Kidney: Renal Oncocytoma

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Classification

Note
Renal Oncocytoma (RO) is a benign renal epithelial neoplasm that comprises approximately 5% 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 are the most frequent renal tumors in patients with Birt-Hogg-Dube syndrome (BHD). BHD is caused by mutations in the folliculin gene (FLCN). The etiology of sporadic RO is not known.

Epidemiology
Renal oncocytomas account for about 3-7% of all renal tumors and shows 2.5:1 male to female ratio. More than 50% of patients with RO are asymptomatic. Some patients have been reported in association with angiomylipoma and/or tuberous sclerosis.

Pathology
Macroscopically, renal oncocytomas are solitary, well-circumscribed, slightly lobulated solid tumors with generally mahogany brown or dark red cut surface. A central scar is frequently observed. Necrosis and hemorrhage are uncommon. Microscopically, tumor cells with abundant, granular cytoplasm are arranged in nests, tubulocystic, solid, or trabecular patterns within edematous, myxomatous or hyalinized stroma. On low power, the epithelial cell nests surrounded by myxomatous stroma gives the appearance of an island archipelago, which is a characteristic feature of oncocytomas. The nucleus is homogenous, round and centrally located, but large bizarre nuclei are frequently observed. Ultrastructurally, tumor cells contain many mitochondria with predominantly lamellar cristae. Some special stains are helpful for differential diagnosis with the eosinophilic or granular form of clear cell carcinoma: most RO show negative vimentin and RCC antigen staining, although positive staining for vimentin in up to 72% has been reported in some series. The immunohistochemical patterns of oncocytoma and chromophobe carcinoma are virtually identical, which often makes distinctions of these tumors with overlapping morphologic features quite difficult. Recently, claudin 8 positivity in oncocytomas has been reported as tool to differentiate these two neoplasms since chromophobe carcinomas are negative for claudin 8 and positive for claudin 7. Some authors have suggested that oncocytoma can progress to chromophobe carcinoma, based on shared abnormalities in chromosome 1, although the occurrence of this transformation has not been conclusively proven.

Treatment
Most patients with RO are treated with nephrectomy. Nephrectomy (radical or partial), enucleation or wedge resection may be performed.

Prognosis
Almost all cases of oncocytoma behave in a benign fashion with no recurrence, metastasis or mortality.
Some atypical features, such as nuclear pleomorphism, perinephric fat involvement and focal necrosis do not seem influence prognosis. Rarely few cases of RO have simulated malignant behavior showing extension to branches of renal vein however this does not correlate with poor outcome. A case of metastatic oncocytoma has been reported.

### Cytogenetics

**Note**

Complete or partial loss of chromosome 1 is the most common cytogenetic abnormality reported in approximately 40% of cases. Other frequent changes include loss of Y (15%) and monosomy 14 (15%). Trisomy 7 has been reported as the most common chromosomal gain in up to 5% of patients. Structural rearrangements involving 11q12-13 have been reported. Approximately 50% of tumors show no chromosomal abnormalities.

The incidence of chromosome 1 abnormalities in bilateral tumors seems to be higher than single tumors. Chromosomal abnormalities seem to be more frequent in sporadic tumors, while familial RO has a higher frequency of cytogenetically normal tumors.

One of the diagnostic pitfalls in renal epithelial tumors is distinguishing between benign RO from the eosinophilic variant of chromophobe RCC. 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**

RO is characterized by dense accumulation of mitochondria and deficient in electron transport chain complex I (CI). CI or NADP-ubiquinone oxidoreductase is the main gateway to the electron transport chain. Mitochondrial proliferation in oncocytic cells could be regulatory response attempting to restore a defective respiratory function since defective oxygen consumption makes mitochondrial proliferation. CI is encoded in part by nuclear genome and in part by the mitochondrial genome for 7 genes (MT-ND1, MT-ND2, MT-ND3, MT-ND4, MD4L, MD5, MD6) yielding 45 subunits. Mitochondrial DNA point mutations are found in all ROs studied (9/9 cases), especially in complex I and none of chromophore RCC.

Mutations in folliculin (FLCN, 17p11.2) cause Birt-Hogg-Dube (BHD) syndrome which is a rare inherited genodermatosis characterized by hair follicle hamartomas, kidney tumors, and spontaneous pneumothorax. RO is the most common renal tumor seen in patients with BHD. The FLCN protein contains a conserved SLS potential phosphorylation site, and shows a highly conserved sequence between human and homologs in mice, Drosophila, and C. elegans. It is believed that FLCN may be involved in energy and/or nutrient sensing through the AMPK and mTOR signaling pathways.

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