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Distinguishing between Renal Oncocytoma and Eosinophilic Renal Neoplasm's: A case report with brief literature review

Dr Indira Shastry K[1] , Dr Swati Sharma[2], Dr Ranjini Kudva[3], Dr Manna Valiathan[4], Dr Sandeep Kumar[5]
[1]Post Graduate, Dept of Pathology, Kasturba Medical College, Manipal University, Manipal, Karnataka
[2]Associate Professor, Dept of Pathology, Kasturba Medical College, Manipal University, Manipal, Karnataka
[3]Professor, Dept of Pathology, Kasturba Medical College, Manipal University, Manipal, Karnataka
[4]Professor and Head, Dept of Pathology, Kasturba Medical College, Manipal University, Manipal, Karnataka
[5]Assistant Professor, Dept of Radiology, Kasturba Medical College, Manipal University, Manipal, Karnataka

***Corresponding author**
Dr Swati Sharma
Email: swatisharma79@yahoo.com

Abstract: Renal oncocytomas are benign epithelial tumors, often asymptomatic, and incidentally diagnosed. Here is a case of 60 year old male where radiological features of the renal mass suggested renal cell carcinoma, but on histopathology and immunohistochemical study, diagnosis of renal oncocytoma was given. In this report, we discuss literature review of clinical, radiological, ultrastructural, pathological and immunohistochemical characteristics of renal oncocytoma and other eosinophilic renal neoplasms.
Keywords: eosinophilic, immunohistochemistry, oncocytoma, renal cell carcinoma.

INTRODUCTION

Renal oncocytoma (RO) is a benign epithelial neoplasm of kidney characterized with mitochondria rich eosinophilic cytoplasm. Oncocytomas account up 3 to 5% of total renal neoplasms [1-4]. Histopathologists face very common problem in distinguishing RO from other eosinophilic renal neoplasms. Most cases can be resolved by careful examination of tumor architecture, nuclear and cytoplasmic features. Immunohistochemistry (IHC) is required for difficult cases [5]. We describe a case where radiology was suggestive of RCC, but on histologic examination and IHC a diagnosis of renal oncocytoma was given. We also highlight the close histologic mimickers of RO and describe the role of IHC in differentiating them.

CASE REPORT

A 60 yr old male diabetic patient was referred to our tertiary care hospital with incidental detection of right renal mass during routine workup. Computerised tomography showed well defined exophytic cortical homogenously enhancing soft tissue lesion in the mid pole of right kidney suggestive of renal cell carcinoma (Figure 1,2). Right radical nephrectomy was done. Grossly, specimen measured 11x7x6 cm. On cut section a well circumscribed encapsulated yellowish tumor mass measuring 4.5x4x4 cm (Figure 3) was noted. There was no capsular invasion or perinephric fat involvement. Microscopy showed well defined nests, acini and tubules composed of round to polygonal cells with abundant coarsely granular eosinophilic cytoplasm, round nuclei, finely dispersed chromatin and central nucleoli (Figure 4,5). There was no infiltration in to renal parenchyma, ureter or blood vessels. On IHC, tumor cells were negative for CD10 (Figure 6) and vimentin, and were positive for CD117 and E-cadherin (Figure 7,8). A diagnosis of renal oncocytoma was given.

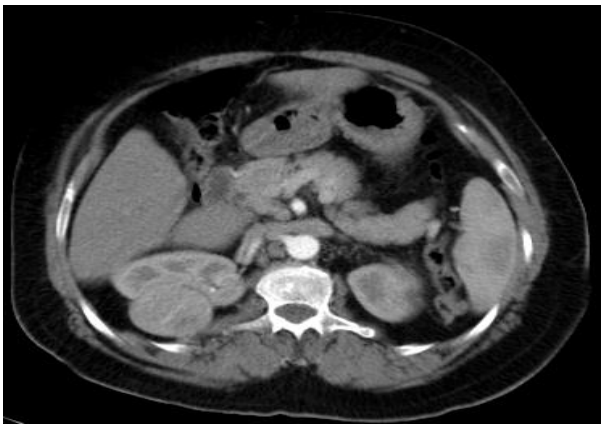

Fig-1: Axial CT images reveal a homogenously enhancing exophytic mass arising from upper pole of right kidney

