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Small Cell Carcinoma of the Upper Urinary Tract: A Case Report and Review of Existing Cases

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Abstract

Primary extra-pulmonary small cell carcinomas (SCC) are rare, with <40 cases reported in the current literature. Only 1% of all primary upper urinary tract tumors are SCCs. We present a new case of a primary SCC of the right upper urinary tract. A 78-year-old male patient presented with frank hematuria and a lump in the left posterior triangle of his neck. CT imaging revealed a right renal pelvic mass associated with suspected liver metastases, cervical and retroperitoneal lymphadenopathy. Rigid ureteroscopy demonstrated a tumor involving the right ureter. Immunohistochemical analysis of neck and ureteric biopsies revealed high proliferative activity and positive CD56 and TTF1 markers, in keeping with a diagnosis of small cell carcinoma. The patient was offered systemic chemotherapy, which he declined. He developed further skeletal metastases and underwent treatment with radiotherapy and dexamethasone. He succumbed to his illness 13 months after initial presentation.

>40% of SCCs of the urinary tract are metastatic on presentation. In these cases, surgical options are limited and prognosis is poor. The literature suggests that neoadjuvant chemotherapy in organ-confined disease improves clinical outcome. However due to rarity of cases, there is limited evidence to guide management of metastatic SCC.

Keywords: Small cell carcinomas; Retroperitoneal lymphadenopathy; Radiotherapy

Introduction

Primary extra pulmonary small cell carcinoma (SCC) is rare, with the most common affected sites being the gastrointestinal (33%) and the genitourinary system (20%) [1]. Its prognosis is poor, as more than 40% of the cases initially present with distant metastasis [2]. Furthermore, primary SCC of the upper urinary tract is extremely rare; it has been previously reported in sporadic case reports, with no more than 40 cases having being so far reported [3,4]. It is exceedingly rare in the western hemisphere, with the biggest relevant retrospective study, identifying an incidence of 1% among all upper tract primary tumors [5].

Successful treatment with neoadjuvant chemotherapy and surgery has been previously reported only in case reports [6]. Indeed, bigger series of extra pulmonary primary SCC have reported a poor outcome of platinum and etoposide based chemotherapy, and radiotherapy, with a 5-year overall survival (OS) at 8.1% [2].

Case Report

A 78-year-old male patient presented with frank hematuria. On clinical examination there were no abnormal findings apart from a palpable lump on the left of his neck.

A CT of neck and thorax with contrast identified a mass of 43 mm, with associated multiple enlarged lymph nodes in the left supraclavicular fossa and lower cervical region, posterior to the sternocleidomastoid muscle. The lungs were found to be clear, however the superior abdominal images partially showed, a right renal mass with retroperitoneal lymphadenopathy, and also a 15 mm suspicious liver lesion. A Computerized Tomography Intravenous Urogram (CT-IVU) demonstrated an atrophic right kidney, with apparent tumor in the renal pelvis and multiple retroperitoneal lymph nodes (Figure 1).

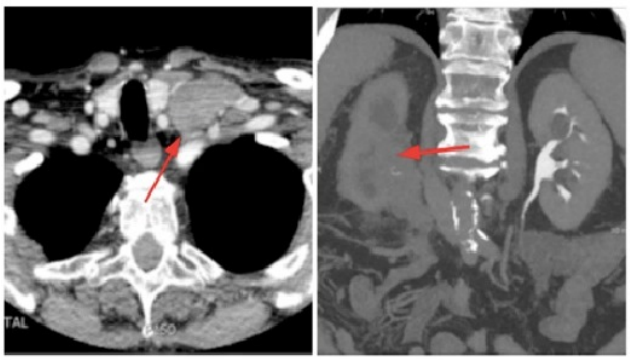

Figure 1: CT of neck and thorax with left supraclavicular nodal mass (left); CT IVU with right renal pelvis occupied by tumour (right).

Given the neck nodal mass, an urgent referral to the head and neck surgeons was made, and a biopsy of the neck node pack followed as a means of a tissue diagnosis.

The patient was also submitted to a right rigid ureteroscopy under general anaesthesia, which verified an aggressive looking tumour in the mid ureter, filling the proximal ureter and the renal pelvis. Biopsies from the ureteric lesion were taken and a ureteric stent was inserted.

The ultrasound guided biopsy of the supraclavicular mass came back positive for small blue cells with abundant apoptotic bodies and mitoses. Immunohistochemical analysis was strongly positive for CD56, and weakly but definitely positive for TTF1. CK 7 and 20, and leukocyte common antigen were negative. There was more than 90% proliferative activity, suggesting an aggressive tumour. The appearances and the immunohistochemical profiles were considered in keeping with small cell carcinoma (Figure 2).

