Case Report

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An Aggressive Urothelial Carcinoma in a Horseshoe Kidney- A Case Report

Pathology Section

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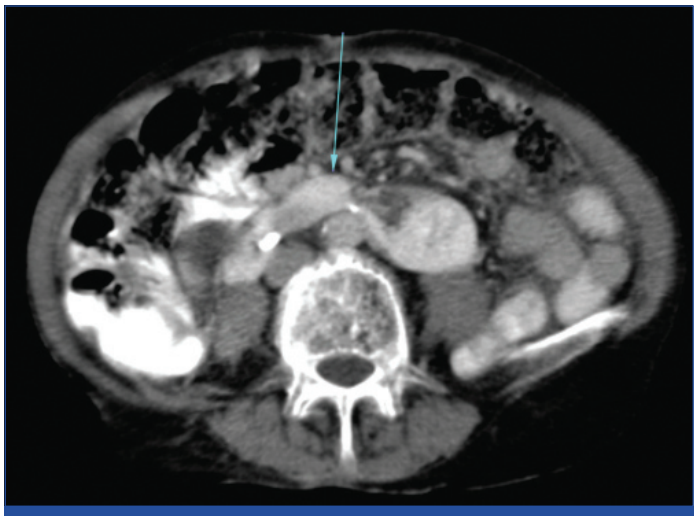
ABSTRACT

Evidence of horseshoe kidney in Indian population is 1 in 600-800 individuals. Horseshoe kidney is predisposed to complications by virtue of its ectopic position, malrotation and associated vascular and ureteral anomalies. Incidence of Renal Cell Carcinoma (RCC) in a horseshoe kidney is same as that in general population. Other pelvic tumours, transitional tumours, Wilms tumour and carcinoids show a greater frequency. High grade urothelial carcinomas are quite rare with a few case reports available. An index case of 75 yeal old male presented with renal mass in an incidentally diagnosed horseshoe kidney on radiologic imaging. The case has been highlighted due to its poorly differentiated tumour morphology and aggressive nature. Further, immunohistochemistry was done to arrive at a correct diagnosis for appropriate treatment. The tumour cells showed positivity for Cytokeratin 7 (CK 7) and CK 5/6. They were negative for p63, PAX-8 (Paired-box gene 8). Also, it is technically difficult to excise large-sized renal mass in an anomalous kidney.

Keywords: High grade malignancies, Anomalous kidneys, Renal anomalies, Renal tumours, Vascular anomalies

