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PRIMARY RENAL CARCINOID TUMOR IN HORSE-SHOE KIDNEY: A CASE REPORT AND REVIEW OF LITERATURE

Urology

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ABSTRACT

Background: Primary renal carcinoid tumors are extremely uncommon. There is a strong association of renal carcinoid tumors with horseshoe kidneys. The presence of carcinoid syndrome and metastases indicates a more malignant disease. Treatment of renal carcinoid tumors is mainly surgical with good outcomes. Preoperative diagnosis without biopsy is rare and most cases are treated as renal cell carcinomas (RCC). Laparoscopic surgery in horseshoe kidney (HSK) is extremely challenging and preoperative CT angiography is very important for successful completion. Our aim was to review the literature for case reports of primary renal carcinoids in horse-shoe kidney and report another case of this rare tumor. **Methods:** Literature was extensively searched for case reports for primary renal carcinoids in Horseshoe kidney. **Results:** A total of 31 cases of primary renal carcinoids in Horseshoe kidney were reviewed. The mean age of presentation was 46.5 ± 13 years with both right (35.48%) and left moiety (38.71%) being equally affected. 35.48% of the cases reviewed were diagnosed as an incidental finding. The mean follow-up time was 3 years, 73.1% of patients had no evidence of disease after surgical treatment (radical or partial nephrectomy). **Conclusion:** Carcinoid tumours in HSK are well differentiated, indolent in nature and rarely associated with metastasis. CT angiography is a must to delineate abnormal vessels before surgery. Surgery is the treatment of choice but is challenging in view of abnormal anatomy.

KEYWORDS

Carcinoid, Renal, Horse-Shoe Kidney

INTRODUCTION

Carcinoid tumours are neoplasms with neuroendocrine differentiation arising from APUD cells. They most commonly arise from gastrointestinal tract and renal carcinoids in the setting of HSK are extremely rare [1]. Among the genitourinary carcinoids reported, the kidney accounts for 19% of the cases with most arising from testis (55%) [2]. Carcinoid tumors have features common to neuroendocrine tumours (NETs) irrespective of the organ of the origin. Carcinoid in the setting of HSK is difficult to differentiate from RCC, TCC preoperatively and diagnosis is based on biopsy. Laparoscopic surgery is extremely challenging and has been reported in few cases only, done in high end laparoscopic centres. This paper seeks to review the literature for primary renal carcinoid tumours in the setting of horseshoe kidney.

CASE PRESENTATION:

A 56-year-old man presented with left flank pain and haematuria from last 1 month. USG was done which showed an oval mixed echogenicity mass of 6.9 x 5.6 cm in the left moiety of horse shoe kidney (HSK). A CT Renal angiography was done, which showed 8 cm mass involving upper and interpolar region of left moiety, projecting into pelvis and abutment of psoas posteriorly suggestive of upper tract transitional cell carcinoma (Fig 1 a, b, c, d).

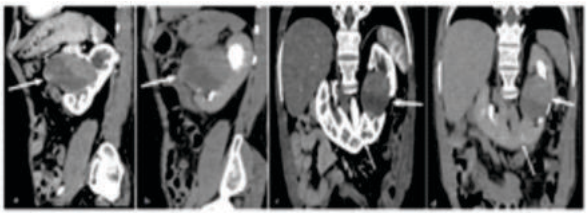

Fig 1 (a, b) Sagittal and (c, d) oblique coronal reformatted images in corticomedullary & excretory phases respectively demonstrating fused lower poles of both kidneys (thin long arrow) and an exophytic mass at interpolar region of left renal moiety (thick short arrow).

There were two renal arteries directly arising from aorta and two renal veins, proximal draining into IVC and distal into renal vein. The patient underwent an uneventful left laparoscopic heminephroureterectomy with bladder cuff excision (Fig 2 a). The final pathologic examination revealed a well-differentiated neuroendocrine tumor, typical of carcinoid, showing eosinophilic trabeculae intermixed with nests of small, monotonous, cuboidal tumor cells (Fig 2 b, c, d).

