Case report

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A young lady with primary amenorrhea and virilization

Khan MH[1], *Morshed MS[2], Sultana N[3], Jahan S[4], Aktar Y[5], Fariduddin M[6]

[1]M A Halim Khan, Associate Professor, Department of Endocrinology, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh; [2]Md. Shahed Morshed, PhD student, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh; [3]Nusrat Sultana, Associate Professor, Department of Endocrinology, BSMMU, Dhaka, Bangladesh; [4]Sharmin Jahan, Associate Professor, Department of Endocrinology, BSMMU, Dhaka, Bangladesh; [5]Yasmin Aktar, Assistant Professor, Department of Endocrinology, Bangladesh Medical College Hospital, Dhaka, Bangladesh; [6]Md Fariduddin, Professor, Department of Endocrinology, BSMMU, Dhaka, Bangladesh

Abstract

An 18-year-old female presented with primary amenorrhea, absent development of breasts, and features of virilization. Investigations revealed high total testosterone and dehydroepiandrosterone-sulfate with normal cortisol and 17-hydroxyprogesterone. Her karyotype was 46XX. CT scan of the abdomen revealed a (4×3) cm sized left adrenal mass. Open adrenalectomy followed by histopathology of the resected adrenal showed a benign adenoma. The patient's clinical and biochemical features improved within six months of surgery. Virilization usually indicates a malignant adrenal tumor, but surprisingly the cause may be a benign one. *[J Assoc Clin Endocrinol Diabetol Bangladesh, January 2024; 3 (1): 31-33]*

Keywords: Virilization, Adrenal adenoma, Dehydroepiandrosterone-sulfate, Adrenalectomy

***Correspondence:** Dr. Md. Shahed Morshed, PhD student, Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, Cell # +88 01738-842019, email: shahedk62@gmail.com

Introduction

Virilization in a female indicates severe hyperandrogenism and is characterized by frontal balding, deepening of the voice, atrophy of breasts, clitoromegaly, and masculine body habitus. Virilization at the time of puberty without secondary sexual features in an apparently looking girl indicates either 46XX virilized or 46XY undervirilized conditions with onset of virilization at puberty.[1] So, the karyotype is an essential component to narrow the differential diagnoses. The differential diagnoses with 46XX karyotyping are late-onset congenital adrenal hyperplasia (CAH), androgen-producing ovarian/adrenal tumor, and 46XX ovo-testicular disorders of sex development (OT-DSD). On the other hand, virilization with a 46XY karyotyping with the uterus indicates ovo-testicular DSD (46XY/46XX chimera) or partial 46XY gonadal dysgenesis. Some 46XY patients with receptor/enzymatic defects (partial androgen insensitivity syndrome, 17-β hydroxysteroid dehydrogenase deficiency, 5-α reductase deficiency) also virilize during puberty without having a uterus. Rarely, severe ovarian hyperthecosis may produce similar features.[2]

Androgen-producing adrenal tumors are very rare (0.2%-0.5% of pediatric tumors) with an incidence of three cases per crore of children. Hyperandrogenism during puberty usually presents with contrasexual precocious puberty and primary amenorrhea without thelarche. Along with dehydroepiandrosterone (DHEA), DHEA sulfate (DHEAS), androstenedione, and testosterone secretion from the tumor, many of the patients may also present with glucocorticoid excess and may be associated with a genetic syndrome. Rapid onset with a short duration of virilization indicates a tumor. The frequency of benign and malignant tumors is usually equal.[3] Here we report a young lady with a benign adrenal adenoma who presented with virilization and primary amenorrhea.

