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*Case Report*

# Congenitaladrenal hyperplasia initially presenting with massive adrenal indcidentalomas: a series of 4 cases

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**Abstract:** Adrenal incidentalomas (AI) are an increasingly prevalent complication in patients with congenital adrenal hyperplasia (CAH). Four late-onset CAH patients (3 with 21-hydroxylase deficiency and 1 with 11β-hydroxylase deficiency) presented with incidental and massive bilateral adrenal masses. Testicular morphology was documented and sperm analysis was performed after 5 days of sexual abstinence. To assess the hypothalamicpituitary-adrenal (HPA) axis, a 24-hour urinary free cortisol excretion test was conducted. Evaluation of the gonadotrophic axis was done by assessing levels of luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone, and estradiol. A gonadotropin-releasing hormone stimulating test was performed in 2 cases. All hormones were analyzed by chemiluminescence immunoassay. All patients underwent testicular ultrasonography. Of the 4 patients, the mean age was 32.25 years. Early indicators of CAH, including short stature and early virilization in the male patients, were evident in all 4 cases. Analysis of the gonadotrope-testicular axis showed that Cases 2 and 4 had higher basal testosterone levels and decreased LH and FSH concentrations. Case 2 showed blunted LH/FSH response to a gonadotropin-releasing hormone stimulating test. Additionally, these 2 patients had much higher dehydroepiandrosterone (DHEAS) and 17-OH-progesterone levels than the other 2 patients. Ultrasound of Cases 1 and 3 showed normal testicular echostructure and volume. Cases 2 and 4 suffered from bilateral testicular diffuse lesions with multiple nodules. CAH should be considered in the presence of AI. If suspected clinically, assays of cortisol, adrenocorticotropic hormone (ACTH), DHEAS, and 17OH-progesterone should be performed.

**Keywords:** CAH, adrenal indcidentalomas, ultrasound, case

## Introduction

Congenital adrenal hyperplasia (CAH) describes a group of rare autosomal recessive disorders categorized by deficient synthesis of cortisol and/or aldosterone [1]. However, the non-classic form of CAH results in only a partial defect in cortisol or aldosterone synthesis, and patients present as late- or adult-onset CAH with features of glucocorticoid or mineralocorticoid insufficiency.

The widespread use and the enhanced quality of high-resolution radiological techniques, including computed tomography (CT) or magnetic resonance imaging (MRI), of the abdomen have resulted in increased discovery of adrenal incidentalomas (AI). Current estimates of the prevalence of such lesions ranges in various studies from 2.3% at autopsy to 4% in retrospective CT series, reaching 5.8% in oncological studies and increasing with patient age [2-4].

Adrenal incidentalomas are an increasingly prevalent complication in patients with CAH. We describe a clinical series to demonstrate anthropometric features, hormonal profiles, and treatment protocols, especially with respect to gonadotropic axis and testicular function in these patients.

## Material and methods

### *Subjects*

Four late-onset CAH patients (3 21-hydroxylase deficiency and 1 11β-hydroxylase deficiency)

**Table 1.** General characteristics of the 4 patients

| Patient | Karyotype | Height (cm) | Parental Height (cm) | Blood Pressure (mmHg) | Penis Length (cm) | Testicular Volume (mL) | Testicular Ultrasound |
|---|---|---|---|---|---|---|---|
| 1 | 46, XY | 163 | ♀: 165<br>♂: 178 | 125/85 | 11 | Left: 12<br>Right: 14 | Normal |
| 2 | 46, XY | 142 | ♀: 158<br>♂: 172 | 135/90 | 8 | Left: 25<br>Right: 25 | Bilateral testicular diffuse lesions, multiple nodules |
| 3 | 46, XY | 158 | ♀: 165<br>♂: 168 | 180/95 | 8 | Left: 25<br>Right: 25 | Normal |
| 4 | 46, XY | 145 | ♀: 157<br>♂: 174 | 90/60 | 8 | Left: 15<br>Right: 12 | Bilateral testicular diffuse lesions, multiple nodules |

