Original Research Paper

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Pathology

NOT JUST CLEAR CELL CARCINOMA-RARE AND UNUSUAL TUMOURS OF KIDNEY.A THREE YEAR STUDY IN A TERTIARY CARE HOSPITAL IN KASHMIR VALLEY.

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ABSTRACT

AIMS: An overall assessment of the clinical behaviors ,histopathological features of non clear cell tumours of kidney

MATERIALS AND METHODS: Retrospective evaluation of uncommon renal neoplasm in a tertiary care center. Twenty cases of uncommon renal tumors were diagnosed in our institution .

RESULTS: Out of 20 cases, fifteen were seen in adults and five in pediatric age group. Rare cases in pediatric age group were 2 cases of clear cell sarcoma (CCS) , one case of rhabdoid tumor , one case of congenital mesoblastic nephroma , one case of multilocular cystic nephroma .Among the adults there were four cases of chromphobe renal cell carcinoma ,three cases each of papillary renal cell carcinoma and renal medullary carcinoma,two cases of oncocytoma,one case each of metanephric adenoma,primitive neuroectodermal tumour and leiyomyosarcoma.

CONCLUSION: The clinical presentations of these uncommon renal tumors are similar to that of clear cell renal carcinoma tumor. Thus, preoperative diagnosis is difficult even with modern imaging techniques. Some of these tumors (CCS, rhabdoid tumor) are rapidly progressing and have a poor outcome. Hence, early intervention in the form of complete surgical resection of the tumor (whenever possible) and postoperative chemo/radiotherapy are imperative for fruitful outcome.

KEYWORDS : Clear cell sarcoma, pediatric, renal tumor, rhabdoid tumor, metanephric adenoma

INTRODUCTION

Clear cell renal cell carcinoma is the most common tumour in adults and Nephroblastoma (Wilms' tumor) is the most common renal tumor in childhood. Clear cell rcc accounts for more than 70% of adult renal tumor. Some unusual tumors like Medullary carcinoma leiyomyosarcoma,primitive neuroectodermal tumour are rarely seen in adult kidney.On the other hand, congenital mesoblastic nephroma (CMN), multilocular cystic nephroma (MCN), are found infrequently in pediatric age group. Clinically all these tumors are indistinguishable. A few case series of uncommon renal tumors are reported in literature till now. We have undertaken a retrospective study of non-Wilms' renal tumors and non clear cell renal tumours in our institution.Each tumor has been evaluated individually in terms of its presentation, preoperative investigations ,preoperative chemotherapy, postoperative recovery, histopathological findings, final outcome, and follow up. The results are tabulated, evaluated, and compared with the other available concerned articles

MATERIALS AND METHODS

This is a retrospective analysis of uncommon renal tumors in both adults and children. We have intentionally excluded common tumor from this study. The study comprised of 20 patients, out of Which 15 were adults(10 males 5 females) and 5 (3 males 2 females)were children. Age ranged from 2 years to 60 years. Most patients were diagnosed clinically as a renal lump,flank pain and some incidentally on ultrasound imaging. . All the patients were investigated in the form of complete hemogram,urine routine examination, chest Xray, ultrasonography(USG)whole abdomen,and contrast enhanced computed tomography (CECT). Magnetic resonance Neo-adjuvant chemotherapies were given in two pediatric cases to make them amenable for complete surgical tumor resection. Radical nephrectomy and surgical staging were done in all cases. Postoperative chemotherapy and radiotherapy were given according to the histopathological reports and TNM staging. IHC was done wherever needed because of limited supply of markers in the department and serum urea/creatinine estimation were done in the follow-up

DISCUSSION

Papillary renal cell carcinoma comprises about 15% of all renal cell carcinoma. Renal tumors arising in patients on chronic hemodialysis tend to be of papillary type.[1]

Papillary renal cell carcinoma is characteristically hypovascular on radiographic studies, and grossly it may exhibit extensive areas of necrosis.[2] Microscopically, complex papillary formations are seen, often accompanied by prominent stromal infiltration by neutrophils or foamy macrophages[3,4] . Psammoma bodies may be numerous. The nuclear grade is variable . Immunohistochemical there is consistent expression of keratin 7. papillary renal cell carcinoma can be further subdivided into two types: *type 1*, in which the papillae are lined by a single layer of cells with scanty pale cytoplasm; and *type 2*, in which the papillae are lined by pseudostratified epithelium composed of cells with abundant acidophilic cytoplasm.[5,6] In our series there were 4 cases of papillary renal cell carcinoma 3 male one female..,the renal mass was found incidentally on ultrasound abdomen.Surgical nephrectomy was done followed by chemotherapy.All 4 patients are doing well on followup

