

Squamous Cell Carcinoma of the Kidney – Rarity Redefined: Case Series with Review of Literature

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Abstract

Squamous cell carcinoma of the renal pelvis and ureter is a rare malignancy, having an incidence of 6% to 15% (of all urothelial tumors). Few cases of primary squamous cell carcinoma of kidney have been reported in the world literature. The insidious onset of symptom and lack of any pathognomonic sign, leads to delay in the diagnosis and subsequent treatment, resulting in grave prognosis for these patients.

Herein, we report 5 cases (three males and two females) of advanced primary squamous cell carcinoma of kidney that were treated at our centre during the last 6 years. The average age was 57 years (range 50-65 years). Three of the patients had history of long standing renal calculus disease while 3 had history of smoking and 1 patient had history of analgesic abuse. These cases were unique because in few of them; all the calyces were involved by the tumor - a field change type of pattern normally seen in transitional cell carcinoma of the kidney. In one patient, thrombus of the inferior vena cava was also present along with infiltration of the duodenum by the tumor. Despite prompt nephroureterectomy, 4 out of 5 patients died within 6 months of treatment. Only one patient was surviving at 5 months of follow up.

Nephrectomy with or without ureterectomy is the treatment of choice in patients suffering from squamous cell carcinoma of the kidney. There is lack of evidence of survival benefits of chemo-radiation following surgery but is advocated by some with the hope that it might increase survival. Biopsy from the renal pelvis or calyceal wall is advocated at the time of stone removal in patients having long-standing history of large renal calculi or staghorn calculus since such patients are capable of harboring occult or overt malignancy.

Keywords: Kidney neoplasms; Carcinoma, Squamous cell

Abbreviations: SCC: Squamous Cell Carcinoma; KUB: Kidney, Ureter and Bladder; IVU: Intravenous Urogram; CECT: Contrast Enhanced Computerized Tomographic; FNAC: Fine Needle Aspiration Cytology; DTPA: Diethylene Triamine Pentaacetic Acid; P: Pathological TNM staging; C: Clinical TNM staging; IVC: Inferior Vena Cava

Introduction

Squamous cell carcinoma (SCC) of the renal pelvis and ureter is rare with an incidence of 6% to 15% of all urothelial tumors (Blacher et al., 1985; Li and Cheung, 1987; Holmang et al., 2007). Very few cases of primary SCC of kidney have been reported in world literature. The insidious onset of symptoms and lack of any pathognomonic sign, leads to delay in diagnosis and treatment.

SCC is frequently associated with calculus disease and hydronephrosis (Li and Cheung, 1987; Busby et al., 2006). Solid mass, hydronephrosis and calcifications are common but nonspecific radiological findings, which may explain why diagnosis is not frequently established before the histopathological examination of the resected surgical specimen (Li and Cheung, 1987; Kinn, 1980; Holmang et al., 2007). Early metastatic spread is common and the prognosis is poor with few patients surviving longer than 5 years (Blacher et al., 1985; Li and Cheung, 1987; Wagle et al., 1974; Holmang et al., 2007). Surgery may sometimes result in cure but radiotherapy or systemic chemotherapy seems to have little benefit (Li and Cheung, 1987; Nakamura et al., 1992; Kimura et al., 2000).

In this case series, other rare events were witnessed with primary SCC. Inferior vena cava (IVC) thrombus was seen; which is a rare

phenomenon. In a few patients, all the calyces were involved – a field change like phenomenon witnessed mainly in cases of transitional cell carcinoma.

Case Series

Case no. 1

A 55 years old female presented with fixed, dull aching left flank pain since 5 months. There was no associated symptom. She was a chronic smoker. Examination of the abdomen was unremarkable. Ultrasound of kidney, ureter and bladder (KUB) revealed left hydronephrosis with dilated upper ureter and a lymph node mass encasing the upper ureter. Urine cytology for malignant cells was negative. Intravenous urogram (IVU) depicted normal right pelvicalyceal system with non-visualization of the left kidney. The contrast enhanced computerized tomographic (CECT) scan of

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abdomen showed left hydronephrotic kidney with an enhancing mass in the region of pelvis and lower pole of kidney with left para-aortic lymph node mass (Figure 1). Fine needle aspiration cytology (FNAC) from that lymph node mass was inconclusive.

