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A Case of 21-hydroxylase Deficiency with Massive Bilateral Adrenal Masses

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Abstract

BACKGROUND: Congenital adrenal hyperplasia (CAH) can lead to bilateral adrenal tumors. Excess adrenocorticotropic hormone is thought to play a role in the development of adrenal nodules. Here, we present a patient with a simple virilizing form of 21-hydroxylase deficiency, a married man, bilateral adrenal tumors, and 46-XX chromosomes.

CASE REPORT: A 39-year-old man suffered from abdominal pain and tension. Abdominal tomography showed macronodular hyperplasia in both adrenal glands, with the largest nodule reaching 4.2 cm on the left side. The patient's old records showed that CAH had been diagnosed at the age of 11 years, but the patient was not taking any medication. The patient was treated with glucocorticoid. Despite irregular use of the treatment, the size of the nodules remained stable for 3 years, and then a significant reduction in nodule size was observed.

CONCLUSION: In patients with bilateral adrenal masses and incidentaloma, CAH should be considered to avoid unnecessary surgery or biopsy. A 17-hydroxyprogesterone test in a suspicious patient is a useful tool for diagnosis.

Introduction

The incidence of adrenal masses varies from 1.4% to 8% [1], [2]. Studies have shown that the prevalence of adrenal incidentalomas increases in both homozygous and heterozygous congenital adrenal hyperplasia (CAH) [3]. Adrenal nodules in CAH can be adenomas, myelolipomas, and less commonly lipomas, and the tumor can be very large [4], [5], [6]. Adrenal nodules are usually discovered incidentally, but sometimes giant myelolipomas in particular can cause swelling, discomfort, and abdominal pain [7], [8]. Adrenocorticotropic hormone (ACTH) excess is thought to play a role in the development of adrenal nodules [7]. There was no significant difference between 17-hydroxyprogesterone (17OHP) levels in CAH patients with adrenal tumors compared with patients without tumors, whereas ACTH levels were higher [5]. Here, we present a patient with a simple virilizing form of 21-hydroxylase deficiency (21OHD), a married man, bilateral adrenal tumors, and 46-XX chromosomes.

Case Report

A 39-year-old man had been suffering from abdominal pain and tension, weakness, and drowsiness for 3 years. He was examined in general surgery. The patient's abdominal computed tomography (CT) and magnetic resonance imaging (MRI) showed macronodular hyperplasia in both adrenal glands, with the largest nodule reaching 4.2 cm on the left side. He was referred to endocrinology clinic for a decision on surgery or biopsy. He was married and had no children. He stated that he had undergone hysterectomy and oophorectomy at the age of 11 years due to menstrual bleeding. He stated that this surgery was performed because of a congenital anomaly. Review of the patient's old records revealed that CAH had been diagnosed at age 11 years and glucocorticoid substitution had been initiated. However, the patient and his relatives stated that they had never used the treatment and stopped going to the hospital for this reason. On physical examination: Blood pressure: 100/70 mm/Hg, pulse: 74/min, height: 145 mm, weight: 65 kg. Beard and body

hair were somewhat sparse. He had mild gynecomastia [Figure 1]. There was hypospadias and the penis was short; the testes could not be palpated in the scrotum. Both testes and epididymis were not visible on scrotal ultrasound.

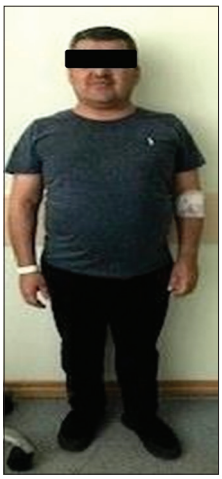

Figure 1: Patient with 21-hydroxylase deficiency

Laboratory analysis revealed normal glucose, electrolyte, renal, and liver function tests and urinary metanephrines. Additional hormone testing revealed: Testosterone: 3.06 ng/mL (1.75–7.81), free testosterone: 18 pg/ml (6.6–30), DHEA-SO4: 470.9 μg/dl (106–464), estradiol: 44pg/ml, FSH: 24.27 mIU/ml, LH: 12 mIU/mL, aldosterone [H]: 609.56 ng/L (25–315), renin: 16.60 μIU/ml (4.4–46.1), cortisol: 7.45 μg/dl (microgram/dl) (6.7–22.6), 17OHP >50 ng/mL (0.2–4.5), ACTH: 70 ng/L (4.7–48.8) was detected. There was a partial cortisol response to the ACTH stimulation test (peak cortizol: 12.77 μg/dL). The genetic result was 21OHD and karyotype analysis revealed 46-XX. The patient was diagnosed with a simple virilization form of CAH and dexamethasone 0.5 mg daily was started. Because of low testosterone levels after the treatment, testosterone replacement therapy was initiated. After therapy, the ACTH level was 12.2 ng/L, the aldosterone level was 11.3 ng/L, and the testosterone level was: 3.12 ng/mL (1.75–7.81), free testosterone: 20 pg/ml (6.6–30), and 17OHP was 27.0. Biopsy or surgery was not considered because the cancer risk of the lesions was very low. Despite the patient's irregular use of the drug, the size of the nodules remained stable for 3 years, and then a marked decrease in nodule size was observed [Figure 2]. Treatment with dexamethasone was changed to hydrocortisone 20 mg/daily as the nodules continued to shrink.

