Case Report

Rare case of upper urinary tract squamous cell carcinoma presenting with significant paraneoplastic syndrome

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Abstract

Squamous cell carcinoma of the upper urinary tract is a rare entity associated with rapidly progressive disease and poor outcomes. Here, we describe a case of a squamous cell carcinoma of the upper urinary tract associated with significant progression and paraneoplastic syndrome. Post-operatively, the patient had near complete resolution of her paraneoplastic syndromes with significant improvements in her functional status.

Keywords: Kidney cancer, paraneoplastic, squamous cell carcinoma, upper urinary tract

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INTRODUCTION

Squamous cell carcinoma (SCC) of the upper urinary tract is a rare disease comprising only 0.5% of renal malignancies and 6%–15% of cancers involving the renal pelvis and ureter.[1-4] The diagnosis is associated with a poor prognosis, and there is a paucity of literature on this condition. We describe here a rare case of SCC of the upper urinary tract in a patient presenting with significant paraneoplastic syndrome.

CASE REPORT

A 76-year-old female presented to the emergency department in March 2019, with progressive weakness, fatigue, and weight loss of over 20 pounds over a period of 3 months and was admitted to the Internal Medicine Service. Her past medical history included stage-3 chronic kidney disease, peripheral vascular disease with multiple bypass surgeries, gastroesophageal reflux disease, gout, appendectomy, and hysterectomy for uterine cancer. She was also a former smoker with a 35 pack-year history having quit 22 years prior.

Initial investigations found her significantly malnourished and anemic, with multiple electrolyte disturbances including profound hypercalcemia. A computed tomography (CT) scan of her abdomen demonstrated a 6 cm mass-like lesion arising from the upper pole of the right kidney with a single prominent retrocaval lymph node measuring 1.1 cm, with no evidence of further metastatic disease [Figure 1a]. Her clinical condition improved with medical optimization including blood transfusions, hydration, and oral nutritional support. Initially, this mass was felt to be consistent with xanthogranulomatous pyelonephritis by the consulting urology service. Follow-up and biopsy of the lesion were arranged as an outpatient, with a tentative plan for a nephrectomy in April 2019, once the patient had been medically optimized.

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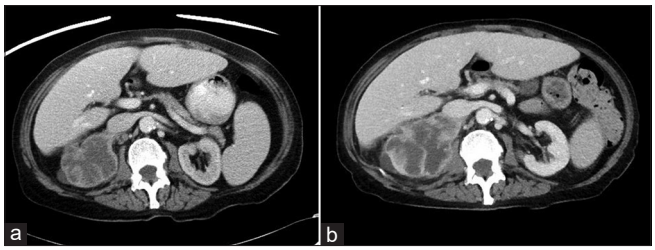

Figure 1: (a) Initial computed tomography scan demonstrating a 5.9 × 5.3 × 6.1 cm heterogeneous mass-like lesion arising from the upper pole of an atrophic right kidney with a single prominent retrocaval lymph node measuring 1.1 cm, with no evidence of further metastatic disease. (b) Repeat computed tomography scan 20 days after the initial computed tomography scan, demonstrating rapid progression of disease. New 0.5 cm × 7.0 cm × 6.8 cm area of cystic change and necrosis within the mass, and local invasion of the renal mass into the right psoas muscle, and the right renal vein abutting the right vena cava with encasement of the solitary right renal artery within the mass

The biopsy demonstrated a poorly differentiated carcinoma with squamous differentiation. With this diagnosis, further investigations including cystoscopy, urine cytology, and CT chest imaging were performed, all of which were normal. Throughout these investigations, her overall performance status began to deteriorate with progressive weakness and anemia after her discharge from hospital.

Given the patient's decline, and after a discussion of her case at multidisciplinary oncology rounds, the plan was to proceed with a right radical nephrectomy with the goal to improve her symptoms and oncological outcomes. It was thought that her anemia and functional decline would progress further without active management of her cancer. A repeat preoperative CT scan demonstrated a significant interval progression of the disease in a 20-day period [Figure 1b]. The renal mass was now found to be locally invasive with possible invasion into the right psoas muscle and the right renal vein abutting the inferior vena cava.

A radical right nephrectomy with inferior vena cava thrombectomy with patch graft angioplasty was performed in early April 2019. Intraoperatively, the mass was noted to be significantly adhered to the adjacent organs including the inferior vena cava. The final pathology demonstrated pT3aN1 SCC measuring 8.5 cm with 50% tumor necrosis with invasion into the renal sinus and collecting system with 1/1 hilar lymph nodes positive [Figures 2 and 3].

The patient recovered quickly and her overall condition improved. She was discharged home in 6 days. Follow-up investigations demonstrated that the patient was normocalcemic, improvement in her anemia, and a CT scan of the abdomen demonstrated no residual tumor or recurrence 2 months postoperatively. Functionally, the patient had a near complete resolution of her preoperative symptoms.

DISCUSSION

SCC is one of the most common nonmelanoma skin cancers. However, SCC in the urothelial tract is a rare condition in Western countries, with a paucity of literature to date and with the majority of available studies focusing of SCC confined to the bladder. We describe here a case of a patient with SCC of the kidney presenting with rapid progression of her symptoms with paraneoplastic syndromes.