presented with massive adrenal masses to the Department of Endocrinology at the PLA General Hospital in Beijing, China between January 2010 and December 2014. The diagnosis of CAH was based on the patients' clinical history, current clinical status, and hormonal profile. The diagnosis of Case 1 was further confirmed by *CYP21A2* gene mutational analysis. These patients' charts were reviewed for demographics, adrenal imaging features, final height, penis length, testicle volume, karyotype, and biochemical results (**Table 1**). Adrenal masses were identified with multi-detector-row computed tomography (CT) and confirmed histopathologically following adrenalectomy. Testicular morphology was documented and sperm analysis was performed after 5 days of sexual abstinence. Sperm status was classified as per the 2010 Guidelines published by the World Health Organization (WHO) [5].

The Chinese PLA General Hospital Ethics Committee specifically approved this study and written informed consent was obtained from all patients.This study have been conducted according to the principles expressed in the Declaration of Helsinki.

*Hormone assays*

Hypothalamicpituitary-adrenal (HPA) axis: a 24-hour urinary free cortisol excretion test was conducted at 0:00, 8:00, 16:00, and 24:00. A dexamethasone suppression test to determine cortisol and adrenocorticotropic hormone (ACTH) levels was also conducted at these same time points. HPA axis hypofunction was defined as a basal serum cortisolconcentration of less than 198.7 nmol/L (normal range: 198.7-797.5 nmol/L).

Gonadotroph axis: luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone, and estradiol levels were assessed. A gonadotropin-releasing hormone (Gonadorelin 100 ug, MaanshanFengyuanPharmaceutical Co., Ltd., China) stimulating test wasperformed in Cases 1 and 2. Normal testosteronerange was defined as 8.4 to 28.7 nmol/L.

All hormones were analyzed by chemiluminescence immunoassay. ACTH was detected using an Immulite 2000 Analyzer (SiemensHealthcare Diagnostics Inc., Los Angeles, USA), while all otherswere measured with an ADVIA Centaur Analyzer (SiemensHealthcare Diagnostics, Tarrytown, NY, USA). Thedifferencesbetween and within-batch were 2.89%-3.69% and 1.86%-5.45% respectively for cortisol and 2.3%-6.2% and 1.4%-4.7% respectively for testosterone in males.

## Results

*Case 1*

A 29-year-old male, father of 1 boy, was referred to our institution in April 2013 due to the discovery of bilateral adrenal masses during a routine check-up. Abdominal ultrasound indicated bilateral adrenal hypoechoic nodules, later confirmed by CT (**Figure 1A**). The patient denied any symptoms attributable to the masses. The patient was assessed for hypercortisolism, aldosteronism, pheochromocytoma, and the presence of a malignant tumor. Malignancy and excess hormone secretion by the lesions were ruled out. Surgery was recommended given the size of the masses and a 3×3×3 cm mass was removed from the left adrenal without complication. Pathological examination confirmed diagnosis of adrenal adenoma. Adrenal CT at 1

