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Original Research Paper

Pathology

A COLLECTION OF INTERESTING RENAL TUMORS

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ABSTRACT We describe five cases of renal tumors characterize the immunohistochemical profiles in detail, and critically review the previously reported cases. Morphologically different five renal tumors with paraffin blocks available for use, were retrieved from the surgical pathology files of the SKIMS. Clinical information was extracted from the medical record. Immunohistochemical stains were performed.

KEYWORDS :

Case histories

Case 1 (PNET)

17yr female presented with complaints of dragging sensation and fullness in the left flank. Examination revealed a large left-sided abdominal mass, confirmed by contrast enhanced computed tomography (CECT) which showed a large left renal mass 10x8 cm replacing mid and lower pole kidney with infiltration in to the sinus tract and encasing the renal pelvis. Another lesion 5x5 cms was seen at renal hilum. Radiological diagnosis of renal cell carcinoma was suggested. The patient proceeded to left nephrectomy.

Case 2 (Reninoma)

8 yr male child presented with complaints of recurrent syncope and on general physical examination was found to have accelerated hypertension and hypokalemia. An ECG revealed a long QT interval. A CT scan revealed a mass lesion 6cm in greatest dimension in the mid-pole of left kidney extending up to pelvis. The patient proceeded to left nephrectomy. VMA and catecholamine levels done pre-op were negative.

Case 3 Metanephric Adenoma

50 yr old male presented with flank pain and hematuria. A CECT abdomen revealed a renal mass in mid pole of right kidney. A right nephrectomy was performed.

Case 4 Mesoblastic Nephroma

4 year old male presented with history of hematuria and mass in lumbar region. Ultrasound revealed tumor in left kidney extending from left hypochondrium to left iliac fossa crossing to hypogastrium. CT scan revealed huge tumor replacing the left kidney. The patient was taken up for left nephrectomy.

Case 5 RCC with angiomyolipoma

53 yr female presented with history of pain in left flank of long duration. CECT abdomen revealed a mass in kidney. Patient proceeded for nephrectomy.

Material & methods

Specimens were fixed in formalin. The specimens were cut-up and processed in the routine manner, with 5-µm sections prepared from paraffin-embedded tissue. Sections were stained initially with hematoxylin and eosin (H & E). Subsequently, histochemical stains like periodic acid-Schiff (PAS) staining were performed as and when needed. For immunohistochemistry, the peroxidase-antiperoxidase technique was applied to tissue sections mounted on Poly L-Lysine coated slides using the following antibodies:

Cd99
CD 45
Desmin
Chromagranin
Synaptophysin

Results

Clinical features

The patients included one female and four males, ranging in age from 4 to 53 years (mean 26.4 years) three patients presented with flank pain, two with hematuria, and one tumor was discovered incidentally. All patients underwent nephrectomy. Follow-up information, available for patients, ranged from 6 months to 4 years 5 months (mean 2.5 years). All patients were alive without evidence of disease.

Gross and microscopic features

PNET

Grossly the kidney weighed 1.2 kg and measured 11×7 cm. The kidney was replaced by a lobulated gray tumor which was solid for the most part but also had areas of necrosis and hemorrhage. The tumor extended through the capsule into surrounding fat with capsule breached at places. Microscopically the tumor consisted of vaguely lobulated proliferations of primitive-appearing round cells with high nuclear to cytoplasmic ratios with small dark blue cell tumor arranged in sheets and cords with focal necrosis (Fig 1.). The tumor cells had indistinct cytoplasm and regular round-to-oval nuclei. In some areas, the cells were arranged into poorly formed rosettes with central fibrillary material and were arranged in a "peritheliomatous" pattern at places . Tumor cells had filigree pattern at places exhibiting arrangement around thin fibrous cores. Mitoses were present but rather inconspicuous, averaging 2 per 10 high-power fields. Vascular invasion was absent. Hilar area was infiltrated by tumor. Single lymph node detected was tumor free. PAS staining revealed that scattered tumor cells contained small amounts of cytoplasmic glycogen. The residual renal parenchyma showed marked chronic inflammation with atrophy. Possibility of Extra skeletal Ewing's sarcoma was suggested with a possible differential diagnosis of blastema-predominant Wilm's tumor. Immunohistochemistry was advised for definitive diagnosis and categorisation. Immunostains performed on the tumor revealed positivity for CD 99

Reninoma

Grossly the kidney weighed 1 kg with a tumor measuring 6x5x3cm which was seen to occupy the middle of the kidney. The tumor was well circumscribed, solid for most part with areas of hemmorhage. A small tumor nodule was seen near the pelvis of the kidney.

