Case report

A case of testicular adrenal rest tumor in a male child with congenital adrenal hyperplasia

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Abstract

Testicular adrenal rest tumors are a well-known complication in male patients with congenital adrenal hyperplasia. Corticosteroid suppressive therapy usually results in the regression of these tumors. We describe a patient with 21-hydroxylase deficiency who developed bilateral testicular masses. Despite steroid suppressive therapy, the tumors did not regress and hormonal control was poor. Consequently, bilateral partial orchiectomies were performed. (Korean J Pediatr 2008;51:1018-1022)

Key Words: Testicular neoplasms, Adrenal rest tumor, Child, Congenital adrenal hyperplasia, Steroid, 21-hydroxylase

Introduction

Congenital adrenal hyperplasia (CAH) is caused by an enzymatic defect in steroid biosynthesis in the adrenal cortex. 21-hydroxylase deficiency is the most common form. In patients with 21-hydroxylase deficiency, precursor steroids, including 17-hydroxyprogesterone (17-OHP), accumulate and are diverted into the sex steroid pathway, resulting in increased androgen production. In CAH, testicular adrenal rest tumors (TARTs) are considered aberrant adrenal tissue that has descended with the testes and has become hyperplastic because of ACTH stimulation. Microscopically, the tumors show features of steroid-producing tissue. The growth of TARTs is stimulated by inadequate corticosteroid suppressive therapy and treatment with adequate doses of corticosteroids results in tumor regression. Although the prevalence of TARTs in male children with 21-hydroxylase deficiency has been reported up to 24%, there were a few reports of TARTs in Korean children with 21-hydroxylase deficiency.

We describe a TART in a Korean patient with 21-hydroxylase deficiency. The patient had bilateral testicular masses and bilateral partial orchiectomies were performed to remove the steroid-unresponsive testicular tumors. Pathology revealed a testicular adrenal rest tumor.

Case report

A 15-year-old boy was admitted with bilateral testicular masses. He weighed 3.31 kg at birth and presented with poor oral intake, vomiting, dehydration, lethargy, and electrolyte imbalance (hyponatremia and hyperkalemia) immediately after birth. His family history was unremarkable. He was initially treated with NaCl and fludrocortisone, based on a diagnosis of pseudohypoaldosteronism. He was diagnosed with the salt-wasting form of 21-hydroxylase deficiency at 1 year of age and was then treated with NaCl and fludrocortisone, based on a diagnosis of pseudoaldosteronism. He was diagnosed with the salt-wasting form of 21-hydroxylase deficiency at 1 year of age and was then treated with corticosteroid (dexamethasone or deflazacort) and fludrocortisone until 10 years of age.

At 10 years of age, he was transferred to our hospital for treatment of nail dysplasia and 21-hydroxylase deficiency. On physical examination, his height was 133 cm (z score of -0.65), and weight was 30 kg (z score of -0.55). The phallus and pubic hair were both at Tanner stage II, and both testes were 3 mL in volume (Fig. 1, Table 1). Predicted adult height (PAH) calculated using the Bayley and Pinneau method was 156.5 cm. He was treated with oral (PO) deflazacort (5 mg) once daily (QD) and fludrocortisone (0.1 mg PO) QD. The plasma 17-OHP level was 55 ng/mL and bone age was compatible to 13 years of age. The elevated 17-OHP level and advanced bone age might result from poor com-
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Fig. 1. Growth chart of the patient, from 10 to 16 years of age. He received growth hormone and leuprolide acetate for three years.

Table 1. Clinical Course, Serial Laboratory Findings and Medications

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>BA (yr)</th>
<th>HC (mg/m²)</th>
<th>FC (mg)</th>
<th>17-OHP (ng/mL)</th>
<th>PRA (ng/mL/hr)</th>
<th>Testes size (mL)</th>
<th>GH/Leup</th>
<th>Events</th>
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<tr>
<td>10.0</td>
<td>133</td>
<td>30</td>
<td>13.0</td>
<td>16.6</td>
<td>0.10</td>
<td>55</td>
<td>&gt;20</td>
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<tr>
<td>10.4</td>
<td>135.2</td>
<td>31</td>
<td>13.5</td>
<td>16.2</td>
<td>0.15</td>
<td>1.7</td>
<td>&gt;20</td>
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<td>10.7</td>
<td>137.5</td>
<td>31.8</td>
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<tr>
<td>11.4</td>
<td>143.6</td>
<td>35.4</td>
<td>14.7</td>
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<td>13.5</td>
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<td>70</td>
<td>19.8</td>
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<td></td>
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<td>47.5</td>
<td>15.6</td>
<td>&gt;125</td>
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<td></td>
<td></td>
<td>Sono/MRI</td>
</tr>
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<td></td>
<td>15.9</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Orchiectomy</td>
</tr>
</tbody>
</table>

Abbreviations: BA, bone age; HC, hydrocortisone daily dosage per body surface area; FC, fludrocortisone; 17-OHP, 17-hydroxyprogesterone; PRA, plasma renin activity; GH/Leup, daily dosage of growth hormone (IU)/monthly dosage of gonadotropin releasing hormone agonist, Leuprolide (mg); D/C, discontinuation; Sono, sonography; MRI, magnetic resonance imaging
year after the operation, 17-OHP level was 27.2 ng/mL and PRA was 31 ng/mL/hr. Treatment with hydrocortisone (15.6 mg/m²/day) and fludrocortisone (0.2 mg/day) was maintained.

Discussion

Occasionally, male patients with CAH, particularly the salt-wasting form of 21-hydroxylase deficiency, develop TARTs in adolescence or early adulthood. The prevalence of TARTs in male children with 21-hydroxylase deficiency has been reported up to 24%\(^7\); these lesions are often bilateral (83%). Concentrations of 17-OHP and androgen are usually elevated. In testicular ultrasonographs, these lesions present as hypoechoic infiltrative nodules and are usually located near the mediastinum testis\(^10\). TARTs have been detected even in childhood\(^7\), recommending that ultrasonographic screening should begin no later than adolescence\(^1\). If TARTs are refractory to medical treatment, partial orchiectomy is recommended\(^11\), \(^12\).

TARTs are hormone-dependent and are not considered true autonomous tumors. During the prenatal period, the gonads and adrenals both develop from the adrenogenital ridge and do not separate until the adrenal groove is prominent. Before separation, adrenal cortical tissue may adhere to the gonad. This aberrant adrenal tissue may then descend with the testis or ovary along the courses of their associated arteries\(^3\). Adrenal rests within the testis occur in 7.5% – 15% of neonates and normally regress in early infancy\(^7\). However, in CAH patients, it is believed that these cells may persist and proliferate with preservation of adrenal-like hormone production properties\(^6\).

Several studies have shown that these tumors are ACTH-dependent, as evidenced by a reduction in tumor size in response to corticosteroid therapy and a recurrence of testicular enlargement in response to ACTH stimulation\(^4\), \(^6\). TARTs may be stimulated not only by elevated ACTH concentrations but also by elevated angiotensin II levels, based on the presence of angiotensin II receptors\(^4\). GH can stimulate differentiation and proliferation of cancer cells or precursor cells, but there are no reports on the effect of GH on proliferation or hyperplasia of adrenal rest tumors.

In CAH patients with testicular masses, clinically useful
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5. Ashley RA, McGee SM, Isotaolo PA, Kramer SA, Cheville


