



Estradiol-secreting adrenal oncocytoma in a 31-year old male

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ABSTRACT

Oncocytic adrenocortical tumors (OAT) are rare and often are non-functional. We report a unique case of an estradiol-secreting adrenal oncocytoma in a 31-year-old male discovered upon an infertility and gynecomastia work-up. After resection of the 9 cm adrenal mass, the patient's estradiol levels normalized from 83.2 pg/ml to 19.0 pg/ml. Gonadotropins and serum dehydroepiandrosterone sulfate also normalized.

1. Introduction

Oncocytic neoplasms that include oncocytomas are rare solid visceral tumors. These have been described in the kidneys, adrenals, parathyroids, lungs, thyroid, salivary gland, pituitary, and ovaries and can vary in biological behavior. Oncocytomas are epithelial tumors composed of cells with eosinophilic mitochondria-rich cells. Overall incidence of oncocytoma is relatively common in other organs and thus more is known about how they behave and how to manage them. However, adrenal oncocytomas are much rarer. Approximately 183 cases of oncocytic adrenocortical tumors (OAT) have been reported globally, with most patients in the age group between 40 and 60¹. The majority of OAT's are detected incidentally. OAT's make up about 1.8% of adrenal tumors and 20–30% are malignant. 30% of adrenal oncocytomas have been reported to exhibit metabolic activity.² In this report, we present a case of an extremely unusual estradiol-secreting adrenal oncocytoma.

2. Case presentation

A 31-year-old male with a history of gynecomastia and infertility presented for evaluation of an adrenal mass which had been discovered 1 year prior to presentation. The patient had undergone a bilateral

cosmetic mastectomy soon after diagnosis of his adrenal mass.

Computed tomography with and without contrast of the abdomen and pelvis demonstrated a 9 cm, heterogeneously enhancing right adrenal mass (Fig. 1). Adrenal metabolic work-up revealed a plasma aldosterone level of 9.2 ng/dL (normal 0.0–30.0 ng/dL), plasma renin activity 1.23 ng/mL/hr (normal 0.167–5.380 ng/mL/hr), plasma free metanephrine level 26.9 pg/mL (normal 0.0–88.0 pg/mL), plasma free normetanephrine level of 43.3 pg/mL (normal 0.0–110.1 pg/mL), random AM serum cortisol of 10 µg/dL (normal 6.2–19.4 µg/dL), and 8AM serum cortisol after 1mg dexamethasone of 1.3 µg/dL (normal 0.0–1.8 µg/dL), making primary aldosteronism, pheochromocytoma, and Cushing syndrome unlikely. The patient's 17-OH progesterone serum level was 153 ng/dL (normal 27–199 ng/dL); however, FSH was low at 0.8 mIU/mL (normal 1.7–8.6 mIU/mL), DHEAS was elevated at 502.0 µg/dL (normal 138.5–475.2 µg/dL), and estradiol was markedly high at 83.2 pg/mL (normal 8.0–35.0 pg/mL).

The patient was advised to undergo open adrenalectomy given concern for malignancy and current guideline recommendation to avoid minimally invasive surgery in patients with adrenal masses >6cm in whom adrenocortical carcinoma is suspected.³ Upon excision through a right modified Makuuchi incision, the mass measured 9.0 × 7.0 × 5.5 cm in size, weighed 240 g, and had microscopically negative margins. On gross examination, red-brown focally hemorrhagic tumor was observed

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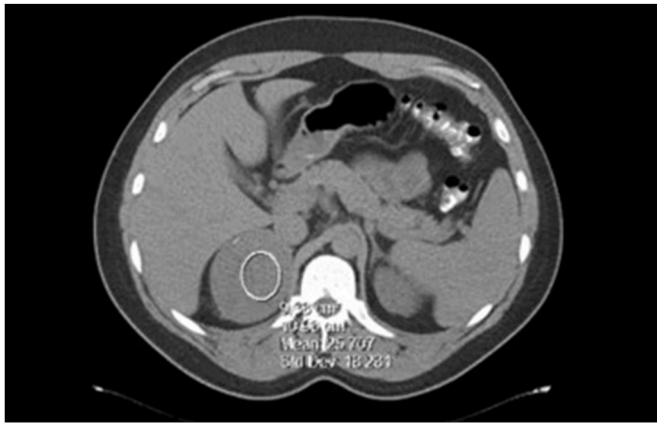
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<https://doi.org/10.1016/j.eucr.2022.102138>

Received 24 April 2022; Received in revised form 31 May 2022; Accepted 16 June 2022

Available online 22 June 2022

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A



B

Fig. 1. Two representative cross-sectional images (A and B) from the patient's CT abdomen and pelvis without contrast demonstrating a right adrenal mass with an unenhanced density of ~26 Hounsfield Units, indicating a lipid-poor lesion.

stemming from a $5.0 \times 1.5 \times 0.5$ cm portion of normal adrenal gland (Fig. 2A).

Microscopically, the tumor featured 2 mitoses/50 hpf and lacked atypical mitotic figures, necrosis, capsular invasion, sinusoidal invasion, and venous invasion (Fig. 2B and C,D). Using the Lin-Weiss- Bisceglia criteria for diagnosing adrenal cortical neoplasms, it was thus deemed to be of uncertain malignant potential.

Postoperatively, the patient did well and was discharged on post-operative day 2. He returned for follow up with labs two weeks later. At that time, his serum estradiol level normalized to 19 pg/ml (8.0–35.0 pg/mL). His serum DHEAS was also normal at 241ug/dL (138.5–475.2 µg/dL) and his 17- OH progesterone was 91 ng/dL (27–199 ng/dL). At 5 month follow-up, his gonadotropins were normal (FSH 2.3 mIU/ml, LH

7.5mIU/ml) with normal serum testosterone of 772 ng/dl (normal, 264–916) and estradiol. Abdominal CT scan showed a normal left adrenal gland and no evidence of disease in the surgical right adrenal bed.

