Urology Case Reports 29 (2020) 101099

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: http://www.elsevier.com/locate/eucr

Oncology

Primary small cell carcinoma of the ureter with hydronephrosis: A case report

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ARTICLE INFO

Keywords:
Small cell carcinoma
Ureteral cancer

ABSTRACT

Small cell carcinoma in the ureter is extremely rare, with few cases reported in the literature. The current report describes the case of a 63-year-old man who presented with right-side back pain. A mass was identified in the right ureter. A nephroureterectomy was performed. Subsequent microscopic examination revealed that the mass comprised a monotonous population of small cells and that the carcinoma cells were positive for cluster of AE1/AE3 and synaptophysin. The tumor was diagnosed as a ureteral small cell carcinoma. Adjuvant chemotherapy was administered with 80 mg/m^2 intravenous cisplatin on day 1 and 100 mg/m^2 etoposide on days 1–3, every 21 days for 2 cycles. The patient has remained disease-free 6 months after surgery.

Introduction

Small cell carcinoma is usually found in the lungs.[1] Primary small cell carcinoma of the urinary tract is a rare cancer: it accounts for less than 0.5% of urinary tract tumors,[2] mostly localized in the bladder and prostate, although its localization in the ureter is extremely rare. Because of its rarity, little is known about the natural history of ureteral small cell carcinoma. The prognosis of small cell carcinoma is poor; surgery is not curative. Adjuvant chemotherapy might extend survival of these patients. We report here a case of primary small cell carcinoma of the ureter with hydronephrosis.

Case report

A 63-year-old man presented with right-side back pain that had persisted for one month without symptoms of bladder irritation or gross hematuria. Physical examination yielded normal results. Routine laboratory examination results were unremarkable. Abdominal ultrasound was performed immediately, revealing grade 3 right hydronephrosis. A computed tomography (CT) scan of the abdomen revealed a 2.5 × 2.0 cm mass in the right ureter, with right hydronephrosis and lithiasis (Fig. 1-a, b). Chest CT was also reviewed, revealing no primary or metastatic lung lesion. We observed no lymphadenopathy in the pelvis, retroperitoneum, or para-aortic region. The patient underwent a right nephroureterectomy. A mass was found within the wall of the right ureter, with grossly negative surgical margins (Fig. 2-a, b). Microscopic examination showed that the tumor comprised small cells with a round to fusiform shape, scant cytoplasm, finely granular nuclear chromatin, and absent or inconspicuous nucleoli (Fig. 3-a, b). Immunohistochemical staining for the tumor cells was positive for cluster of AE1/AE3 and synaptophysin. The patient was diagnosed with small cell carcinoma of the ureter. The surgical margins were negative. The pathological stage at diagnosis was pT3N0M0. After diagnosis of primary small cell carcinoma of the ureter and absence of metastasis, adjuvant chemotherapy was administered, followed by 80 mg/m^2 intravenous cisplatin on day 1 and 100 mg/m^2 etoposide on days 1–3, every 21 days for two cycles. The patient has remained disease-free 6 months after surgery. The patient is living uneventfully.

Discussion

The bladder is the most common location of small cell neuroendocrine carcinomas, but they are extremely rare in the ureter, with fewer than 50 earlier cases reported in the literature since the first case was

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https://doi.org/10.1016/j.eucr.2019.101099
Received 2 October 2019; Accepted 10 December 2019
Available online 14 December 2019

