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LOW GRADE RENAL ONCOCYTIC TUMOR OF KIDNEY: A DIAGNOSTIC DILEMMA

Pathology

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ABSTRACT

Renal neoplasms with oncocytic features includewide range of morphological entities including Oncocytoma, chromophobe RCC, eosinophilic variant of clear cell RCC etc ,posing a diagnostic challenge. We are presenting a rare case of newly described entity in the exhaustive list of renal oncocytic neoplasm , Low grade oncocytic tumor.In this paper, we discuss the diagnostic aspect and clinical behavior of this rare tumor including histologic as well as immunophenotypic profile.

KEYWORDS

Oncocytoma, Chromophobe RCC, Unclassified oncocytic tumour

INTRODUCTION:

Oncocytic renal neoplasms remain a significant area of challenge between new entities and unclassified oncocytic tumors.

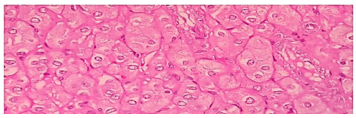
Low grade oncocytic tumor is a new entity not included in WHO classification but was proposed by Trpkov et al[1] who described a group of distinct oncocytic tumors with uniform low grade morphological features that are unexpectedly CD117 negative but are diffusely CK7 positive. These tumors show overlapping morphologic features with oncocytoma and chromophobe RCC but do not fit into either of these entities based on morphologic features and immunohistochemical profile.

CASE REPORT

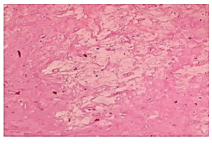
A 70 year male presented with complaints of hematuria and flank pain since 3 months. On radiological evaluation CT scan revealed a left renal mass in upper pole posteromedial aspect measuring 4x3x3 cm in size. No syndromic association was identified.The patient underwent left radical nephrectomy.

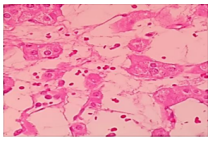
Grossly, a well circumscribed cortical tumor was identified at the upper pole of kidney beneath the capsule measuring 4.5x3.5x3cm in size. Cut surface of the tumor was solid, homogenous tan brown. No areas of hemorrhage or necrosis were identified.Renal sinus fat and renal vein resection margins were uninvolved by the tumor.

Microscopy revealed an unencapsulated tumor composed of sheets and solid nests of polygonal cells showing abundant pale to granular eosinophilic cytoplasm, round nuclei with inconspicuous nucleoli. Perinuclear halos were not identified. No characteristic wrinkling or raisionoid appearance of nuclei was seen. Central part of the tumor shows loose edematous areas showing dispersed tumor cells and fresh areas of hemorrhage. Scattered and clusters of lymphocytic infiltration noted in the compact nests and loose myxoid areas .No significant cellular atypia, nuclear pleomorphism, mitotic activity or necrosis were seen.



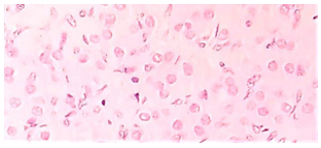
1.A



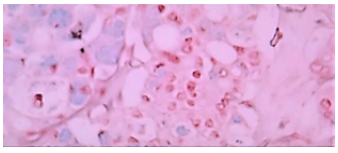


1.B 1.C

Figure 1 (A-C) .H&E stain showing an oncocytic tumor with loose and myxoid areas



2.A

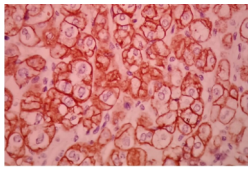


2.B

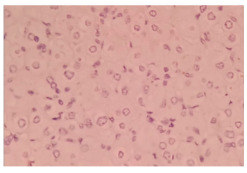
Figure 2.Hale's colloidal iron negative in tumor cells 2A, positive control 2B.

Based on morphology a broad range of differential diagnosis were considered including Eosinophilic variant of Chromophobe RCC, Oncocytoma and Eosinophilic variant of clear cell RCC and immunohistochemical panel was decided and done with following antibodies including PAX8, CD117,CK7, CD10, AMACR and vimentin.

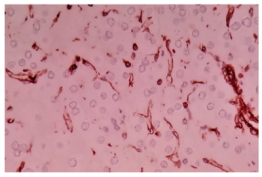
The tumor cells were strongly positive for CK7, PAX8 while immunonegative for other markers.



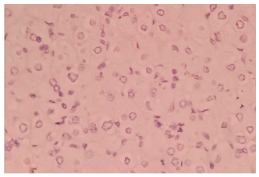
3.A



3.B



3.C



3.D

Figure 3.(A-D) Tumor cells showing CK7 positivity3A, CD 117 negative3B ,Vimentin3Cand CD10 negative3.

Based on morphologic and immunohistochemical profile, a diagnosis of Low grade oncocytic tumor of kidney (CD117 negative and CK7 positive) was suggested.