Case presentation

An 18-year-old female, 2nd issue of non-consanguineous parents presented to the Endocrinology Department with hirsutism, acne, frontal balding, and masculinization of body habitus without deepening of voice for six months. (Figure-1). She had not started menarche yet. On

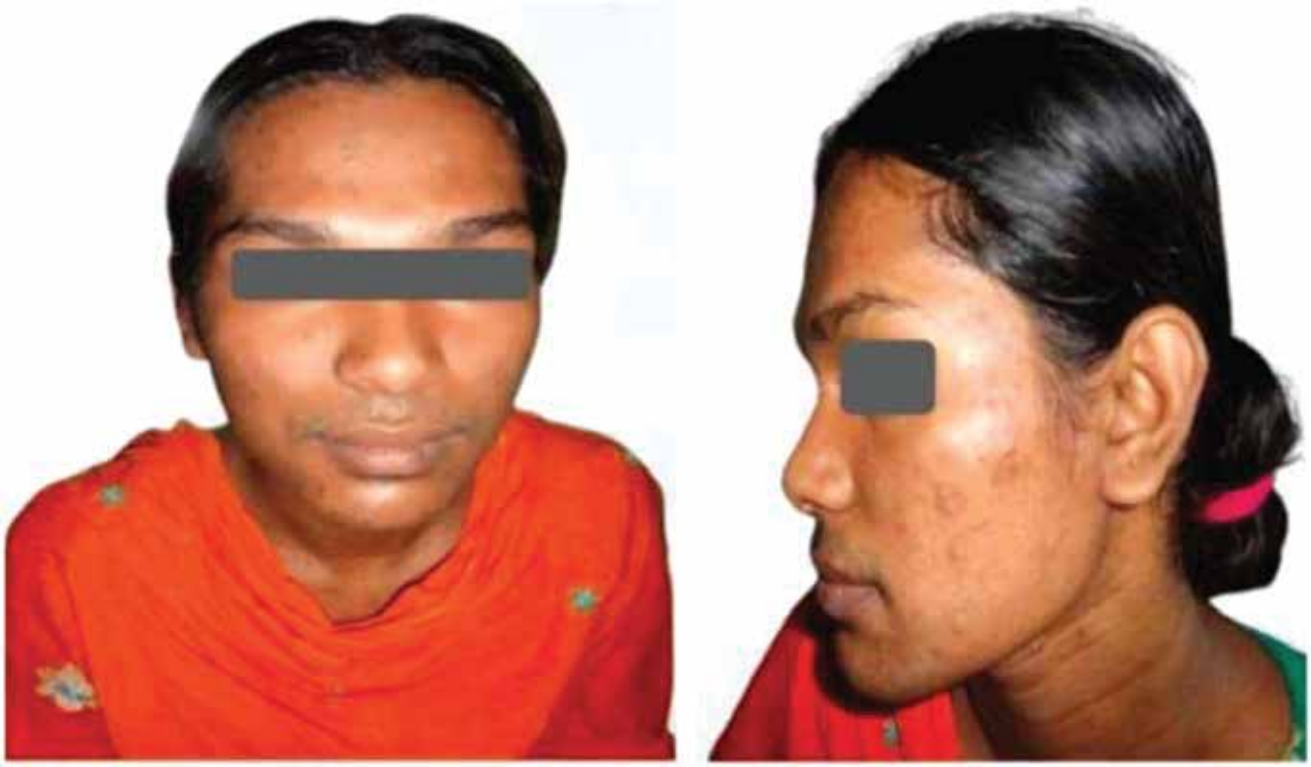

Figure-1: Features of acne, hirsutism, frontal balding, and masculine body habitus of the patient (frontal and left lateral view)

examination, she had moderately severe hirsutism (18 points on modified Ferriman Gallwey score), the clitoris was two cm in length and 1.5 cm in breadth (clitoral index: 3.0 cm^2), breast development at Tanner stage-B1, P-5, and vital signs were normal. A hormonal evaluation revealed high levels of total testosterone (TT) with DHEA-S. Serum cortisol, adrenocorticotropic hormone (ACTH), and 17-hydroxy progesterone were not elevated. Her karyotype was 46XX (Table-I). The pelvic ultrasound showed a small uterus with multiple tiny follicles in both ovaries. CT scan of the abdomen revealed a left adrenal mass, 4x3 cm in size (Figure-2). Open adrenalectomy followed by histopathological examination of the adrenal mass indicated a benign adrenal adenoma. The postoperative progress of the patient was clinically satisfactory with normalization of DHEAS and TT levels and the onset of menstruation after induction by six months of estrogen. Now the patient is on follow-up with cyclical estrogen and progesterone supplementation.

