

Synchronous bilateral urothelial carcinoma of the upper urinary tract – case report

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Abstract

There are approximately 30 case reports in the literature of synchronous bilateral upper tract urothelial carcinoma (UTUC) without bladder involvement^[1-11]. Surgical treatment, either open, laparoscopic or robotic approach, remains the standard therapy, but choosing the appropriate technique is crucial in this situation. Some patients with low-risk disease may benefit from a more conservative approach (e.g., endoscopic ablation, segmental resection), in order to preserve the renal function.

No specific guidelines for management have so far been formulated, given the rarity of disease.

We present the case of a patient with synchronous bilateral UTUC, involving renal pelvis, in which we decided radical nephrectomy on one side and a conservative intervention on the contralateral side, with very good clinical and functional results. The challenges in diagnosis and surgical management of such a case are highlighted and various available treatment options are presented.

Keywords: synchronous, urothelial carcinoma, upper urinary tract

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Introduction

Upper tract urothelial carcinoma (UTUC) represents approximately 5% of all urothelial carcinomas^[12], renal pelvis being four times more frequent involved than the ureter^[13,14]. Bilateral tumors may be synchronous or metachronous. Synchronous bilateral UTUC without bladder involvement are extremely rare.

Different behaviors of urothelial carcinoma of the renal pelvis and ureter have been reported in terms of tumor invasion and prognosis^[15]. Ureteral urothelial carcinoma is associated with a higher local or distant recurrence rate compared to urothelial carcinoma of the renal pelvis.

Renal urothelial carcinoma most frequently arises in the extrarenal part of the pelvis, followed by the infundibulocaliceal region^[16]. Tumor spread occurs by mucosal extension or local, hematogenous, or lymphatic invasion. The most common sites for metastases are the liver, bone, and lungs.

The development of minimally invasive surgery, which allows renal preservation in selected patients, makes accurate tumor staging mandatory to determine the appropriate therapy; staging is usually performed with computed tomography (CT) or magnetic resonance (MR) imaging.

Materials and methods

Patient I.A., female, 65-years old, without urologic history, presents total macroscopic hematuria and upper abdominal pain. She was diagnosed on a CT scan with right renal pelvis tumor and she was admitted in our institute, a tertiary urologic center, for further investigation and treatment.

The patient's medical history was significant for Hashimoto tiroiditis, high blood pressure and peptic ulcer.

At admission, the patient was asymptomatic and the clinical exam was in normal limits. She had no renal dysfunction on laboratory findings. Pulmonary radiography showed no pathological findings.

CT scan, made in other center, revealed right renal pelvis mass. (Fig. 1).

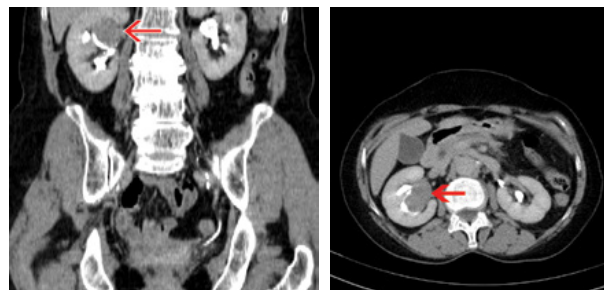


Fig. 1: Computed tomographic scan: right renal mass (red arrow)

Surgical intervention was performed with subtotal right nephroureterectomy by lumbar approach, with favorable postoperative course.

Gross examination revealed right kidney with dilated calyceal system with tumor invasion, which was whitish, friable and with areas of necrosis and intratumor hemorrhage. Microscopic examination revealed papillary urothelial carcinoma, well/moderately differentiated, G1/G2 (low-grade), pT2 stage. Rest of the renal parenchyma had an aspect of nonspecific chronic nephritis with spots of sclerogenic tendency. (Fig. 2).

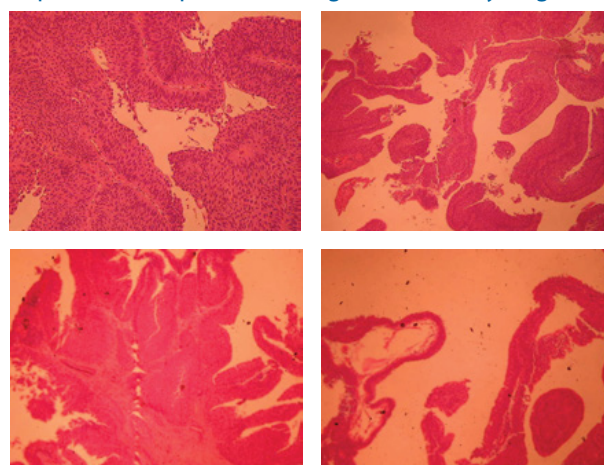


Fig. 2: Histopathologic aspects.