The patient will undergo routine follow-up with endocrine labs every 6 months, and CT scans every 6–12 months for at least 5 years given the uncertain malignant potential.

3. Discussion

AOTs are rare adrenal tumors, with functional oncocytomas making up only a small minority of these tumors. Of the reported functional oncocytomas, there have been 19 reported cases of androgen secreting oncocytomas that result in virilization of females, but we believe this is only the second reported case of an estrogen secreting adrenal oncocytoma in a male.⁴ Our patient's estradiol secreting oncocytoma was likely responsible for his gynecomastia and fertility difficulties which had been an issue for at least 6 years prior to resection of the mass. The patient had undergone a bilateral cosmetic mastectomy 1 year prior to adrenalectomy.

Bisceglia and colleagues first described diagnostic criteria of OAT's known as the Lin-Weiss-Bisceglia criteria. Based on these criteria, for an oncocytic tumor to be considered malignant it must meet any 1 of the 3 major criteria: mitotic rate of more than 5 mitoses/50 high power field, any atypical mitoses, or venous invasion. If the tumor meets one of the major criteria, it is considered to be malignant. The following minor criteria were also described: >10 cm and/or >200 g, presence of necrosis, demonstration of capsular invasion, and/or sinusoidal invasion. If any minor criteria are present, the tumor is deemed of uncertain malignant potential, while benign designation is given if none of these features are observed. As such, our case was considered to have uncertain malignant potential due to the absence of any of the major criteria and the presence of 1 minor criteria (weight of the tumor >200 g).⁵

To our knowledge, this is the second reported case of an estrogen secreting adrenal oncocytoma. Other feminizing adrenal tumors (FAT) have been reported. Such tumors are also exceedingly rare, making up 1–2% of all adrenal neoplasms. These tumors are more often malignant and tend to have a poor prognosis.⁵ Men harboring such tumors often present with gynecomastia. The LH and FSH tend to be low due to the inhibitory effect of the high estrogen level on the hypothalamic-pituitary-gonadal axis, while the precursors to estrogen and testosterone (DHEAS) tend to be elevated. For FATs, estrogen testing in follow-up can be used as a tumor marker for monitoring of recurrence.⁶

Of the reported cases of functional oncocytomas, none have had recurrence of disease during follow-up ranging from 2 weeks to 64 months.¹

4. Conclusion

Adrenal oncocytomas, especially those that exhibit metabolic function, are extremely rare. Estrogen-producing adrenal tumors are also extremely uncommon and can contribute to infertility and gynecomastia. This case report adds to the world's literature and underscores the central role of adrenal surgery in managing these rare solid neoplasms.

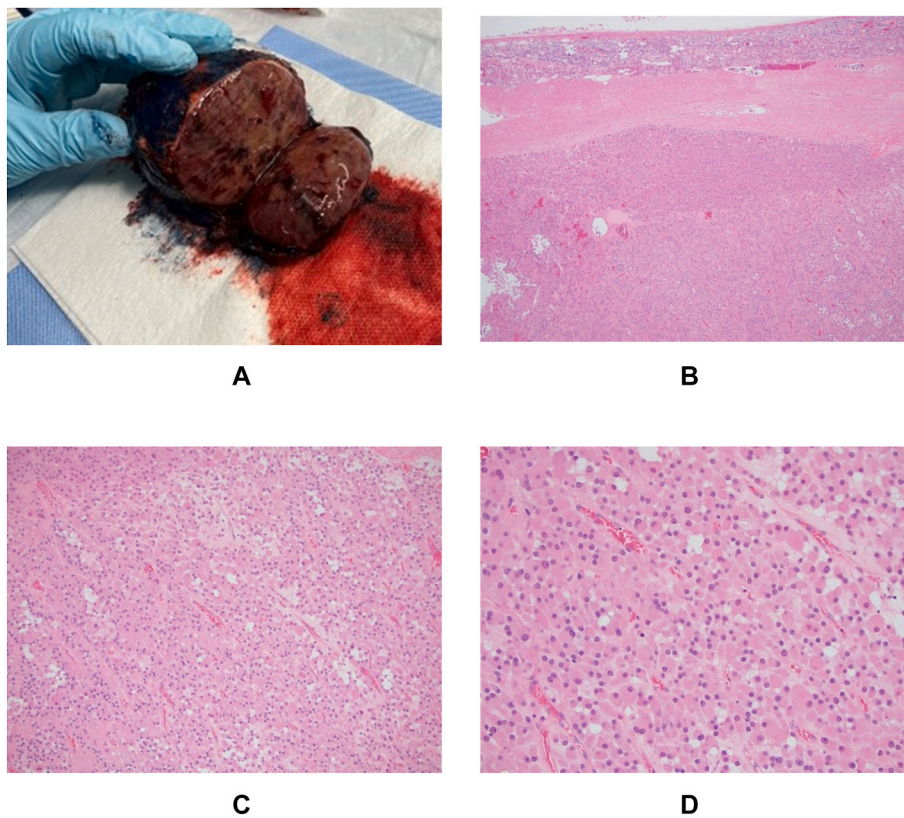


Fig. 2. 2A Gross appearance of the resected adrenal mass, demonstrating the focally hemorrhagic surfaces 2B. This tumor is encapsulated with a rim of adrenal gland tissue (top). 2C. Oncocytic tumor cells without increased mitotic Fig. 2D. High-power view shows tumor cells with eosinophilic cytoplasm and prominent nucleoli.

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