Left radical nephroureterectomy (till the lower end) with excision of the para-aortic lymph node mass was performed. Cut section of the specimen revealed infiltration of the pelvis and all the calyces by the tumor mass; mass was extending to the perinephric region (Figure 2a). Histopathological examination of the specimen revealed it as moderately differentiated SCC (Figure 2b and 2c). The tumor was highly cellular and showed extensive infiltration of the renal parenchyma. The lymph node mass also showed squamous cell metastasis and there was involvement of the wall of proximal ureter by the tumor (pT3N2M0). The patient was given chemo-radiation following the surgery and is doing well at 5 months of follow-up. At last follow-up, there was no evidence of local or distal metastasis.

Case no. 2

A 60 years old man presented with history of flank pain and intermittent painless hematuria since last 3 months. He was suffering from left renal calculi since last 6 years. On examination, there was a hard and non-tender left renal lump. The ultrasound KUB revealed left staghorn calculus with hydronephrosis. Urine cytology for malignant cells was negative. IVU depicted non-visualization of the left kidney. The CECT scan of the abdomen showed left hydronephrosis with a large calculus and a normal right kidney. Diethylene triamine pentaacetic acid (DTPA) scan revealed left split renal function of 5%. Surgical exploration was undertaken; consistency of the kidney was hard and nodular on palpation and there were few enlarged lymph nodes at the hilum. Left radical nephrectomy with excision of the left proximal ureter and left para-aortic lymph nodes was performed. The excised specimen consisted of a hard mass involving the pelvis and the lower pole of the kidney with large staghorn calculus. Histopathology of the specimen revealed this mass as moderately differentiated SCC which was also involving the lymph nodes (PT3N2M0). Despite surgical treatment, the patient died due to extensive metastases within 6 months of surgery.

Case no. 3

A 55 years old female patient was referred to our centre with history of attempted (failed) left nephrectomy elsewhere for non-functioning kidney due to calculi. She had osteoarthritis with positive history of analgesic abuse but her renal function tests were normal.

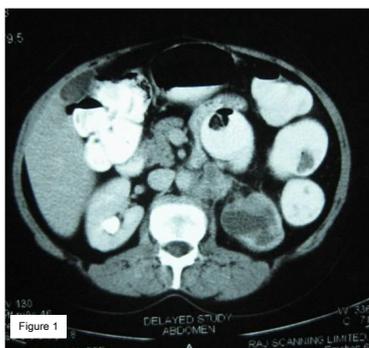


Figure 1: CECT scan depicting enhancing left renal mass with hydronephrosis and para-aortic lymph nodes. The para-aortic lymph node mass with a renal tumor suggest the presence of local metastatic lymph nodes.

