Unsuspected primary renal urothelial carcinoma with squamous differentiation in a background of long standing renal calculi: A case report

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Abstract

Introduction: Primary upper urinary tract tumors are quite uncommon. Most of these are malignant epithelial tumors out of which 90% are urothelial carcinomas. The majority of patients are male and elderly. Long standing renal calculus is a common etiology. Insidious onset of disease, lack of specific signs and symptoms and the inability of routine radiological investigations to detect tumour areas lead to delay in diagnosis.

Aims and Objectives: to study the histo-morphological features of incidental primary urothelial carcinoma of kidney with squamous differentiation.

Materials and Methods: formalin fixed, hematoxylin and eosin stained sections of a nephrectomy specimen submitted in the Pathology department of SN Medical College, Agra, were observed microscopically and findings were noted.

Result: A nephrectomy specimen was submitted for histopathological examination. Grossly, kidney was severely hydronephrotic with dilated calyces and multiple calculi. No tumour or growth was noted. Histology revealed primary urothelial carcinoma with squamous differentiation. Vascular and perineural invasion was also noted. Hilum showed presence of urothelial carcinoma in situ with dysplasia. Extensive areas of necrosis were also seen.

Conclusion: In patients presenting with long standing renal calculi and poorly functioning kidney, urothelial malignancy should be suspected and radiological investigations like CT scan should be done pre operatively. Squamous differentiation is common in urothelial carcinomas and is associated with aggressive disease.

Keywords: Urothelial carcinoma, Non-functioning kidney, Squamous differentiation.

Introduction

Primary upper urinary tract tumors are quite uncommon. Most of these are malignant epithelial tumors out of which 90% are urothelial carcinomas. Urothelial carcinomas of upper urinary tract account for 5-10% of all urothelial carcinomas.[1,2] The majority of patients with UTUC are male and elderly.[3] The common etiologies include long standing renal calculus disease, previous history of renal calculus surgery, chronic analgesic abuse or radiotherapy. The strongest association has been reported with long standing kidney stones. Most common presenting symptoms are pain and hematuria. Insidious onset of disease, lack of specific signs and symptoms and the inability of routine radiological investigations to detect tumour areas lead to delay in diagnosis. Unfortunately, this leads to invasive disease and advanced stage at presentation leading to poor prognosis.[4]

Materials and Methods

Formalin fixed, hematoxylin and eosin stained sections of a nephrectomy specimen submitted in the Pathology department of SN Medical college, Agra, were observed microscopically and findings were noted.

Result

A 60 year old male presented with pain right side of abdomen for one year along with burning micturition. Patient was a non-smoker with no relevant medical history. He was operated for right sided kidney stone 24 years back, the details of which are not available. Pre-operative ultrasound examination revealed a severely hydronephrotic right kidney with complete cortical loss and with multiple right sided renal calculi (18 mm) in upper calyx [Fig. 1]. Left kidney was normal. Intravenous pyelogram revealed a poorly functioning right kidney. CT scan was not done pre-operatively. Serum urea was 23.8 mg/dl and serum creatinine was 0.8 mg/dl. Urine culture was sterile. Patient underwent a right sided simple nephrectomy and specimen was submitted for histopathological examination. On gross examination, a severely hydronephrotic kidney was seen with dilated calyces and multiple calculi. No tumour or growth was noticed on gross examination [Fig. 2]. Microscopic examination revealed primary urothelial carcinoma with squamous differentiation in the form of individual cell keratinization and intercellular bridges. The tumour involved the upper pole of kidney and showed invasion in renal pelvis. Vascular and perineural invasion was also noted. Hilum showed presence of urothelial carcinoma in situ with dysplasia, along with features of pyelonephritis [Fig. 3]. Extensive areas of necrosis were also seen. Peri-renal fibrofatty tissue was infiltrated by cells with squamous differentiation. Lower pole of kidney and renal capsule were not involved by tumour. Patient was put on follow-up and advised a post-operative CT scan to look for local spread and metastatis of tumour. Post-operative CT scan showed presence of a mass lesion in the renal fossa, involving the right adrenal and invading into the

right psoas [Fig. 4]. Patient is complaining of pain in the loin area post-operatively and he is contemplating chemotherapy.

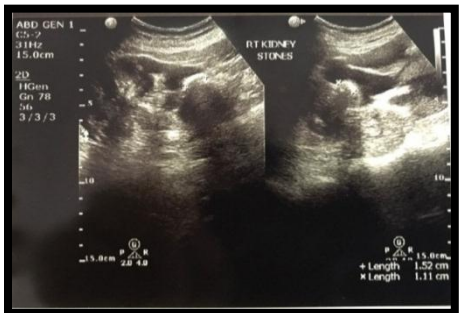

Fig. 1: USG shows severely hydronephrotic right kidney with complete cortical loss and with multiple right sided renal calculi

Fig. 2: Gross examination shows a hydronephrotic kidney with dilated pelvi-calyceal system and complete loss of cortico-medullary demarcation.