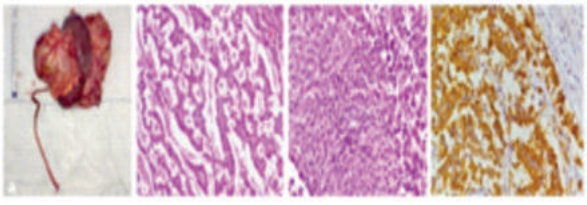

Fig 2 a Heminephroureterectomy with bladder cuff specimen (post-Surgery)
Fig 2 b Tumor cells arranged in trabecular pattern against a loose vascular stroma. (H&E x 200)
Fig 2 c Higher magnification showing tumor cells with moderate amount of cytoplasm, relatively uniform round-oval nuclei with stippled chromatin and inconspicuous nucleoli. (H&E X 400)
Fig 2 d Tumor cells showing strong diffuse cytoplasmic Synaptophysin immunoreactivity. (Synaptophysin x 400)

Post-surgery octreotide scan was negative.

Results: The clinical and pathologic data of the 31 cases are shown in Table 1.

The mean age of presentation was 46.5 ± 13 years. with both right (35.48%) and left moiety (38.71%) being equally affected. 63.3% were males. 35.5% of the cases were incidentally detected. Most patients presented with pain (58%). Other presenting symptoms were hematuria, weight loss, pyelonephritits, pruritis, constipation, back pain and facial flushes in one patient. Mean size of the tumor was 6.67 ± 3.4cm, largest tumor being 14.9 cm in greatest dimension. Except 1 case, all were operated by open surgery. The mean follow-up time was 3 years, 73.1% of patients had no evidence of disease after surgical treatment (radical or partial nephrectomy). Only one patient with liver metastasis died of disease. Even though none had extrarenal disease at

presentation, but still 8 out of 31(25.8%) of the patients had nodal/extranodal metastasis on follow up.

DISCUSSION

Primary Renal carcinoid tumor is very rare, with peak incidence in the fifth and sixth decades of life [2]. Carcinoid tumor in HSK presents at an earlier age compared to normal kidneys (relative risk 62-120) [3]. In our review, the mean age of presentation was 46.5 ± 13 years which is earlier compared to the primary renal carcinoid in normal kidney (mean age 50 years) [4]. Carcinoid tumor is thought to originate from neuroendocrine cells in association with intestinal metaplasia of the renal collecting system or from the teratomatous intestinal or respiratory epithelium within the HSK, which may explain why it is common in HSK [5]. The male: female ratio is 1.7:1 which is in accordance with the findings of Romero et al and is postulated to be due to the higher incidence of horseshoe kidneys in males [2]. Primary renal carcinoids not associated with HSK have equal male: female predisposition. Also, both moieties are equally affected in our study, which is unusual as right kidney is more affected than left in primary renal carcinoids, as reported by Romero et al [3]. There is frequent occurrence of renal carcinoids in the isthmus of the horseshoe kidneys [3] and all our cases had involvement of Isthmus. Our case was 49 years male who had tumor involving left moiety and isthmus.

There may be associated Wilms tumour, neoplasms of the renal pelvis and teratoma associated with carcinoid tumor of HSK [3]. Teratoma containing carcinoid has been reported in one case which also had synchronous adenocarcinoma in the other moiety. The prognosis in such cases is determined by the most aggressive tumor. No such associations were seen in our study, implying that these are rare associations.

Most of the primary renal carcinoids are detected incidentally. This is not the case in carcinoids associated with HSK. Most cases in this review were symptomatic (64.52%) and most commonly reported with abdominal or flank pain [6]. They may also present with haematuria, constipation, urinary frequency, fever, epigastric discomfort, weight loss, and abdominal mass [6]. Our case too was symptomatic at presentation with pain and haematuria with imaging suggesting upper tract urothelial carcinoma.