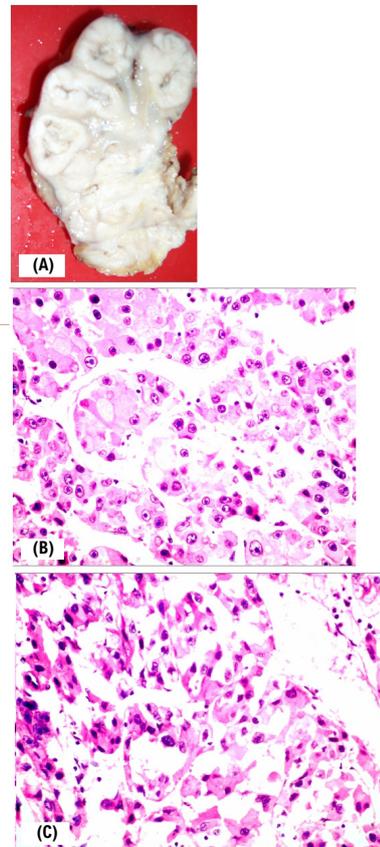


Figure 2: **A:** Cut section of the kidney showing all the calyces and pelvis infiltrated by SCC. The field change pattern of pelvicalyceal involvement is classically described for the urothelial malignancy; in SCC such involvement may occur but is extremely rare. **B:** Histopathological depiction of tumor cells. The malignant cells have completely replaced the pelvicalyceal urothelial architecture. Few intervening vessels are seen; normal renal architecture is obliterated. **C:** Microphotograph showing large malignant cells with intervening fibrous tissue as intervening sheets. At places, squamous tumor cells show keratinized deposition. The presence of keratin is pathognomonic of SCC.

The referral operative details mentioned a hard kidney mass which was infiltrating the psoas muscle. She was investigated further at our centre; CECT scan of the abdomen showed a left heterogeneous renal mass with 3 cm calculus in the kidney. She was re-explored by a midline laparotomy. On exploration, a large renal mass of 10x12 cm size, adherent to the psoas muscle was found. Left radical nephroureterectomy with partial excision of the psoas muscle was performed. Excised specimen consisted of a mass which was involving the entire kidney, along with a calculus in the renal pelvis. Histopathological examination of the mass revealed high-grade SCC (pT4N2M1). Patient died after 5 months of surgery due to extensive metastases and disease recurrence.

Case no. 4

A 50 years old male patient presented with right renal lump and intermittent hematuria. He was a chronic smoker and suffered from renal calculus disease for last 12 years. CECT scan abdomen revealed a large renal mass (right), large multiple retroperitoneal lymph nodes, possibility of invasion of the duodenum and thrombus in the inferior vena cava (Figure 3a and 3b). The cephalad end of the thrombus was reaching till the retro-hepatic level. X-ray Chest (postero-anterior

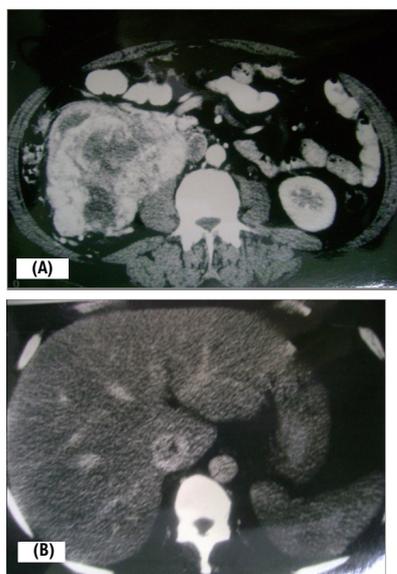


Figure 3: **A:** CT scan showing large heterogeneous right renal mass with thrombus in vena cava. Vena cava thrombus is commonly described for renal cell carcinoma. In SCC, occurrence of such thrombus is rare. **B:** CT scan showing retro-hepatic thrombus. The distal end of the thrombus is extending till the retro-hepatic portion of inferior vena cava.

view) depicted right pleural effusion. Trucut biopsy of the mass confirmed it as moderately differentiated SCC (cT4N2M1). In view of the grave prognosis, the patient and his relatives were psychologically counseled. The patient died after 1 month from extensive chest metastases.

Case no. 5

A 65 years old male patient presented with intermittent painless hematuria. The abdominal examination was unremarkable. He was chewing tobacco for last 20 years. He underwent right pyelolithotomy 8 years back. Ultrasound KUB showed right gross hydronephrosis. IVU depicted non-visualized right kidney. CT scan of abdomen showed right hydronephrotic kidney with thin renal parenchyma and a heterogeneous mass at the lower pole with few enlarged lymph nodes near the renal hilum. He was managed by right radical nephroureterectomy. Histopathology of the mass confirmed it as moderately differentiated SCC; also infiltrating the perinephric fat. The lymph nodes were infiltrated by the tumor cells too (pT3N2M0). Patient died after 4 months of surgery because of metastatic disease.