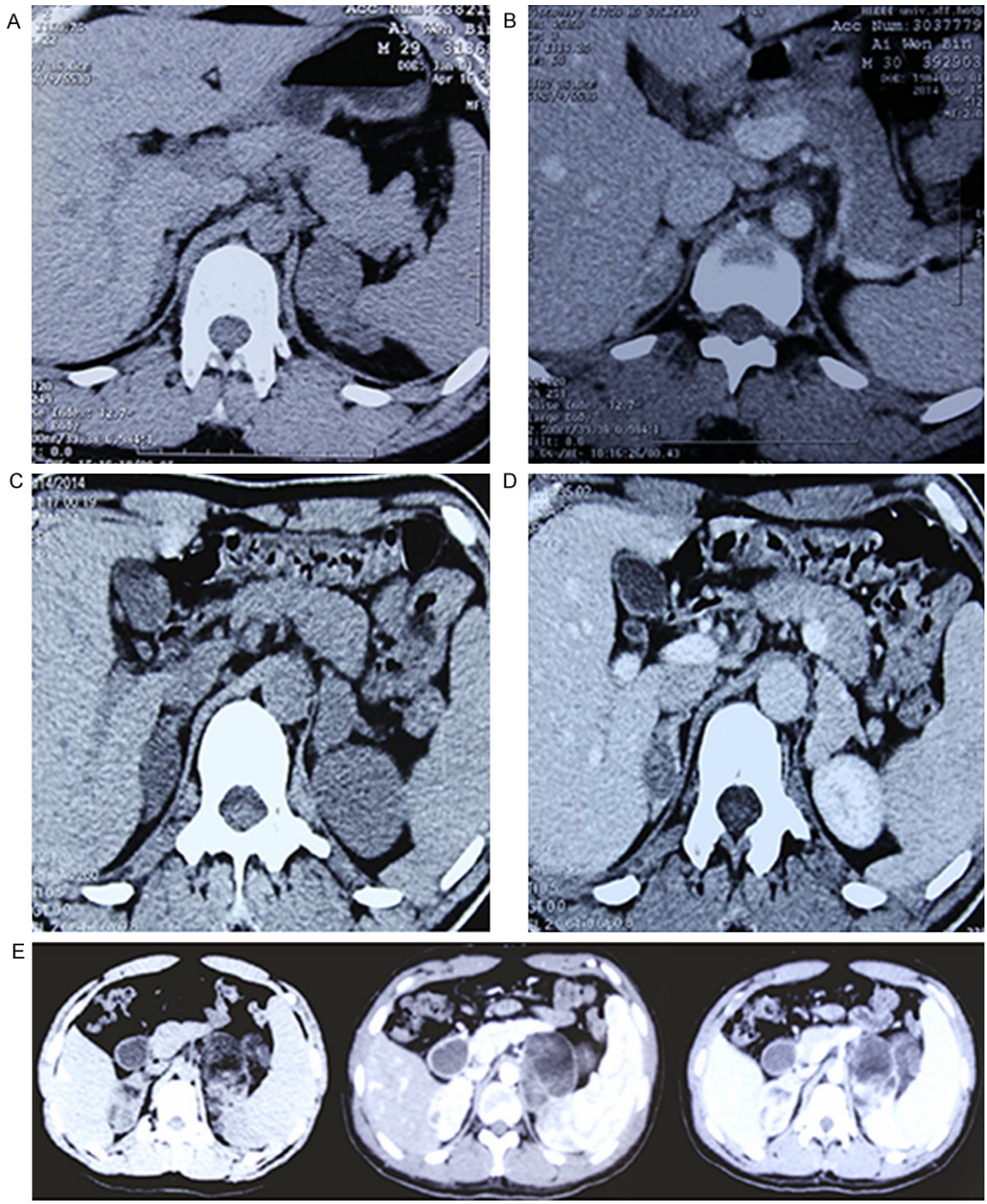


**Figure 1.** Computed tomography images of the adrenal glands of Case 1. A. Preoperative CT showing bilateral adrenal masses (left: 3.6×3.1 cm; right: 2.1×0.8 cm). B. Adrenal CT at 1 year postoperative follow-up showing enlargement of the left adrenal and a mass of the right adrenal (2.4×1.6 cm). C and D. Computed tomography images of the adrenal glands of Case 3. Bilateral adrenal masses are seen. E. Computed tomography images of the adrenal glands of Case 4. Bilateral adrenal masses are seen.

year follow-up showed enlargement of the remaining left adrenal and the presence of a right adrenal mass (**Figure 1B**). Further investigation revealed remarkably high ACTH levels and low cortisol levels (**Tables 2** and **3**). The patient had a higher basal level of 17-OH-progesterone, which was suppressed after a dexamethasone test (**Table 2**). DNA sequenc-