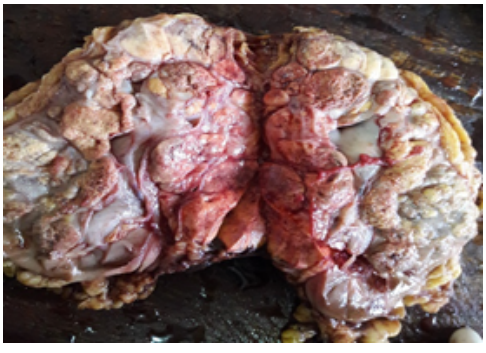

Fig1a Gross picture showing cut section of tumour with necrotic hemmorhagic areas

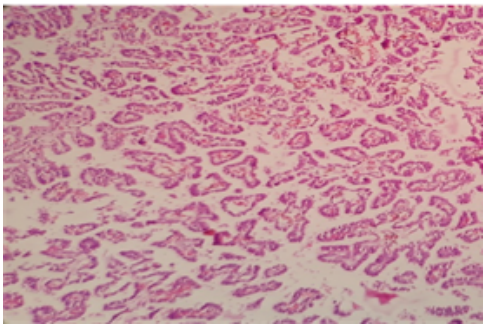

Fig1b Photomicrograph showing papillary formations of papillary tumour at 10x

Chromophobe renal cell carcinoma comprises about 5% of all cases of renal cell carcinoma. It is grossly well circumscribed, solitary, with a homogeneous gray to brown cut surface devoid of hemorrhage or

necrosis[7] (Fig.2a). Microscopically, there is a characteristic nesting ('alveolar') arrangement of the tumor cells, sometimes associated with microcystic and adenomatous patterns of growth.[8] The tumor cells have sharply defined borders and abundant cytoplasm[9] (Fig2b.). The latter has a pale, acidophilic quality, and there is often a clear perinuclear region. This cytoplasmic appearance is due to the presence of numerous cytoplasmic vesicles that are well appreciated by electron microscopy[10] . These vesicles stain for Hale colloidal iron, indicating the presence of acidic mucins[11,12,13,14] . Calcification is present in nearly half of the cases. Immunohistochemically, chromophobe renal cell carcinoma is positive for EMA, keratin 7, CD9, CD82,[15] paxillin, claudin-7 and -8,[16,17] Ep-Cam (an epithelial adhesion molecule),[18] and E-cadherin, but not N-cadherin or vimentin.[1] Despite earlier claims to the contrary, a high percentage of chromophobe cell carcinomas have been found to be immunoreactive for CD10.We reported 4 cases of chromophobe renal cell carcinomas(2males 2 females)One patient presented with flank mass one with flank pain and two were detected incidentally. Surgical nephrectomy was done followed by chemotherapy.All 4 patients are doing well on follow up.

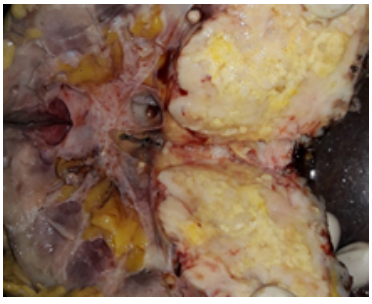

Fig 2a Gross picture of cutsection of chromophobe renal cell carcinoma

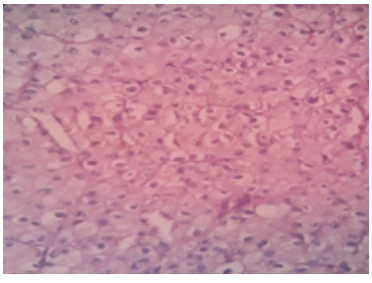

Fig 2b Photomicrograph showing eosinophillic uniform cells arranged in small nests