Microscopically, it was composed of sheets of tumor cells with rich delicate vasculature. Tumor cells were medium sized and uniformly round to polygonal with abundant, pale eosinophilic cytoplasm, and nuclei were round with inconspicuous nucleoli (Fig 2). The tumor nodule near pelvis also showed a similar morphology. Based on the H&E morphology, clinical history of accelerated hypertension and a multicentric tumor possibility of Reninoma was suggested.

Metanephric Adenoma

Grossly the kidney showed a protruding tumor nodule in mid pole of kidney measuring 4.5 cms in greatest dimension. The tumor was well encapsulated and within the confines of the renal capsule. Cut surface revealed a friable growth with no hemmorhage or necrosis. The renal vessels, pelvis, ureter and Gerota's fascia were all free of tumor. Microscopically, the tumor was well encapsulated with cells arranged as tubules and exhibited focal papillary architecture with round to oval nuclei, irregular nuclear membranes and inapparent nucleoli. Few calcospherites were present, and no mitotic activity was noted. There was no parenchymal, vascular, or capsular invasion.

Mesoblastic Nephroma

Grossly, the tumor replaced more than half of the kidney measuring 20x 17x 8 cm, was well encapsulated with very little normal kidney parenchyma discernible at one end. The tumor had a fleshy, firm, whorled appearance and was solid for most part with few areas of hemmorhage(Fig3). Microscopically, the tumor exhibited interlacing fascicles of fibroblastic cells with thin tapered nuclei, pink cytoplasm, low mitotic activity, and an abundant collagen deposition(Fig4).

RCC with Angiomyolipoma

Grossly the kidney revealed a necrotic growth towards one pole measuring 4 cm in greatest dimension. Capsule seemed to be infiltrated grossly. Rest of the parenchyma was unremarkable. Microscopically, the tumor revealed two components. One component was that of a classic (clear cell type) renal cell carcinoma with typical cells having centrally placed nuclei surrounded by clear cytoplasm and having thin cell borders. The other component was composed of tumor having blood vessels, smooth muscle and fat cells. The blood vessels were seen to have clear cells surrounding them, arranged in a radial fashion around the vessels(Fig 5).

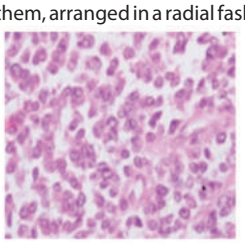

Fig 1-Microscopy of PNET(40X)

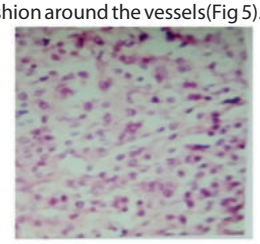

Fig 2 Microscopy of Reninoma(40X)

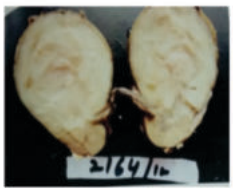

Fig 3-Gross of Mesoblastic Nephroma

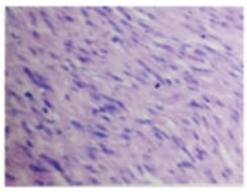

Fig 4 Microscopy of Mesoblastic Nephroma (40X)

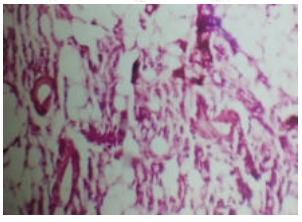

Fig 5- Microscopy of Angiomyolipoma (40X)

Discussion

Case 1 of the series is PNET of the kidney occurring in a 17-year-old girl. The diagnosis was suggested by the architectural and cytological appearance of the tumor on H & E staining. The nuclei were round to oval with little pleomorphism and scanty cytoplasm. Mitoses were few for such a primitive-looking tumor, a characteristic feature of PNETs (2). In some areas, rosettes of Homer-Wright type were seen, indicative of neural differentiation. The results of immunohistochemistry also strongly suggested a PNET. Positivity was detected with antibodies to the *MIC2* gene product: O13. These antibodies recognize a cell-surface glycoprotein involved in rosette formation with erythrocytes, with a molecular weight of 30/32 kDa that is overexpressed in ES and PNET (3). These markers are sensitive for such tumors but are not entirely specific. Membrane immunoreactivity is more specific than cytoplasmic. The clinical, histological and immunohistochemical findings in this case pointed to a diagnosis of PNET. Among the differentials, secondary tumor to the kidneys could be excluded with some certainty by thorough examination and investigation. The possible differentials were excluded by staining for respective antibodies which included: LCA for lymphoma, desmin for rhabdomyosarcoma.