**Table 2.** Adrenal Steroid Precursors, ACTH, and PRA

| Parameter | Patient 1 | | | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|---|---|
| | Preoperative | Postoperative | Post-GC Admin | Postoperative | Postoperative | Postoperative |
| 17-OHP (ng/ml) | - | >20 | - | >20 | 7.53 | >20 |
| DHEAS (ug/dl) | - | 86.2 | - | 179.0 | 112 | 255 |
| 24hr-UFC (nmol/L) | 133.9 | 340.6 | - | 73.9 | 203.8 | 32.7 |
| ACTH [0:00] (pmol/L) | 7.64 | 5.53 | <1.1 | 7.86 | 2.71 | 5.28 |
| Cortisol [0:00] (nmol/L) | 32.2 | 33.15 | <25.7 | 29.69 | 38.35 | <25.7 |
| ACTH [8:00] (pmol/L) | 16.1 | 180.0 | <1.1 | 2.34 | 96.8 | 143.0 |
| Cortisol [8:00] (nmol/L) | 126.8 | 152.26 | <25.7 | 182.65 | 334.67 | 138.18 |
| ACTH [16:00] (pmol/L) | 8.55 | 17.9 | 2.21 | 1.34 | 30.2 | >278 |
| Cortisol [16:00] (nmol/L) | 57.9 | 153.76 | <25.7 | <25.7 | 345.93 | 147.2 |
| ACTH [1mg-DST] (pmol/L) | <1.1 | 1.25 | - | <1.1 | - | - |
| Cortisol [1mg-DST] (nmol/L) | <25.7 | <25.7 | - | <25.7 | - | - |
| PRA [supine] (ug/L/h) | 3.6 | 3.9 | - | 7.5 | <0.1 | 10.6 |
| Aldosterone [supine] (pmol/L) | 712.3 | 648.7 | - | 530.4 | 330.1 | 772.4 |
| PRA [upright] (ug/L/h) | 10.3 | 12.3 | - | 12.9 | <0.1 | 10.6 |
| Aldosterone [upright] (pmol/L) | 809.9 | 481.2 | - | 698.2 | 291.3 | 698.2 |

-, data unavailable; GC, glucocorticoid; 17-OHP, 17-OH-progesterone; DHEA, dehydroepiandrosterone; ACTH, adrenocorticotropic hormone; DST, dexamethasone suppression test; PRA, plasma renin activity.

**Table 3.** Mid-Dose Dexamethasone Suppression Test (0.75 mg, q6h, 5 days)

| Patient | Time | 17-OHP (ng/ml) | DHEA (ug/dl) | ACTH (pmol/L) | Cortisol (nmol/L) |
|---|---|---|---|---|---|
| 1 | Baseline | 18.9 | 152.6 | 180 | 152.26 |
| | Day 4 | 1.82 | 20 | 1.33 | <25.7 |
| | Day 6 | - | - | - | - |
| 2 | Baseline | >20.0 | 179 | 2.34 | 182.65 |
| | Day 4 | 2.39 | <15 | <1.1 | <25.7 |
| | Day 6 | 2.77 | <15 | <1.1 | <25.7 |
| 3 | Baseline | 14.9 | <15 | 84.6 | 361.33 |
| | Day 4 | 0.87 | 20.0 | 2.22 | <25.7 |
| | Day 6 | 0.78 | 24.4 | 2.09 | <25.7 |
| 4 | Baseline | >20.0 | 316 | 79.3 | 127.8 |
| | Day 4 | 2.25 | 40.4 | 1.22 | <25.7 |
| | Day 6 | - | - | - | - |

-, data unavailable; 17-OHP, 17-OH-progesterone; ACTH, adrenocorticotropic hormone, DHEA, dehydroepiandrosterone.

ing of the *CYP21* gene indicated NG_0079-41.2:g.C/A5774A/G and T518T/A point mutations which confirmed the diagnosis of 21-hydroxylase deficiency (**Figure 2**). Additionally, the patient had a short stature and mild skin pigmentation. Dexamethasone (0.375 mg) was given nightly and the right adrenal mass was left in situ. Radiological tests confirmed that the tumor and left adrenal hyperplasia shrank over the following 1 year. 17-OH-progesterone level decreased to the normal range.

