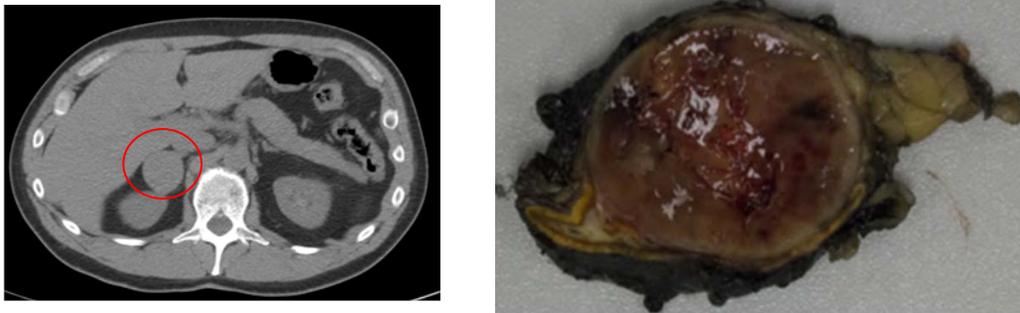


**Case title:** A 47 year-old man with a right adrenal mass

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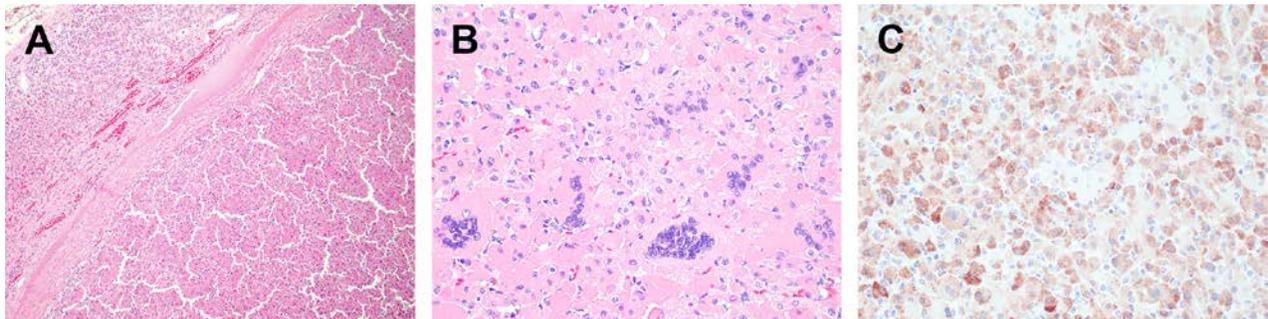
**Clinical history:** A 47 year-old man with a 2 year history of a slowly growing right adrenal mass. The patient had no significant previous medical history and denied any symptoms of adrenal hormone excess. Laboratory studies failed to reveal abnormalities with testosterone, aldosterone, cortisol or renin levels. Urine metanephrines study was also negative. The CT scan showed indeterminate washout characteristics atypical for an adenoma. The patient had no family history of endocrine disorders. The tumor was resected by laparoscopic adrenalectomy.

**Gross findings:** Gross examination of the adrenalectomy specimen revealed a 5 x 4.5 x 2.5 cm well circumscribed encapsulated pink-tan mass with discrete areas of hemorrhage (Figure 1).



**Figure 1. Radiographic (circle) and gross photographs of the right adrenal gland, revealing a well-circumscribed pink-tan mass with a thin capsule on sectioning.**

**Microscopic examination and immunohistochemistry:** Microscopy demonstrated an encapsulated tumor composed of oncocytes organized in diffuse, solid or sheet-like patterns (Figure 2 A and B). The polygonal oncocytic cells were remarkable for a moderate degree of nuclear pleomorphism with occasional multinucleated cells (Figure 2B). Mitotic activity was 1/50 HPF. No atypical mitotic figures, venous invasion, necrosis or sinusoidal invasion was identified. Immunohistochemical studies showed that the lesional cells were reactive with antibodies to melan-A (Figure 2C) and non-reactive with antibodies to alpha-inhibin. Ki67 revealed less than 5% positive tumor cells.



