THE ADRENALECTOMY IN RARE ENDOCRINE TUMORS – 2 CASES REPORT

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THE ADRENALECTOMY IN RARE ENDOCRINE TUMORS-2 CASES REPORT (Abstract):
Adrenal tumors are a rare finding. The endocrine profile is complex. The adrenalectomy is a major step in their therapy but it also brings out major information regarding the possible aggressive profile based on pathological exam and immuno-hystological findings. We present two cases cured by surgical procedure that also provided material for elucidating the diagnosis. Case 1 is 58-year-old female with metabolic syndrome. She is incidentally diagnosed by a routine abdominal ultrasound with a left adrenal mass. This apparently doubled the size in only 3 months, up to 9.3 by 8.5 cm, as pointed by the computed tomography scan, suggesting an adrenal carcinoma. The laparoscopic left adrenalectomy was performed and the pathological report revealed an adrenal adenoma with osteoid metaplasia, a rare finding in such tumors. The evolution after surgery was good. The prognostic was better that seemed initially before. Case 2 is a 50-year-old female patient presenting progressive hirsutism. The investigations suggested an adrenal carcinoma, based on: very high serum testosterone levels (5 times above normal) and 24-hours urinary ketosteroids (5 times as normal). The computed tomography showed a right adrenal tumor of 11.5 by 11 by 12 cm. Because of these findings, a carcinoma was suspected and right open adrenalectomy was performed. The pathological report showed that the tumor was gigantic, up to 14 cm, with a weight of 780 g. The structure was complex: trabecular and compact zones, anisocytosis, anisocaryosis, hemorrhage, calcar impregnations, osteoid metaplasia. No invasion into the capsule or the vessels was found. The immuno-hystochemistry showed positive reaction for melan A, vimentin, and synaptophisin. For the moment, no therapy is necessary. Further follow up by serum endocrine markers and serial imagistic scan are necessary. Both cases are suggestive for the importance of adrenalectomy in the cure of adrenal tumors.

KEY WORDS: ADRENALECTOMY, LAPAROSCOPY, ADRENAL TUMOR

INTRODUCTION
The adrenal tumors represent a wide panel of phenotypes varying from non-secreting small adenomas to adrenal carcinoma. Some of them are very rare, thus a vast statistical experience is lacking. Nevertheless, the adrenalectomy is the major step in elucidating the diagnosis and prognosis of rare adrenal tumors.
CASES REPORT

Case 1

58-year-old female patient is known with arterial hypertension, type 2 diabetes mellitus and hyperlypidemia since the last decade, under adequate therapy. A routine abdominal echography was performed and a nodule of 5.58 cm was discovered at the level of the left adrenal. On admission, 3 months later, the abdominal computed tomography (CT) revealed a left adrenal tumor of 9.3 by 8.5 cm, with polycyclic borders, iodophylia, diffuse mycrocalcifications and no metastasis. (Fig. 1A). This apparently doubled the size in only 3 months, under the reserve of proper imagistic interpretation. Based on the large size, apparently increasing diameter and high vascularization, an adrenal carcinoma was suspected. Moreover, the endocrine profile showed normal function despite the metabolic complications that might suggest a Cushing’s syndrome. The plasma basal cortisol was 11.14 µg/dL (normal 8-22), with suppression at the 2 mg x 2 days dexametason standard suppression test. The plasma metanephrines and normetanephrines were within normal limits: 13 pg/mL, respective 43 pg/mL (normal <45, respective <90). Laparoscopic left adrenalectomy was performed with no complications (Fig. 1B).

Fig. 1 Abdominal CT scan
A. Left adrenal tumor; B. After left adrenalectomy

No adrenal insufficiency was registered after surgery. The pathological report revealed an adrenal adenoma with osteoid metaplasia, myelolipomatosis metaplasia, microcalcifications, hemorrhage and cysts (Fig. 2).

The osseous metaplasia is not an uncommon finding. There are cases reported in colonic adenomas or adenocarcinomas, gallbladder, phyllodes tumor of the breast, renal cancer etc [1-5]. Osseous metaplasia was found in endometrium, too and the DNA analysis showed that does not originates from the fetus. [6] Immuno- staining reaction was positive for melan A, inhibin and CD 34 into the vessels, suggestive for adrenal origin (Fig. 3).

The patient will be followed up by serial CT scan. The unexpected benign aspect improved the prognosis. Also, despite the large size, laparoscopy was successfully performed which helped the recovery of the patient.
**Case 2**

50-year-old female patient is admitted for progressive hirsutism since the last few months. The physical exam showed no other anomalies. The biochemical profile was normal except for hypercholesterolemia (total serum cholesterol - 266 mg/dL, with normal < 200 mg/dL).

![Pathological examination](image1)

**Fig. 2 Pathological examination (HE×100)**

A Corticoadrenal adenoma; B Areas of myelolipomatos and osteoid metaplasia; C Cysts and hemorrhage; D Osteoid metaplasia

![Immunohistochemistry](image2)

**Fig. 3 Immunohistochemistry**

A Melan A zonal +ve reaction (×200); B Inhibin zonal +ve reaction (×200); C CD34 +ve reaction in the vessels (×100)
The endocrine investigations revealed: an extremely high total plasma testosterone (3.34 ng/mL, with normal between 0.14 and 0.76 ng/mL); high levels of 17-hydroxi progesterone (6.19 ng/mL, with normal between 0.2 and 3.5 ng/mL); extremely increased androgens and glucocorticoids metabolits as 24-hours 17-ketosteroids (95.4 mg/24-h, with normal between 12 and 19 mg/24-h) and 24-hours 17-hydroxi corticosteroids (18.25 mg/24-h, with normal between 3.5 and 5.5 mg/24-h). The basal plasma cortisol as well as plasma metanephrines and normetanephrines were normal. The high values of testosterone and the relatively acute onset of the hirsutism suggest rather an adrenal origin than ovarian one. The CT scan showed a right adrenal tumor of 11.5 by 11 by 12 cm, with hemorrhage, calcifications, inhomogeneous contrast and hypervascularisation. The tumor had mass effect over the liver and right kidney (Fig. 4A).

