalji W et al</td>
<td>72</td>
<td>A large left-sided tumor of bladder</td>
<td>TURBT + BCG, cystoprostateurectomy (recurrence)</td>
<td>G2 pT1, Tis, with prostatic invasion</td>
<td>10 years</td>
<td>Left, testicular pain</td>
<td>Para-aortic lymphadenopathy</td>
</tr>
<tr>
<td>3</td>
<td>Manav AN et al</td>
<td>56</td>
<td>Left hydronephrosis, an 8.5 × 7.5 cm lymph node surrounding the left proximal ureter</td>
<td>Systemic gemcitabine-cisplatin chemotherapy</td>
<td>NA</td>
<td>The same time</td>
<td>Left, painless swelling</td>
<td>Left para-aortic lymph nodes, pelvic bone, left sixth rib</td>
</tr>
<tr>
<td>4</td>
<td>Oppong FC et al</td>
<td>67</td>
<td>Flat tumor on the anterior bladder wall with extension to the lateral walls</td>
<td>Intracavity doxorubicin and subsequent radiotherapy</td>
<td>Poorly differentiated, T1</td>
<td>2 years</td>
<td>Bilateral, painful swollen testis with hydrocele</td>
<td>Not noted</td>
</tr>
<tr>
<td>5</td>
<td>Watkin NA et al</td>
<td>68</td>
<td>NA</td>
<td>Cystodiathermy and radical radiotherapy</td>
<td>Poorly differentiated, T2</td>
<td>6 years</td>
<td>NA, a painful, hard testicular swelling</td>
<td>Not noted</td>
</tr>
<tr>
<td>6</td>
<td>Kozak GN et al</td>
<td>84</td>
<td>A small tumor below the bladder neck and a larger tumor to the left of the original tumor</td>
<td>TURBT + BCG</td>
<td>Poorly differentiated, T1</td>
<td>15 months</td>
<td>Right, bilateral hydroceles</td>
<td>Paratesticular lymph node</td>
</tr>
<tr>
<td>7</td>
<td>Binkley WF et al</td>
<td>69</td>
<td>A mass in the bladder trigone region</td>
<td>TURBT + local radiation</td>
<td>Transitional cell carcinoma (TCC) of urinary bladder and adenocarcinoma of the prostate</td>
<td>8 months</td>
<td>Left, tender and slightly enlarged</td>
<td>Lungs, scalene lymph nodes, liver, vertebra</td>
</tr>
<tr>
<td>8</td>
<td>Morgan K et al</td>
<td>74</td>
<td>A 2-cm papillary tumor</td>
<td>TURBT, cystoprostatectomy (recurrence)</td>
<td>G2, noninvasive (TURBT), high-grade TCC invading the trigone, prostate, and seminal vesicles (recurrence)</td>
<td>9 months</td>
<td>Right, firm and tender testis</td>
<td>Not noted</td>
</tr>
<tr>
<td>9</td>
<td>Thwaini A et al</td>
<td>74</td>
<td>NA</td>
<td>TURBT + radical cystoprostatectomy</td>
<td>G2 pT3 with involvement of the trigone</td>
<td>3 years</td>
<td>Left, painless swelling</td>
<td>Not noted</td>
</tr>
<tr>
<td>10</td>
<td>Kiely G et al</td>
<td>71</td>
<td>A large bladder mass</td>
<td>TURBT</td>
<td>G3T2, with squamous differentiation</td>
<td>1 year</td>
<td>Left, painless swelling</td>
<td>Pulmonary and paraatracheal tissue</td>
</tr>
<tr>
<td>11</td>
<td>Doherty AP et al</td>
<td>64</td>
<td>NA</td>
<td>Radical radiotherapy</td>
<td>Moderately differentiated, T3</td>
<td>6 years</td>
<td>Bilateral, enlarged</td>
<td>Not noted</td>
</tr>
<tr>
<td>12</td>
<td>Wang CN et al</td>
<td>64</td>
<td>Complete obstruction in the mid-third ureter</td>
<td>Radical nephroureterectomy with bladder cuff excision + radiotherapy + systemic chemotherapy</td>
<td>G2,T2</td>
<td>5 months</td>
<td>Left, painful swelling</td>
<td>Not noted</td>
</tr>
<tr>
<td>13</td>
<td>Present case</td>
<td>69</td>
<td>Left renal pelvis mass</td>
<td>Radical nephroureterectomy with bladder cuff excision</td>
<td>Moderately differentiated, with invasion to the muscularis</td>
<td>10 years</td>
<td>Left, painless swelling</td>
<td>Not noted</td>
</tr>
</tbody>
</table>