Discussion

Chronic irritation of urothelium is presumed to be a cause of squamous metaplasia with subsequent malignant progression to SCC (Holmang et al., 2007; Gahagan and Reed, 1949). The common causes of chronic irritation in decreasing order are long duration of renal calculus disease, previous history of renal calculus surgery, chronic analgesic abuse or radiotherapy (Li and Cheung, 1987; Holmang et al., 2007; Gahagan and Reed, 1949). The strongest association has been reported with renal calculus disease (Blacher et al., 1985; Holmang et al., 2007; Gahagan and Reed, 1949; Booth et al., 1980).

Unfortunately, our current knowledge of squamous cell carcinoma is based on few case reports (Blacher et al., 1985; Li and Cheung, 1987; Holmang et al., 2007; Gahagan and Reed, 1949; Booth et al., 1980). Female sex predilection was reported earlier but now it

is not considered valid since this disease is found equally in both the sexes. The mean age of presentation is 56 years with no predilection for side (laterality) (Blacher et al., 1985; Holmang et al., 2007; Booth et al., 1980). Pain and hematuria are the most common presenting symptoms. Pain is due to pelviureteric junction obstruction and/or local extension (Blacher et al., 1985; Holmang et al., 2007; Gahagan and Reed, 1949; Booth et al., 1980). Hematuria may be due to primary tumor mass or calculus disease.

The patients may present for the first time with anorexia, weight loss and/or lethargy, particularly in advanced cases (Blacher et al., 1985; Gahagan and Reed, 1949; Booth et al., 1980). The diagnosis is usually confirmed by histopathological examination of the surgical specimen. Late onset pain, solid mass with or without hydronephrosis and rarity of the tumor are possible culprits behind late diagnosis of this entity (Li and Cheung, 1987; Holmang et al., 2007; Gahagan and Reed, 1949; Booth et al., 1980; Kimura et al., 2000; Holmang and Johansson, 2006). Insidious onset of the disease and lack of any pathognomonic sign or symptom confounds the delay in diagnosis. Due to this delay in diagnosis, invasion of the renal parenchyma occurs in few patients. Radical nephroureterectomy with excision of the bladder cuff (guidelines proposed by Johansson and Wahlqvist (1979)) appears to be the treatment of choice for patients not having distant metastasis (Blacher et al., 1985; Holmang et al., 2007; Holmang and Johansson, 2006; Johansson and Wahlqvist, 1979). Unfortunately, majority of the patients have locally advanced or metastatic disease at the time of presentation and in these patients, nephrectomy with or without ureterectomy is recommended (Holmang et al., 2007; Kimura et al., 2000; Holmang and Johansson, 2006). Nephrectomy is necessary even in the face of metastatic disease; to establish a histological diagnosis, for control of symptoms such as pain, fever and hematuria or to eliminate the source of infection before systemic chemotherapy can be instituted (Blacher et al., 1985; Holmang and Johansson, 2006; Johansson and Wahlqvist, 1979). The common finding on surgical exploration is local invasion of the tumor into renal parenchyma, perirenal fat, psoas muscle or vascular invasion; which suggests that lymphadenectomy has limited value in this disease. Cisplatin based chemotherapy and palliative radiotherapy have been advocated for the control of local symptoms in metastatic disease but have failed to show any survival benefit (Blacher et al., 1985; Holmang et al., 2007; Booth et al., 1980; Johansson and Wahlqvist, 1979).

In the present study, 3 patients (60%) had stone disease and one patient had history of pyelolithotomy (Table 1); this is comparable to the incidence reported in the literature (Blacher et al., 1985; Holmang et al., 2007; Booth et al., 1980; Johansson and Wahlqvist, 1979).