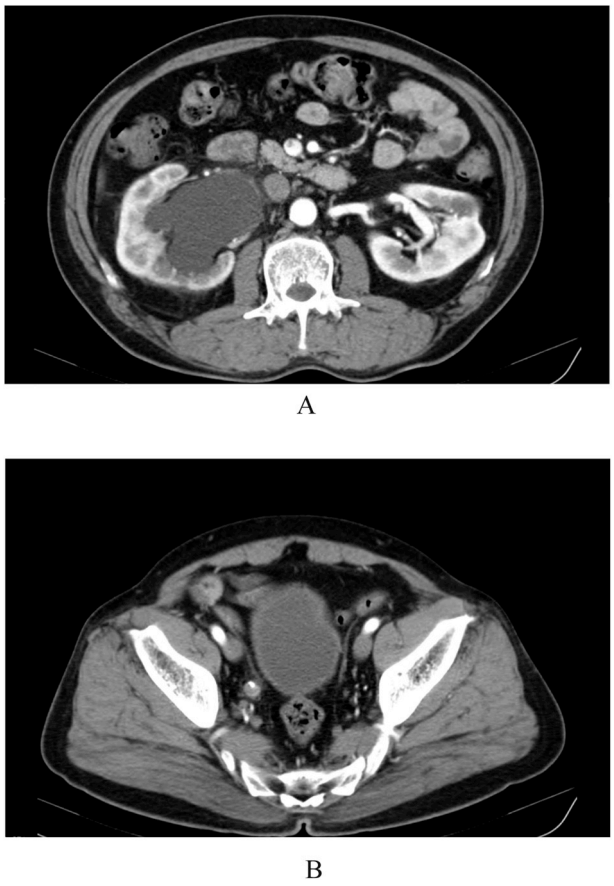


Fig. 1. Computed tomography (CT) scan of the abdomen showing a 2.5 × 2.0 cm mass in the right ureter, with right hydronephrosis (a) and lithiasis (b).

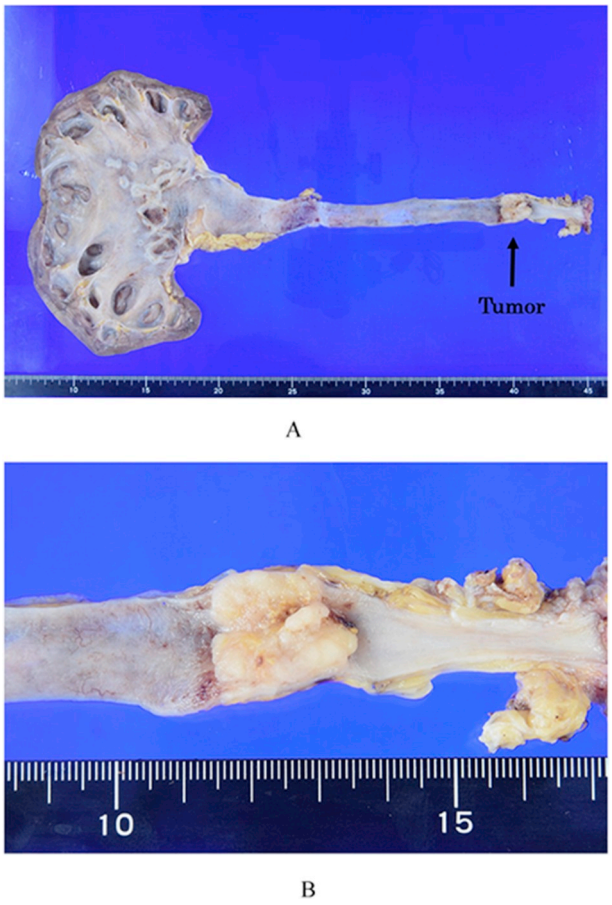


Fig. 2. Mass with grossly negative surgical margins found within the wall of the right ureter (a, b).

reported by Ordonez et al. in 1986.[3] The origin of small cell carcinoma of genitourinary systems remains unclear, but the urinary tract contains neuroendocrine cells that might be a source of small cell carcinoma.[4]

Hematuria and pain are the most commonly reported symptoms of this tumor. Hematuria, usually gross, results from vascular invasion, whereas pain is secondary to hydronephrosis following obstruction of the ureter.[5] The pain increases gradually over time, becoming chronic, allowing a differential diagnosis from lithiasis, which presents as acute pain. Ultrasonography is the initial choice for imaging in a suspected obstruction of the urinary tract. A second-level procedure is CT scan, which can establish the presence of a mass, confirm an associated hydronephrosis because of the obstruction, and confirm tumor extension.[2]