The postoperative ultrasonography evaluation showed a 14 mm tumor on the left posterior pelvis wall. Amagnetic resonance imaging (MRI) with intravenous contrast agent confirmed the finding, on the left pelvis posterior wall with slight extension in the middle calyceal groups, of a lacunar image of about 17/13 mm, with T1 and T2 hyposignal, without significant restriction on water diffusion sequence, that did not retain contrast agent; note that when changing the patient in ventral decubitus position, the lesion described above remained fixed on the posterior pelvis wall. The MRI appearance suggested both hematic and inflammatory substrate, but a tumor substrate could not be excluded

with certainty. (Fig. 3). Radiologist's recommendation was to reevaluate the patient.

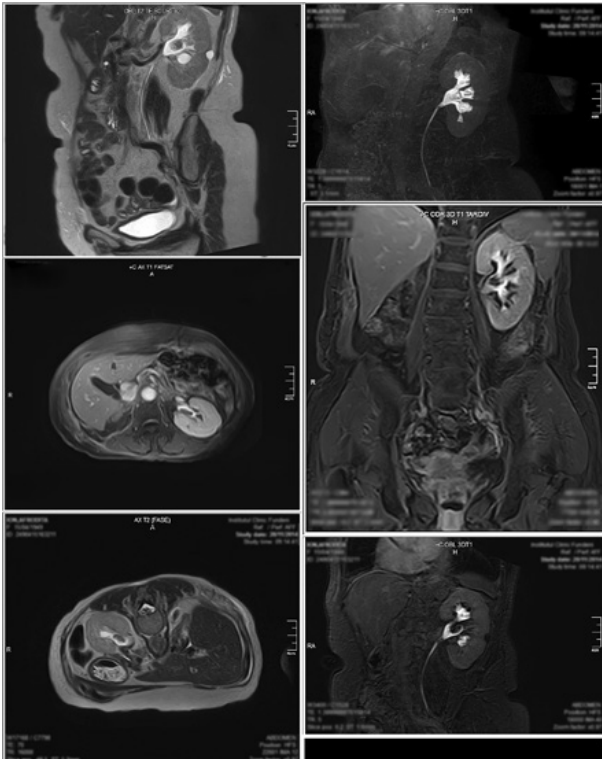


Fig. 3: Multiple MR aspects of left renal mass. Middle left – patient facing up. Lower left – patient facing down.

It was decided to delay surgery for the left renal pelvis tumor in order to allow the patient to recover after the first intervention. She was discharged with good general condition, afebrile, with clear and facile micturition.

Patient was readmitted after 4 weeks, asymptomatic. Left pyelotomy with resection of the pelvis tumor was performed, using lumbar approach. Histological examination confirmed the suspicion of urothelial tumor, revealing an urothelial papillary carcinoma with low malignant potential (PUNLMP). Macroscopic, the tumor was vegetant, whitish and friable. (Fig. 4).

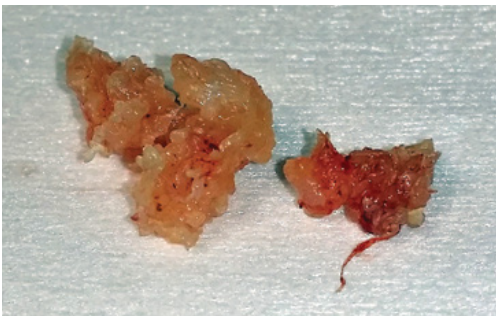


Fig. 4: Intraoperative aspect of left renal tumour.

Postoperative evolution was marked by macroscopic hematuria in day 4, possibly secondary to prophylactic anticoagulant therapy, for which a 3 way Foley catheter was inserted.

Control CT examination performed on day 5 postoperatively revealed spontaneously hyperdense content (content hematic) on the left pielocalyceal system and ureter, which appeared slightly dilated (Grade I) and a small accumulation of fluid thickness approx. 14 mm at the lodge of right nephrectomy. Under conservative treatment, the evolution has been favorable, subsequent scans showing total remission of the hematoma and left hydronephrosis.

The patient, asymptomatic, was periodically reassessed every 6 month, clinic and imagistic, without pathological elements.

Discussions

Synchronous bilateral UTUC has been reported to occur in 1%–2% of cases of renal lesions and 2%–9% of cases of ureteric lesions.