Imaging cannot reliably differentiate carcinoid from other renal tumors. No distinctive imaging features differentiate them from other primary renal masses. On Ultrasound they are usually hyper echoic mass and on Computed tomography, they are solid or solid with cystic component with minimal contrast enhancement corresponding to their hypo vascular or avascular nature [7]. CT angiography is important in any case of renal tumor associated with HSK from surgical point of view, as aberrant renal vessels arise from many sources. Common site of origin of aberrant renal artery is common iliac artery (CIA). Right moiety has more chances of getting aberrant vessel from CIA than left [2].

Histopathologic differentiation between Renal Carcinoid and RCC is essential because the treatment and prognosis are entirely different. On histopathology, cut surface is yellow-orange to tan-red and most are confined to the kidney while some involve perirenal fat. In view of Somatostatin receptor expression, Somatostatin receptor scintigraphy (SRS) is used for the location of the disease elsewhere in the body and treatment of tumor recurrence and metastasis with good sensitivity and specificity.

Approximately 10% involve the renal vein. In our review, the mean size of the tumor was 6.67 ± 3. 38cm.The neoplastic cells are monomorphic with granular amphophilic to eosinophilic cytoplasm. The nuclei are round to oval, uniform in size, with granular salt and pepper chromatin. Neoplastic cells contain membrane bound electron dense neurosecretory granules (100 to 400 nm) usually with a polar distribution. The mitochondria and rough endoplasmic reticulum are poorly developed [3]. Perinuclear aggregates of intermediate filaments have also been reported [2]. Immunohistochemical Staining is positive for a variety of neuroendocrine markers like neuron-specific enolase, chromogranin, Leu-7, synaptophysin, and cytokeratins (broad-spectrum and low-molecular-weight) [3,8].

In our review, all the tumors were confined to the kidney. None had renal vein or IVC involvement. Only 3 cases of metastasis were reported. All these are suggestive of their indolent nature when associated with HSK. Carcinoid tumour in HSK is less aggressive compared to RCC. Distant spread has been reported for up to 7 years after nephrectomy which makes long-term follow-up care imperative [8].

Surgical resection of the tumor is the treatment of choice in the management of localized primary renal carcinoid via Open or Laparoscopic approach. In this review, except our case, all were operated by open surgery in view of complex anatomy which poses severe difficulty while manoeuvring the tumor laparoscopically. Being a high-volume centre of laparoscopy, our case was managed by laparoscopic surgery without any difficulty. Metastatic renal carcinoid is chemo resistant [8]. Somatostatin receptor expression has been reported in 87% of the cases [9]. However, there is limited data in the literature regarding the use of somatostatin analogues in the treatment of primary NETs of the kidney.

Syndromes like carcinoid syndrome, Cushing syndrome, Verner Morrison have been reported to occur in approximately 12.7% of patients with renal carcinoids [2] but only one patient had carcinoid syndrome (3.23%) in this review

CONCLUSION:

Carcinoids associated with HSK have a better prognosis than those occurring in normal kidneys. Renal carcinoids arising within HSK are benign however when bilateral, course is more aggressive with likely metastasis on follow up. Outcome does not appear to be directly related to presence of nodal metastases or type of surgery. Development of distant metastasis after surgery does not seem to worsen the prognosis.