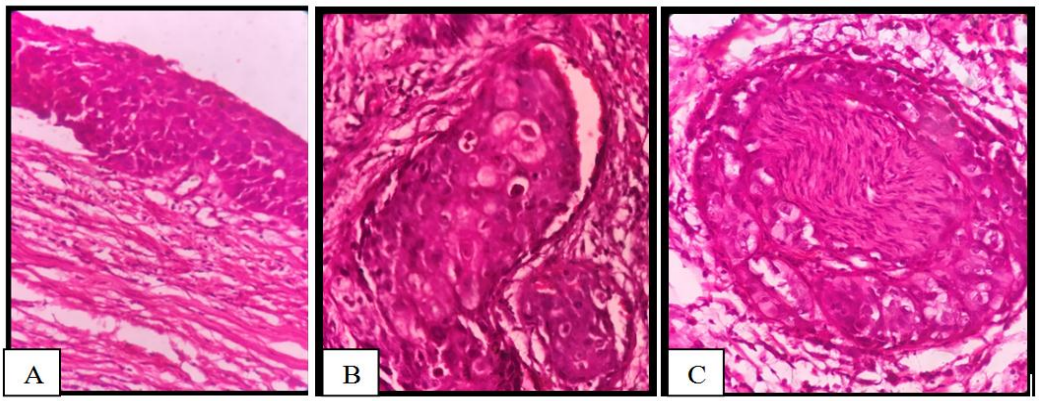

Fig. 3: A) Urothelial carcinoma in situ B) Intravascular invasion with tumor cells showing squamous differentiation. C) foci of perineural invasion. H&E, 40x

Fig. 4: post-operative CECT showing absence of right kidney due to nephrectomy along with presence of a mass lesion in the renal fossa involving right adrenal and right psoas

Discussion

Urothelial carcinomas of the upper tract have an epidemiology similar to those of the bladder, in that there is a male predominance, they are most common in older individuals, and tobacco and industrial carcinogen exposure are risk factors.[4] In the case discussed, the patient was an elderly male with history of long standing renal calculi and was also operated for the same complaint 24 years back. Although there were no clinic-radiologic clues towards cancer, yet the clinical history is consistent with this diagnosis.

The histopathology of upper tract tumors show the same spectrum as carcinomas of the urinary bladder with 90-95% represented by urothelial carcinoma. Morphologic variants of urothelial carcinoma include mixed (squamous and glandular) differentiation, nested variant, micropapillary variant, lymphoepithelioma like, inverted papilloma like, trophoblastic differentiation and sarcomatoid carcinoma. Features reported to have a negative impact on survival include architecture (sessile vs papillary), multifocality, concomitant carcinoma in situ, the presence of lymphovascular invasion and the presence of extensive (>10%) tumour necrosis.[4] In this case, on histopathology, the tumour showed foci of malignant urothelium with squamous differentiation in the form of individual cell keratinization and intercellular bridges. These foci of primary urothelial carcinoma were invading the renal parenchyma of the upper pole and renal pelvis. Hilum showed presence of urothelial carcinoma in situ with dysplasia. Renal parenchyma and hilum also demonstrated features of

chronic pyelonephritis. Intravascular and perineural invasion was noted. Extensive areas of necrosis were also seen.

If the urothelial dysplastic element is identified along with urothelial carcinoma in situ, the tumour should be classified as primary urothelial carcinoma with squamous differentiation.[8] Chronic irritation of urothelium is presumed to be a cause of squamous metaplasia.[5] Makise et al reported that squamous differentiation is the most common histological variant of urothelial carcinoma and its presence correlated significantly with the presence of histological grade 3 tumors, lymphovascular invasion, concomitant carcinoma in situ, advanced tumor stages, and lymph node metastasis.[6] Another previous study showed that squamous differentiation in urothelial carcinoma is associated with high recurrence of tumours in patients with bladder Ta/T1 carcinomas.[7] Tyagi et al studied 9 cases of primary malignant tumours of the renal pelvis in which they reported the mean being 41.7 years. Male/female ratio was 8:1. Pain & haematuria were the most common complaints. The commonest was transitional cell carcinoma seen in 7 patients (77.8%). Hydronephrosis, chronic pyelonephritis and nephrolithiasis were noticed in 66.7%, 44.4% and 22.2% of patients respectively.[9] Extensive tumour necrosis is independently associated with disease recurrence.

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. The common finding on surgical exploration is local invasion of the tumor into renal parenchyma, perirenal fat, psoas muscle or vascular invasion. Cisplatinum based chemotherapy and palliative radiotherapy have been advocated for the control of local symptoms in metastatic disease but have failed to show any survival.[5]

Conclusion

Urothelial malignancy should be suspected in patients with a long standing staghorn calculi, pyelonephritis and hydronephrosis. Squamous differentiation is common in urothelial carcinomas and is associated with aggressive disease. Radiological investigations like intravenous urography, ultrasound or computed tomography should be done pre-operatively in every patient presenting with long standing renal calculi and poorly functioning kidney. Unfortunately, in resource poor countries like India, such tumours often go un-noticed for long duration and present only at high stage leading to poor patient outcome.

Consent

Informed consent was obtained from the patient for publication of this case report.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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