**Figure 2. Microscopic and immunohistochemical studies: An adrenal tumor is composed of oncocytes arranged in sheet-like pattern (A); Occasional multinucleated and bizarre tumor cells are noted (B); The tumor cells react with antibodies to Melan A in cytoplasmic pattern.**

**Final diagnosis:** Oncocytic adrenal cortical neoplasm of low malignant potential

**Discussion:** Adrenal oncocytic neoplasm is one of the histological subtypes of incidentally detected adrenal masses that are usually large, benign, nonfunctional adrenal tumors, with prevalence in women and on the left side<sup>1</sup>. These tumors are exceedingly rare and have been reported of variable size (3-20 cm) and weight (12-2,415 g)<sup>2</sup>. No imaging modality can differentiate benign from malignant adrenal oncocytic neoplasms. Only pathologic criteria are able to best predict clinical behavior. Histopathologic parameters that define oncocytic adrenal cortical neoplasms include predominantly (>90%) cells with eosinophilic and granular cytoplasm, variably enlarged and irregularly shaped nuclei, and a diffuse architectural pattern. The Weiss morphologic classification system of adrenocortical tumors that predicts their biological behavior is not applicable for oncocytic neoplasms since they already possess three “positive” criteria, i.e. three mentioned above histopathologic parameters that define an oncocytic adrenocortical neoplasm, they would all be automatically malignant. Bisceglia et al proposed major and minor criteria modified from the Weiss system for nononcocytic adrenocortical tumors (Table 1) and applied them to oncocytic adrenal cortical neoplasms. The limited study was based on 10 analyzed cases plus literature review.

**Table 1. Histologic criteria for diagnostic characterization of biologic behavior of oncocytic adrenocortical neoplasms**

Major Criteria	Minor Criteria
A mitotic rate above 5/50HPF	Large size (>10 cm and/or >200g)
Any atypical mitoses	Necrosis
Venous invasion	Capsular invasion
	Sinusoidal invasion

The presence of one major criterion indicates malignancy (adrenal cortical carcinoma), while one to four minor criteria indicate uncertain malignant potential (borderline) and none of the criteria is indicative of benignancy (adrenocortical oncocytoma). Due to rarity of the adrenal cortical neoplasms however, additional clinicopathologic studies are necessary to accumulate more supportive evidence for this diagnostic approach. Given the lack of clearly delineated criteria we have generally placed these into either the malignant or low malignant potential categories.

The differential diagnosis includes oncocytic pheochromocytoma, conventional adrenocortical carcinoma with focal oncocytic changes, conventional renal carcinoma with oncocytic features or eosinophilic variant of chromophobe renal cell carcinoma involving adrenal gland, and hepatocellular

carcinoma. Therefore, the use of immunohistochemistry is beneficial to resolve the differential diagnosis. In general, the immunophenotypic profile of an oncocytic tumor is: diffuse positivity for vimentin, melan-A, synaptophysin and alpha-inhibin<sup>4</sup> and no reaction with antibodies to chromogranin while oncocytic pheochromocytoma should be positive for chromogranin and negative for inhibin and melan-A. Involvement by renal cell carcinoma or metastatic hepatocellular carcinoma can be evaluated immunohistochemically in patients with history or imaging evidence of malignancies in the respective organs.

Adrenalectomy is the mainstay of therapy. The prognosis depends on histopathologic classification. A regular judicious follow-up for the first five years is recommended due to lack of the objective data in regard to malignant behavior<sup>2</sup>. A reporting pathologist should be aware of uncertainty associated with malignant behavior of these adrenal cortical neoplasm since the current proposed histopathologic classification is based on a limited number of cases due to rarity of such lesions.

### **List of References**

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