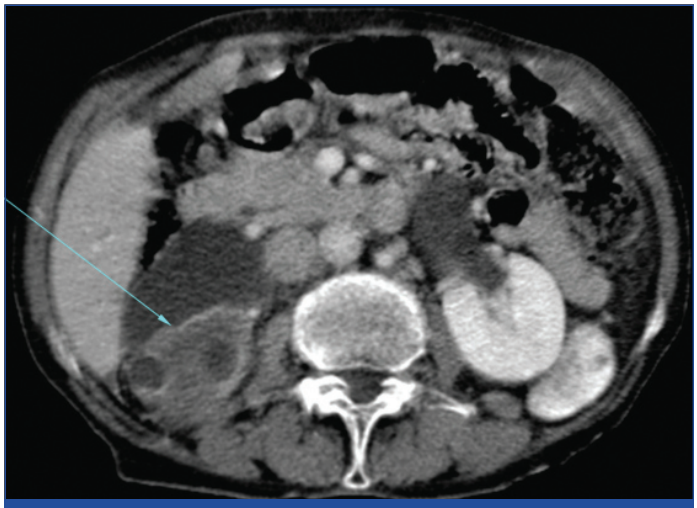
CASE REPORT

A 75-year-old male presented to the urology department with the chief complaints of one month history of abdominal pain and one episode of gross haematuria. The pain was sudden in onset, colicky and intermittent in nature. He was a known hypertensive on oral anti-hypertensive medications. His clinical examination revealed right lumbar and renal angle tenderness and no abnormalities were detected on systemic examination. No evidence of lymphadenopathy/oedema was noted. CT scan revealed horseshoe kidney united at the lower pole [Table/Fig-1]. Also, seen was a heterogeneously enhancing lesion in the upper pole of the right kidney measuring 7.4×7.3×5.2 cm [Table /Fig-2]. Another well-defined heterogeneously enhancing lesion was seen arising from the isthmus measuring 2.3×2.5×3.9 cm. Radiological diagnosis of heterogeneously enhancing mass lesion in a horseshoe kidney which was evident on scan was made [Table/Fig-1,2]. Routine blood and urine investigations as well as kidney function tests were within normal limits except for microscopy of urinary sediment which revealed 15-20 RBCs/hpf (Red Blood Cells/high power field). A provisional diagnosis of incidental radiologic evidence of horseshoe kidney with right renal mass was then given. A probability of RCC was considered. The patient underwent a right radical nephrectomy.



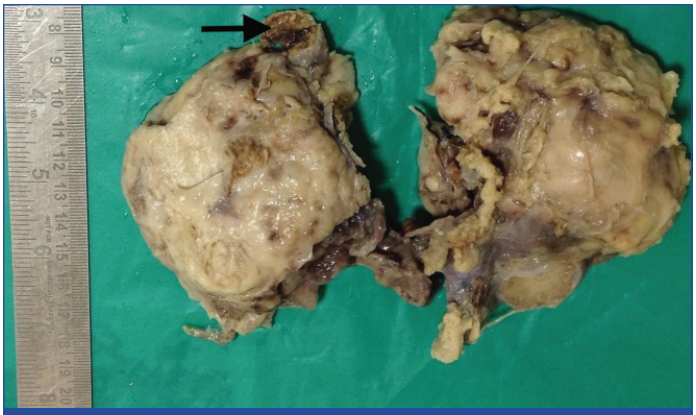
[Table/Fig-1]: CT scan showing horseshoe kidney with midline isthmus (arrow).

Intraoperatively, enlarged para-aortic lymph nodes were noted and hence, these too were subjected to a histopathological examination. Grossly, the kidney measured 11×9×3.5 cm. The external surface was irregular, bosselated and bulky at the upper pole with capsule adherent at places [Table/Fig-3]. Cut surface showed irregularly infiltrating, grey white solid growth measuring 9×6.5×4.8 cm involving the entire kidney and exhibiting focal yellow areas [Table/Fig-4]. The adjacent adrenal gland showed haemorrhage on cut-surface.



[Table/Fig-2]: Axial CT scan image showing heterogeneously enhancing mass lesion in the upper pole of right kidney (arrow).

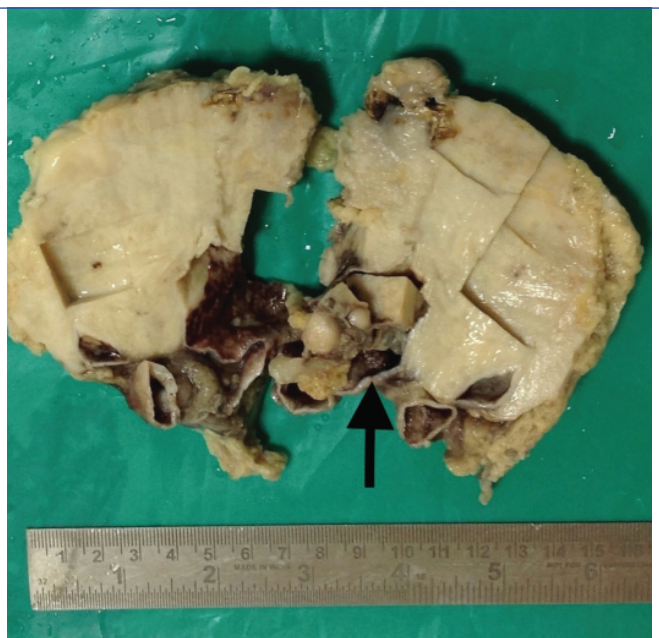
Microscopy revealed a poorly differentiated malignant epithelial tumour infiltrating the renal parenchyma and invading the perinephric fat. The tumour cells were arranged in sheets and nests with extensive areas of necrosis [Table/Fig-5]. Tumour cells were oval to polygonal with markedly pleomorphic nuclei, prominent nucleoli and eosinophilic cytoplasm, which diffusely infiltrated and destroyed the normal renal parenchyma [Table/Fig-6]. Mitoses were seen 5/10 hpf. Areas of vascular emboli were also evident. The pelvicalyceal lining epithelium showed ulceration, haemorrhage and fibrosis. Scanty compressed renal parenchyma showed areas of cystic degeneration. The adrenal gland showed infiltration by nodules of tumour, necrosis and haemorrhage. Three lymph nodes isolated from the perinephric fat showed metastasis in one lymph node with