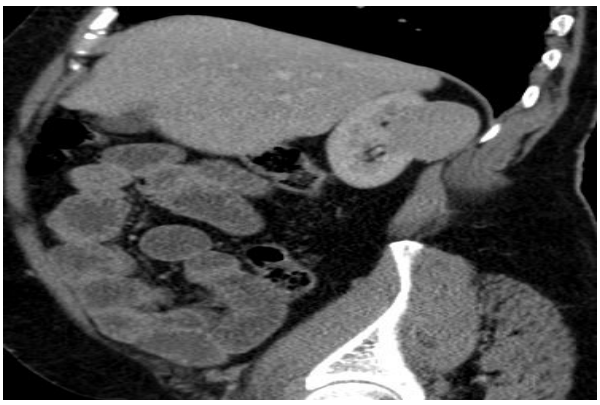

Fig-2: Sagittal view showing exophytic mass from upper pole of right kidney

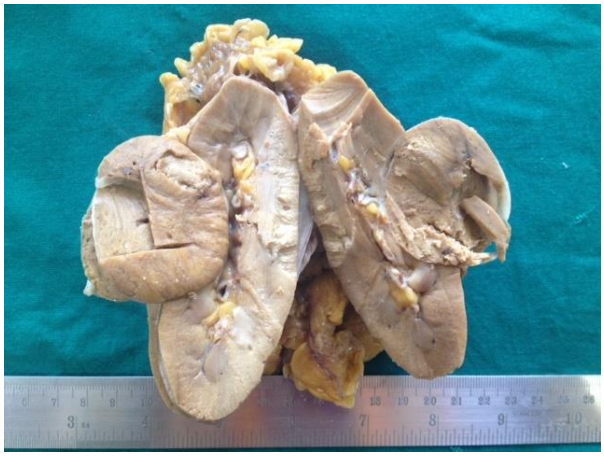

Fig-3: Gross, Well circumscribed encapsulated yellowish tumor

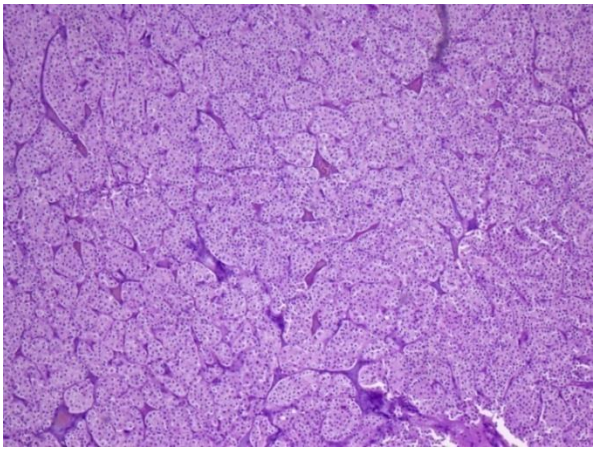

Fig-4: Well defined nests, acini and tubules composed of round to polygonal cells H& E X40

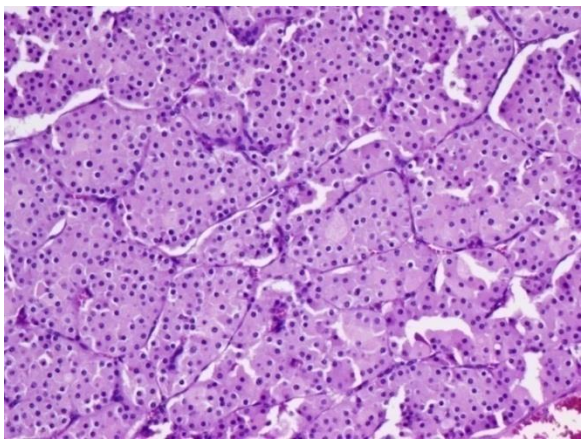

Fig-5: Cells with abundant coarsely granular eosinophilic cytoplasm, round nuclei, finely dispersed chromatin and central nucleoli H&E x100