Extra skeletal Ewing's sarcoma (EES)/PNET is a rare lesion that accounts for about 1% of all soft tissue sarcomas. The "round cell" tumors of the kidney include a wide range of unrelated neoplasms with overlapping morphologic features and different prognostic/therapeutic implications (6). Its morphologic, immunohistochemical, and molecular genetic features are analogous to those of Ewing's sarcoma/ PNET of other sites. Most patients are young adults and the clinical course is very aggressive (7). The tumors usually included in this differential diagnosis include blastema-predominant WT, ES/PNET, metastatic neuroblastoma, synovial sarcoma, desmoplastic round cell tumor, small cell carcinoma, clear cell sarcoma, and lymphoma. This differential diagnosis is further complicated by the relatively rare occurrence of most of these entities in the kidney. Renal ES/PNET was first reported by Mor et al. (8). Most of the previously reported cases have occurred in young adults (mean age, 28 yr; range, 4–69 yr), with a slight male predominance (male: female, 1.5:1). There has been some debate as to whether renal ES/PNET is an entity distinct from extra renal ES/PNET and one that carries a worse prognosis (9, 11). The identification of the same EWS-FLI-1 gene fusions in renal ES/PNET as in extra renal tumors, by Parham et al., (12) and the roughly similar outcome of renal tumors and of adult non-renal ES/PNET (13) suggest that this is not the case.

In case 2 of the series we present a young child with a rennin producing tumor. Our differentials in this case included Wilm's tumor, pheochromocytoma and RCC. Possibility of pheochromocytoma was ruled out by pre-op urinary VMA levels. Also confirmed by a negative staining for chromagranin , synaptophysin ,S 100 . The tumor was positive for CD 34 ,CD117 Immunostains..

Primary reninism is a very rare cause of secondary hypertension.(14) More than 80 cases of juxtaglomerular cell tumors have been described since the first case reported by Robertson *et al.* in 1967.(15) Juxtaglomerular cell tumors are seen more frequently in women than in men, and they usually occur during adolescence or early adulthood.(1) In our case the patient presented at a much younger age of 8 yrs. Juxtaglomerular cell tumors are commonly associated with hypertension, secondary aldosteronism and hypokalemia. Although both renal (16, 17) and extrarenal5–10 renin-secreting neoplasms have been reported, such tumors usually arise in the kidney from the juxtaglomerular apparatus. Diagnosis of juxtaglomerular cell tumors is not always easy, and the tumors can be small and distally located in the renal cortex. Patients usually present with severe, uncontrollable hypertension, hyperaldosteronism, and hypokalemia. A juxtaglomerular cell tumor is usually a surgically curable cause of hypertension (18) and the hypertension usually returns to normal immediately or gradually after the removal of the tumor. (19).As in our case the child

was normotensive after the surgery. Other tumors which rarely have been reported to produce renin include renal cell carcinoma, Wilm's tumor, congenital Mesoblastic Nephroma, hepatoblastoma, lung carcinoma, ovarian tumor, soft tissue tumors and glioblastoma multiforme (20). This tumor type has usually been considered benign. However, these tumors have a potential for vessel invasion as has been reported in few cases of Reninoma with metastases (21). One typical feature of this tumor was its multicentricity.

Case 3

Metanephric adenoma formed third case of the series. These tumors usually behave in a benign fashion (33). It has been suggested that these tumors are related to the developing proximal tubule of the fetal kidney or nephrogenic rests, based on similar morphologic features and an immunohistochemical profile that is similar to that of developing metanephric tubules (34). Although the histogenesis of MA is unclear, a morphologic similarity to Wilm's tumor (WT) complex exists. Metanephric adenoma occurs in children and adults, most commonly in the fifth and sixth decades. In our series the patient presented at 53 yrs. There is a 2:1 female preponderance (29). Patients with Metanephric adenofibroma have ranged from 5 months to 36 years (median = 30 months) (30). Grossly, range widely in size; most have been 30 to 60 mm in diameter (29). In our case the tumor was 4.5 cm. Multifocality is uncommon. The tumours are typically well circumscribed but not encapsulated.