Because of these findings, a carcinoma was suspected. Right open adrenalectomy was performed with no complications. The pathological report showed that the tumor was gigantic, up to 14 cm, with a weight of 780 g. The structure was complex: trabecular and compact zones, anisocytosis, anisocaryosis, hemorrhage, calcium impregnations, osteoid metaplasia. Apparently, no invasion into the capsule or the vessels was found that improved the prognosis of the diagnosis (Fig. 5).
Immunohistochemistry showed positive reaction for melan A, vimentin, inhibin and synaptophysin (Fig. 6). 3 months after surgery, no metastasis was found at CT scan (Fig. 4B). The patient had no adrenal insufficiency and the hormonal panel was normal. The serum neuro-endocrine markers (serotonin, chromogranin A) were within normal limits. Immunostaining for somatostatin was presented, proving the neuroendocrine origin. As no adrenal remnants were found, the adrenolytic medication was not necessary. Further follow up by endocrine markers and serial imagistic scan are necessary.

**DISCUSSIONS**

The first case was an incidental diagnosis based on a routine ultrasound. Adrenal incidentalomas are most frequently cortical adenomas. The management of an adrenal incidentaloma refers to evaluate the endocrine and imagistic profile in order to decide the secretory profile, the mass effect and the surgical indication [7].

The cases point the importance of surgery in the diagnosis of adrenal tumors. Specific diagnostic tests that can accurately differentiate between benign and malignant features before surgery and pathological exam are lacking [8]. The most useful parameter is the size of the tumor, but there is no specific threshold. In one study, out of 198 adrenalectomies performed between 1989 and 2007, after complete clinical, endocrine and imaging exam, mass size was the only indication for 16 adrenalectomies (15.1%). Adrenal mass size in these patients was 5.9 +/- 0.6 cm. Three tumors of these were malignant. In total, 8 malignant tumors were identified in this series (7.5%, size range 4-14 cm, mean 8.0 +/- 1.3 cm). A cut-off of 4 cm is considered by some the major
tool for adrenalectomy indication [8]. Generally, the most controversial management is for tumors between 4 and 6 cm. For example, in 152 patients with adrenal incidentalomas the mean pathologic size of the tumors was 5.6 +/- 3.2 cm (range 0.5 to 22.0 cm). Based on the size criterion of 6 cm, the incidence of adrenal cancer is higher but there is not the same statistically significant difference for a cut-off of 4 or 5 cm [9].

The options for the surgical management of adrenal tumors include techniques like open anterior and posterior, transabdominal laparoscopic, retroperitoneal laparoscopic, thoracoabdominal, and partial adrenalectomy [10]. Since its first description in 1992, laparoscopic adrenalectomy has become the most useful method for adrenal disease [11]. Regarding the type of the surgical procedure, there are only a few head-to-head comparisons between laparoscopic and open methods at the same institution. For example, in one study over 88 patients who underwent adrenalectomy between January 1997 and October 2008 (51 with laparoscopic method and 37 with classical procedure) showed that the first group experienced significantly less blood loss, shorter hospital stay and earlier oral intake after surgery. Laparoscopy was performed including in 8 cases of tumors larger than 6 cm and 2 adrenal cancers. Mostly, laparoscopic adrenalectomy is regarded as the gold standard procedure for adrenal tumors, irrespective of whether the tumor is benign or malignant [12]. However, some consider laparoscopy controversial for malignant adrenal tumors. A prospective randomized study in these cases is difficult because of the rarity of the disease. In adrenal cancer, the laparoscopic surgery may be performed only when it possible complete tumor resection, including the adrenal capsule. Conversion to an open procedure should be decided before tumor morcellation or fracture of the tumor capsule. Patients who clearly have indication for open procedure are those with local invasion or large tumors [13].

Adrenocortical carcinomas are rare. They have mix features as they originate both from medulla and from adrenal cortex. There are also some mix adrenal adenomas reported in the literature but the data are inconsistent [14]. The median follow-up in adrenal carcinoma is 25.5 months (with ranges between 1 up to 102 months). Generally, these tumors have more than 5 cm. The adrenalectomy is the only curative therapy. Recurrence was found in 13 % in one series [15]. The exact role of adjuvant therapy in the management of adrenocortical carcinoma is not as well established. Adjuvant therapy includes adrenolytic medication as mitotane and cytotoxic drugs. The first class, even there are some controversies, is more used than the second. In case of apparently curative surgical procedure, follow up by endocrine markers and imagistic scan is adequate. The prospects of identifying diagnostic and prognostic markers or gene profiles for adrenal cancer have lately improved with the development of genome-wide gene-expression analysis. Since 2003, several studies have reported distinct gene-expression profiles between benign and malignant adrenocortical tumors that may have diagnostic and prognostic clinical utility [16]. The prognosis depends on clinical onset regarding the symptoms and the short time onset, the dimensions of the tumor and the spreading of the disease at the moment of diagnosis.

CONCLUSIONS

The finding of these cases highlights the importance of surgery in rare adrenal tumors, as being the only tool to cure the disease. Also, it associates the possibility of pathological examination and immuno-staining in order to obtain a specific diagnosis and correct management.
REFERENCES