Table 1: The clinical and pathologic data of the 31 cases

Reference	Sex/Age	presentation	Gross	Laterality	Treatment	Extrarenal invasion	Metastasis	Clinical Outcome	IHC
Fetissof et al., 1984 Lanson et al., 1978a	65/M[1]	Fever, flank mass	2-cm tumor nodule arising within cystic teratoma ("dysplastic" horseshoe kidney)	Right	Right nephrectomy	No	No	NA[3]	Glucagon, Serotonin and somatostatin +ve
Acconcia et al., 1988	29/F[2]	pain, hematuria	10 × 7-cm, circumscribed, lower pole	Right	Right nephrectomy	No	No	NED[4], 3 years	Somatostatin and adreno-corticotropic hormone negative
Machet et al., 1994	79/F	Abdominal pain	6 cm, cystic mass rt lower pole, non-enhancing	Right	Right Partial Nephrectomy with Isthmectomy	No	No	NED,3 years	Somatostatinand Serotonin +ve
Van den Berg et al., 1995	55y/F	Atypical chest pain	5cm, circumscribed, isthmus	Isthmus	Partial Nephrectomy with Isthmectomy	No	No	NED,3years	Pancreatic polypeptide
Kurl et al., 1996	62y/F	Flank pain	9 ×5× 5-cm, isthmus, cystic component		NA	No	No	Yes(liver at 24 months). Alive with disease	Pancreatic polypeptide,glucagon,serotonin

Krishnan et al., 1997	48y/M	Pyelonephritis	6× 5 × 2.5 cm cystic lesion involving isthmus containing multiple carcinoids.	Isthmus	Open Partial Nephrectomy with Isthmectomy	No	No	NED,2 years	Glucagon, pancreatic polypeptide, VIP, serotonin,calcitonin somatostatin,neuron specific enolase +ve
Lodding et al., 1997	23y/M	Abdominal pain	2cm, circumscribed, stone like	Right	Open right heminephrectomy	No	No	NED 3 years	NA
Be´gin et al.,1998	43y/M	Testicular pain	3.5-cm solid, circumscribed tumor located in the left medial aspect close to the isthmus	Left	left radical nephrectomy	No	No	NED at 20months	NA
Isobe H et al,2000	51y/F	Incidentally detected	7.0 x 5.0 x 5.0 cm surrounded by a capsule and was reddish-brown and fragile on cut surface	Left	Isthmectomy, left nephrectomy and lymphadenectomy	No	No	NED, 3 years	Neuron-specific enolase, chromogranin-A, cytokeratin, pancreatic polypeptide, vasoactive intestinal peptide and CEA +ve
Soulie M et al 2001	NA	Incidentally detected	Cystic lesion in kidney	Left	Left partial nephrectomy	No	No	NED,3years	NA
McVey JR et al 2002	39y/M	Pruritis,weight loss	4x3cm lesion in left moiety	Left	Partial Nephrectomy and alcohol injection liver metastasis	No	Yes (liver,spine)	4y survival	Synaptophysin, pancytokeratin +ve
Faucompret S et al 2002	42y/M	Incidentally detected	6cm left moiety lesion	Left	Left heminephrectomy	No	No	NED,3 years	Chromogranin and Serotonin +ve
Motta L et al 2004	45y/M	Gross Hematuria	13-cm left-sided renal mass	Left	left radical nephrectomy with symphysiotomy followed by Octeotride therapy	No	At 9 months,liver metastasis and an osteolytic lesion on the iliac bone	NA	Chromogranin and Serotonin +ve
Cerulli C et al,2005	56y/M	Incidentally detected while being evaluated for renal stones	A large mass in the lower pole of the right kidney	Right	right open partial nephrectomy with resection of the lower half of the right kidney and isthmectomy	No	No	NA	Chromogranin and Serotonin +ve
Rodríguez-CovarrubiasF et al,2006	33y/F	Constipation, lower back pain. and right flank abdominal mass	Bilateral tumor arising in a HSK	Both	Right radical nephrectomy and left partial nephrectomy with isthmectomy	No	Liver metastasis after 5 months of surgery, followed by new liver and lung lesions	Alive at 3 years	Synaptophysin, Neuron-specific enolase (NSE) and Chromogranin +ve
Hartman MS et al,2006	32y/M	Pain abdomen	Bilateral enhancing, partly cystic renal masses involving both moieties as well as isthmus. The largest enhancing mass, within the right kidney, measured 11 x 7 cm	Both	Sandostatin on a monthly basis	No	Thyroid,Pleura and left Metastasis	Alive at 2years	Synaptophysin, pancytokeratin +ve
Lane et all 2007	68y/F	Incidental	4.5cm	Right	Partial Nephrectomy	No	Liver	Died of disease at 24 months	NA
Lane et al 2007	51y/M	Incidental	8cm	Right	Radical Nephrectomy	No	No	NED at 11 months	NA
Lane et al 2007	51y/M	Pain	3.5cm	Left	Radical nephrectomy	No	No	NED at 6 years	NA