DISCUSSION

Low grade oncocytic tumor is a recently described entity showing distinct morphologic and immunoprofile.

The renal tumors with oncocytic morphology included in the differential diagnosis are oncocytoma, chromophobe RCC, borderline / hybrid oncocytic tumors, eosinophilicvariant of clear cell carcinoma ,papillary oncocytic RCC, Epithelioid angiomyolipoma, eosinophilic solid and cystic RCC and SDH deficient RCC.

The broad categorization for renal neoplasms with eosinophilic cytoplasm includes:1. Chromophobe RCC VS oncocytoma,2. Tumors resembling oncocytoma and chromophobe RCC,3. Eosinophilic but not chromophobe or oncocytoma.

The distinction between chromophobe and oncocytoma is well defined based on morphologic features and immunohistochemical profile[2,3]

The distinction between chromophobe RCC and oncocytoma is well defined based on morphologic features and immunohistoc hemicalprofile[4]. Histomorphologically LOT shows loosely arranged connective tissue stroma and myxoid areas. In contrast to oncocytomas, LOT exhibit diffuse immunoreactivity for CK 7 and negative for CD117. Hale's colloidal iron is negative in LOT ,positivity with apical snots are described in oncocytoma.

Eosinophilic variant of Chromophobe RCC show prominent cell membranes, raisinoid nuclei and Hale's colloidal iron, CK7 and CD117 strongly positive, whereas, LOTshows low grade morphological features, negative Hale's colloidal iron stain .Expresses CK7 and negative for CD117 .

The second category includes eosinophilic variant of clear cell RCC,Xp11/TFE3 RCC, Birt-Hogg-Dube associated RCC, and tubul ocystic RCC. The distinction between these subtypes can also be established based on integrated morphological and immunohist ochemical approach.As clear cell RCC show strong CD10 positivity and are negative for CK 7 and Cd117.

Oncocytic papillary renal cell carcinoma show papillae with oncocytic cytoplasm and are CD10, AMACR and vimentin positive and negative expression for CD117.LOT lacks the adipose tissue component shows low grade morphology where asEpitheloid AML oncocytic subtype shows, large tumor cells with prominent ganglion like cells and multinucleation, immunohistochemically HMB45 positive and CK7 negative.

Newly described entity SDH deficient RCC show vacuolated eosinophilic or clear cells, arranged in solid nests and tubules and have flocculent cytoplasmic vacuoles with low grade nuclei. Immunohistochemicallyit shows loss of expression of SDHB and negative forvimentin, CK7 and CD117[(4).]

The tumors which lie in the grey zone showing morphological and immunohistochemical overlap cannot be categorized into anyexisting subtypes. These tumors were previously reported as unclassified renal tumors[1].

Trpkov etal[(1)]recently, who studied 28 such tumors showing solid and compact nested growth, areas with edematous stroma and loosely arranged cells. The tumor cells described in this study showed oncocytic cytoplasm with uniform round to oval nuclei and focal perinuclear halos. Immunohistochemically, all cases in their study were CD117 negative and CK7 positive. They designated these tumors as Low grade oncocytic tumor which is similar to our case.

A new entity oncocytic variant of chromophobe RCC was proposed in 2016 by Kuroda et al[(5)] who described 5 such cases that were similar to renal oncocytomas morphologically but were CD117 negative and diffusely CK7 positive.

Another extensive study[(6)]was carried out in cases of unclassified RCC tumorsby Perrinoet al examined 136 cases and categorised into thesehistological groupsoncocytoma/ chromophobe RCC-like; clear cell RCC-like; papillary RCC-like; collecting duct-like; and pure sarcomatoid differentiation. The majority of the Oncocytoma /chromophobe and clear cell RCC-like phenotypes were low stage (pT1 or pT2). The papillary RCC-like, collecting duct-like and pure sarcomatoid phenotypes were mainly high stage (pT3 or pT4).They also concluded that the renal neoplasms exhibiting cells with eosinophilic cytoplasm posed the greatest diagnostic challenge.

Chandra K Flack et al [(7)] compared the clinical outcomes in 351 patients diagnosed as renaloncocytoma, oncocytic neoplasm and chromophobe tumors. They found that there was no significant difference in the median survival or recurrence rate or metastases seen between oncocytoma or oncocytic neoplasms.

Our case was a diagnostic dilemma as it showed nested growth pattern with low grade nuclear features and loose areas along with immunopostivity for CK7 and negative immuno-expresssionof CD117.Post surgery six month follow up of our case did not show any recurrence or metastasis.

CONCLUSION

Low grade oncocytic tumor is an emerging entity distinct from oncocytoma and chromophobeRCC, shows indolent behaviorand should always be considered in the differential diagnosis of renal oncocytic tumors. Further extensive studies are required to assess the biological behavior and prognosis of these cases.

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