Oncocytic Tumors: An Uncommon Benign Adrenal Gland Lesions With Features of Malignancy

Zineb Elazime 1, Lamiaa Elazizi 1, Hayat Aynaou 1, Houda Salhi 1, Hanan Elouahabi 1

1. Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Hassan II University Hospital Center, Fez, MAR

Corresponding author: Zineb Elazime, zineb.elazime@gmail.com

Abstract

Oncocytic cell neoplasms are usually found in the thyroid or salivary glands and the kidneys. Adrenal oncocyto...
Considering that the patient had neither hypertension nor hypokalemia, we wanted to rule out pheochromocytoma and Cushing’s syndrome. The results of this study are as follows: a negative urinary fractionated metanephrines test, 1 mg dexamethasone overnight of 0.6 ug/dl µg/dl. In the presence of atypical features of the adrenal lesion on the chest CT scan, an MRI was performed and detected a large mass in the external portion of the left adrenal gland. The mass was well limited with regular contours, encapsulated with intermediate T2 signal with areas of high T2 signal, restrictive in diffusion, without signal drop in out-of-phase (OOP) sequences, and with progressive heterogeneous enhancement following a type III enhancement curve, outlining areas of necrosis (Figures 2-3). It measured 59 x 43 mm, responsible for the reflow of the external splenic vein, without any signs of kidney or pancreas invasion.

**FIGURE 1:** (A) Adrenal CT, axial section: left adrenal lesion, solid-necrotic with a spontaneous density of 40UH. (B) Axial image on portal phase (CT) scan showing a left adrenal mass, heterogeneously enhanced

**FIGURE 2:** Voluminous mass in the external part of the left adrenal gland, well limited, with regular contours (orange circle), encapsulated, described in intermediate T2 signal with areas in marked T2 hypersignal (orange arrow), restrictive in diffusion (red circle), not showing any signal decrease in the OP sequences (red arrow)
The patient underwent a left adrenalectomy via laparotomy and had an uneventful recovery.

The histological analysis revealed large polygonal cells with abundant granular and eosinophilic cytoplasm and a vesicular nucleus without cytonuclear atypia. The immuno-histological analysis showed an intense and diffuse marking of anti-synaptophysin and anti-MelanA antibodies, anti-chromogranin antibodies, and cytokeratin, which were all negative. The proliferation index evaluated by Ki67 is less than 5% (2%). Besides, the PS100 antibody showed the presence of scattered star cells. Hence, the diagnosis of adrenocortical oncocytoma was made.

A month after the surgery, the patient was completely asymptomatic, with no evidence of surgical wound infection or incisional hernia. He is now under follow-up.

Discussion

The oncocytic cells have been described initially in 1931 by Hamperl as cells with a granular and eosinophilic cytoplasm [3]; these characteristics were the consequence of several mitochondria [8]. Although the mechanisms of oncocytosis are not fully known, two theories exist to explain it: the first one is that the proliferation of mitochondria is the consequence of a mutation and the second one is the result of an epigenetic event resulting from the cellular hypoxia [9].

Adrenal oncocytoma is extremely rare; nearly 200 cases have been published since Kakimoto et al. reported the first case [1]. They affect a wide age group (15-77 years), more prevalent in women and in the left adrenal gland [10]. They usually manifest as an incidentaloma.

According to current recommendations, an adrenal incidentaloma greater than 4 cm and over 10 HU is presumptively malignant. Despite this fact, an adrenal oncocytoma is usually benign. Approximately, 25% of AOs reported in the literature are malignant, but in some recent series, a percentage greater than 60-70% have been found [11]. Also, AO has been reported to be associated with hormonal hypersecretion in 31.5% of cases, principally as a Cushing’s syndrome, virilizing syndrome, or pheochromocytoma-like syndrome [12].

Imaging techniques (e.g., CT, MRI) have limited sensitivity for adrenal oncocytoma because it is hardly distinguishable from a malignant tumor. Basically, AOs are in general large (8.5 cm on average), low in lipids, with increased attenuation on the CT from 20 to 40 HU, and have malignant features such as heterogeneous contrast enhancement or fibrous encapsulation.

Macroscopically, the AO is a well-circumscribed enclosed lesion, in which areas of bleeding and/or necrosis can be detected. The defining histological characteristic of these tumors is a proliferating oncocytic cell, with an increased size and an eosinophilic granular cytoplasm, due to the accumulation of mitochondria. They are usually positive for vimentin, calretinin, alpha-calretinin, alpha-inhibin, and melanin-A and negative for S100 and chromogranin [13].

In terms of prognosis, while the Weiss criteria [14] are used to establish the malignant behavior of adrenocortical carcinomas, these standards are not appropriate for AO. Thus, for better stratification, the Lin-Weiss-Bisceglia system has been proposed for AO [15], which distinguishes major criteria (>5 mitoses/50 hpf, presence of atypical mitoses or venous invasion) and minor criteria (height >10 cm or weight >200 g, presence of tumor necrosis, capsular or sinusoidal invasion). The presence of any major criteria would classify the tumor as malignant, while minor criteria, such as a lesion of uncertain potential, and the absence of all criteria would suggest a benign lesion.
Concerning the treatment of these tumors, their association with hormonal hypersecretion and their suspicion of malignancy make surgery the first option. Adrenalectomy is usually performed by laparotomy for large tumors or by laparoscopy for smaller ones if imaging shows a well-encapsulated tumor with no invasion.

There are few recommendations for follow-up. No recurrent benign or indeterminate oncocytomas have been reported. Patients with malignant oncocytomas, however, have a five-year survival rate of 50-60% after surgery. Out of the nine cases of malignant oncocytoma, five were reported disease-free in six months, whereas four experienced a recurrence [3].

It is recommended that regular monitoring should be maintained for at least five years [3,7].

**Conclusions**

Adrenal oncocytoma is a rare tumor. Surgical removal remains the primary method of treatment and it can be considered in most cases as a benign tumor. This case report is a valuable contribution to understanding adrenal oncocytoma due to the lack of information based on cases reports. However, large clinical studies are much needed to confirm the results as well as in order to evaluate the prognosis and establish follow-up strategies.

**Additional Information**

**Disclosures**

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

**References**