Clinical case

Corticomedullary mixed tumor of the adrenal gland

Tumeur surrénalienne corticomédullaire

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Résumé

Une femme âgée de 34 ans est explorée pour obésité, hirsutisme avec aménorrhée secondaire et HTA récente. Les explorations biologiques et hormonales ont objectivé une hypokaliémie, un hypercorticisme et une hyperandrogénie. Les métanéphrines urinaires étaient normales ainsi que l’aldostéronémie. L’imagerie abdominale par résonance magnétique nucléaire a montré une masse surrénalienne hétérogène mesurant 4 × 6 cm, avec une double composante tissulaire et graisseuse évoquant un corticosurrénalome. L’évolution après surrénalectomie droite a été marquée par une normalisation des chiffres tensionnels et de la kaliémie. La patiente a présenté une insuffisance surrénalienne secondaire traitée par l’hémisuccinate d’hydrocortisone. L’étude histologique a montré une masse unique mixte, composée de cellules corticales et médullaires surrénauliennes. L’étude immunohistochimique a mis en évidence une positivité pour la chromogranine A.

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Mots clés : Surrénale ; Syndrome de Cushing ; Corticomédullaire ; Hypertension

Abstract

A 34-year-old woman presented with weight gain, hirsutism, recent hypertension and secondary amenorrhea. Laboratory findings showed hypokalemia, elevated cortisol and androgen levels with normal urine metanephrines and normal aldosteronemia. Abdominal magnetic resonance imaging showed a right heterogeneous adrenal mass measuring 4 × 6 cm with mixed component of fat and adrenal tissue suggesting corticosurrenaloma. After right adrenalectomy, blood pressure normalized and hypokalemia resolved. In the postoperative course, the patient presented adrenal insufficiency treated with hydrocortisone hemisuccinate. Histological examination showed a single tumor mass composed of an admixed population of adrenal cortical and medullary cells. Immunohistochemical evaluation was positive for chromogranin A.

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Keywords: Adrenal; Cushing’s syndrome; Corticomedullary; Hypertension

1. Introduction

Corticomedullary mixed tumors are rare primary benign tumors of the adrenal gland characterized histologically by the presence of a single tumor mass formed by an admixture of adrenal cortical and medullary cells [1,2]. Since they have no specific clinical features, these tumors are discovered frequently on histological examination. No data has been published regarding the prevalence of these tumors. Only a small number of cases have been described in the literature [1–9]. In this work, we report a case of corticomedullary mixed tumor of the right adrenal gland.

2. Case report

A 34-year old woman presented in our endocrine department with hirsutism, weight gain and secondary amenorrhea. Symptoms occurred within 6 months. There was no relevant past medical history and the patient was taking no medication, especially corticosteroids. On physical examination, the patient was 97 kg in weight and 176 cm in height, with a body mass index of 30 kg/m². Obesity involved the face, the neck, the
Table 1
Hormonal findings.
Tableau biologique.

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Result</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>FUC (µg/24 h)</td>
<td>190</td>
<td>25–120</td>
</tr>
<tr>
<td>ACTH (pg/ml)</td>
<td>&lt;10</td>
<td>50</td>
</tr>
<tr>
<td>Testosterone (ng/ml)</td>
<td>1.2</td>
<td>&lt;0.7</td>
</tr>
<tr>
<td>DHEAS (ng/ml)</td>
<td>2395</td>
<td>300–3300</td>
</tr>
<tr>
<td>Delta-4 (ng/ml)</td>
<td>3</td>
<td>0.3–3.1</td>
</tr>
<tr>
<td>17 OH (ng/ml)</td>
<td>1.4</td>
<td>&lt;5</td>
</tr>
<tr>
<td>FUC/low DXM test</td>
<td>550</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Cortisolemia/low DXM test</td>
<td>185</td>
<td>&lt;25</td>
</tr>
<tr>
<td>FUC/high DXM test</td>
<td>520</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Cortisolemia/high DXM test</td>
<td>315</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Aldosterone (pg/ml)</td>
<td>22</td>
<td>10–180</td>
</tr>
<tr>
<td>Renine (ng/ml)</td>
<td>2.5</td>
<td>1.1–20.2</td>
</tr>
<tr>
<td>Urinary metanephrines (mg/24 h)</td>
<td>0.8</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>


Trunk and the abdomen. Ferriman and Gallway index was evaluated at 22 with acne and increased muscle mass consisting with virilization without clitoromegalia. There were no purplish abdominal striae. Blood pressure monitoring revealed high blood pressures at excess of 150/100 mmHg and a pulse rate of 80/minute. Laboratory investigations showed hypokalemia and normal glucose tolerance. Hormonal findings showed elevated cortisol and androgen levels but normal urine metanephrines and normal aldosteronemia (Table 1). Adrenocorticotropin hormone (ACTH) was blunted suggesting primary adrenal origin of cortisol excess. Magnetic resonance imaging (MRI) identified a heterogeneous mass of the right adrenal gland measuring 6 × 4 cm, with mixed component of fat and adrenal tissues suggesting corticosurrenaloma (Fig. 1). Preoperative medication with antihypertensive and anticortisolic agents (ketoconazole 400 mg/day) was given to reduce blood pressure and metabolic effects of cortisol excess. The patient underwent surgical adrenalectomy by right lombotomy. Postoperative course was marked by improvement of the blood pressure levels and normalization of serum potassium. Secondary adrenal insufficiency was confirmed and the patient was treated with hydrocortisone hemisuccinate. Macroscopic study of the removed adrenal showed a 5 × 4 × 4 cm, yellowish-orange encapsulated tumor, nodular and fleshy in consistency, with focal areas of hemorrhage (Fig. 2). On microscopic examination, the tumor was composed of distinct cell populations: adipocytes, adrenal cortical cells and pheochromocytes, which were intimately admixed in haphazard arrangement (Fig. 3). Immunohistochemical evaluation was positive for chromogranin A (Fig. 4).

