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Advanced small-cell bladder cancer into a ureterocele: A case report and literature review

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ABSTRACT

Small cell bladder cancer (SCBC) is found in 0.5–1.2% of all bladder tumors. Ureteroceles are dilatation of the distal portion of an ectopic ureter, which association with tumors are rare. This article reports the first case described of an SCBC developed into a ureterocele, beyond a literature review.

Introduction

Bladder cancer causes approximately 150,000 deaths per year and it is the second most prevalent genitourinary malignancy, after prostate adenocarcinoma. Urothelial carcinoma represents 90% off all bladder tumors, while small cell bladder cancer (SCBC) is found in only 0.5–1.2% of patients.[1] Originally identified in 1981, SCBC is a rare and aggressive subtype tumor, most frequently presenting with haematuria,[2] which often shares morphologic and biologic features of small cell lung carcinoma: rapid progression, early metastasis, and high mortality rate.

Ureteroceles represent a version of the ectopic ureter with cystic dilatation of its distal portion, which is located either within the bladder or urethra. It can be associated with a single or duplex system and, in duplicate patients, they are associated with the upper pole ureter obstruction.

There are few reported cases of ureterocele malignant tumors, none with SCBC.

Case presentation

A 68-year-old female patient, non-smoker and without previous contact with anilines or other chemicals, presented with a three-month-old illness macroscopic haematuria. Computed tomography showed a duplicated ureter, dilatation of the upper kidney pole, a ureterocele with an expansive lesion and without metastases [Fig. 1]. Cystoscopy exhibited a solid white lesion occupying the ureterocele, which size filled the bladder beyond its midline. Transurethral resection was done without complications.

Histological fragment of mucosa showed a high-grade noninvasive papillary urothelial carcinoma.

With these results, intravesical immunotherapy was initiated with Bacillus Calmette-Guérin, six weekly sessions (40 mg); however, before finishing treatment (after second application), the patient returned to the emergency room with low back pain; a new CT scan was performed, presenting multiple metastatic lesions.

Beyond this evolution, anatomopathological immunohistochemistry was performed, which showed expression for cytokeratin with a Golgi pattern, CD56, synaptophysin, with a high proliferation index (Ki67 > 95%). Standard-compliant with SCBC [Table 1/Fig. 2].

Platinum-based chemotherapy 4-cycles was started, but with a low response, evolving to death in 3 months.

Discussion

A duplex ureter and urinary collecting system is a frequent anatomical variance that can be asymptomatic or associated with vesicoureteral reflux, incontinence, ureterocele or obstruction. The incidence of it variates at 0.7–4% of the population, affecting females more than males.[3]

In complete duplication, there are two collector systems for one single kidney and two ureters on the same side, which lead to the bladder into separate orifices.

According to Weigert-Meyer rule, the ureter that drains the kidney's upper pole inserts inferiorly and medially to the normal place insertion. Often, this insertion is abnormal and associated with ureterocele. The

Abbreviations: SCBC, small cell bladder cancer; CT, computerized tomography

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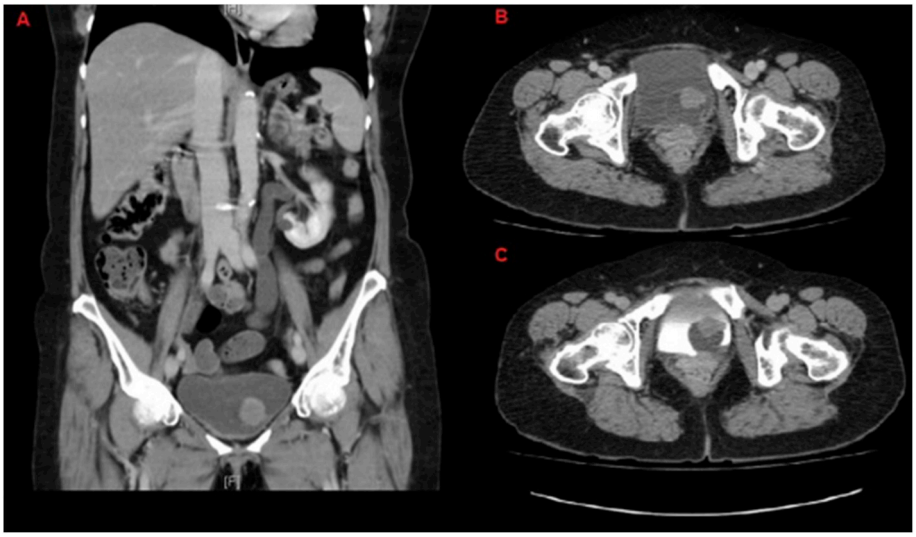

Fig. 1. Abdominal C: A (coronal) - presence of ureterocele and duplicate pelvic-calyx system. B and C (axial)- cuts showing hypercaptive lesion inside the ureterocele, in arterial and excretory phases.

Table 1
Description of antibodies positivity in immunohistochemistry.

