

Solid Tumour Section

Review

Kidney: Renal Oncocytoma

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Identity

Phylum

Urinary

system:Kidney:Adult:Oncocytoma/oncocytosis

Classification

Note

Renal Oncocytoma is a benign renal epithelial neoplasm that comprises approximately 5-9% of renal tubular epithelial tumors.

Clinics and pathology

Note

The first case of renal oncocytoma was reported by Zippel in 1942. Since then this tumor have been described as proximal tubular adenoma with oncocytic features and later oncocytoma became the generally accepted term.

Embryonic origin

Many investigators have suggested that these tumors originate from intercalated cells of the collecting system.

Etiology

Renal oncocytomas can present in familial or sporadic forms. Oncocytomas may be seen in patients with Birt-Hogg-Dube syndrome (BHD, who

carry germline mutations in the folliculin gene (FLCN). However, sporadic cases are much more common and have an unknown etiology.

Epidemiology

Renal oncocytomas account for about 5-9% of all renal tumors and occur across a broad age range, peaking in the seventh decade. There is a male predominance (2:1) and tumors are frequently small and found incidentally. A rare association between oncocytoma and angiomyolipoma or tuberous sclerosis has been reported..

Pathology

Macroscopically, renal oncocytomas are well-circumscribed, slightly lobulated solid tumors with generally mahogany brown or dark red cut surface. The tumors are typically solitary, but can be multifocal or bilateral. A central scar is frequently observed. Some cases show involvement of the perinephric fat or rarely the renal vein with no change in prognosis. Microscopically, the tumor is composed of nests and tubular structures made up from oncocytic cells, and is frequently associated with fibrous or edematous stroma. The tumor cells are large round eosinophilic cells with granular cytoplasm that is packed with mitochondria. Nuclei are round and monomorphic and contain small nucleoli. Tumor cells around the central scar are small with scant cytoplasm. Bizarre cells with

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pleomorphic nuclei may be present in some tumors and have no effect on outcome. Mitoses and necrosis are not seen. Tumor cells are typically immunoreactive for KIT, S100A (multifocal), and HNF1beta, and are negative for CD10, AMACR and vimentin. CK7 is usually negative or patchy positive with immunoreactivity in single scattered cells; this

is in contrast to chromophobe renal cell carcinoma which shows diffuse membranous positivity.

Rare cases that show multiple oncocytic tumors can be referred to as oncocytosis. Oncocytosis, as well as hybrid oncocytic tumors may occur sporadically or in association with Birt-Hogg-Dubé syndrome. .

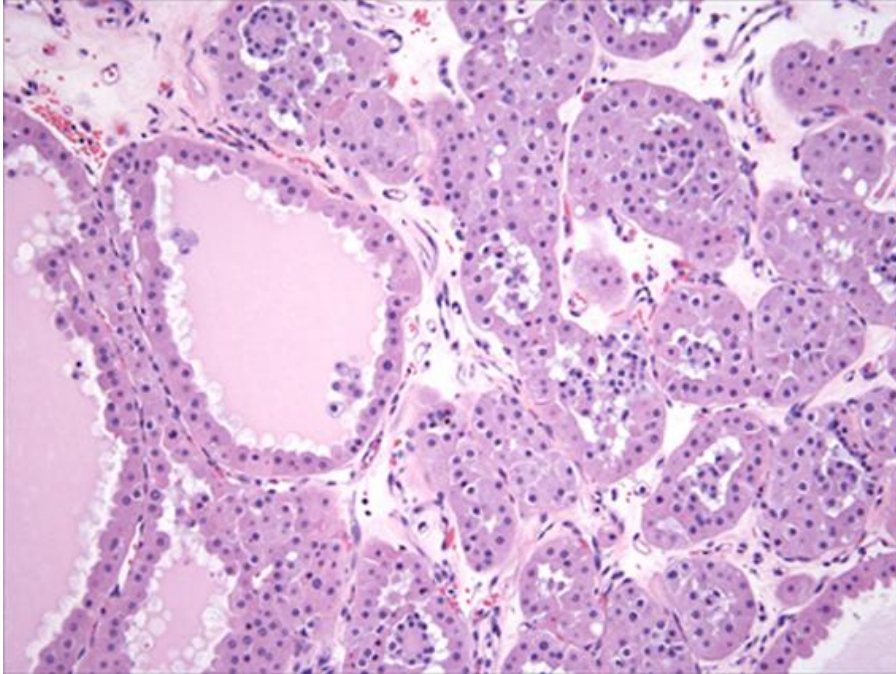


Figure 1A: Oncocytoma is a benign renal epithelial neoplasm. Oncocytomas contain small oncocytic cells with round, regular nuclei that sometimes contain a small nucleolus. Architecturally the tumors are solid, nested or tubular, and are frequently associated with edematous stroma.