*Case 2*

A 48-year-old male, father of 1 girl, presented to our emergency department in April 2013 complaining of acute right abdominal colic. Abdominal ultrasonography confirmed this to be the result of a kidney stone. Incidental bilateral adrenal masses were also noted. Adrenal CT showed pronounced bilateral adrenal hyperplasia and bilateral lower-density adrenal masses (left: 5.6×3.4 cm; right: 2.3×1.5 cm) described as typical adrenal myelolipoma with a capsule, heterogeneous stroma, and calcifications.

The patient had a short stature and mild skin pigmentation. A detailed medical history revealed that his growth and development had been accelerated at 6 years of age. Upon inquiring into the patients past medical history, the patient revealed that his growth and development were ahead of his peers at age 6. Genital examination showed normal penile size and testicular volume. Biochemical investigation revealed low cortisol levels, which barely increased after a hypoglycemia stimulation test. In addition, the patient had a higher basal level of 17-OH-progesterone, which was suppressed after a dexamethasone test (**Tables 2**

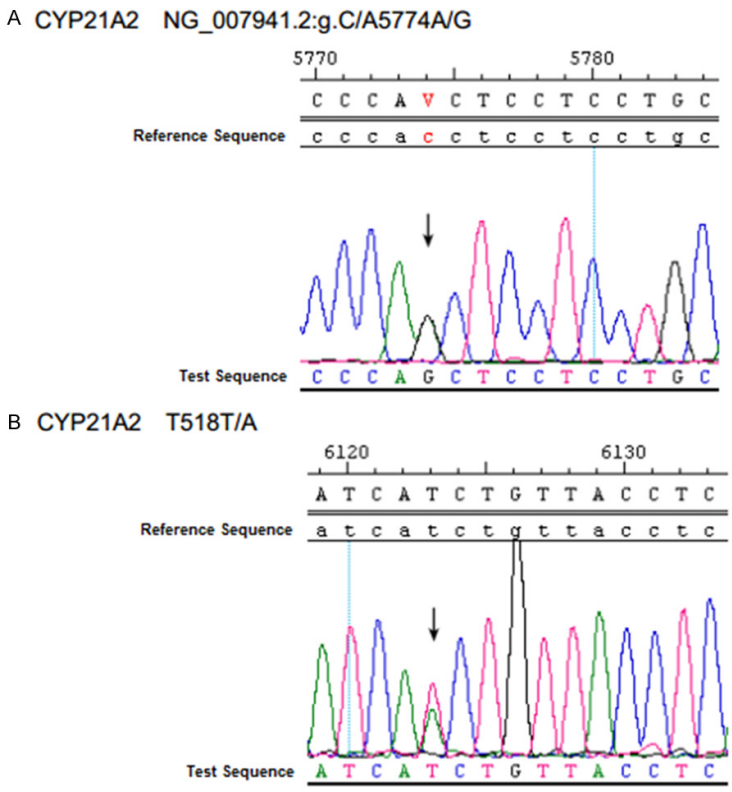


**Figure 2.** Genetic analysis of Case 1. DNA sequencing of the *CYP21* gene indicated NG_007941.2:g.C/A5774A/G and T518T/A point mutations confirming diagnosis of 21-hydroxylase deficiency.

and **3**). Dexamethasone (0.1875 mg) was given once nightly. The masses were asymptomatic and were left untreated. No radiological changes of the tumor and/or hyperplasia were observed over the subsequent 8 months. 17-OH-progesterone level was normalized.

*Case 3*

A 26-year-old male presenting with bilateral adrenal masses (**Figure 1C** and **1D**) was referred to our department in December 2014. A detailed medical history revealed precocious puberty beginning at age 6 and a history of hypertension for the past 8 years. The patient had been diagnosed with "cerebral infarction" 4 years prior became severely hyperkalemic during that hospitalization. During this time, bilateral adrenal masses were found incidentally. In addition, the patient had 11β-hydroxylase deficiency that had not been diagnosed until he was 23 years old. Physical examination upon admission to our department indicated shorter stature but no signs of increased pigmentation. The patient was hypertensive at 170/95 mmHg. Laboratory investigations revealed hypokalemia (2.67 mmol/L), slightly decreased cortisol excretion, and elevated 17-OH-progesterone which was suppressed after a dexamethasone test (**Tables 2** and **3**). The patient had normal aldosterone levels but severely inhibited plasma renin activity consistent with 11β-hydroxylase deficiency.