Smoking or tobacco chewing was also observed in 60% of the patients (Table 1) which is a known predisposing factor for this malignancy. One patient (case no. 4) was inoperable due to inferior vena cava thrombus, duodenum invasion and lymph node metastasis. Vena cava thrombosis is extremely rare in squamous cell carcinoma and is considered a bad prognostic sign (Holmang et al., 2007; Kimura et al., 2000).

Follow-up of these patients' includes physical examination, X-ray chest and liver function tests. Check cystoscopy for the recurrence in urinary bladder is not recommended since bladder tumor is unusual after upper tract squamous cell carcinoma. Similarly, abdominal CT scan is not recommended due to lack of palliative or therapeutic treatment for recurrences in the abdomen. Prognosis in the setting of metastatic disease is poor with reported median survival of 5

Patient characteristics	Case No. 1	Case No. 2	Case No. 3	Case No. 4	Case No. 5
Age (in years)	55	60	55	50	65
Sex	Female	Male	Female	Male	Male
Associated Kidney stone	Absent	Present	Present	Present	Absent
Previous history of stone surgery	Absent	Absent	Absent	Absent	Present
Hydronephrosis	Present	Present	Absent	Absent	Present
Smoking/tobacco intake	Present	Absent	Absent	Present	Present
Analgesic abuse	Absent	Absent	Present	Absent	Absent
Operation done	Radical nephroureterectomy	Radical nephroureterectomy	Radical nephroureterectomy	Inoperable	Radical nephroureterectomy
Pathological staging	pT3N2M0	pT3N2M0	pT4N2M1	cT4N2M1	pT3N2M0
Survival in months	5*	6	5	1	4

*Still surviving (other patients have deceased)

Table 1: Patient Characteristics.

months (Blacher et al., 1985; Li and Cheung, 1987; Holmang et al., 2007; Gahagan and Reed, 1949; Booth et al., 1980; Kimura et al., 2000; Holmang and Johansson, 2006). In our study, the mean survival was only 4.2 months.

Conclusion

Squamous cell carcinoma of the renal pelvis and ureter is a rare entity. Because of non-specific sign and symptoms, most of the patients present with advanced disease (stage pT3 and pT4). Nephrectomy with ureterectomy is the treatment of choice in these patients. Even in the face of metastatic disease, nephrectomy should be performed to establish the histological diagnosis, for local control of symptoms such as pain, hematuria and elimination of source of infection particularly if associated with renal calculi. There is lack of evidence regarding survival benefit with chemo-radiation following surgery but it is still advocated by some with the hope of increasing survival. Overall prognosis is dismal. Biopsy from the renal pelvis or calyceal wall should be considered during the treatment of stone disease, in patients having long-standing history of large renal calculi or staghorn calculus. Such patients are susceptible of harboring occult or overt malignancy along with the renal stone disease.

Consent

Written informed consent was obtained from all the patients included in this study. Ethical clearance for this study was obtained from the institutional ethics committee and was in accordance with the Declaration of Helsinki. Moreover, the patients in this study are anonymous and there is no reason to think that the patients or their families would object to publication of this study.

Competing Interests

- None of the authors have any financial or non-financial potential conflicts of interest.
- None of the authors have funding from or shares in organizations that stand to gain or lose from the publication of this study, none of the authors hold any patents related to this study, or have any other competing interests that may cause embarrassment were they to become public after the publication of this case series.

Authors' Contributions

"VS and SNS treated these patients. VS analyzed and interpreted the patient data. He also wrote the initial draft of the manuscript. RJS contributed to the

manuscript by editing it and contributing the initial information about the patients. SNS analyzed the data and did the editing and correction of the manuscript and added information wherever necessary. BM performed the histopathological examination and was a major contributor in writing the manuscript. NA and SM contributed by correcting and revising the manuscript. All the authors read and approved the final manuscript."

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