UTUC typically occurs in the 6th and 7th decades of life, with males affected three times more often than females^[16]. Besides increasing age and male gender, the most important risk factor is smoking, with smokers being two to three times more likely to develop UTUC than nonsmokers. Other known risk factors are: chemical carcinogens (aniline, benzidine, aromatic amine), cyclophosphamide therapy, analgesic abuse, particular long-term use of phenacetin^[17-21], heavy caffeine consumption, stasis of urine and structural abnormalities such as horseshoe kidney. Higher incidence was noted in areas in which Balkan nephropathy or Taiwan black-foot disease is endemic. These conditions are associated with interstitial nephritis, uremia, and multifocal and bilateral urothelial tumors. Blackfoot disease in Taiwan is associated with the contamination of drinking water with arsenic and other heavy metals, whereas the etiology of Balkan nephropathy remains an enigma^[22, 23, 24].

Patients with multiple recurrences of multifocal bladder carcinoma also have an increased incidence of bilateral tumors. Many hypotheses have been suggested:

1. that upper tract tumor cells originate in the bladder and that multiple resections damage the antireflux function of the ostiae^[25]
2. some genetic evidence support the theory that multifocal bladder tumors can arise from the uncontrolled spread of a single transformed cell^[26]

- the entire urothelial surface has undergone a neoplastic change (the so-called field effect).

Hematuria is the main presenting symptom. Other initial presenting symptoms are incidental findings on physical examination and lower abdominal or flank pain.

Compared with bladder, the upper urinary tract has few anatomical differences, structural and histological. One of them is the rich vascular and lymphatic network, which causes rapid metastasis in retroperitoneum. Macroscopic, UTUC are highly variable in appearance from small areas neof ormation up to large tumors, infiltrative, ulcerating or with necrosis areas. Eighty-five percent of UTUC are low-stage, superficial, papillary neoplasms with a broad base and frondlike morphologic structure [27]. These tumors are usually small at diagnosis, grow slowly, and follow a relatively benign course [28]. Histologically: 95% have epithelial origin, the rest have mesenchymal origin.

Several studies found a correlation between grade and pT stage, i.e. that tumors at a lower stage tended to be lower grade tumors while those at a higher stage tended to be higher grade tumors.

Conventional imaging modalities such as excretory urography (EU), retrograde pyelography (RP), and renal ultrasonography (US) still play a key role in the assessment of hematuria, in combination with endourologic techniques. However, multiphasic CT urography offers superior detection of urothelial tumor and allows accurate staging of detected lesions at the same examination. MR imaging, including the newer techniques of MR angiography and MR urography, offers comparable evaluation in patients who cannot tolerate iodinated contrast material and in whom multiplanar, vascular, and collecting system imaging is required.

Surgical treatment, open, laparoscopic or robotic approach, remains the standard therapy, but choosing the appropriate technique is crucial in this category of patients.

Research in recent years has led to a better understanding of the evolution and prognostic factors in this kind of neoplasia, conservative surgical treatment indications list being open. The main indications for segmental resection should be:

- low-grade, low-stage transitional cell carcinoma;
- solitary kidney with a ureteral tumor;
- bilateral synchronous ureteral tumors;
- poor renal function;
- high-risk patients.

The major problem in conservative surgery approach remains the high rate of relapse and disease progression, between 15 and 45% in various studies. Associated renal insufficiency, high grade and stage of disease, and positive lymph node status are known poor prognostic factors. BCG or Mitomycin C administration in situ decreases the risk of recurrence and / or progression.

In patients with conservative surgery, close follow up is extremely important, local recurrence being frequently asymptomatic. The risk of recurrence persists even at 5-10 years, so surveillance should be continued for 10 years and perhaps longer. Up to 50% of patients initially presenting with UTUC, more commonly with ureteric tumors than with renal tumors, will develop metachronous tumors in the bladder, typically within 2 years of surgical treatment. [29, 30]

According to the National Comprehensive Cancer Network guidelines, regional lymphadenectomy and neoadjuvant chemotherapy should also be considered in selected patients with high-risk disease.

Conclusions

Synchronous bilateral tumors are very rare. The long-term outcome for patients with synchronous tumors is largely unknown, because our current knowledge is based primarily on approximately 30 case reports with short follow-up.

The treatment and follow-up of patients with bilateral ureteral or renal pelvic tumors must be individualized on the basis of the type of surgery performed. Vigilant urologic and radiologic follow-up is warranted to assess for metachronous lesions and recurrence, at least during the early years, when the risk of tumor recurrence is greatest, are appropriate.

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