NA: not available.
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![Image](image.jpg)

**Figure 1.** Microscopic section of the left testicle shows a nested and infiltrated growth pattern of urothelial carcinoma. The heteromorphism of the tumor cells was obvious and nuclear mitosis was common (hematoxylin and eosin 100×).

**Figure 2.** The neoplastic cells exhibited marked positivity for cytokeratin (CK) 20 (CK20 immunostain; 40×).

of intravesical Epirubicin. Regular follow up and cystoscopic surveillance lasted two years after TURBT and showed no evidence of tumor recurrence. In July 2015, he presented to our urology department complaining of a one-month history of gross hematuria and painless left testicular swelling. Physical examination found a 2- to 3-cm mass in the left testicle and he was slightly tender on palpation. A scrotal ultrasound demonstrated a hypoechoic and hypervascular soft tissue mass, measuring 3.0×2.5×2.0 cm, within the left testicle and a normal right testicle. Cystoscopy revealed a flat cauliflower-like mass on the posterior wall of the bladder. Computed tomography (CT) showed thickening of the bladder wall and a possible mass in the posterior aspect of the bladder. No other hypermetabolic activity was observed anywhere else.

On July 22, 2015, he underwent TURBT and left radical orchiectomy. The resected left testicle with intact tunica albuginea measured 6.0×4.0×3.0 cm. On cut section, the testicle contained a well-circumscribed grayish-yellow mass about 2.6×2.1 cm. The lesion was confined to the testicle with no involvement of the tunicas, epididymis, paratesticular soft tissue, or spermatic cord. Microscopically, the tumor had a nested and infiltrated growth pattern. The heteromorphism of the tumor cells was obvious and nuclear mitosis was common (Figure 1). There were multiple intratubular tumor thrombus. The neoplastic cells exhibited marked positivity for cytokeratin (CK) 20 (Figure 2) and were negative for cluster of differentiation (CD) 117, placental alkaline phosphatase (PLAP), vimentin (VM), inhibin a. The spermatic cord and resection margins were negative. The pathologic diagnosis was metastatic UC of the left testicle.

The patient had an uneventful recovery and received adjuvant chemotherapy of cisplatin and gemcitabine.

**Discussion**

When radical nephroureterectomy with bladder cuff excision is performed, local recurrence of UTUC is rare and the risk of distant metastases is directly related to the risk factors such as tumor location, surgical waiting time, tumor stage and grade, lymphovascular invasion, surgical margins, pathological factors. The distant metastasis of UC to the bone, lung, and liver is not rare. By contrast, testicular metastasis from UC is exceptionally rare. Metastases to the testis are most commonly incidental findings at autopsy or in therapeutic orchiectomy specimens performed for the treatment of prostate cancer [16]. Prostate and lung together account for over 50% of the primary sites [10]. Clinically, there are no specific features that differentiate primary from secondary testicular tumors, as both may present with local pain, tenderness, painless swelling. Also, serum tumor markers such as alpha-feto protein (AFP) and human chorionic gonadotropin (hCG) are not helpful in distinguishing primary from secondary testicular tumors. Thus in older patients presenting a solitary testicular mass, the differential diagno-
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sis must include metastatic carcinoma. A personal history of cancer should first be investigated. The mean age of 13 patients with secondary testicular neoplasms in this series was 69 years with an age range from 56 to 84 years. In contrast, patients with primary testicular neoplasms are generally younger. According to the reviewed cases, 3/13 (23%) were in right side, 7/13 (54%) in left side, and 2/13 (15%) in bilateral testis. Four patients 4/13 (31%) felt testicular pain, 2 patients 2/13 (15%) first presented as hydrocele. Two patients were initially diagnosed as epididymitis and treated with antibiotics which turned out to be no effect. Most of the patients 10/13 (77%) had their primary tumor in the bladder and only 2/13 (15%) in the ureter. Only the case in our report found the primary tumor was from the renal pelvis. The length of time from the diagnosis of primary tumor to testicular metastasis ranged from 5 months to 10 years. Except in one case, the primary tumor and multiple metastasis were found at the same time [6].