*Case 4*

A 26-year-old male presented to our hospital in April 2010 with severe pain in both testes was referred to our hospital in April 2010. Testicular ultrasound indicated bilateral diffuse testicular lesions, as well as multiple nodule and bilateral adrenal masses (**Figure 1E**). The patient was assessed for pheochromocytoma and the presence of a malignant tumor. Malignancy and excess hormone secretion by the lesions were ruled out.

Upon examination, the patient was noted to have a short stature. A detailed medical history revealed that he had undergone surgery to remove an 85×80 mm myelolipoma from his left adrenal gland 4 years prior.

Biochemical investigation revealed a low cortisol level as well as high basal levels of 17-OH-progesterone and dehydroepiandrosterone (DHEAS)-both of which were suppressed following a dexamethasone test (**Tables 2** and **3**). Samples from a percutaneous ultrasound-guided fine needle biopsy of the tumor confirmed that the lesions were testicular adrenal rest tumors (TART). The patient was diagnosed with CAH due to his 21-hydroxylase deficiency.

## Discussion

Due to the widespread increase in frequency of cross-sectional imaging, AI's are becoming a common clinical problem. Malignancy and functionality are the 2 main clinical issues upon identification of AI. Guidelines issued by the American Association of Clinical Endocrino-

logists (AACE) and the American Association of Endocrine Surgeons (AAES) in 2009 [6] recommend that patients with AI's undergo clinical, biochemical, and radiographic evaluation for signs and symptoms of hypercortisolism, aldosteronism (if hypertensive), the presence of a pheochromocytoma, or a malignant tumor. But is it enough just to do the above? Both homozygous and heterozygous patients with CAH exhibit an increased susceptibility to AI [7], yet assessing for undiagnosed, non-classical CAH is not explicitly recommended in these guidelines.

Although the tumorigenesis of AI is still poorly understood, it is clear that CAH, mainly 21-hydroxylase deficiency, predisposes for adrenal tumors that are usually not malignant [7, 8]. CAH patients typically exhibit abnormally high levels of adrenocorticotropic hormone (ACTH) due to the lack of negative feedback from cortisol [8]. Long-standing elevation of ACTH secretion may lead to adrenocortical hyperplasia [9, 10]. Tumor formation may then take place in the hyperplastic adrenal cortex [7, 11]. The prevalence of adrenal tumors detected by CT or MRI has been reported at widely varying ranges [7, 12, 13]. Nermoen et al. found 7 individuals with adrenal tumors (2 bilateral, 4 with myelolipoma) in a cohort of 62 CAH patients [12]. Jaresch et al. found adrenal masses in nearly 82% of homozygous and 45% of heterozygous CAH patients, and consequently recommended that patients with adrenal incidentaloma be evaluated for undiagnosed CAH [7]. It is worth noting that not only CAH patients may have high frequency of adrenal tumors but also 45% of CAH carriers were reported to have adrenal tumors [7]. Manifest CAH and CAH carriers may be overrepresented among patients with AI's. Sabina M et al. used genetic analysis in patients with non-functional AI's found that 16% were CAH carriers and 2%-5% were undiagnosed CAH [14, 15]. Patients with gene mutations that cause CAH are clearly overrepresented in adrenal incidentaloma cases, and oftentimes patients with non-classic CAH remain undiagnosed until later in life; the oldest undiagnosed CAH case in the literature was an 88-year-old woman [16]. Here, we present 4 patients with non-classical CAH who were referred to our department because of AI's.

