□ Case Report □

A case of adrenocortical adenoma following long-term treatment in a patient with congenital adrenal hyperplasia

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As a result of the widespread use and enhanced quality of high-resolution radiological techniques, a recent report has revealed a relatively high prevalence of small adrenal tumors in patients with untreated congenital adrenal hyperplasia due to 21-hydroxylase deficiency. However, there are scarcely any pediatric cases of adrenocortical tumor following long-term treatment in patients suffering with congenital adrenal hyperplasia. We report here on a pediatric female case of adrenocortical adenoma despite adequate long-term treatment for the salt-losing type of congenital adrenal hyperplasia. **(Korean J Pediatr 2007;50:302-305)**

Key Words : Congenital adrenal hyperplasia, Adrenocortical tumor

Introduction

It is well known that adrenal adenomas could develop from hyperplastic tissues under increased corticotropin stimulation of the adrenal cortex in patients who are suffering with congenital adrenal hyperplasia (CAH)[1]. CAH is an inherited syndrome characterized by inefficient cortisol synthesis[2]. Decreased production of cortisol leads to increased secretion of corticotropin releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) from the hypothalamus and pituitary gland, respectively, resulting in the overproduction of active androgens and hyperplasia of the adrenal glands[2]. The prevalence of adrenal tumor is relatively high in those patients suffering from untreated CAH due to 21-hydroxylase deficiency[1]. A recent report shows a high incidence of adrenal masses: nearly in 82% of the homozygous and in 45% of the heterozygous CAH patients[1].

Most cases of adrenal incidentaloma have been reported in adult patients with CAH[1, 3]. We report here on a girl with the salt-losing form of CAH due to 21-hydroxylase deficiency, who developed an adrenocortical tumor at 6 years of her age despite of adequate steroid treatment after birth.

접수 : 2006년 11월 20일, 승인 : 2007년 2월 15일
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Case Report

A 12 year-old girl, who was diagnosed as the salt-losing form of 21-hydroxylase deficiency by clinical findings immediately after birth, was admitted for the evaluation of an incidentally discovered adrenal tumor. She weighed 3.87 kg at birth. She presented with ambiguous genitalia, hypernatremia and hyperkalemia. Her family history was unremarkable. She has been treated with hydrocortisone at 20 mg/m^2/day and mineralocorticoid after birth. Clitoroplasty was done at 12 months of age. The mass was first discovered at 6 years of age by routine ultrasonography that was performed for assessment of the adrenal gland. The mass was a 2.3×2.6 cm-sized well-marginated isoechoic solid mass in the right adrenal gland (Fig. 1). At that time, she had no clinical features of Cushing syndrome, virilization or secondary sexual differentiation.

On admission, her body weight was 55.0 kg (90-97th percentile), her height was 134 cm (3-10th percentile), and the body mass index (BMI) was 30.6 kg/m^2 (>97th percentile). She had moderate truncal obesity, but she did not have plethora or purple striae on her trunk. She did not show hyperpigmentation of the skin or mucosa. Her sexual maturation showed breasts at Tanner stage I and pubic hair at Tanner stage II. The bone age was 12 years according the method of Greulich and Pyle.

Laboratory examination revealed serum sodium and potassium values of 143 and 3.8 mmol/L, respectively. The serum 17α-hydroxyprogesterone (17-OHP) level was 0.16 ng/mL (normal: 0.11-0.98 ng/mL). The serum testosterone and estradiol levels were 6.8 ng/dL (normal, <3-10 ng/dL in Tanner I and 7-28 ng/dL in Tanner II) and 2.35 ng/dL (normal, 0.5-2.0 ng/dL in Tanner I and 1.0-2.4 ng/dL in Tanner II), respectively. The serum dihydroepiandrosterone sulfate (DHEAS) concentration was 6.19/dL (normal: 10-144/dL in Tanner I and 34-129/dL in Tanner II). The serum ACTH and cortisol levels at 8 AM were 30.7 pg/mL (normal, 25-100 pg/mL) and 0.47/dL (normal, 5-23/dL), respectively. The plasma renin activity was 31.0 ng/mL/hr (normal, <5.9 ng/mL/hr). The 24 hour urine vanillymandelic acid, metanephrine and normetanephrine levels were 5.6 mg/g Cr (normal, <8 mg/g Cr), 0.12 μmol/g Cr (normal. <10.5 μmol/g Cr), and 150 g/24hr (normal, 72-410 g/24hr), respectively.