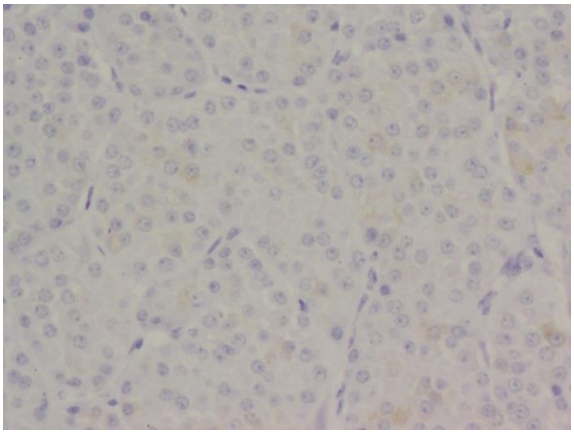

Fig-6: CD10 negative in tumor cells x 20

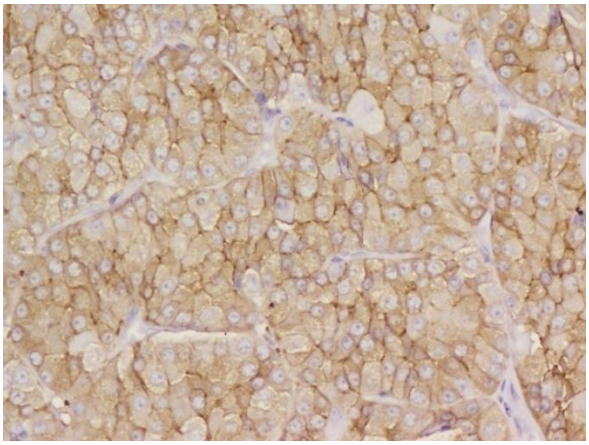

Fig-7: CD117 positive in tumor cells x20

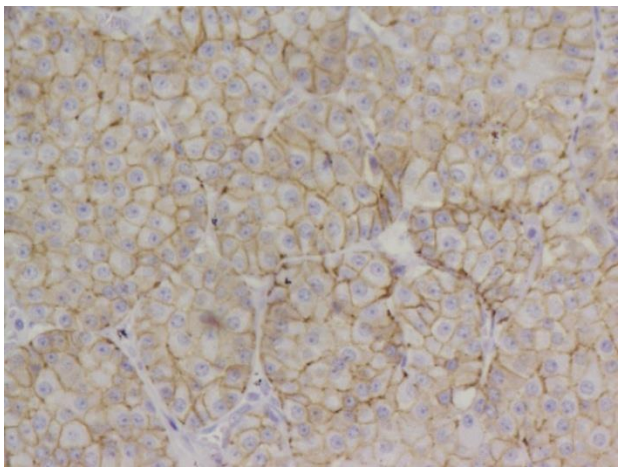

Fig-8: E-Cadherin positivity in tumor cells x20

Table-1: Morphological and Histopathological differences between RO and other eosinophilic renal neoplasms