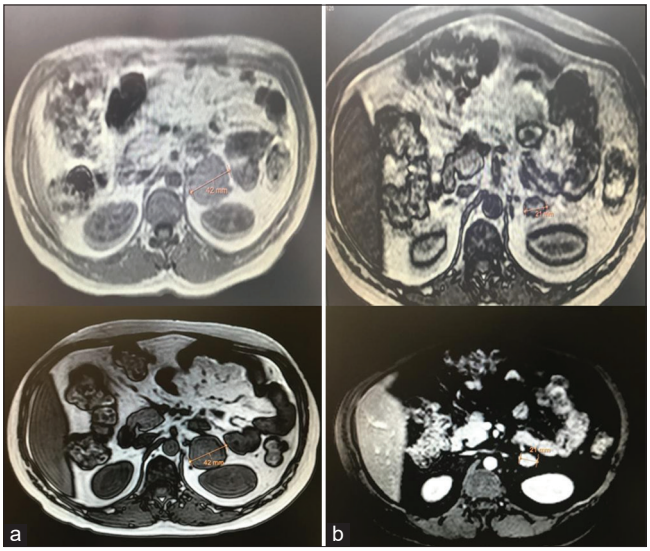

Figure 2: Adrenal mass in left adrenal gland in MRI scan, (a) before the treatment. (b) After the treatment

Discussion

Our patient was diagnosed with 21OHD based on elevated serum 17OHP levels and confirmed by CYP21 gene analysis. The patient denied any episodes of adrenal insufficiency in the history. Most untreated CAH patients, including 21OHD patients, have adrenal masses [3], [9]. Reisch *et al*. reported adrenal nodules in 19 of 26 (73%) patients with CAH [4]. Our patient was born with hermaphrodism but did not go to a hospital for this reason until the age of 11 years and lived as a male. When he was 11 years old, he was diagnosed with CAH, but he did not go for follow-up after surgery and did not take medical therapy. Jaresch *et al*. studied 22 patients with homozygous CAH (of whom 20 had 21-OHD) who received replacement therapy with hydrocortisone and reported that adrenal tumors were detected in 82% of patients at CT [3]. In one study, the presence of nodules was assessed by classifying patients according to their hormonal status and compliance with therapy. Of the 26 patients, eight had a nonclassical form, four had a salt-wasting form, and 14 had a simple virilization form. All patients underwent CT or MRI. Those with nodules were reexamined after 12 months of adequate replacement therapy. Nodules were found in four of eight untreated patients and in two of three patients with poor control, whereas no nodules were found in 15 patients with good control. In these six patients, the adrenal nodules shrank significantly and in some even disappeared after adequate replacement therapy [10]. In this study, the shrinkage after treatment confirms that these nodules are caused by ACTH. In the study conducted by Nermoen *et al.*, adrenal tumors were detected in nine of 101 patients with 21OHD, four of which were defined as adrenal myelolipoma, and one as pheochromocytoma [4]. In one case of salt wasting CAH, histopathologic examination revealed bilateral giant adrenal lipomas [7]. A systematic review that included 420 cases of adrenal myelolipomas found that 10% of cases were associated with CAH [11]. It is said that small incidentalomas do not require biopsy or surgery for follow-up because the risk of cancer is very unlikely compared with large incidentalomas [12]. Although the nodules in our case were large, no biopsy or surgery

was performed because they were not suspicious on imaging and were defined as macronodular hyperplasia. The delayed shrinkage of the masses on treatment was attributed to the patient's lack of compliance. Despite the irregular use of treatment, the size of the nodules remained stable for 3 years, and then a significant shrinkage of the nodules was observed.

Conclusion

In patients with a bilateral adrenal mass and incidentaloma, CAH should be considered to avoid unnecessary surgery or biopsy.

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