3. Discussion
We report a rare case of corticomedullary mixed tumor revealed by hyperandrogenism and weight gain. In the current case, symptoms and hormonal findings were suggestive of corticosurrenaloma. In fact, weight gain with central obesity is characteristic of Cushing’s syndrome. The severity of hirsutism with symptoms of virilization as well as MRI trunk and the abdomen. Ferriman and Gallway index was evaluated at 22 with acne and increased muscle mass consisting with virilization without clitoromegalia. There were no purplish abdominal striae. Blood pressure monitoring revealed high blood pressures at excess of 150/100 mmHg and a pulse rate of 80/minute. Laboratory investigations showed hypokalemia and normal glucose tolerance. Hormonal findings showed elevated cortisol and androgen levels but normal urine metanephrines and normal aldosteronemia (Table 1). Adrenocorticotropin hormone (ACTH) was blunted suggesting primary adrenal origin of cortisol excess. Magnetic resonance imaging (MRI) identified a heterogeneous mass of the right adrenal gland measuring 6 × 4 cm, with mixed component of fat and adrenal tissues suggesting corticosurrenaloma (Fig. 1). Preoperative medication with antihypertensive and anticortisolic agents (ketoconazole 400 mg/day) was given to reduce blood pressure and metabolic effects of cortisol excess. The patient underwent surgical adrenalectomy by right lombotomy. Postoperative course was marked by improvement of the blood pressure levels and normalization of serum potassium. Secondary adrenal insufficiency was confirmed and the patient was treated with hydrocortisone hemisuccinate. Macroscopic study of the removed adrenal showed a 5 × 4 × 4 cm, yellowish-orange encapsulated tumor, nodular and fleshy in consistency, with focal areas of hemorrhage (Fig. 2). On microscopic examination, the tumor was composed of distinct cell populations: adipocytes, adrenal cortical cells and pheochromocytes, which were intimately admixed in haphazard arrangement (Fig. 3). Immunohistochemical evaluation was positive for chromogranin A (Fig. 4).

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Fig. 1. Magnetic resonance imaging identifying a mass of the right adrenal gland measuring 6 × 4 cm, heterogeneous with mixed component of fat and adrenal tissue.

Imagerie par résonance magnétique identifiant une masse de la surrénale droite mesurant 6 × 4 cm, hétérogène avec une double composante intriquée de tissu adipeux et surrénalien.
findings suggested corticosurrenaloma. The diagnosis of corticomedullary mixed tumor was a surprising finding on histological examination. Mixed tumors involving the cortical and medullary components of the adrenal gland are rare because of the distinct embryological origin of the adrenal cortex and medulla. Corticomedullary mixed tumor represents a single tumor mass composed of an admixed population of adrenal cortical and medullary cells [2]. They were first described in 1969 by Mathison and Waterhouse [1]. This definition excluded cases of simultaneously occurring adrenal cortical adenomas and pheochromocytomas as well as cases of adrenocorticotrophic hormone producing pheochromocytomas with associated adrenal cortical hyperplasia [2]. In the current case, we described a well-circumscribed tumor mass, easily distinguished from the remaining adrenal cortical and medullary tissues. Adrenal cortical and medullary cells were intimately admixed. Severe hirsutism, hypokalemia and hypertension are secondary to the adrenocortical component of the tumor, which produces both cortisol and androgen. Urinary metanephrines were normal, but didn’t exclude paroxysmal secretion of catecholamines usually encountered in pheochromocytoma. Immunohistochemical positivity for chromogranin A excluded corticosurrenaloma. Concurrent myelolipoma associated with corticomedullar mixed tumor have been described in literature [3]. However, in our case the presence of adipocytes may only represent myelolipomatous foci as seen in more common adrenal lesions.

The pathogenesis of such corticomedullary mixed tumors is different from that of simultaneous occurrence of separate adrenal cortical adenomas and pheochromocytomas. In fact, ectopic corticotropin production by some pheochromocytomas is thought to be a mechanism leading to adrenal cortical hyperplasia, which in turn may develop into an adrenal cortical adenoma [10]. Additionally, catecholamines secreted by pheochromocytoma are thought to stimulate the anterior pituitary to secrete corticotropin, which may lead to adrenal cortical hyperplasia and/or adrenal cortical adenoma. Some authors suggested the mechanism of collision, composition or combination tumors [2]. We think that a paracrine secretion of growth factors
may be evoked. None of the cases reported to date has shown evidence of malignancy. The prognosis is mainly related to metabolic features resulting from cortisol excess. Recurrence of the tumor on the contralateral adrenal gland has been described in one case of the literature [11]. Thus, long-term follow up is suggested.

4. Conclusion

Corticomedullary mixed tumors are very rare, frequently discovered on histological examination. Clinical findings are not specific including symptoms of hypercortisolemia, hyperandrogenism and catecholamine excess. Treatment is based on surgical resection. Long-term outcome is still now unpredictable.

References