Sl. no	Features	Renal oncocytoma	Chromophobe RCC	CC-RCC with eosinophilic cytoplasm	Oncocytic variant of papillary RCC	Oncocytic variant of renal AML
1	Macroscopy	Non encapsulated mahogany brown coloured mass with central scar	Well circumscribed mass with slightly lobulated surface	Well circumscribed, multifocal with necrosis and hemorrhage	Well circumscribed with hemorrhage, necrosis and cystic degeneration	Yellow tan well demarcated mass.
2	Architecture	Nests, acini or tubules	Solid sheets of oncocytic cells	Nests surrounded by sinusoids	Papillae lined by tall eosinophilic cells	Sheets or nests of oncocytic cells
3	Cytoplasm	Eosinophilic	Eosinophilic	Eosinophilic	Eosinophilic	Eosinophilic
4	Nucleus	Uniform, round evenly distributed chromatin	Resinoid hyperchromatic nuclei with small nucleoli	Uniform, round evenly distributed chromatin	Hyperchromatic with anisonucleaosis	Monomorphic nuclei, evenly distributed chromatin
5	Nucleoli	Inconspicuous / +	Prominent nucleoli	+/-	Prominent macronucleoli	Nucleoli +/-
6	Perinuclear halo	Absent	Present	Absent	-	absent
7	Clear cells	Absent	Mixed with eosinophilic cells	Mixed with eosiophilic cells , Necrosis +	Absent	Adipocytes +/-
8	Halle's colloidal iron	Negative	Diffuse cytoplasmic positive	Negative	Negative	Negative
9	Ultra structural features	Numerous, uniform tightly packed mitochondria	Numerous vesicles 150-300nm with dilated mitochondria.	Lipid and glycogen vacuoles with pleomorphic swollen mitochondria	Numerous mitochondria with lamellar cistern	Intracytoplasmic membrane bound dense bodies and crystals

Table-2: Immunohistochemical panel to differentiate between RO and other Eosinophilic renal neoplasms [1,12,20,21, 16]

Sl no	Antibodies	Renal Oncocytoma	Chromophobe RCC	CC-RCC with eosinophilic cytoplasm	Oncocytic variant of papillary RCC	Oncocytic variant of renal AML
1	Vimentin	Neg	Neg	Pos	Pos	Neg
2	CD10	Pos/neg	Pos/neg	Pos	Pos	Neg
3	CK7	Patchy	Pos	Neg	Pos	Neg
4	CD117	Pos	Pos*	Neg	Pos/neg	Neg
5	E-Cadherin	Pos	Pos	Neg	Pos/neg	Neg
6	HMB-45	Neg	Neg	Neg	Neg	Pos
7	S100A1	Pos	Neg	Pos	Pos/neg	-
8	RCC marker	Neg	Neg	Pos	Pos/neg	Neg

Pos: Positive, Neg: Negative,*Positive with membrane accentuation.

DISCUSSION

RO is a common benign renal epithelial neoplasm, first described by Zippel [6] in the year 1942 and was acknowledged after publication of 13 cases by Klein and Valensi in the year 1976 [7]. It can manifest at any age but peak incidence occurs around 6^{th} -7^{th} decade. Males are affected 2-3 times more than females [1,8]. Surrounding adipose tissue invasion and vascular invasion have been described even though it is a benign tumor [1]. Majority of patients are asymptomatic and RO is discovered during workup of unrelated condition, as seen in our case. While a few may present with hematuria, flank pain or mass. Rarely RO can be associated with renal Angiomyolipomas (AML), around 15 cases have been described in literature [9]. Patients with the rare genetic disorder, Birt-Hogg-Dubé syndrome can present with oncocytomatosis – the presence of multiple oncocytomas in both kidneys [10]. Other sites where oncocytoma can be seen include salivary gland, thyroid, larynx, skull base and adrenal gland. First line of investigation for renal mass is imaging studies, although it is difficult to distinguish RO from RCC. On CT, RO appears as sharply demarcated lesion of variable size and appears iso attenuating or slightly hyper attenuating relative to the kidney parenchyma [11]. One helpful sign is presence of central scar, but it is present in only 30% of cases, and hence one should remember that absence of central scar does not exclude the diagnosis of RO [8].

