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Oncology

Low back pain revealing a primary small cell neuroendocrine carcinoma of the upper urinary tract: A case report and review of the literature

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ABSTRACT

Small cell carcinoma of the upper urinary tract is very rare. Their aggressiveness and their poor prognosis make it grave. We report the management of a patient who consulted in the emergency room for low back pain and to whom the radiological and endoscopic assessments found a tumor of the upper urinary tract with lung, liver, bone and adrenal damage. Anatomopathological study of biopsies obtained by flexible ureteroscopy and percutaneous liver biopsy confirmed the diagnosis and the metastatic nature of secondary lesions.

Introduction

Carcinomas of the upper urinary tract represent 5% of urothelial carcinomas, their incidence is estimated at 1/100 000 inhabitant/year.

Small cell neuroendocrine carcinomas of the upper urinary tract are very rare. Little is known about their incidence, a review of the literature allowed us to count only less than forty cases reported.[1]

The rarity of these tumors, their aggressiveness and their poor prognosis make them all the seriousness. We report the case of a patient who consulted in the emergency room for hematuria and low back pain in a context of deterioration of the general state in whom the examinations showed a small cell neuroendocrine carcinoma of the upper calyx with lung, liver, bone and adrenal metastasis.

Case presentation

An 63-year-old Arab male Moroccan with a past of heavy smoking and transient hematuria for the past year, without other comorbidities. His family history was unremarkable for cancers in any first- or second-degree relatives. The patient went to the emergency room for low back pain for the past 2 months and impaired general condition made of asthenia, loss of appetite and weight loss. Biological tests showed renal failure and hepatic cytolysis. A first-line ultrasound showed moderate right ureterohydronephrosis and liver damage. CT imaging of the chest, of the abdomen and pelvis revealed a upper calyx tissue process with lung nodule-like lesions of the upper segment of lingual measuring 25 mm long axis and as well as micronodules of the culmen; multiple lesions involving the entire liver segments; two adrenal masses in bilateral and multiple osteocondensing lesions of the hipbone with blurred boundaries (Fig. 1).

The patient underwent right flexible ureteroscopy which revealed a large, friable, endophytic mass of the upper calyx (Fig. 2). Cold cup biopsies were obtained and a ureteral stent was placed. Histologic evaluation revealed small cell neuroendocrine carcinoma. Immunohistochemical analysis revealed moderate positive staining for synaptophysin, highly and diffuse staining for CD 56. The tumor stained negative for cytokeratin AE1/AE3 as well as chromogranin (Fig. 3).

Percutaneous liver biopsies were also performed and revealed metastasis of small cell neuroendocrine carcinoma of the upper urinary tract. After discussions between oncologist, pathologist, and surgeon, considering the metastatic stage of the disease, the patient was proposed palliative chemotherapy consisted of cisplatin and etoposide. In a context of lockdown due to Covid 19, the patient did not adhere to the treatment and died 3 months after the diagnosis.

Discussion and review of the literature

Neuroendocrine carcinoma are mostly occurs in the tracheobronchial tree. Outside the lung, the genitourinary system is the second most affected after the gastrointestinal tract. Within the genitourinary tract, the bladder and prostate are the most frequently affected sites.

Hypotheses put forward on the genesis of neuroendocrine tumors of

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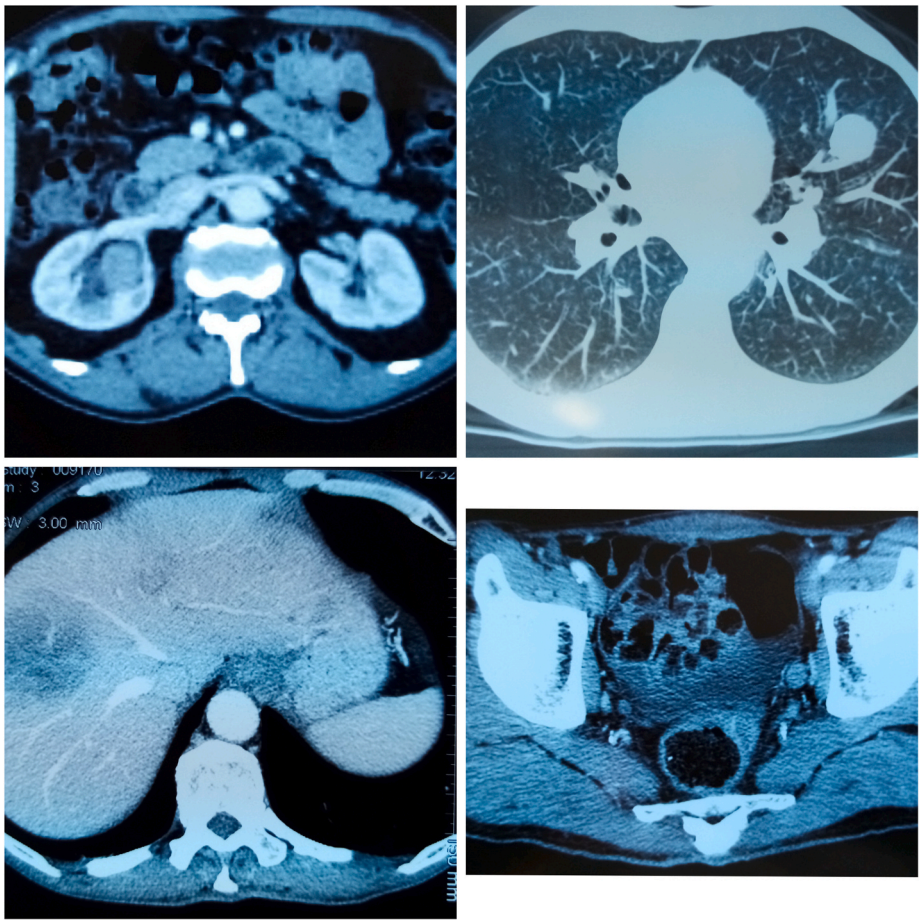