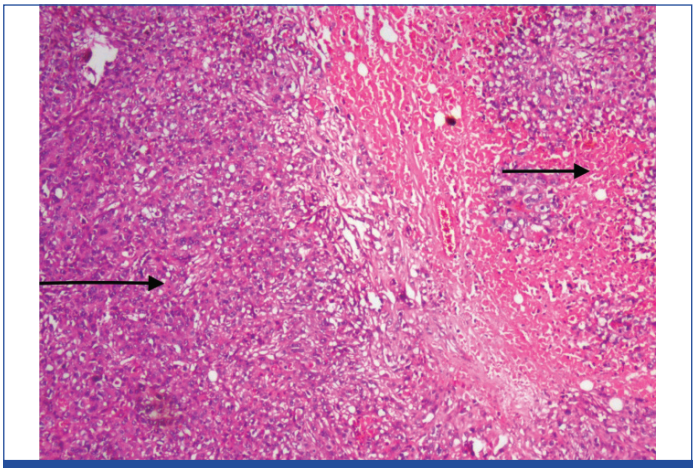
[Table/Fig-3]: Gross appearance of the excised kidney with irregular bosselated surface and capsule adherent at places with right adrenal gland, Arrow shows right adrenal gland.

perinodal spread. Paraaortic lymph node sent separately showed extensive metastasis with perinodal spread. Histopathological impression of poorly differentiated carcinoma was made with possibilities of high grade RCC, Squamous Cell Carcinoma (SCC) and Urothelial Carcinoma (UC). Immunohistochemical markers were used to come to a final diagnosis of the type of tumour. The immunohistochemical workup planned out at this stage was to confirm/rule out RCC, SCC and/ or UC. This workup was mandated in view of a poorly differentiated tumour cell morphology on haematoxylin eosin staining which consisted of CK 7, CK 5/6, PAX-8 and p63. The neoplastic cells showed diffuse and strong positivity for CK 7 [Table/Fig-7a]. They showed scattered positivity for CK 5/6 [Table/Fig-7b]. The cells were negative for p63 and PAX-8. PAX-8 positivity is associated with RCC. p63 negativity ruled out SCC and confirmed high grade nature of UC. CK 7 positivity is associated with UC. CK 5/6 positivity is associated with 70% cases of UC thus acting as a specific marker. A confirmatory diagnosis of a high grade UC in a horseshoe kidney with paraaortic lymph node involvement was made. The patient was doing well post-surgery and was discharged on the 7th day. Advice offered on discharge was follow-up with adjuvant chemotherapy after surgery.