Medullary carcinoma was first described byDavis and associates (1995) . The most common clinical presentation is hematuria and flank or abdominal pain. Very often, symptoms referable to distant metastases are the initial presentation. Patients show a male gender predilection (2:1), and an age range of 5 years to 39 years with 75% of patients in their second and third decades. Radiologic features with local invasion of the renal sinus in the clinical setting of a young patient with sickle cell trait are strongly suggestive of the diagnosis of medullary carcinoma..Microscopically, the tumor cells are organized in large irregularly shaped nests infiltrating a fibrous stroma. This desmoplastic stroma may equal or exceed the tumor in forming the tumor mass . Immunohistochemical stains including AE1/AE3, EMA, CAM 5.2, and CEA are positive.[19,20,21,22] High molecular weight cytokeratin stains are negative. Epithelial mucin is usually present.In our series 3 patients of medullary carcinoma presenting with abdominal pain were noted (2 males and one female) .All 3 patients had sickle cell trait. And are doing well on therapy after nephrectomy

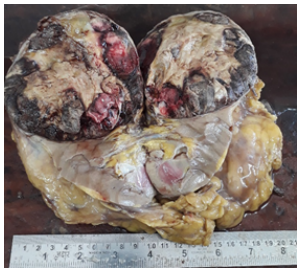

Fig3a Gross picture of cut surface of renal tumour showing well circumscribed tumour with variegated appearance

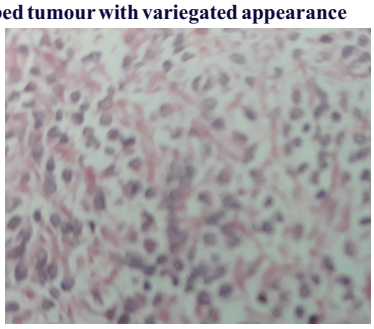

Fig3b Photomicrograph showing pleomorphic tumour cells with hyperchromatic enlarged nuclei with some cells having rhabdoid features(High power magnification)

Oncocytoma patients range in age from 15 years to 102 years with a peak frequency in the sixth to eighth decades (75% occur in the ages 50 years–79 years). Approximately 67% of patients are males.[23] This neoplasm is most frequently identified as an incidental diagnosis in the course of a radiologic examination. Grossly it is solid and well circumscribed, sometimes focally encapsulated. The color of the cut surface is red-brown to mahoganyThe common morphology shows rounded aggregates of small oncocytes in an acellular stroma . Clones of smaller cells with scant cytoplasm (oncoblasts) may be admixed . A central scar is typically, but not invariably, present.[24,25] Most nuclei are smoothly rounded to oval, show minimal pleomorphism, and often show prominent nucleoli. Focal areas often have prominent nuclear pleomorphism with hyperchromasia, but large, bizarre cells may be widely scattered .Two patients of oncocytoma(one male,one female) in our series were diagnosed incidentally and operated with nephron sparing surgery.No chemotherapy or radiotherapy was given Both patients are doing well.

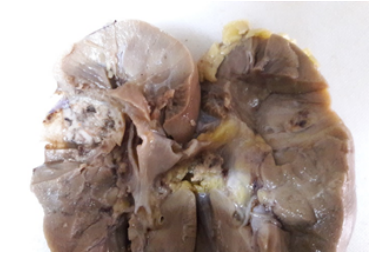

Fig4a Gross picture showing small encapsulated tumour grey white in color

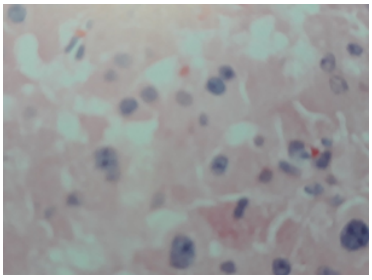

Fig 4b photomicrograph showing oncocytic cells on 40x magnification,

Metanephric adenomas are uncommon, densely cellular neoplasms of the kidneys peak age frequency is 40 years to 69 years. There is a female preponderance (69%). The neoplasm is incidentally discovered in approximately 50% of cases. Alternatively, some patients present with hematuria, and abdominal or flank pain. Ten percent of patients present with polycythemia. The neoplasms are solid, firm, yellow-tan to gray, well circumscribed, and unencapsulated. The cut surface commonly shows foci of hemorrhage and necrosis. Small cysts and calcifications are present in 10% of cases. They range in size from millimeters to the largest reported at 15 cm.[26] Fifty-percent of cases are 5 cm or less in diameter. Microscopically, the metanephric adenoma shows very small cells with very little cytoplasm forming very small tubules in an acellular stroma . Similar cells may line branching tubular structures (F. Nodules of closely packed small tubules, suggesting blastemal nodules, are less often seen . The intervening stroma is