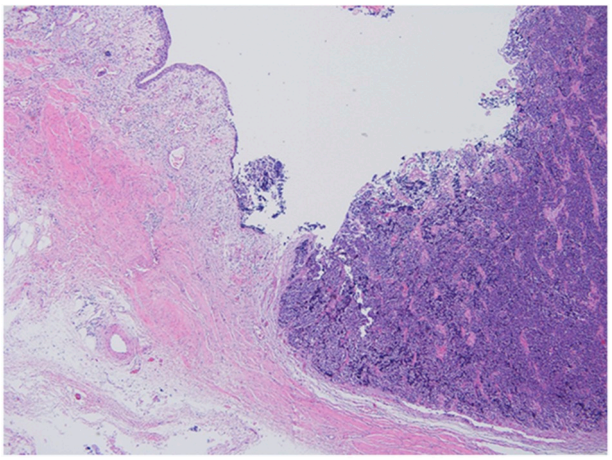
The diagnosis of these tumors depends on their pathology and immunohistochemistry. Histologically, these tumors are rarely pure. They are frequently admixed with other components including adenocarcinoma, chondrosarcoma, leiomyosarcoma, and urothelial cell carcinomas. These tumors consist of small cells, with prominent nuclei, scant cytoplasm, and granular chromatin. In addition, a high mitotic index might be observed. Furthermore, immunohistochemical staining for specific neuroendocrine markers, including CD56, neuron-specific enolase, Syn and CgA, might distinguish neuroendocrine small cell carcinoma from other tumors.[3]

The clinical course of these tumors is usually aggressive. Median survival is only 17 months, with a 51.9% 1-year survival rate. The lymphatics, the lung, and the liver are common metastatic sites for small cell carcinoma of the ureter. High incidence exists of early dissemination and a frequent recurrence of these tumors, which might be attributable to occult metastasis at initial presentation.[1]

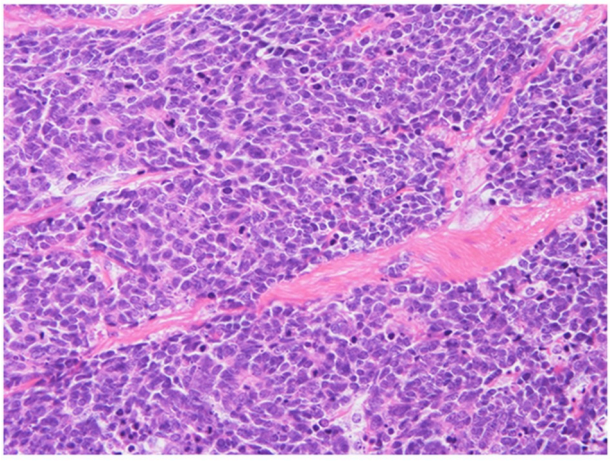
The primary treatment is surgical remotion of the tumor by ureterectomy or nephroureterectomy depending on the clinical status of the patient, stage, and localization of the tumor. Because of the aggressive course of small cell carcinoma of the ureter, the surgeon must address the radicality of the excision as early as possible, considering that in most cases the resection alone does not seem to stop progression of the disease. Many clinicians have proposed that multimodality therapy, including surgery, radiation, and chemotherapy is fundamentally important for patients with small cell carcinoma of the urinary tract. The surgical treatment is usually followed by adjuvant chemotherapy and radiotherapy.[2,4]

Earlier, Ouzzane et al. reported that the median survival time of patients with upper urinary tract small cell carcinoma was 24 months for those administered with chemotherapy versus 12 months for those who underwent surgery alone. Furthermore, patients administered platinum-based chemotherapy appeared to exhibit a higher median survival time than those who were not administered a regimen containing platinum. The combination of etoposide and cisplatin is a very frequently used regimen, with a response rate of 69% found in one study of the treatment of extrapulmonary small cell carcinoma.[3,4] In the present case, the patient received 80 mg/m^2 intravenous cisplatin on day 1 and 100 mg/m^2 etoposide on days 1–3, every 21 days for two cycles. The patient has remained disease-free 6 months after surgery. Clinical results indicate that etoposide and platinum might also be effective for ureteral small cell carcinoma.

However, for most patients with small cell carcinoma of the ureter, these treatments are insufficient to achieve a cure. Other strategies must be used to improve outcomes for patients with this lethal cancer. New molecular therapeutic approaches have been investigated for this tumor. Reportedly this tumor expresses c-kit and carries a platelet-derived growth factor receptor-α (PDGFRA) mutation, which might be



A



B

Fig. 3. The tumor comprised small cells with round to fusiform shape (a), scant cytoplasm, finely granular nuclear chromatin, and absent or inconspicuous nucleoli (b).

potential therapy targets.[5]

Conclusion

Small cell carcinoma of the ureter is an aggressive disease. Surgery combined with adjuvant chemotherapy of the combination of etoposide and platinum might improve survival rates. Although this is a rare tumor, effective targeted therapies are anticipated for application to improve overall survival.

Financial support and sponsorship

None.

Declaration of competing interest

The authors have no conflict of interest, financial or otherwise, in relation to this study.

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