These tumors are highly cellular, epithelial tumours composed of small, uniform, embryonic-appearing cells. Long branching and angulated tubular structures also are common. The stroma ranges from inconspicuous to a loose oedematous stroma. Hyalinized scar and focal osseous metaplasia of the stroma are present in 10- 20% of tumours (29). Immunohistochemical studies of metanephric adenoma have given variable results. Positive reactions with a variety of antibodies to cytokeratins have been reported; as have positive reactions with antibody to vimentin (31). Positive intranuclear reactions with antibody to WT-1 are common in metanephric adenoma (32). Epithelial membrane antigen and cytokeratin 7 are frequently negative and CD57 is positive.

Case 4

Congenital mesoblastic nephroma, while rare, is the most common kidney "Neoplasm" diagnosed in the first three months of life and accounts for 3-5% of all childhood renal neoplasms(35). Congenital Mesoblastic nephroma in a malignant tumorous growth of the kidney's mesenchyme (i.e. connective tissue cells). Histologic examination of these tumors provides critical information on their prognoses. This examination divides congenital mesoblastic nephroma into three types:

- 1) The classic type occurs in 39% of patients. Its tissues show interlaced spindle-shaped smooth muscle cells evidencing low mitotic activity with no evidence of tumor encapsulation; and infiltration into and entrapment of normal kidney tissue (35). .
- 2) The cellular type occurs in 42% of patients.[1] Its tissues show densely packed fibrosarcoma-like cells evidencing high rates of mitosis, less infiltration of normal kidney tissue, and multiple areas of hemorrhage and cysts. (35,36)
- 3) The mixed type occurs in 19% of patients. It shows a mixture of the classic and cellular types in different areas of the neoplasm (35).

Case 5

Renal cell carcinoma with angiomyolipoma formed case 5 of the series. AMLs account for approximately 1% of surgically removed renal tumours. It has been considered an uncommon neoplasm, but its frequency is increasing because it is detected in ultrasonographic examinations performed to evaluate other conditions. It can occur sporadically or in patients with TS, an inherited autosomal dominant syndrome. Most surgical series report four times as many sporadic AMLs as AMLs associated with TS (27). Simultaneous occurrence of AML with renal cell carcinoma (RCC) and oncocytoma in the same kidney has also been reported (22). Although this situation is very rare, from a clinical and pathological point of view it is important to consider the possibility that RCC might arise within AML. As seen in this case of the series. Classic angiomyolipoma is a triphasic tumor that shows varying amounts of myoid spindle cells, lipid-distended cells, and dysmorphic vessels. Although angiomyolipoma was originally considered to be a hamartoma, a number of different lines of evidence now strongly support its neoplastic nature. (28) Angiomyolipoma is the most common member of a family of tumors that has been recently referred to as the perivascular epithelioid cell (PEC) family of tumors (23); the other members include lymphangioleiomyomatosis, (24) the clear cell "sugar" tumor of the lung, (26) and the rare clear cell tumors of the pancreas (25) and uterus. Angiomyolipoma occurs most commonly in the kidney and liver, but may involve a variety of unusual sites. The majority of angiomyolipomas show typical triphasic morphologic features and are easily diagnosed. However, it has become increasingly apparent that angiomyolipoma may be somewhat protean in appearance, depending on the relative proportions of each element, and on the morphologic forms taken by these elements. AMLs are characterized by a coexpression of melanocytic markers (HMB45, HMB50, CD63, tyrosinase, Mart1/MelanA and microophthalmia transcription factor) and smooth muscle markers (smooth muscle actin, muscle-specific actin and calponin); CD68, neuron-specific enolase, S-100 protein, estrogen and progesterone receptors, and desmin may also be positive, whereas epithelial markers are always negative (27).

S.No.	Case	Age/sex	Signs/symptoms	Radiographic findings	Gross findings	Follow-Up
1	PNET	17/F	Dragging sensation and fullness in left flank	Large renal mass in mid and lower pole	Solid tumor with necrosis and capsular infiltration	6 months
2	Reninoma	8/M	Accelerated hypertension, QT prolongation	Tumor mass in mid pole kidney, Tumor nodule pelvis	Solid tumor, areas of hemmorhage	Normotensive 5 months
3	Metanephric Adenoma	50/M	Flank pain, hematuria	Tumor mass in mid pole kidney	Friable tumor, well encapsulated. No hemmorhage	5 months
4	Mesoblastic Nephroma	4/ M	Mass, hematuria	Tumor mass replacing whole of kidney	Firm, whorled, fleshy tumor	6 months
5	RCC with Angiomyolipoma	53/F	Pain left flank of long duration	Tumor mass 4 cm, upper pole	Necrotic growth	2 months

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