The rarity of metastatic involvement of testis remains unexplained. The low incidence of secondary tumors to the testis is apparently due to the lower temperature of the scrotum, which could impair the metastatic ability of tumor cells from solid organs. It may also be due to blood-testis and blood-epididymis barrier. The tight junctions between Sertoli cells and epididymis epithelial cells respectively, build a functional barrier of utmost competence [17]. Various routes of spread of metastatic tumors to the testes have been suggested, including arterial embolization from the tumor, retrograde venous spread, retrograde lymphatic spread, direct spread along the vas deferens to the epididymis, and transperitoneal seeding through a patent tunica vaginalis. The dissemination mechanism seems to vary with type and location of the primary tumor, and one does not exclude the other [18]. Metastatic pathways from UCs to the testis remain speculative. There were only three UTUC cases in this series and one case was not confirmed by pathologic diagnosis [6]. Wang CN, et al [15] thought that the mechanism of ureteral cancer metastasis to the testis may be reflux from vas deferens. Tumor cells invaded into the vas deferens through cross of the ureter and the vas deferens. However, we don’t agree with them. Only metastasis in the condition that the ureteral tumor located near the vas deferens can be explained by their hypothesis. We think that lymphatic spread is a very important route and past transurethral surgery may promote the metastasis. In the present case, multiple intra-tubular tumor thrombus were found in the testicle specimen, suggesting lymphatic metastasis. In the reviewed cases, we find eight patients 8/13 (62%) accepted transurethral surgery before testicular metastasis. In our case, the patient underwent transurethral surgery for recurrent tumors of bladder and prostatic urethra. The bladder recurrence and transurethral operation may cause the tumor cells spread to the testicle. Another possible mechanism is through retrograde descent whereby tumor cells can directly seed via descent through the testicular veins. This theory may potentially explain the ipsilateral deposit of metastasis in our case.

Testicular metastases usually are a manifestation of widely disseminated tumors. Five patients 5/13 (38%) had other synchronous sites of metastasis in the reviewed cases. Therapeutic strategies used for any metastatic tumor include palliative chemotherapy, radiation, and sometimes surgery. Because there are no randomized clinical trials on resection of testicular metastasis from UCs, the benefit for resection of testicular metastasis is not clear. We suggest that surgery be done if the patient could endure. First, it can clarify the diagnosis. Then surgery can palliate symptoms and control tumor growth. And most importantly, resection of testicular metastasis from UCs may improve survival for these patients. There were two patients doing well at 1.5 years [11] and 21 months [15] after orchietomy. Post-operative platinum-based chemotherapy remains of clear benefit in improving survival and should be considered.

In conclusion, we present an extremely rare case of testicular metastasis from renal pelvis carcinoma. We hypothesized that the most possible pathway for testicular metastasis from UC is the lymphovascular system and transurethral surgery may promote the metastasis. Excision of local lesions is suggested and may provide satisfactory management for such patients.

Disclosure of conflict of interest

None.

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