A review of 65 patients with SCC of the renal pelvis and ureter by Holmäng *et al.* demonstrated that patients with SCC of the upper urothelial tract were more likely to present with local symptoms compared to those with urothelial cell carcinoma.[4] The prognosis of patients treated with advanced SCC (pT3) is poor and was found comparable to patients diagnosed with pT4 upper tract urothelial cell carcinoma.[4] A median survival of only 7 months postoperatively was noted and only 5 (5.5%) patients survived longer than 5 years with a diagnosis of SCC.[4]

Patients with upper tract SCC have been retrospectively described to present with paraneoplastic syndromes such as leukocytosis, thrombocytosis, anemia, or hypercalcemia.[5-8] Such as in the case of our patient, the radiological findings can be difficult to interpret and are nonspecific, such as hydronephrosis, nephrolithiasis, calcifications, and solid mass.[3,5,8-11] Given these nonspecific findings, the diagnosis of SCC is difficult to make before a histopathological review of the mass.[3,5,8-11] There has even been a case of SCC of the renal pelvis diagnosed postnephrectomy in the absence of any masses on CT, with the only findings being a staghorn calculus, renal parenchymal thinning, and hydronephrosis, demonstrating the difficulties in diagnosing this rare condition.[12] It is believed that chronic tissue irritation with infection, inflammation, and calculi would lead to dysplasia with malignant transformation of the normal urothelial lining into SCC, although a definitive pathophysiology has not yet been elucidated.[4,11,13]

Previous cases have demonstrated the highly aggressive nature of this cancer as was the case with our patient and others have reported rapid metastatic progression of the mass and resulting death of the patient.[7,9-12] This makes the timely diagnosis and urgent treatment of this rare condition crucial to ensure that patients have timely access to care.

Surgery remains the mainstay of treatment for nonmetastatic disease with either nephrectomy or nephroureterectomy, sometimes combined with adjuvant cisplastin-based

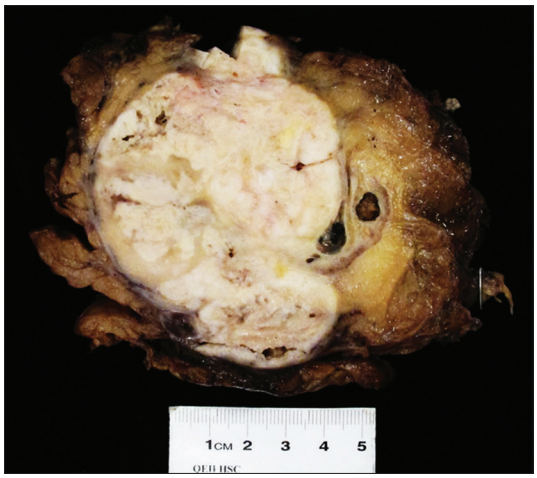

Figure 2: Gross pathology of the surgical specimen demonstrated a 8.5 cm × 6.5 cm × 6.2 cm whitish-tan and solid tumor with the involvement of the renal sinus and collecting system. The noninvolved kidney demonstrated marked end-stage changes with stone formation

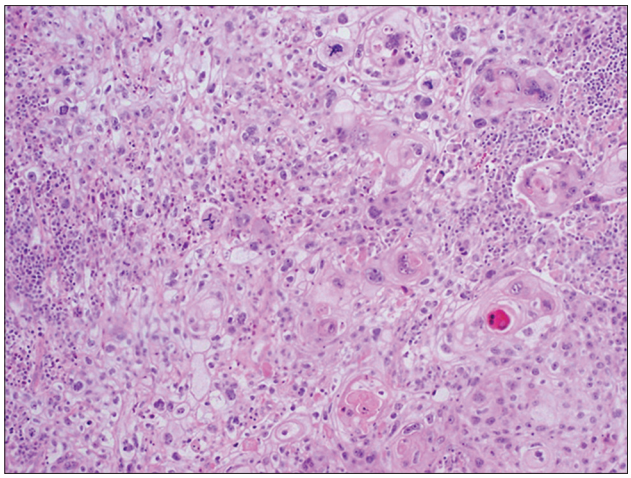

Figure 3: Hematoxylin and eosin stain of the radical nephrectomy specimen showed a moderately differentiated squamous cell carcinoma composed of nests or sheets of highly atypical squamous cells with focal squamous keratin pearl formation (×200)

chemotherapy and/or radiation.[1,4,11,12] However, owing to the rarity of this condition, the efficacy of various chemotherapeutic regimens is unknown.[1,4,11,12] Recently, a study demonstrated that in squamous differentiation of upper urothelial tract malignancies, the programmed death ligand 1 expression was found in all 14 cases (100%) tested.[14] This novel study presents a potential immunotherapy target in patients diagnosed with SCC where other cisplatin-based chemotherapy regimens have known to be unsuccessful in improving clinical outcomes in these patients. However ultimately, the optimal treatment regimen for these patients remains unknown.

CONCLUSION

SCC of the upper urothelial tract is a rare condition that can be difficult to diagnose during its initial presentation. This condition should be suspected when patients present with a complex renal or upper urothelial tract mass with indeterminate radiological findings or significant paraneoplastic syndrome in the absence of metastatic disease. If the diagnosis is questioned, a biopsy may expedite the timely diagnosis and potential definitive surgical treatment of this rare and aggressive cancer. Although there has been some research in the field of SCC differentiation of the upper urothelial tract tumors, more studies and research into this disease will need to be done to determine the best course of treatment for these patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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