Case report

Functional adrenal oncocytoma presenting as Cushing’s syndrome: Case report and literature review

Yung-Shu Lee\textsuperscript{a}, Wun-Rong Lin\textsuperscript{b,\textsuperscript{*}}, Chi-Kuan Chen\textsuperscript{b}, Yi-Wei Pai\textsuperscript{b}, Marcelo Chen\textsuperscript{b}

\textsuperscript{a} Department of Urology, Mackay Memorial Hospital, Taitung, Taiwan
\textsuperscript{b} Department of Pathology, Mackay Memorial Hospital, Taipei, Taiwan

\textbf{A R T I C L E  I N F O}

Article history:
Received 28 November 2010
Received in revised form 26 January 2011
Accepted 17 February 2011
Available online 15 November 2011

Keywords:
adrenal tumor
Cushing’s syndrome
oncocytoma

\textbf{A B S T R A C T}

Adrenocortical oncocytomas are very rare, with only 47 cases reported in the English literature. They are usually benign and nonfunctional. Herein, we report on a 30-year-old female patient presenting with extreme weight gain (17 kg in a year), moon face, buffalo hump, central obesity and edema in both legs. Computed tomography revealed a 3.2 cm solid left adrenal tumor. A clipless laparoscopic adrenalectomy was performed. Pathology revealed an adrenocortical oncocytoma.

\textsuperscript{*} Corresponding author. Department of Urology, Mackay Memorial Hospital, 92 Chung Shan North Road, Section 2, Taipei 104, Taiwan.
E-mail address: vincen@ms1.mmh.org.tw (W.-R. Lin).

\texttt{1. Introduction}

Oncocytomas are neoplasms comprised of cells replete with eosinophilic granular cytoplasm packed with swollen mitochondria. They can arise in the kidney, thyroid, salivary glands, parathyroid, lung, pituitary gland and ovaries.\textsuperscript{1,2} The term “oncocyte” was first used by Hamperl in 1950 to describe large, highly eosinophilic granular cells associated with a Hurthle cell tumor of the thyroid gland.\textsuperscript{3} Adrenocortical oncocytomas are very rare, with only 47 cases reported in the English literature.\textsuperscript{4} They are usually benign and nonfunctional. Only seven cases of functional adrenal oncocytoma have been reported.\textsuperscript{5} Herein, we report on a rare case of functional adrenal oncocytoma in a patient presenting with Cushing’s syndrome.

\texttt{2. Case report}

A 30-year-old female patient presented with extreme weight gain (17 kg in 1 year) and bilateral leg edema for 3 months. She had a history of essential hypertension since 2008 and obesity. The family history was noncontributory. She had complained of proximal muscle weakness and thigh soreness for a year and of getting fatter, especially in the face. In the past 3 months, she had experienced palpitations, insomnia, anxiety and persistent swelling in her lower legs. She had irregular menstrual cycles with menorrhagia. Her body weight increased from 71 to 79 kg in 20 days. A physical examination revealed a moon face, buffalo hump, central obesity and edema in both legs.

Blood tests showed that cortisol (morning, afternoon and dexamethasone suppression test), aldosterone (standing and lying down), adrenocorticotropic hormone, thyroid-stimulating hormone, luteinizing hormone, follicle-stimulating hormone and prolactin levels were all within normal ranges. Her testosterone level (1.43 ng/mL) was high. Her dehydroepiandrosterone (121.0 \textmu g/dL) and free T4 (0.64 ng/dL) levels were low. Urine cortisol (638.40 \textmu g/day), 17-ketosteroids (27.6 mg/day) and 17-OH progesterone (43.2 mg/day) levels were high.

Adrenal computed tomography (CT) revealed a 3.2 cm well-defined, nearly homogeneously solid mass with a mean Hounsfield unit (HU) number of around 30 on precontrast scans, favoring a relatively lipid-poor adenoma (Fig. 1). An Adrenal scans with Radioiodine - Labeled Norcholesterol (NP-59) showed unilateral visualization of the left adrenal gland, and a left adrenal adenoma was diagnosed.

Adrenal computed tomography (CT) revealed a 3.2 cm well-defined, nearly homogeneously solid mass with a mean Hounsfield unit (HU) number of around 30 on precontrast scans, favoring a relatively lipid-poor adenoma (Fig. 1). An Adrenal scans with Radioiodine - Labeled Norcholesterol (NP-59) showed unilateral visualization of the left adrenal gland, and a left adrenal adenoma was diagnosed.

Due to the presenting symptoms and signs and the high urine cortisol level, the impression was of a functional adrenal adenoma with Cushing’s syndrome, and a clipless left laparoscopic adrenalectomy was performed via a retroperitoneal approach. On gross examination, the specimen was 3.5 cm \times 2.5 cm \times 2.0 cm and weighed 16.5 g. Microscopically, the tumor was composed of trabecular and solidly arranged oncocytc cells with mild nuclear...
atypia and no mitotic activity. There was no tumor necrosis. Extramedullary hematopoiesis was seen within the tumor and in the periadrenal soft tissue. Immunohistochemical staining showed that the tumor was strongly positive for alpha-inhibin and negative for cytokeratin (AE1/AE3), vimentin, chromogranin A, epithelial membrane antigen and HepPar1 antigen. The Ki-67 index was very low. Pathological impressions were a left adrenal oncocytoma and extramedullary hematopoiesis (Fig. 2A and B).

