Oncocytic adrenocortical carcinoma: a rare adrenal tumor subtype

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Oncocytic tumors arising from the adrenal gland are rare. Oncocytic adrenal neoplasms (OAN) may mimic adrenocortical carcinoma (ACC) at presentation, and can only be definitively diagnosed histologically. Most OANs are benign, and carry a favorable prognosis. We report on an 83-year-old female who, while being investigated for anemia and weight loss, was found to have a 23 cm adrenal mass concerning for ACC. Adrenalectomy and histopathology confirmed a malignant OAN, based on the Lin-Weiss-Bisceglia criteria. We report on the largest non-functional, malignant OAN cited in the literature to date. OAN's, though rare, can be considered in the differential diagnosis of large adrenal tumors.

Key Words: adrenal cortex neoplasms, carcinoma, histopathology

Introduction

Oncocytic tumors are uncommon neoplasms, occurring most often in the thyroid, kidney, parotid, salivary or pituitary glands.[1] They are defined histologically by a predominance (> 75%) of oncocytes,[2] which are large epithelial cells with highly eosinophilic cytoplasm and abundant mitochondria.[1] They are typically benign,[3] but malignant oncocytic adrenocortical neoplasms (OANs) have been reported. Since the first description of OANs in 1986 by Kakimoto, only 150 cases have been reported.[3,4] The majority of OANs are non-functional, and discovered incidentally. They present at a mean age of 47, with a strong female predominance (2.5:1), and are more frequently left sided.[3-5] Grossly, OANs tend to be large, round, well-circumscribed, and tan in color.[3,4] A challenge in the diagnosis and management of OANs is that their biologic behavior is difficult to predict.[5-8]

OANs can be classified as benign (adrenocortical oncocytoma), borderline (oncocytic neoplasm of uncertain malignant potential), or malignant (oncocytic adrenocortical carcinoma).[7]

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They generally portend a more favorable prognosis compared to non-oncocytic adrenocortical tumors.[2,5] The two largest case series in the literature report that 80% of OANs are benign.[5,7]

Generally, functional adrenal tumors or tumors > 4 cm are surgically excised.[4,9] Due to the large size of most OANs upon diagnosis, they are usually managed with open adrenalectomy.[3] Herein, we describe a case with the largest reported non-functional, malignant OAN, found incidentally in an 83-year-old woman being investigated for anemia, early satiety and weight loss.

Case report

An 83-year-old woman was referred for management of a 23 cm, heterogeneous, enhancing mass in the left retroperitoneum, appearing to arise from the adrenal gland. On CT, the mass displaced the left kidney caudally, and abutted the pancreas, spleen, and great vessels, Figure 1. The patient had lost 15 kg over 6 months, and complained of early satiety, and fatigue. Past medical history revealed hypertension and multiple surgeries, including cholecystectomy, appendectomy, and hysterectomy. Medications at presentation included terazosin, atenolol, ASA, and potassium supplements. Family history revealed an aunt who underwent adrenalectomy for a functional tumor. On examination, there was a left-sided large, firm palpable mass, extending from the costal margin to the pelvic brim. The differential diagnosis at

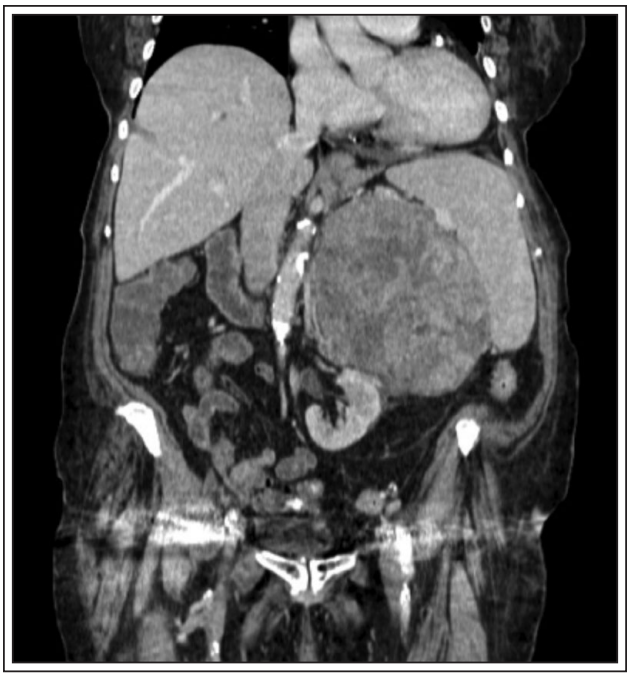

Figure 1. Preoperative computed tomography.

presentation included an adrenocortical carcinoma (ACC), or functional adrenal tumor. Adrenal functional work up, including 24 hour urinary free cortisol, serum metanephrines, aldosterone, renin and plasma electrolytes, was normal. Staging CT showed no distant metastases.

Open left adrenalectomy and locoregional lymph node dissection was performed via a Chevron incision. Grossly, there was displacement, but no invasion, of adjacent organs. Estimated blood loss was 150 cc, the left kidney and renal vessels were spared, and there were no peri-operative complications.

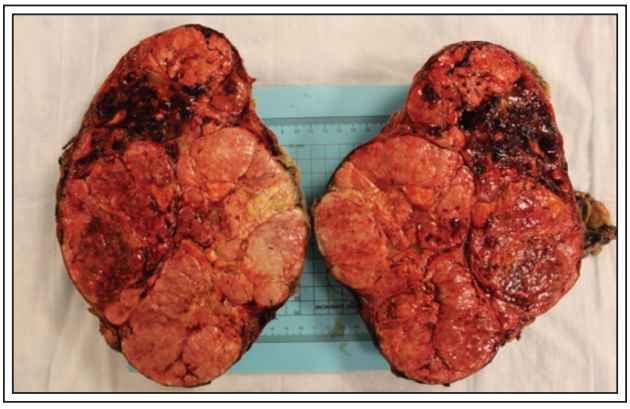

Figure 2. A well circumscribed, lobulated mass with yellow – tan cut surfaces and geographic necrosis replacing the entire adrenal gland parenchyma. The capsule is intact.