Table-I: Investigation profile of the patient

Test	Result	Normal values
Complete blood count	Normal	
S. Total testosterone, ng/mL	11.15	63-120
S. DHEAS, µgm/dL	760.2	35-430
S. FSH, mIU/mL	9.76	4-13
S. LH, IU/L	6.15	2-15
S. Basal Cortisol, nmol/L	495	138-690
Plasma ACTH, pg/mL	61.5	ND-46
S. 17-OH Progesterone, ng/mL	1.1	0.16-2.83
Stimulated 17-OHP*, ng/mL	2.06	0.80-4.20
Karyotype	46XX	-
USG of the whole abdomen	Small uterus,multiple tiny follicles in right ovary, small cyst in left ovary	-
CT scan of the abdomen	Left adrenal mass (4×3) cm	

*1-hr after 250 µg Synacthen injection

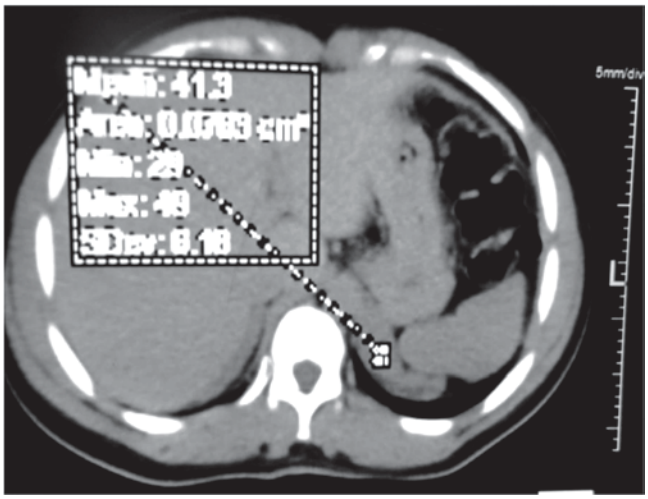

Figure-2: CT scan of abdomen showing left adrenal mass

Discussion

As our patient's karyotyping was 46XX, the receptor/enzymatic defects were excluded. Patients with 46XX OT-DSD usually present with ambiguous genitalia, cryptorchidism with inguinal hernia, breast development, and cyclic hematuria. The absence of these features as well as the presence of only ovaries exclude this diagnosis. Late-onset CAH usually presents slowly and was excluded by low 17-OHP. The source of androgen from the adrenal rather than the ovary was confirmed by elevated DHEA-S, the presence of adrenal tumor in imaging.

In an older case series reported by Del Gaudio et al. (1993), 10 (5.3%) of 190 cases (age: 20-66 years) of adrenal tumors presented with features of virilization. Seven out of 10 tumors were malignant and the mean duration from the onset of 1st symptom to diagnosis was 18.4 months.[3] Our patient noticed her features of virilization started about six months back.

The prognosis of adrenal adenoma after adrenalectomy is promising.[4,5] Our patient also improved within six months of adrenalectomy.

Conclusion

Virilization during the pubertal period has many differential diagnoses. Virilization due to an adrenal adenoma is a rare diagnosis with a good prognosis following adrenalectomy.

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Disclosure

The authors have no multiplicity of interest to disclose.

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Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethical Approval and Consent to Participate

Written informed consent was obtained from the patient. All methods were performed in accordance with the relevant guidelines and regulations.

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