The patient’s postoperative recovery was uneventful. Intravenous hydrocortisone sodium succinate was given postoperatively, and on the second postoperative day the patient was switched to oral cortisone acetate. The patient had lost 4 kg of weight by the 30th postoperative day.

3. Discussion

Adrenal masses are usually silent and are incidentally detected in 1–2% of abdominal CT scans.6 These adrenal incidentalomas may be cortical adenomas, myelolipomas, pheochromocytomas, cysts, ganglioneuromas, adrenocortical carcinomas or adrenal metastases, with nonfunctioning cortical adenomas being the most common.7 In order to distinguish nonfunctional from functional adrenal masses, a biochemical evaluation should be performed. Surgical removal is indicated for adrenal masses that are functional or >6 cm in size.

Adrenal oncocytomas are very rare, and only 48 cases have been reported to date.4 Many such tumors are benign and nonfunctional, and are detected incidentally. Adrenal oncocytomas are reported to be more common on the left-hand side (2:1), with tumor size ranging from 3 cm to 15 cm (median 8 cm) and weighing from 30 g to 865 g (mean 281 g). The mean age of diagnosis is 46 years and the condition is prevalent in females. Only two cases of a malignant adrenal oncocytoma have been reported: one was an adrenal oncocytoma with local invasion and distant metastases8 and the other was a 51-year-old male with a 15.0 cm × 16.0 cm × 17.2 cm adrenal mass. In the latter case, the man had enlarged periarterial lymph nodes, elevated serum
the oncocytoma is benign. Immunohistochemical and molecular biological malignant. If no major or minor criteria are met, the tumor is considered malignant. If the tumor meets one or more minor criteria, it is considered as malignant. If a tumor meets one or more major criteria, it is de
ciated (Table 1).

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Major criteria</th>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitotic rate ≥5 mitoses/50 high power fields</td>
<td>Large tumor size: &gt;10 cm and/or &gt;200 g</td>
<td></td>
</tr>
<tr>
<td>Atypical mitosis</td>
<td>Necrosis</td>
<td></td>
</tr>
<tr>
<td>Venous invasion</td>
<td>Capillary invasion; sinusoidal invasion</td>
<td></td>
</tr>
</tbody>
</table>

dehydroepiandrosterone sulfate, elevated serum cortisol following an overnight 1-mg dexamethasone test and increased urinary excretion of 17-hydroxycorticosteroids. The mass was unresective due to tumor invasion of the inferior vena cava.9

Tahar et al have reported that the clinical symptoms of functional adrenocortical oncocytomas include virilization in three female cases, Cushing’s syndrome in a male case, bilateral gynecomastia in two male cases and pseudopuberty in a female child. A MEDLINE search revealed that only one case of Cushing’s syndrome has been reported. The presence of Ki-67 proliferative index was very low, and no major or minor criteria were met.

A diagnosis of an oncocytoma is based on histological and immunohistochemical studies. Oncocytomas are neoplasms made up of cells with large amounts of eosinophilic granular cytoplasm filled with swollen mitochondria. In immunohistochemical studies, vimentin and keratin are frequently identified, and the tumors are strongly positive for antimitochondrial antibodies. In the present case, the tumor was composed of trabecular and solidly arranged oncocytes, with mild nuclear atypia and no mitotic activity. The tumor was strongly positive for alpha-inhibin and negative for cytokeratin (AE1/AE3), vimentin, chromogranin A, epithelial membrane antigen and HepPar1.

Bisceglia et al have produced new criteria for the differentiation of benign from malignant adrenocortical oncocytomas (Table 1). If a tumor meets one or more major criteria, it is defined as malignant. If the tumor meets one or more minor criteria, it is considered borderline malignant. If no major or minor criteria are met, the oncocytoma is benign. Immunohistochemical and molecular profiles can be used to determine the tumor’s nature and predict its behavior. The presence of Ki-67 (+), p21 (+), p27 (+) and Mdm-2 (-) can be used to predict malignancy and distant spread of adrenal cortical tumors. The sensitivity of these proteins is low, however, and only 13% of adrenal cortical carcinomas expressed this phenotype. In the present case, the tumor was functional, 3.5 cm in size, the Ki-67 proliferative index was very low, and no major or minor criteria were met.

4. Conclusion

In patients presenting with symptoms and signs of Cushing’s syndrome, 24-h urine cortisol is a valuable test for the diagnosis of Cushing’s syndrome if plasma cortisol levels are normal. Adrenocortical oncocytomas are rare and usually benign and nonfunctional. A functional adrenal oncocytoma may, however, present as Cushing’s syndrome. This must therefore be taken into consideration in differential diagnosis.

References