



Poorly differentiated urothelial carcinoma of ureter presenting as Bulbar Palsy-An unusual presentation

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Summary

Urothelial neoplasms of the kidney and ureter (upper urinary tract) are uncommon, accounting for approximately 5% of all epithelial tumors of the urinary tract, with most urothelial tumors occurring in the urinary bladder¹⁻⁸. Patients with upper tract urothelial neoplasms usually seek care because of gross hematuria (80%), flank pain (20%), and/or a palpable mass (10%).^{7,15,16}. Here, we present a case of poorly differentiated urothelial carcinoma from upper ureter with a unique presentation with bulbar palsy.

Case Report

A 55 years old Female patient presented with H/O low back ache since 6 months, difficulty in swallowing both for liquids and solids since 1 month.

On examination- she was found to have left 9th to 12th cranial nerve palsies. She was admitted and evaluated for bulbar palsy. Her MRI brain revealed a fairly well defined altered intramedullary signal involving the clivus on the left with mild expansion of bone – features suspicious for metastasis.

Hence patient was evaluated to search for the primary with CECT abdomen and chest which revealed possibility of neoplastic lesion in the left upper ureter (? TCC) with retroperitoneal adenopathy, hepatic & skeletal metastasis. Well defined lobulated intense heterogeneously enhancing hypodense lesion in the left

paratracheal region extending superiorly into the lower neck.

Excision biopsy of the paratracheal lesion revealed poorly differentiated carcinoma. IHC of the sample revealed metastatic poorly differentiated urothelial carcinoma.

This was unique presentation where poorly differentiated urothelial carcinoma presented as bulbar palsy.



Fig.1 Left hypoglossal weakness

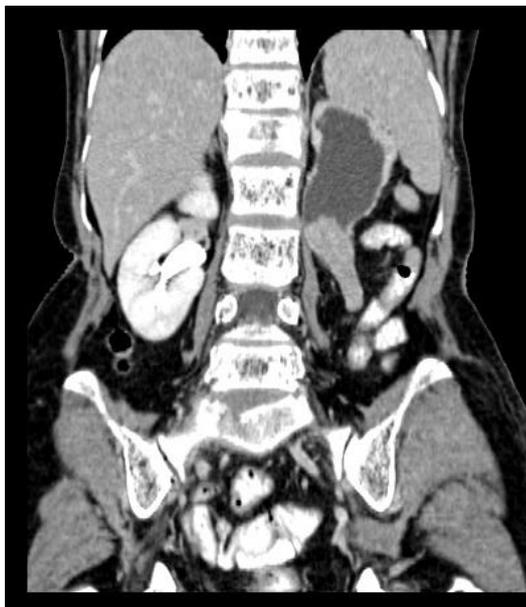


Fig.2 CT Abdomen-left Ureteric mass with hydronephrosis and vertebral metastasis

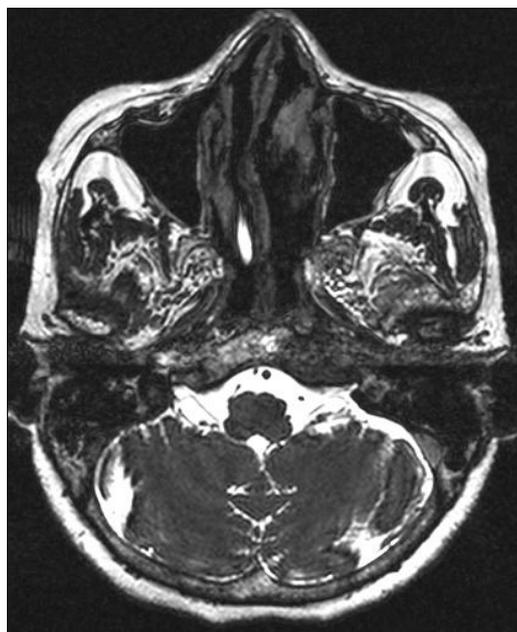


Fig.3 MRI Brain-Metastasis to clivus on left side

Discussion

Urothelial neoplasms of the kidney and ureter (upper urinary tract) are uncommon, accounting for approximately 5% of all epithelial tumors of the urinary tract, with most urothelial tumors occurring in the urinary bladder¹⁻⁸.