Three of the patients in our study were confirmed to have myelolipomas. Myelolipomas tend to be the most common type of adrenal tumor in CAH patients, with adenomas coming in a step behind. Myelolipomas are relatively rare, benign endocrine inactive tumors composed of adrenal, adipose and myeloid tissue. Chronic ACTH and androgen stimulation may play a causative role in the generation of myelolipomas in patients with untreated CAH. Almeida MQ et al. study demonstrated ACTH (MC2R) and androgen (AR) receptors overexpression in giant bilateral myelolipomas from poor-compliance CAH patients [17]. On CT images, the presence of low attenuation fat in the lesion, which has a density of -30 HU, is a specific and diagnostic finding. Cases 2, 3, and 4 all possessed typical imaging features of a myelolipoma (**Figure 1C-E**). However, the presence of hemorrhage and necrosis features, especially massive lesions, tended to emulate the radiological aspect of an adrenal carcinoma. Adrenal carcinoma is typically not associated with CAH, and the likelihood of tumors smaller than 6 cm in diameter being carcinomas is markedly less than those larger than 6 cm in diameter [6, 18-20]. Thus it appears reasonable to follow up CAH patients with AI's both clinically and with periodic CT scans. Our first patient received dexamethasone (0.375 mg) and periodic CT scans after diagnosis, and the tumor and adrenal hyperplasia were observed to be shrinking radiologically over the subsequent 1 year observation period. The tumors in Cases 2, 3, and 4 were unchanged on follow-up CT scans. As AI's in CAH are typically benign tumors, biopsy and surgery in this situation need to be routine, even with massive size [19].

In CAH, increased ACTH levels stimulate steroidogenesis and cortisol precursors are shunted into androgen production [1, 21, 22, 8]. Excess androgens result in masculinization, premature puberty, and short stature resulting from early skeletal maturation [8]. In addition, childhood steroid exposure with glucocorticoids and androgens has been reported to influence final height [23]. All 4 patients in this study had abnormally low final heights based on parental heights, resulting from androgen exposure in childhood. This feature should have been an early indication of possible non-classical CAH, but was ignored when all 4 patients were initially admitted. Thus, we recommend

**Table 4.** Gonadal Function Tests

| Parameter | Patient 1 | | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|---|
| | Preoperative | Postoperative | Postoperative | Postoperative | Postoperative |
| Testosterone (nmol/L) | 8.23 | 13.64 | 34.64 | 14.96 | >52.05 |
| Estradiol (pmol/L) | 108.3 | 92.7 | 153.57 | 102.27 | 121.91 |
| Progesterone (nmol/L) | 54.94 | 53.85 | 52.98 | 6.70 | 47.93 |
| LH (mIU/mL) | 1.71 | 1.93 | <0.07 | 1.58 | <0.07 |
| FSH (IU/L) | 5.47 | 5.22 | <0.3 | 2.31 | <0.3 |
| Sperm Parameters | | | | | |
| Volume (mL) | 3.0 | - | - | 2.0 | 2.8 |
| Sperm Count ($10^6$/mL) | 3.86 | - | - | 7.07 | 4.34 |
| Vitality (%) | 57 | - | - | 40 | 36 |

-, data unavailable; FSH, follicle stimulating hormone; LH, luteinizing hormone.

**Table 5.** Gonadotropin-Releasing Hormone Stimulating Test

| Patient | Parameter | -15 min | 0 min | 30 min | 60 min | 120 min |
|---|---|---|---|---|---|---|
| 1 | LH (mIU/mL) | 2.35 | 2.07 | 37.97 | 32.20 | 18.44 |
| | FSH (IU/L) | 6.06 | 5.94 | 12.93 | 14.70 | 14.36 |
| 2 | LH (mIU/mL) | <0.07 | <0.07 | 0.81 | 1.13 | 1.41 |
| | FSH (IU/L) | <0.3 | <0.3 | 1.17 | 1.00 | 1.79 |

FSH, follicle stimulating hormone; LH, luteinizing hormone.

that when an AI is confirmed as "non-functional", final height and other possible indicators of non-classical CAH should be considered.

In addition, Case 3 exhibited the typical features of precocious puberty, resistant hypertension, and hypokalemia that should have been indicative of CAH. His delayed diagnosis was an unfortunate result of an insufficient recognition of CAH. Analysis of hormonal profile provided useful information for the final diagnosis.