Fig. 1. CT image showing a upper calyx tissue process of right upper urinary tract; the lung, liver and bone damage.

the bladder, which can be extrapolated to the upper urinary tract, suggest three suppositions. If for some these neuroendocrine tumors result from seeding from normal neuroendocrine cells in the urinary tract; others think they result from undifferentiated stem cells that differentiate into neuroendocrine, which would moreover make logical the frequent association between neuroendocrine carcinoma and urothelial carcinoma on the same slide. The third group thinks these tumors result from urothelial metaplasia.

In the meta-analysis by Ouzzane and al[1] on the data from 39 clinical cases of small cell neuroendocrine carcinoma of urinary tract reported in the literature, men seem to be more affected (sex ratio 2 men for 1 woman), the average age is 66 and symptomatology dominated by hematuria and pelvic pain. It also emerges from this meta-analysis that at the time of diagnosis, 47% of patients have already reached a locally advanced or metastatic stage and the remaining 53% develop metastases after 13 months of survival, which makes it a cancer with a very poor prognosis. All of these ascertainments are consistent with our patient who was a 63-year-old man who consulted for low back pain and impaired general condition and who at the time of diagnosis already had pulmonary, hepatic, bone and adrenal metastases.

As for the therapeutic attitude, the low incidence of these tumors strongly limits the realization of randomized studies.

For low-risk tumors, conservative treatment is possible provided that the patient is informed of the risk of recurrence and local progression and that the latter accepts strict and close supervision.[2]

For high-risk tumors, radical treatment with nephroureterectomy is the standard treatment. The POUT trial recently demonstrated a clear benefit in adding adjuvant chemotherapy to nephrouretectomy, highlighting a 51% improvement in survival without recurrence in the adjuvant chemotherapy arm.[3]

Ouzzane et al. also found increased survival with Platinum plus etoposide as an adjuvant compared to nephroureterectomy alone.

For metastatic forms, local treatment, whether surgery or radiotherapy, only has a place in a palliative and symptomatic approach; the reference treatment for these forms being chemotherapy based on platinum salt, most of the data in the literature being extrapolated from prospective trials of metastatic bladder tumors.[4] Patrick J et al.[5] report an 80-month survival, the longest to our knowledge, in a patient who had nephrouroterectomy plus multiple metastasectomy followed by chemotherapy based on octreotide and then with temozolomide and capecitabine. This is the first reported use of the somatostatin analogue in the management of upper tract SCC. Having no fairly large series capable of allowing a randomized study Patrick's approach remains to be confirmed by broader studies.

Conclusion

Small cell neuroendocrine carcinomas are an extremely rare entity. Their aggressiveness and their poor prognosis make it a real challenge for hospital practitioners. The case we are publishing once again shows the need for rapid diagnosis and, above all, progress in targeted therapy.

Author contributions

Dr. CAT conducted the study and wrote the manuscript. Drs. AM, TM, AEH and MR participated in the care of the patient. Teacher AB supervised the writing.