acellular, hyalinized, or edematous. Psammoma bodies are common, frequently embedded in dense stroma. Mitoses are rare or absent .Our one patient of metanephric adenoma was a male patient presenting with incidental finding on ultrasound.He underwent nepphrectomy and is doing well on regular follow up

Peripheral neuroectodermal tumors are most frequently observed in the soft tissues of the paravertebral region and chest wall, less frequently in the extremities. PNETs arising in the kidney were first reported in 1994, Patients show a male predominance (58%), and there is no side predilection. The age range of patients reported in the literature is 4 years to 69 years, with 85% of cases diagnosed during the second to fourth decades. Most patients are between the late teens and early thirties. Patients present most frequently with abdominal or flank pain. These neoplasms are typically large, with 65% measuring greater than 10 cm in diameter. Only occasional cases are 5 cm or smaller. Usually, much of the kidney is involved, with evidence of local invasion into the peri renal tissue. The cut surface of the solid tumor is gray-tan with random areas of necrosis and hemorrhage,., Microscopically, the neoplastic cells are small with scanty, clear, or eosinophilic cytoplasm. Glycogen can often be detected with the PAS stain. The nuclei are round and centrally located. Nucleoli are not prominent. Mitoses are frequent, as are small, round hyperchromatic nuclei of pyknotic cells. These tumor cells are dispersed in sheets or poorly defined lobules of discohesive cells. Perivascular pseudorosettes are common, and in many cases Homer-Wright rosettes are present . Foci of tumor necrosis are also common. Immunostaining procedures include positive vimentin, Cd99

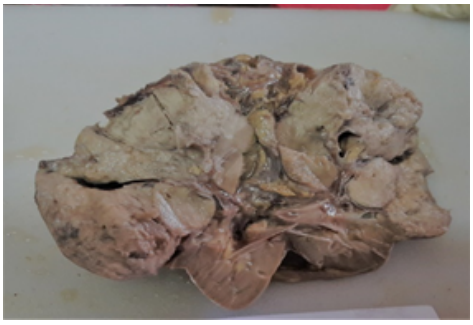

Fig5a Gross picture showing irregularl fleshy cut surface of tumour

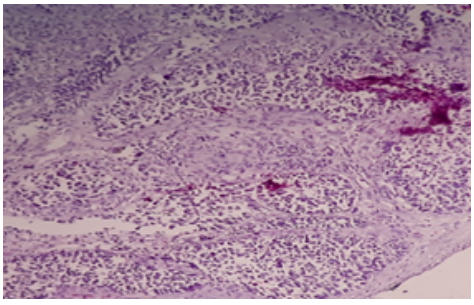

Fig5b Photomicrograph showing round to oval tumour cells arranged in nests.fibrovascular bundles traversing through the tumour

Sarcomas of various types can arise in the adult kidney, including the renal capsule. Before a diagnosis of primary sarcoma of the kidney of any type is made, the more common possibilities of sarcomatoid renal cell carcinoma and primary retroperitoneal soft tissue sarcoma (particularly liposarcoma) with secondary renal invasion should be considered.

CCSK is also known as “Bone metastasing tumor of childhood.” It comprises of 3% of all primary childhood renal tumor. It is classified separately from Wilms' tumor due to several distinctive features such as unilateral,unicentric in the medullary region of kidney with foci of necrosis and cyst formation, and presence of intracytoplasmic vesicles. CCSK has propensity to permeate through renal and perirenal vascular system.[27]Bone and brain metastasis is the characteristic features of CCSK. CCSK is rare below 1 year of age, peak incidence 3-5 years and is more common in male (male:female =2:1). Various patterns of CCSK have been described such as classical, myxoid, sclerosing, cellular, epitheloid, palisading verocay body, spindle cell, storiform, and anaplastic. Most common is classic type (90%) where the tumor cell appears as monomorphic with cords ornests of 10 cells separated by fibrovascular septa. Cells in the core of the tumor may assume a spindle shape.Nuclei are overall uniform with fine dirty chromatin without prominent nucleoli. Empty appearing Orphan Annie Eye nuclei are a frequent occurrence. Cytoplasm is sparse with indistinct borders.[28] CCSK is vimentin and Bcl-2 positive. CCSK is managed by aggressive surgical approach followed by chemotherapy and radiotherapy as per NWTSG protocol. Relapses although late are common even in stage-1 tumor. The overall survival is 69%[29] In this series, we have encountered two patients.