Nevertheless, urothelial tumors of the renal pelvi-calyceal system are rare and are thought to account for 4% to 15% of primary kidney neoplasms in the United States.^{1,3-6,9-12}

Ureteral tumors are even less common, representing 1% of all urothelial tumors.^{1,10,13,14}

Epidemiology and Risk Factors

Most studies have found urothelial neoplasms of the kidney and ureter to be more common in men than in women.^{1-3,5-7,9-17}

These tumors peak in the six and seventh decades of life, with a mean age at initial diagnosis of about 65 years, and appear to affect whites more often than other races in the United States.^{5,9,12}

Urothelial neoplasms are more common in the renal pelvises and calyces than in the ureters.^{1,10,13,17,20-22}

No definitive predilection for involvement of the right or left side has been found, and fewer than 3% are synchronous and bilateral.^{9,12,16,23,24}

Many of the risk factors for developing urothelial neoplasms of the upper tract are similar to those of the bladder and include cigarette smoking,^{4,17,25} exposure to industrial chemicals (dye, petroleum, rubber, and leather industries),^{4,15,17} and chronic irritation (stones and infection).^{7,26,27}

Exposure to radiographic contrast agents that contain thorium has also been associated with the development of upper tract tumors.¹⁷

Patients with various forms of tubulointerstitial nephritides are also at greater risk for developing urothelial neoplasms of the renal pelvis, as are people in certain regions of the world.

Analgesic nephropathy, which develops secondary to abuse of phenacetin-containing analgesics, is associated with renal papillary necrosis, capillarosclerosis (increased basement membrane around subepithelial capillaries), and urothelial neoplasms.¹⁷

In regions where phenacetin abuse is high, urothelial neoplasms represent up to 24% of kidney neoplasms. Unlike most patients with urothelial neoplasms of the renal pelvis, the male/female ratio is lower

for analgesic-related tumors, and the mean age at diagnosis is about 5 years earlier.

Patients with endemic nephropathy, described in the Balkan countries (Romania and Bulgaria and

[the former]Yugoslavia), have a high frequency of upper tract urothelial neoplasms. Patients are most commonly diagnosed between the third and fifth decades of life, and the incidence of bilateral tumors is approximately 10%.

Renal failure, which is often the cause of death, develops in most patients.

The exact cause of the disease is unknown, but it is postulated to be silicates in the drinking water.

A fairly recently described nephropathy, Chinese-herb nephropathy, has been linked to the development of urinary tract neoplasms, particularly in the upper tract. This disease originally was described in Belgian women who were enrolled in a “slimming clinic.” The cause of the nephropathy is the ingestion of various agents, including Chinese herbs, with the main causative agent purported to be aristolochic acid. Urothelial neoplasms develop in approximately 40% of patients with this nephropathy.

In certain regions of Taiwan where “blackfoot disease,” a peripheral vascular disease due to sustained exposure to arsenic, is endemic, there is an unusually high incidence of renal pelvic and ureteral urothelial neoplasms. The cause is postulated to be related to the ingestion of compounds in well water.

In certain regions, urothelial neoplasms arise in women slightly more often than in men and account for approximately 10% and 40% of all urothelial carcinomas and renal carcinomas, respectively.

Certain syndromes, including hereditary nonpolyposis colorectal carcinoma (Lynch type II syndrome) and Muir-Torre syndrome, may also be associated with an increased risk for developing urothelial neoplasms of the upper tract.