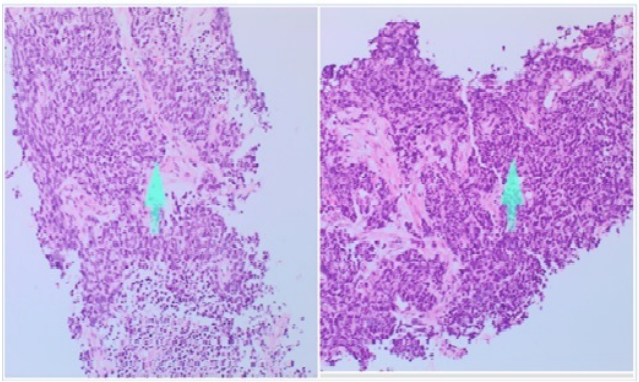

Figure 2: Lymph node with features of small cell carcinoma (left); ureteric biopsy with similar characteristics (right).

The biopsies taken from the right ureter came back with exactly the same immunohistochemical features as the supraclavicular ones, confirming a small cell carcinoma of the right ureter. Again a high proliferative pattern was evident, as most cells were positive on Ki67 antibody (Figure 3).

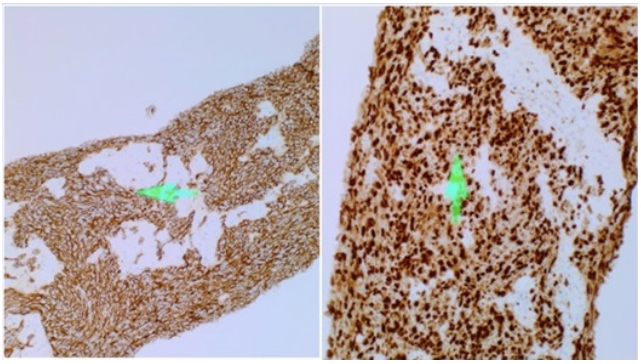

Figure 3: The tumour is positive with CD56 Immunostain, a marker for small cell carcinoma (left); there is a high proliferation index, as most cells are positive with Ki67 antibody (right).

It was concluded that the disease was a primary upper urinary tract small cell carcinoma with lymph node and liver metastasis. The patient was therefore referred to the oncology team for systemic chemotherapy. He was offered the option of systemic treatment with etoposide and cisplatin, but the patient declined.

He thereafter developed multiple skeletal metastases, with right sciatica and neuralgia in L1-L2 dermatomes. He underwent 5 fractions of radiotherapy and high dose dexamethasone to control spinal cord compression symptoms. Further to his progressive disease, he passed away 13 months post his original presentation.

Discussion

This is a report of a primary SCC of the urinary tract, with distant lymph node involvement and liver metastasis on presentation. The prognosis of these tumours is exceedingly poor, due to the aggressiveness of the disease and due to the fact that more than 40% of these cases are metastatic on presentation [2]. Our patient was palliated soon after his diagnosis, and his survival of 13 months from the moment of diagnosis underlines the bad prognosis of such patients. The biggest research on this field covered a 40-year period (1970-2010), with a total 40 cases collected [3]. The median overall survival (OS) of these patients was of 15 months, with a 23.8% 3-year survival.

Effective management with surgery for these patients is rarely available, due to the advanced character of their disease on diagnosis. There have been very few patients reported, who underwent timely a nephroureterectomy, with or without adjuvant chemotherapy, and were considered as completely cured for their disease [6].

Neoadjuvant and adjuvant chemotherapy has been reported to be highly effective in SCC of the urinary tract. The biggest relevant study from Lynch et al. [7] reports an improvement of the OS survival by 141 months (159.5 vs 18.3), for patients with resectable bladder SCC, if compared to radical cystectomy only. The chemotherapeutic regimes used were mainly of cisplatin/etoposide and ifosfamide/doxorubicin, but other schemes have been tested successfully. The outcomes of the authors underline the great chemosensitivity of SCC. This study included only patients with radiological features of organ confined or resectable locally advanced disease (up to T4aN0M0).

In the case of our patient, chemotherapy of cisplatin/etoposide was offered to the patient as a palliative treatment, considering that the patient had already distant lymph node and liver metastatic disease. The patient's decision was to opt out from chemotherapy. Palliative radiotherapy managed to offer a partial benefit with regards to his pain, caused by vertebral metastasis. His survival from diagnosis was close to the reported median OS of 15 months.

As the incidence of primary upper urinary tract SCC is extremely rare, there is currently no space for firm evidence on the optimal management of these patients. Considering however the similar cellular features of these SCCs, we should strongly consider offering neoadjuvant chemotherapy and radical surgery to patients presented with localized SCC of the upper urinary tract, based on the strong evidence coming from Lynch et al. [7].

Conclusion

Upper urinary tract SCC is an exceedingly uncommon condition with poor prognosis. Almost half of the patients are metastatic on presentation and no surgical options are available. In the eventuality of a radiologically organ confined disease, neoadjuvant chemotherapy associated with nephroureterectomy is expected to improve the OS.

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