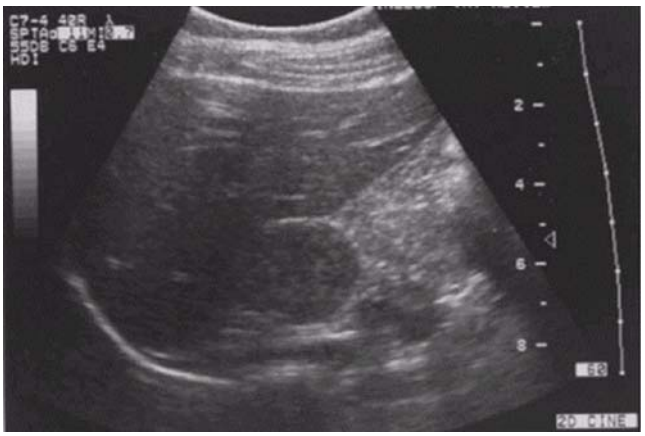

Fig. 1. Ultrasonogram done at 6 years of age through the right flank shows a well marginated round to ovoid isoechoic solid mass in the right suprarenal region. This mass is measured about 2.3×2.6 cm with relatively homogeneous internal echogenecity without discernable calcification or cystic change.

The ultrasonogram revealed a 3.9×2.8 cm-sized right adrenal mass with internal calcifications. Upon magnetic resonance imaging (MRI), it measured 3.2 cm and showed homogeneous low signal intensity on the T1-weighted images without metastasis (Fig. 2).

The mass was 4.4×3.1 cm with internal calcification on the follow-up ultrasonogram at 13 years of age. At present, she is being treated with hydrocortisone 20 mg/m^2/day.

Discussion

Adrenocortical tumors complicating untreated or inadequately treated CAH have occasionally been reported in the past[4-6]. With the progressive improvements of ultrasonography, computed tomography (CT), and MRI techniques, adrenal tumors are being detected more frequently in CAH patients. Jaresch et al[11] reported a high incidence of adrenal tumor, nearly 82% in homozygous CAH patients and 45% in heterozygous patients with CAH, and there was no correlation between tumor size and the serum 17-OHP con-

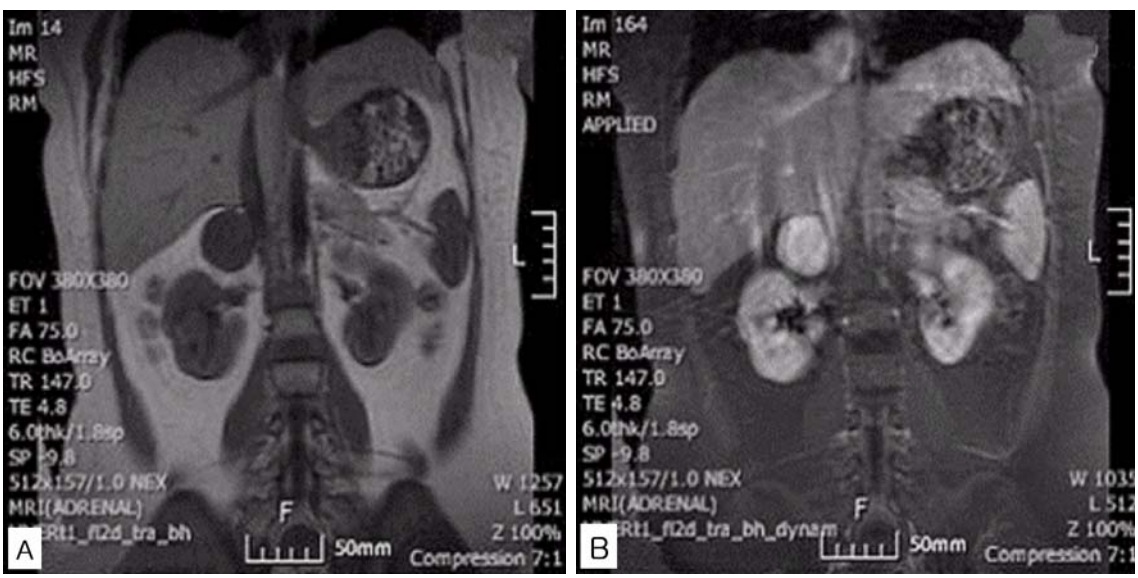

Fig. 2. A well defined mass in right adrenal gland shows homogeneous T1 low signal intensity (A) and heterogeneous T2 high signal intensity (B) on abdominal magnetic resonance image at 12 years of age. There are no evidence of periadrenal infiltrates or invasion into adjacent organs.