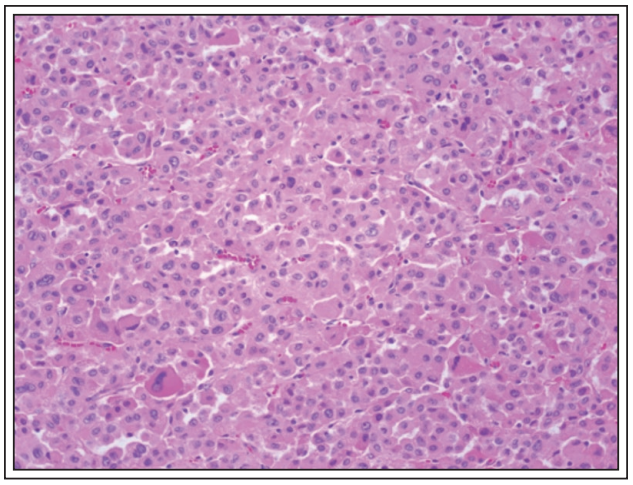

Figure 3. (200x) The tumor is composed of large polygonal cells with abundant, eosinophilic and granular cytoplasm. The nuclei are round with a single small nucleolus. Some tumor cells have large pleomorphic hyperchromatic nuclei. Mitotic rate is 7/50 hpf (x400). Atypical mitotic figures are not present.

Gross pathology revealed the tumor was 2020 grams, measuring 23.3 cm x 19.5 cm x 8 cm, Figure 2. Surgical margins were negative. Microscopy revealed a mitotic count of 7/50 high power field (hpf), and clear cells comprised < 25% of the tumor. Atypical mitoses and capsular invasion were absent, Figure 3. Thus, on the Modified Weiss system,[10] the tumor was given a score of 5 (out of 7), indicating malignant potential (≥ 3). On the Lin-Weiss-Bisceglia (LWB) criteria, Table 1, the lesion met one major and two minor criteria, again classifying it as malignant.

TABLE 1. **Lin-Weiss-Bisceglia criteria[7] for assessing biological behavior of oncocytic adrenal neoplasms (OANs)***

Major criteria
- Mitotic rate of > 5 mitoses per 50 hpf
- Atypical mitoses
- Venous invasion

Minor criteria
- Large size (> 10 cm and/or > 200 g)
- Necrosis
- Capsular invasion
- Sinusoidal invasion

*≥ 1 major criteria = malignant; ≥ 1 minor criteria = borderline; no major or minor criteria = benign

The patient convalesced well, and was discharged from hospital on postoperative day 6. At 4 week follow up she was doing well, and reported her energy and appetite had improved significantly.

Discussion

We report on a 23 cm, malignant oncocytic adrenocortical neoplasm detected during work up of anemia, weakness, and early satiety. Oncocytic tumours arising from the adrenals are extremely rare, and it is uncommon for them to be malignant. To our knowledge, the case presented here is the largest non-functional OAN reported in the literature. As adrenal cortical carcinoma (ACC) accounts for 25% of adrenal tumors that are larger than 6 cm,[4] that was the most likely preoperative diagnosis. This case shows that although rare, an OAN could be considered in the differential of a large adrenal mass.

There are no imaging characteristics that can reliably differentiate OANs from other adrenal tumors preoperatively.[3,8] Khan et al did note that malignant OANs tended to be larger, lipid-poor and exhibit central necrosis.[2]

Definitive diagnosis of OANs can only be established with histopathology. Fine-needle aspiration of large adrenal tumors is not routinely recommended, and is often non-diagnostic.[9]

It has been recommended that determination of malignancy for OANs be done using a different set of criteria than conventional (non-oncocytic) adrenocortical tumors.[7] The Lin-Weiss-Bisceglia (LWB) criteria proposed in 2004 is the currently recommended classification system for OANs. The major criteria of this system include a mitotic count of greater than 5 per 50 hpf's, atypical mitoses, and venous invasion, and minor criteria include a tumor size larger than 10 cm, or mass > 200 g, necrosis, capsular invasion, and sinusoidal invasion. The presence of any major criteria defines malignancy, the presence of any minor criteria indicates uncertain malignant potential, and the absence of any major or minor criteria defines a benign tumour.[7] Due to the large size of most OANs at diagnosis, open adrenalectomy is usually required.[3] Smaller adrenocortical tumors may be removed laparoscopically.[9]

Following successful excision of malignant OANs, the 5-year survival rate has been reported as 50-60%.[3] In the largest case series to date, 3 out of 8 patients with malignant OANs had local recurrences, 1 developed distant metastases, and 3 died of their disease, with a mean follow up time of 26.5 months (range 1-108 months).[5] A 5-year survival is poor for malignant OAN's; however, these represent the minority. The majority of OAN's are benign and can be followed conservatively postoperatively, in contrast to the aggressive nature of ACC.[3]

Conclusion

We present a case of a 23 cm adrenal tumor that was found to be a malignant oncocytic adrenocortical neoplasm. OANs are a very rare subtype of adrenal tumor that are typically benign and carry a better prognosis than non-oncocytic adrenal malignancies. Imaging cannot reliably differentiate OANs from other adrenal tumor types. They should be classified using the Lin-Weiss-Bisceglia criteria. Surgical resection is the only curative treatment, and open adrenalectomy is the gold standard approach. □

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