Bhalla et al 2007	32/M	Pain abdomen	14.cm mass lesion	Right	NA	No	Lymph node Thyroid	Alive at 1 year	NA
Armah et al, 2009	50y/M	Low back and right hip pain	5x4 cm mass involving lower pole of left kidney	Left	Partial nephrectomy	No	No	NA	Chromogranin, synaptophysin-+ve
de Hoog JP et al.2010	51y/M	lumbar back pain and sciatica	6x4.2x3.5 cm mass involving the right lower pole	Right	Open Heminephrectomy and isthmectomy	No	No	NED, 1year	Chromogranian, synaptophysin and neuron-specific enolase +ve
Anand A et al, 2010	35y/M	Right flank pain, haematuria	9x7cm mass involving isthmus of HSK extending to lower pole of right kidney	Right	Right nephrectomy with isthmusectomy	No	No	NED ,3 years	Cytokeratin (CK), neuron specific enolase (NSE), chromogranin and synaptophysin +ve
Litwinowicz et al 2011	66/M	Incidental	8cm mass	Left	Radical Nephrectomy	No	Lymph nodes	NA	NA
Sun K et al, 2013	37y/M	Incidentally detected	1.Cystic mass (5.2×5.2) in lower pole of right kidney and isthmus. 2.(2.4×2.4 cm) at the lower pole of the left kidney and in isthmus	Both	Bilateral Partial Nephrectomy	No	No	NED ,9months	Carcinoid component was pancytokeratin , synaptophysin , chromogranin A +ve Left mass -cRCC
Amira et al,2014	33y/M	left hypochondrial mass	(9.6 cm × 9.2 cm × 9.5 cm) mass hilum of the left compartment of horseshoe kidney extending to the lower pole and isthmus, cystic with wide area of haemorrhage	Left	left open nephrectomy	No	No	NA	cytokeratin + synaptophysin+ chromogranin -ve
Seker KG et al,2017	37y/F	Incidentally detected	1.8 x 1.25 cm mass in left kidney lower pole	Left	Left open Partial Nephrectomy	No	No	NED, 2 years	Chromogranin, synaptophysin-+ve
Khatami R et al,2018	42y/F	Incidentally detected renal mass while being evaluated for hypertension	7.8 x 6.8 x 6.7 cm lobulated heterogeneous mass arising from the midline bridging cortical tissue; enlarged retroperitoneal lymph node	Isthmus	Open partial nephrectomy	No	No	NED,2 years	Chromogranin, synaptophysin-+ve Neuron specific enolase+ve
Rosenberg JE et al,2018	51y/F	Facial Flushes	3.5cm endophytic mass in right moiety	Right	Open right Partial Nephrectomy	No	No	NA	Cytokeratin (CK), neuron specific enolase (NSE), chromogranin and synaptophysin +ve
Gupta S et al,2021	40y/F	Hematuria	14.9-cm mass arising from the isthmus	Isthmus	Open partial nephrectomy	No	Yes (retroperitonealLymph nodes)	NA	Chromogranin, synaptophysin-+ve
Present case, 2022	49/M	Flank Pain, Hematuria	6.5 x 6 cm mass in hilum, solid and cystic with extension into Pelvis	Left	Lap left heminephrectomy with Bladder cuff excision	No	No	NED at 1 year	Cytokeratin (CK), neuron specific enolase (NSE), chromogranin and synaptophysin +ve

1M- Male, 2F- Female, 3NA- Not Available, 4NED- No Evidence of disease

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