If CAH is suspected clinically, assays of cortisol, ACTH, DHEAS, and 17-OH-progesterone should be performed. All of the 4 patients had remarkably increased ACTH and DHEAS levels and a higher basal level of 17-OH-progesterone, which was suppressed after a dexamethasone test. Their cortisol levels were also lowered.

Additionally, Cases 1 and 2 underwent hypoglycemia stimulation tests that hardly increased cortisol levels. This emphasizes how crucial correct diagnosis of CAH in cases of AI, as patients with undiagnosed CAH are at risk of adrenal crises [24]. Such patients may benefit from glucocorticoid therapy and should at least be equipped with emergency medication.

Analysis of the gonadotrope-testicular axis showed that Cases 2 and 4 had higher basal testosterone levels and decreased LH and FSH concentrations (**Table 4**). Case 2 showed blunted LH/FSH response to agonadotropin-releasing hormone stimulating test (**Table 5**). Additionally, these 2 patients had much higher DHEAS and 17-OH-progesterone levels than the other 2 patients, suggesting that the lower gonadotropin levels might be linked to the synergistic antigonadotropic effect of the elevated levels of these 17-OH-progestogens and testosterone precursors [25-27]. Knowledge of this gonadotropin profile may have therapeutic implications. Case 4 exhibited azoospermia, which may result from gonadotropin inhibition linked to elevated DHEAS and 17-OH-progesterone levels. Treatment with glucocorticoids, which is typically considered when patients are diagnosed with CAH, can lead to a decrease in these adrenal precursors, normalizing gonadotropin levels and improving the sperm count [28-32]. Therefore, follow-up of cases like those presented herein should include gonadotropin and semen analysis.

TART's are well-defined hypoechoic lesions of the testicle near the rete testis. They are benign and often bilateral, and possibly arise from precursor steroidogenic stem-like cells in the testicle under ACTH-stimulation. The localization of the tumors within the rete testis renders them difficult to identify by clinical examination [33, 34]. Testicular ultrasound examination is therefore mandatory to diagnose TART's [26]. Previous studies, which generally use small sample sizes and vary with regards to patient

selection and tumor detection, have reported results of between 0% and 94% for the prevalence of TART's in CAH men [12, 35-38]. However, numerous reports of TART's in CAH support the hypothesis that they are a relatively common phenomenon in CAH men [39, 40].

All of our patients underwent testicular ultrasound examination. Cases 1 and 3 had normal testicular echostructure and volume. Cases 2 and 4 suffered from bilateral testicular diffuse lesions with multiple nodules. Case 4 initially presented with painful testis and samples from a percutaneous ultrasound-guided fine needle biopsy of the lesions confirmed the cause to be a TART. Long-standing TART's have previously been linked to obstructive azoospermia, gonadal dysfunction, and infertility [12, 38, 41]. Intensifying glucocorticoid treatment is recommended in these patients and might lead to a reduction in tumor size by suppression of ACTH secretion [42, 43]. The follow-up period of our 2 patients with TART's was too short to observe a definitive size increase.

The main limitation of the present study is its retrospective nature. Some study parameters were not available for all 4 cases. As such, only 2 patients underwent gonadotropin-releasing hormone stimulating testing. The follow-up period was also short and the information reported was limited to the available data.

## Conclusions

We report the clinical features, CT characteristics, adrenal function, gonadotrope-testicular axis function, and testicular ultrasound findings from 4 patients with non-classical CAH and AI's. The patients all had reduced height and their hormonal profiles indicated remarkably increased ACTH, DHEAS, higher basal levels of 17-OH-progesterone, and relatively lower cortisol levels. We also found alterations of the gonadotrope-testicular axis, TART's, and azoospermia. Thus, we recommend that CAH should be included in the differential diagnosis of AI's. If suspected clinically, assays of cortisol, ACTH, DHEAS, and 17OH-progesterone should be performed. Testicular ultrasound and semen analysis seems advisable once CAH is confirmed.

## Disclosureof conflict of interest

None.

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