Table 11
Classification of Urothelial Neoplasms of the Kidney and Ureter*

Papillary neoplasms
Inverted papilloma [†]
Papilloma
Papillary urothelial neoplasm of low malignant potential
Papillary urothelial carcinoma
Low-grade
High-grade
“Flat” lesions
Urothelial dysplasia
In situ urothelial carcinoma
Invasive urothelial carcinoma
Conventional
With aberrant differentiation (squamous, glandular, small cell/neuroendocrine)
Spindle cell carcinoma (sarcomatoid carcinoma)
Carcinosarcoma
Other [‡]

* Extrapolated from Epstein et al.¹⁸

[†] Not truly papillary.

[‡] Includes the following variants of urothelial carcinoma: nested, micropapillary, microcystic, lymphoepithelial, and plasmacytoid.

Manifestations and Clinical Evaluation

In the upper tract, urothelial neoplasms may arise at any site lined by urothelium, including the renal papillae, calyces, pelvis, ureteropelvic junction, and ureter.

Patients with upper tract urothelial neoplasms usually seek care because of gross hematuria (80%), flank pain (20%), and/or a palpable mass (10%).^{7,15,16.}

Hydronephrosis or hydroureter may occur secondary to obstruction. Evaluation of the patients consists of a detailed history and physical examination followed by urinalysis, bladder cytology, upper tract radiographic imaging, and cystoscopy. Contrast studies of the upper tract consist of intravenous urograms, computed tomography, and, possibly, retrograde pyelography. Radiologic filling defects found on contrast studies may represent nonneoplastic or neoplastic processes and require confirmation by a cellular or a tissue diagnosis.

Cellular diagnosis begins with bladder cytology, which has a relatively high false-negative rate in cases of upper tract urothelial neoplasms, especially with low-grade tumors.^{26.} Brush cytology, which requires ureteral manipulation, anesthesia and fluoroscopic control, has an accuracy of 78%.²⁶

The most accurate diagnostic modality and one that has been accepted as a standard of care for the evaluation of abnormal filling defects and obstruction is ureteroscopy with tissue biopsy under direct visualization. Stroom et al²⁷ found that standard evaluation of 12 patients with upper tract urothelial neoplasms, using intravenous urograms, computed tomography, cystoscopy and cytology provided the correct provisional diagnosis in 7 patients. The addition of ureteroscopy increased the number of patients with correct provisional diagnoses to 10.

Additional Patient and Tumor Characteristics

Several studies have found that patient age correlates with survival, and women may have a worse outcome.

Patients with upper tract urothelial neoplasms have a high rate of multifocal tumor and tumor recurrence. In a review by Charbit et al,²⁴ multifocal disease was present in 30% of patients with clinically identified solitary lesions who underwent radical surgery.

From 7% to 58.5% of patients with upper tract disease have urothelial neoplasms elsewhere, before, concomitant to, or after the renal or ureteral tumor,^{2,3,5,6,9,10,12,23,24} and in a significant proportion of patients (5%-56%), bladder carcinoma develops after an upper tract tumor.^{6,10,20,21,23}

In contrast, only 4% of patients with bladder cancer develop upper tract disease (the percentage does not include those with involvement of the distal ureter at cystectomy).¹⁵

In general, the presence of multiple urothelial neoplasms and tumor shape are considered to be prognostic indicators,^{2,6,11,23} although a few reports have not found these features to be significant predictors of survival in upper tract disease.²⁵

The presence of vascular invasion is an adverse predictor of survival and usually is associated with high-grade and high-stage disease.

As expected, vascular invasion and high tumor grade and stage have been shown to correlate with metastases.

The most common sites for metastasis in patients with upper tract urothelial neoplasms are regional lymph nodes, lungs, liver, and bone.^{10,11,15,17,25.}

A multivariate analysis of 109 patients with upper tract urothelial neoplasms by Okikawa et al demonstrated that lymph node status was an independent predictor of survival.

Conclusion

Urothelial carcinoma of ureter is extremely rare malignancy with typical presentation with haematuria, flank pain or as a mass. Here is a rare presentation of poorly differentiated urothelial carcinoma presenting with bulbar weakness with no prior typical symptoms of the disease.

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