The classical gross description for RO is well circumscribed mahogany brown coloured tumor with central stellate scar. Color of the tumor can be tan to pale yellow as seen in our case. Hemorrhage can be associated in 20% cases, however necrosis is extremely rare [1,8]. Microscopy shows nests, acini, tubules of round to polygonal cells with abundant densely granular eosinophilic cytoplasm, centrally placed round nuclei with evenly distributed chromatin in hypocellular hyalinised stroma or myxoid stroma. Small populations of cells show feature of degenerative atypia in form of high nuclear: cytoplasmic ratio and nuclear hyperchromasia. No atypical mitosis is seen [1]. As per definition RO lacks significant areas of clear cell change, papillary projections and necrosis [8,12]. But in up to 15% cases focal clear cell change may be seen especially around areas of hyalinisation. Focal small papillary projections have also been documented [1,8], although pure or extensive papillary architecture is not a well recognised feature. Also presence of small foci of necrosis does not exclude oncocytoma [1]. Extra renal involvement can be appreciated in 11-20% cases and this should not be considered as a sign of malignancy [8]. On electron microscopy, oncocytes contain numerous tightly packed mitochondria which are of normal shape and size with long and lamellar cistern. Other cytoplasmic organelles are sparse and unremarkable. Typically microvesicles are absent which are seen in chromophobe RCC. Clear cell RCC with eosinophilic cytoplasm show lipid and glycogen vacuoles with pleomorphic swollen mitochondria [13]. Oncocytic variant of papillary RCC show numerous mitochondria with lamellar cistern. Whereas oncocytic variant of renal AML show intracytoplasmic membrane bound dense bodies, crystals and granules (rhomboid and spherical) [1] .

Histological mimickers of RO include chromophobe RCC, clear cell RCC (CC-RCC) with eosinophilic cytoplasm, oncocytic papillary RCC and oncocytic variant of AML [5]. Diagnosis of RO is difficult in cases demonstrating cellular pleomorphism, atypical nuclear features and invasion. For such cases ancillary techniques are needed to establish the correct diagnosis. On IHC, RO is negative with few scattered weak positive cells (around 5%) for CK 7 in contrast to chromophobe RCC and oncocytic papillary RCC which show diffuse strong staining. Nevertheless, pitfall of this immunostain is 14-18% of chromophobe RCC can be negative for CK7. CC-RCC with eosinophilic cytoplasm and oncocytic variant of renal AML are negative for CK7 [14-16]. RO, chromophobe RCC and oncocytic variant of renal AML are negative for vimentin and RCC marker. Whereas CC-RCC with eosinopohilic cytoplasm and oncocytic papillary RCC are positive for both. Oncocytic papillary RCC is

positive for CD 10, whereas RO and chromophobe RCC show variable positivity. Renal AML is positive for HMB 45, while rest of the others are negative. RO shows both cytoplasmic and membranous positivity for CD117, unlike chromophobe RCC which shows cytoplasmic positivity with peripheral membranous accentuation and oncocytic variant of papillary RCC which may be variable positive [17]. CC-RCC with eosinophilic cytoplasm and oncocytic variant of renal AML are negative for CD117. E- Cadherin is a cell adhesion glycoprotein expressed in distal tubules of nephron. It is expressed in majority of both oncocytoma and chromophobe RCC, but predominantly cytoplasmic staining in oncytoma , but membranous or cytoplasmic staining in chromophobe RCC[5]. Others are negative for E-Cadherin. S100A1 is a calcium binding protein of S100 gene family. RO, CC-RCC with eosinophilic cytoplasm and oncocytic variant of papillary RCC are positive for S100 A1, whereas chromophobe RCC show negative staining [5,8,16-19]. Differences in morphological and immunohistochemical expression pattern for these tumors are summarised in table 1& 2. As far as special stain Halle's colloidal iron is concerned, this histochemical stain is not properly standardised in many labs and hence its utility in chromophobe RCC remains in doubt[5].

CONCLUSION

RO is a benign tumor seen in old age and has male preponderance. Establishing a diagnosis of RO can be difficult in some cases and other eosinophilic renal neoplasms like chromophobe RCC, CC-RCC with eosinophilic cytoplasm, oncocytic papillary RCC and oncocytic variant of AML must be ruled out. We can use panels of different IHC markers depending on tumor histology.

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