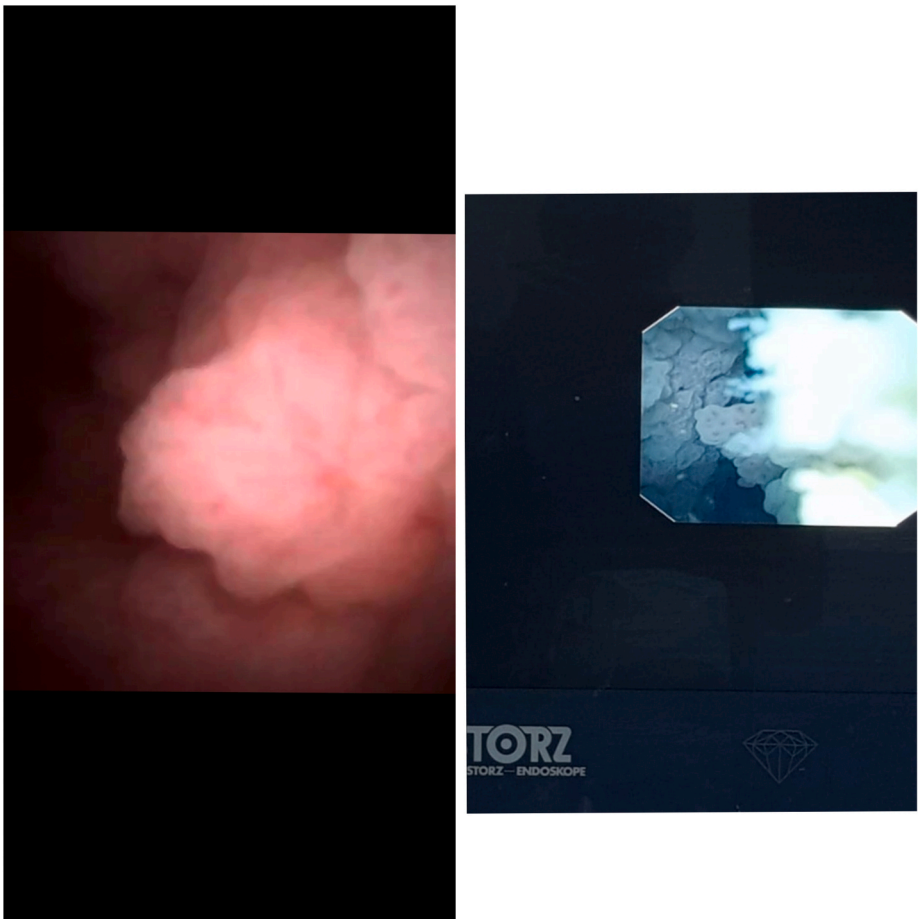

Fig. 2. Endoscopic image showing the tumor in the upper calyx.

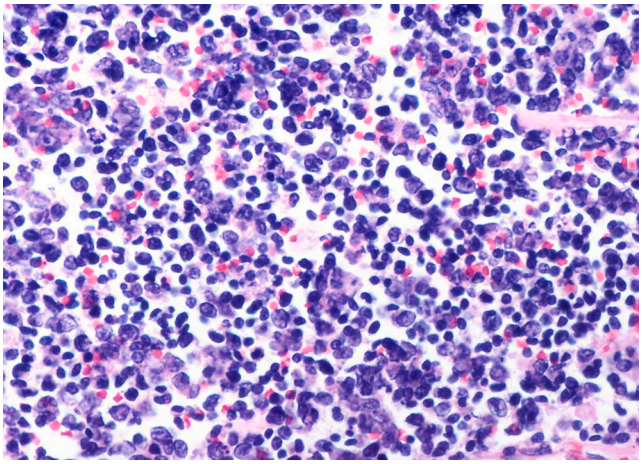

Fig. 3. Microphotography showing a proliferation made of sheets of small blue cells. The nucleocytoplasmic is high with numerous mitotic figures. (HE, 400X). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Consent

Written informed consent was obtained from the patient's next of kin for publication of this case report.

Declaration of competing interest

The authors do not declare any conflict of interest.

References

1. Ouzzane A, Ghoneim TP, Udo K, et al. Small cell carcinoma of the upper urinary tract (UUT-SCC): report of a rare entity and systematic review of the literature. *Canc Treat Rev.* 2011;37(5):366–372.
2. Pignot G, Colin P, Roupret M, Traxer O. Conservative management of urothelial carcinomas of the upper tract: systematic review for the yearly scientific report of the French National Association of Urology. *Prog Urol.* 2014;24(15), 1011—20.
3. Birtle AJ, Chester JD, Jones RJ, et al. Results of POUT: a phase III randomised trial of perioperative chemotherapy versus surveillance in upper tract urothelial cancer (UTUC). *J Clin Oncol.* 2018;36(suppl 6S) [abstr 407].
4. Rouprêt M, et al. Recommandations françaises du Comité de Cancérologie de l'AFU — actualisation 2018—2020 : tumeurs de la voie excrétrice supérieure. *Prog Urol.* 2018:11.
5. Hensley PJ, Bhalodi AA, Gupta S. Primary upper urinary tract small cell carcinoma: a case series and literature review. *J. Endourol.Case Rep.* 2017;3(1):165–168. https://doi.org/10.1089/cren.2017.0103.