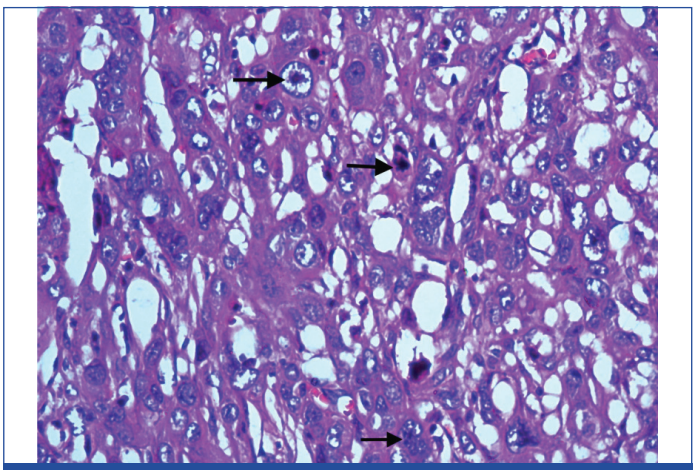
The prognosis generally in such types of cases depend on the surgical technique employed because of vascular anomalies associated with horseshoe kidney, in present case the patient was lost to follow-up.



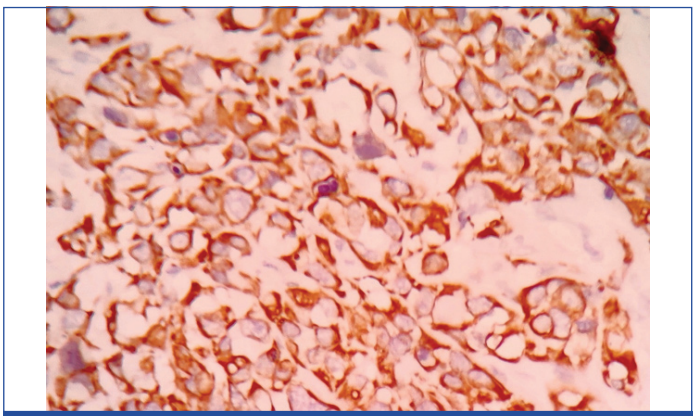
[Table/Fig-4]: Cut surface shows entire kidney involved by a grey white mass with focal necrosis, Arrow shows dilated calyx (arrow).



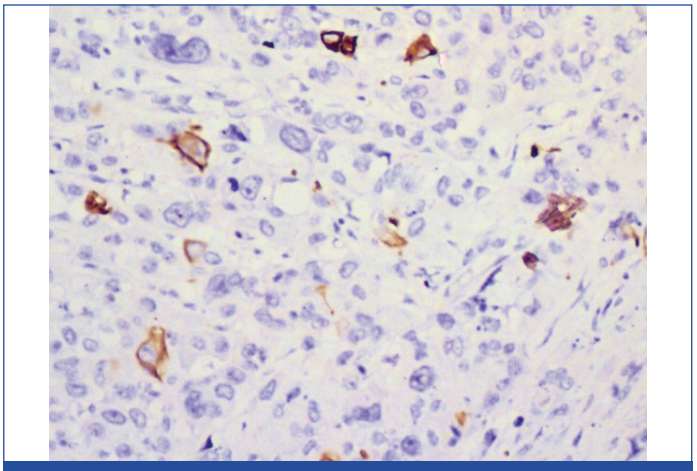
[Table/Fig-5]: Photomicrograph of poorly differentiated carcinoma with cells arranged in sheets and foci of necrosis (arrows) (H&E, X100).



[Table/Fig-6]: Photomicrograph showing tumour cells with bizarre nuclei and atypical mitotic figures (arrows) (H&E, X400).



[Table/Fig-7a]: Diffuse and strong positive cytoplasmic staining of tumour cells for CK 7 (IHC, X200).



[Table/Fig-7b]: Scattered cytoplasmic positivity of tumour cells for CK5/6 (IHC, X200).