Antibody	Clone	Results
Cytokeratyns 40, 48, 50 and 50,6 kDa	AE1.AE3	Positive Golgi
Chromogranin A	DAK-A3	Negative
Synaptophysin	DAK-SYNAP	Positive rare
Protein p63	DAk-p63	Negative
GATA-3	L50-823	Negative
APX-8	MRQ-50	Negative
Ki-67	M1B1	Positive 95%
CD56	123C3	Positive

ureter of lower pole inserts near the normal site, but normally presents vesicoureteral reflux, caused by the angle that it crosses the urinary bladder wall.

Cancers presenting into a ureterocele are rare, and only a few cases have been reported in the literature, including pheochromocytoma (Cabanas et al. 1973), leiomyoma (Sekar et al. 1980), adenocarcinoma (Yenilmez et al., 2007) and urothelial carcinoma (Atisgueta et al. 2016, Perego et al. 1974, Heyman et al. 1984, Fukunaga et al. 1993). There is no reporting of the SCBC and this abnormality.

SCBC is a rare subtype with a poor prognosis and a deficiency of standardized treatment options. In most cases, they will be locally advanced or metastatic at diagnosis, which most common sites are regional and distant lymph nodes, liver and bones. Ghervan et al. describe that these lesions are macroscopically large, with a polypoid or nodular aspect and superficial necrosis. They generally do not have macroscopically difference from urothelial carcinoma and, in 40% of cases, they may co-exist.[4]

The immunohistochemical study usually shows both epithelial and neuroendocrine differentiation. According to Moreto et al. the markers that are normally positive are neuron-specific enolase (25–100%), chromogranin A (22–89%), synaptophysin (67–76%), CD 57, CD 56 and protein gene product. The differential diagnoses are large-cell carcinoma and carcinoid cancer of the bladder,[5] high-grade urothelial carcinoma, lymphoma, lymphoepithelial-like carcinoma from the lung, metastases from another neuroendocrine tumor, neuroendocrine carcinoma of the prostate infiltrative and rhabdomyosarcoma.[4]

Treatment options for SCBC are not standardized, nonetheless, the neoadjuvant platinum-based chemotherapy (4 cycles) followed by radical cystectomy offers better results, except when existing metastases

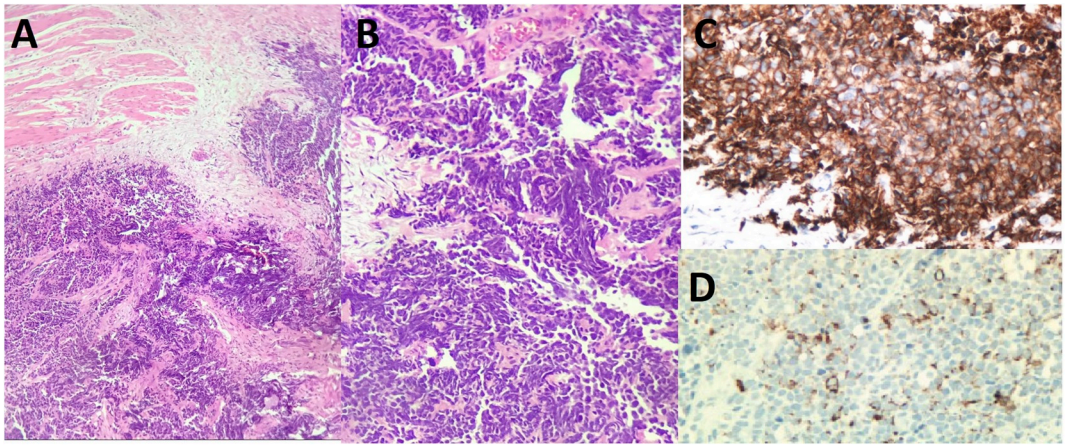

Fig. 2. Pathological: Fragments of bladder revealed inflammatory infiltrate with granulomatous reaction and areas with small round cell neoplasia (A and B). There was the expression for CD56 (C) and cytokeratin with a Golgi pattern (D), compatible with small cell neuroendocrine carcinoma.

at diagnosis, in which exclusive chemotherapy offers palliative support (4–6 cycles). The transurethral resection of the bladder tumor is not considered adequate treatment, but it can be used for the removal of any large tumor burden, before chemotherapy.

Lynch at al. and Siefker-Radtke et al. exposed that in combined treatment modalities, the median overall survival of neoadjuvant chemotherapy + cystectomy is bigger than cystectomy + adjuvant chemotherapy. For limited diseases, survival varies from 12 to 83 months, while extensive disease, survival does not exceed 4–13 months.[4,5]

Conclusion

The development of tumors in ureteroceles are very rare, with SCBC never previously described. The most common sign is haematuria and imaging studies can suggest alterations of the ureterocele walls.

The management protocol is not defined. Neoadjuvant platinum-based chemotherapy followed by cystectomy proposals better results. The utilization of treatment modalities varies significantly depending on TNM status. The prognosis is short because of the aggressiveness of this subtype and palliative therapy is common.

Consent

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Conflict of interest statement

All the authors declare no conflict of interest regarding this scientific communication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eucr.2019.100986.

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