centration in the patients suffering from CAH. The pathogenesis of developing adrenal tumor in CAH patients is still obscure. Some authors stress that persistent adrenocorticotropin (ACTH) stimulation in CAH may result in adenomatous change of the adrenal cortical tissue, which in the end may lead to neoplastic transformation of hyperplastic adrenal cortical tissue in CAH patients[6]. Takayama et al.[7] reported that the adrenocortical tumor cells had the same 21-hydroxylase activity deficiency as adrenocortical hyperplasia in a 21-hydroxylase deficiency patient with combined adrenocortical tumor.

On the other hand, an adrenocortical tumor complicating the long-term treatment with anadequate dose of steroid in a 32-year-old woman with 21-hydroxylase deficiency was reported by Takahashi et al.[8]. But Jaresch et al.[1] reported that small adrenal tumors frequently occur in the heterogygous carrier and they do not usually demonstrate corticotropin hypersecretion. Therefore, they suggested that ACTH hypersecretion alone cannot explain the pathogenesis of adrenal tumors in CAH[1].

In a study that concerned hormonal evaluation and mutation screening for 21-hydroxylase deficiency in 19 bilateral and 31 unilateral adrenal incidentaloma patients, Patocs et al.[9] reported that five patients with unilateral adrenal incidentalomas had heterozygous *CYP21B* mutations, but four of them showed 17-OHP concentrations lower or slightly higher than the normal limit after ACTH stimulation. So, Patocs et al.[9] suggested that adrenocortical tumor formation might also involve mechanisms that are independent of the ACTH-induced changes in 17-OHP secretion.

Some adrenocortical tumors may result in masculinization in girls and precocious puberty in boys, or in other hormonal abnormalities. Functioning adrenocortical tumors in CAH patients are very rare, and all of them are virilizing tumors[10-13]. Their virilizing symptoms improved after surgical excision of the tumors. Most of the adrenocortical tumors in CAH patients are nonfunctioning tumors[1, 14]. They didn't have any virilizing symptoms or other hormonal abnormalities.

Several investigators have presented paradigms for evaluating and treating incidental adrenal masses in adults[15-17]. It is generally agreed that hormonally active tumors should be removed regardless of their size. However, for hormonally inactive tumors, various investigators have proposed different sizes for which it is considered safe to observe these lesions. The recommendation of the size at which an adrenal mass may be safely observed varied from 3 to 6 cm[15-17].

Unfortunately, there have been no recommendations about what to do when adrenal tumor were found in children with CAH. Several reports suggested that hormonally inactive adrenal tumors smaller than 6 cm in diameter in pediatric CAH patients should not be removed and routine follow up imaging study should be performed every 2 years[1, 8]. Any reported cases of combined adrenal carcinoma and CAH are extremely rare[13]. Of course, several authors have recommended that a hormonally inactive adrenal tumor greater than 6 cm in diameter should be removed because adrenocortical carcinoma was frequently greater than 6 cm in diameter[18].

In our case, the patient didn't have any hormonal abnormalities, the tumor size was less than 6 cm and it has been growing very slowly during 6 years with no metastases. We are performing follow up imaging studies every 6 months to ensure this tumor is benign, with no surgical treatment.

한 글 요 약

장기간 치료받은 부신 피질 과형성증 환아에서 발생한 부신 피질 종양 1례

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최근 해상도가 향진된 방사선학적 검사가 널리 사용되면서, 21-수산화효소 결핍증에 의한 선천성 부신 피질 과형성증 환아에서 부신피질종양이 발견되는 경우가 많아지고 있다. 일반적으로 적절한 스테로이드 호르몬 치료를 받은 21-수산화효소 결핍증 소아에서 부신피질 종양의 발생률는 매우 드물다. 저자들은 생후 초기부터 적절한 용량의 스테로이드 치료로 잘 조절되고 있는 염분소실형 21-수산화효소 결핍증을 가진 12세 여아에서 부신 종양이 우연히 발견된 1례를 보고하고자 한다.

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