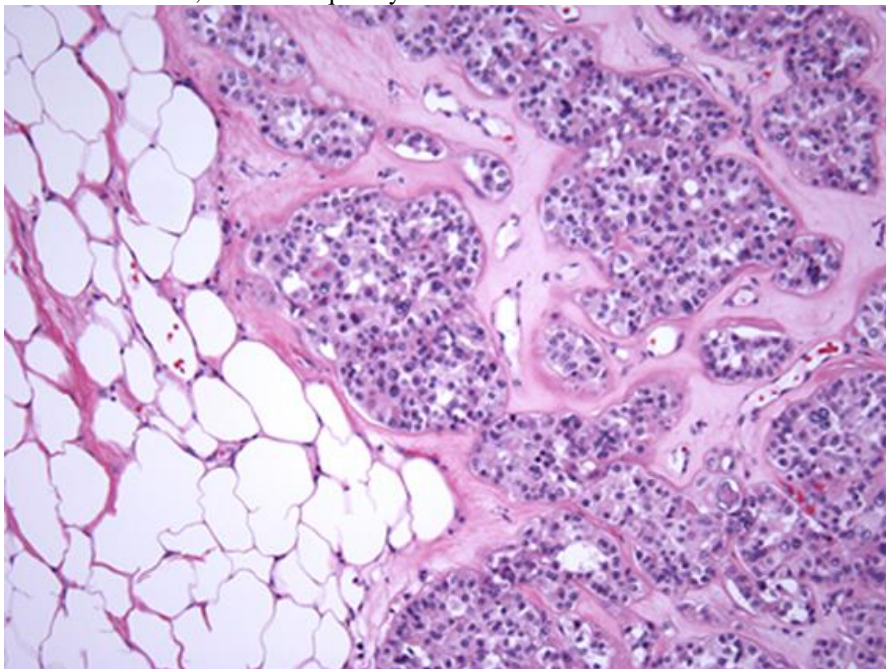


Figure 1B: Occasionally oncocytomas extend into perinephric adipose tissue; this finding has no effect on clinical outcome (i.e., the tumor is still benign).

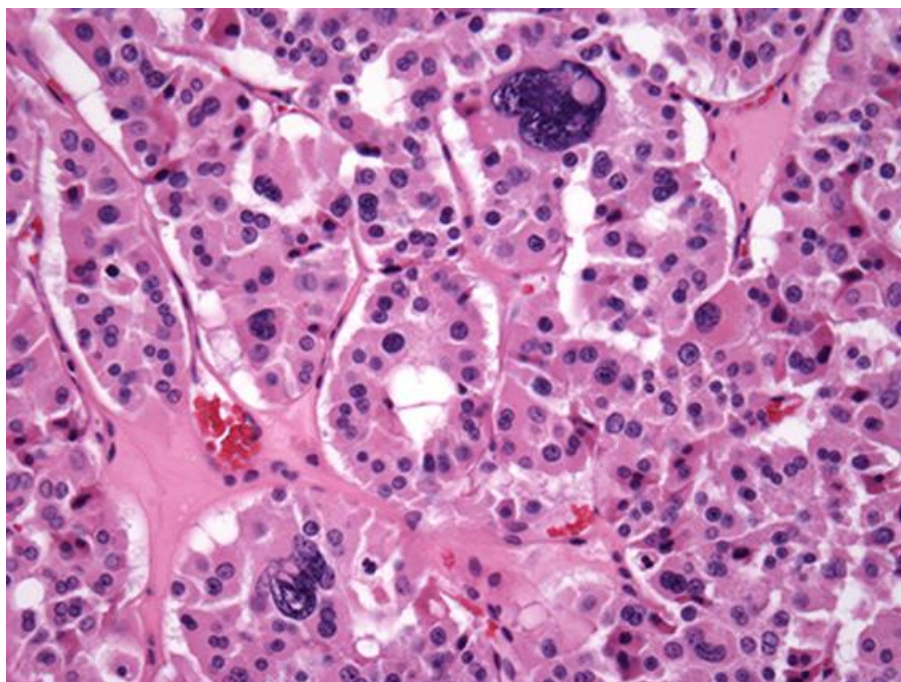


Figure 1C: A small subset of oncocytomas demonstrate nuclear atypia and/or multinucleation. Some think this is due to degenerative change. Regardless, these nuclear features do not affect clinical outcome (i.e., the tumor is still benign).

Treatment

Most patients with RO are treated with nephrectomy. Nephrectomy (radical or partial). Enucleation, wedge resection or ablation may also be considered for treatment options but are less common.

Prognosis

Oncocytomas behave in a benign fashion. Atypical pathologic features, such as nuclear pleomorphism, perinephric fat involvement and extension into renal vein branches do not influence prognosis.

Cytogenetics

Note

Oncocytomas frequently exhibit losses of chromosome 1/1p-, chromosome 14 and/or a sex chromosome. Structural rearrangements of 11q13 have been reported, with t(5;11) and t(9;11) representing the most common translocations. A t(6;9)(p21;p23) has been reported in three cases of oncocytoma (Balzarini et al., 1999; Hudacko et al., 2011). A subset of oncocytomas exhibit non-recurrent numerical or structural abnormalities. A normal karyotype is also frequently observed.

One of the diagnostic pitfalls in renal epithelial tumors is distinguishing between benign RO from the eosinophilic variant of chromophobe carcinoma. Many studies have reported that chromophobe RCC shows complex simultaneous losses of chromosomes 1, 2, 6, 10, 13, 17, and 21. Although occasional losses of all these chromosomes have been reported in RO, the simultaneous loss of all

these chromosomes has not been seen in oncocytomas.

Genes involved and proteins

Note

Mitochondrial DNA mutations that disrupt components of complex I in the electron transport chain can be found in bilateral and multifocal oncocytomas (Lang et al., 2015).

FLCN (folliculin gene)

Location

17p11.2

Note

Germline mutations in FLCN cause Birt-Hogg-Dubé syndrome, an inherited disorder characterized by follicular hamartomas, renal tumors, pulmonary cysts, and spontaneous pneumothorax. Hybrid oncocytic/chromophobe tumors and chromophobe renal cell carcinomas are the most common renal tumors in Birt-Hogg-Dubé syndrome, but oncocytomas may be seen in a subset of cases. The renal tumors are typically bilateral and multifocal.

Protein

Folliculin is a putative tumor suppressor that plays a role in the regulation of energy homeostasis and AMPK and CC: TXT: mTOR ID: 40639> signaling.

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