DISCUSSION

Horseshoe kidney is the most common renal fusion anomaly accounting for 1 in 600-800 population with slightly higher incidence in males (M:F=2:1) [1]. Incidence is higher in the patients presenting with complaints related to obstruction, infection, malrotation or development of a tumour and with chromosomal anomalies such as Edward and Turner syndrome. This developmental anomaly occurs between 4 to 6 weeks of gestation. It occurs as a result of anomalous fusion of inferior pole of kidneys around the origin of the inferior mesenteric artery forming an isthmus and thus, giving rise to a U-shaped structure that is unable to ascend [2]. The kidney is usually lower than normal and the renal pelvis becomes oriented anteriorly. This gives rise to various vascular and ureteral anomalies, complications such as pelviureteric junction obstruction, renal stones, tumours, trauma and infection [2]. The incidence of malignancy is 3 to 4 times greater than in normal population and is thought to be due to secondary teratogenic factors at birth [3]. According to the world literature reviewed, there are 200 cases of tumours developed in horseshoe kidney been reported [4]. A few tumours associated with increased frequency include, renal pelvic urothelial carcinoma Transitional Cell Carcinoma (TCC), Wilms tumour, Carcinoid, SCC and Oncocytoma [1]. Among these, as mentioned by Balawender K et al., the most common tumour detected is RCC which constitutes 45% of the tumours, followed by Wilms and TCC which account for 20% of tumours seen in horseshoe kidney patients [5]. Though RCC occurs with same frequency in normal as well as in a horseshoe kidney, it is the most common in a horseshoe kidney [4]. The patients are of elderly age group presenting with painless haematuria and no other significant pathology and thus, it is picked up mostly on radiological examination [3]. Patients with horseshoe kidney may be asymptomatic throughout and present with symptoms related to obstruction, infection as a complication or may present with symptoms arising due to an obviously malignant tumour arising in an anomalous kidney. In present case too, the patient had an episode of haematuria and the horseshoe kidney was picked up incidentally on radiologic investigation.

Survival depends upon co-morbid status of the patient at surgery, pathology and stage of tumour at diagnosis and surgery depends on renal anomaly. In present case, the microscopic features were that of a poorly differentiated carcinoma. The possibilities included high grade RCC which is the most commonly developing malignant tumour arising in association with a horseshoe kidney [5]. The second differential diagnosis based on histopathologic assessment was that of a high grade SCC, hence to confirm the origin of tumour cells immunohistochemical markers were required due to its non-descriptive morphologic features. The third differential diagnosis based on morphology of tumour cells in certain foci of the tumour was that of high grade UC. Majority of the UC which are high grade show papillary configuration. In present case, the tumour cells were arranged in diffuse non-descriptive sheets. To establish the origin of the tumour and to type it, a panel of immunohistochemical markers had to be applied to establish an accurate diagnosis, due to the fact that high grade UC can have foci of squamous or glandular differentiation [6,7]. The profile of the tumour was highly characteristic, the tumour cells were diffusely positive for CK 7 which is seen in 60% of UC and is considered as a highly specific marker for UC of the kidney. Scattered positivity for CK 5/6 was noted which is usually the picture seen in UC of the kidney. The tumour cells were negative for p63 which ruled out SCC and confirmed the high grade aggressive nature of UC [8]. The tumour cells were negative for PAX-8 which ruled out RCC. The standard treatment of pelvic UC is nephroureterectomy. The overall 5-year survival rate in the surgically resected cases is about 50%. Unfortunately, progressive advanced stages of clinical presentation makes surgical procedures difficult and also brings down the prognosis [3,9]. In present case, adequate resection of the tumour was done with paraaortic lymph node dissection. Definitive diagnosis was arrived at due to complete immunohistochemical workup which was done.

CONCLUSION(S)

This case has been presented due to its uncommon occurrence in an anomalous kidney, aggressive nature and poor prognosis. Co-morbid factors such as hypertension, elderly age would influence the prognosis.

The poor prognostic factors in this case were older patient age, solid tumour pattern, high tumour grade, extensive tumour necrosis, nodal and vascular metastasis. The knowledge of consortium of anomalies, associated complications, their imaging features, complete pathologic examination including appropriate immunohistochemical workup for accurate diagnosis plays a crucial role in guiding most suitable treatment to the patients.

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