RTK accounts for 2% of all renal tumors. It was described early in 1978 as a rhabdomyosarcomatoid variant of Wilms' tumor.[30] The term “rhabdoid tumor”was coined by Haas in 1981 because of absence of muscle differentiation. RTK is the most aggressive renal tumor in pediatric age group. Usually, it presents in advanced stage and resistant to chemotherapy.[31]Diffuse hematogeneous and lymphatic spread occur in infancy. Macroscopically,it is solid, nonencapsulated with extensive intratumoral hemorrhage and necrosis. Microscopically, it comprises sheets of cells with prominent nucleoli and nuclear pleomorphism. Important histologic features are open vesicular nuclei and scattered hyaline eosinophilic cytoplasmic inclusions of intermediate filament in a whorled pattern.In our series, we encountered one male patients with RTK. They presented with rapidly progressing renal lump. There was no hematuria and no clinical evidence of distant metastasis.

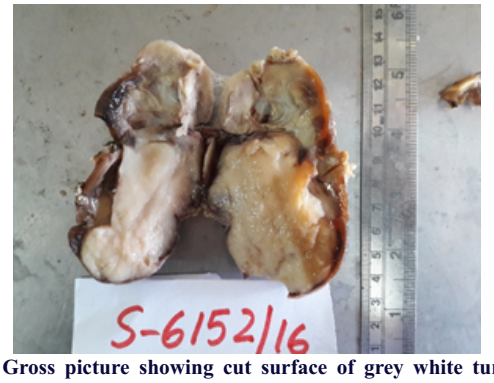

Fig6 Gross picture showing cut surface of grey white tumour completely replacing whole renal parenchyma

CMN is the most common renal tumor in newborn and infancy. Bolande *et al*. were the first to describe the tumor as a separate entity from Wilms' tumor.[32]Macroscopically, it is a firm tumor. Cut section showsyellowish gray trabeculations like leiomyoma. Three histological subtypes have been described. Classical (24%) looks like infantile myofibromatosis, cellular (66%) looks like infantile fibrosarcoma, and mixed type(10%).[33] Relationship between mixed CMN and two main histologic subtypes is not clear.[34] Classic CMN reflects intrarenal fibromatosis and cellular CMN isintrarenal infantile fibrosarcoma. Most cases of CMN are cured with radical nephrectomy with lymph nodes sampling. Metastasis to lung, liver, brain, and heart have been reported.

Cystic nephroma, also known as MCN, is a rare nongenetic lesion of unknown etiology. According to the “WHO classification of the renal neoplasms,” it is grouped along the mixed epithelial-stromal tumor of the kidney.[35]Histologic feature include cyst lined by flat, cuboidal,or hobnail epithelium and septa variably lined by fibrous and/or ovarian-like stroma. Clinically, all patients presented to us with renal lump and hematuria. USG and Doppler study of the abdomen revealed no vascularity of the tumor. CECT of whole abdomen showed cystic mass with sharp demarcation with renal parenchyma. No lymphadenopathy or metastasis was found. Radical nephrectomy was done. Cut surface revealed multiple cysts pushing renal pelvis, cysts were filled with serous fluid, and rim of normal renal tissue.

Cysts were lined by cuboidal or flattened epithelium.Edmun ds reported first case.

CONCLUSION

We had encountered different types of uncommon renal tumors such as CCSK, RTK, CMN, etc., in this study. Among them, RTK had shown a poor prognosis.CCSK is an aggressive and rapidly progressive renal tumor, but the final outcome has changed for better with improvised

chemo- and radio-therapies.CMN has very good prognosis as with cystic nephroma.

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Conflicts of interest
There are no conflicts of interest

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