THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India (March–April 2019) 69(2):188–191
https://doi.org/10.1007/s13224-018-1193-6

CASE REPORT

Successful Treatment Outcome in a Woman with Congenital Adrenal Hyperplasia

Sheela Shenoy[1] · **Madhuja Gopishyam**[1,2]

Received: 22 June 2018 / Accepted: 17 November 2018 / Published online: 30 November 2018

About the Author

Prof. Sheela Shenoy is currently Head of Department of OBG at Cosmopolitan Hospital, Trivandrum and imparts training for the National Board of Examinations. She has served as Head of Department at Govt. Medical College, Trivandrum and as a Faculty in Clinical Epidemiology Research and Training Centre affiliated to INCLEN. She has contributed to the projects on bacterial vaginosis, maternal mortality and acupressure in the INCLEN Reproductive Working Group and as a collaborator in the medical abortion studies under the WHO Reproductive Unit. She has publications in National and International journals and authored a monograph on Challenges in Safe Motherhood Initiative. She is an active member of FOGSI and served as President of Kerala Chapter.

Keywords Congenital adrenal hyperplasia · Ambiguous genitalia · Primary amenorrhea

Prof. Sheela Shenoy is currently Head of the Department of OBG at Cosmopolitan Hospital, Trivandrum and imparts training for the National Board of Examinations.Dr Madhuja Gopishyam, DGO, DNB is a Specialist at Renai Medicity Multi Super Speciality Hospital, Ernakulam.

✉ Madhuja Gopishyam
dr.madhuja@gmail.com

[1] Department of OBG, Cosmopolitan Hospital, Thiruvananthapuram, India

[2] Present Address: Department of OBG, Renai Medicity, Ernakulam, India

Introduction

Congenital adrenal hyperplasia is a group of autosomal recessive disorders characterized by defects in the adrenal hormone biosynthesis pathway due to mutations in the CYP21A2 gene. In 90% of cases, it is caused by deficiency of 21 hydroxylase enzyme [1]. It can also be caused due to deficiency of 11 beta hydroxylase or 3 beta hydroxysteroid dehydrogenase. CAH is divided into a classical type consisting of salt wasting and simple virilizing type and a nonclassical type. Classical CAH is the most common cause of sexual ambiguity at birth. Incidence varies with ethnicity, overall incidence being approximately 1 in 16,000 live births [2]. Menstrual, sexual and reproductive function is reduced in untreated cases due to multiple factors like excessive adrenal androgens, progesterones and abnormalities of external genitalia. In the nonclassical or

late onset type, the external genitalia are usually normal and presentation is in the form of menstrual irregularities and hirsutism.

Case Report

A 19-year-old presented with primary amenorrhea, ambiguous genitalia and hirsutism. She had first sought medical help at the age of 16 years for primary amenorrhea. A perineal surgery was done at 16 years elsewhere, but she had not attained menarche. She was born out of a nonconsanguinous marriage and had a male sibling with normal development. Her schooling was appropriate for age and she scored average grades. There was no history of cyclical pain in abdomen or chronic illnesses.

Her height was 150 cm, weight 42 kg, BMI 18.6 and blood pressure was in the normal range. She had normal intelligence and a feminine voice. There was no palpable abdominal mass. Breast was Tanner 2 and pubic hair Tanner 3. Her Ferriman–Gallway score for hirsutism was 10. She had clitoromegaly with clitoral length of 4 cm (Fig. 1). She had a pinpoint urethral orifice at the vestibule. Labia minora was hypoplastic, and lower two-thirds of labia majora were fused in the midline. Vagina could not be visualized.

Karyotyping showed female genotype. Pelvic ultrasound showed normal uterus and bilateral polycystic ovaries. MRI showed adrenal hypertrophy, polycystic ovaries, clitoromegaly and normal uterus. Hormonal assays revealed markedly elevated 17OH progesterone levels (22 ng/ml), and testosterone was in the male range. DHEAS was in the normal range.

She was diagnosed to have CAH of simple virilizing type and started on prednisolone 5 mg, titerd to 7.5 mg per day after 2 months. She attained menarche in 3 months following initiation of treatment. She had irregular scanty periods, only on taking medroxy progesterone for withdrawal bleeding. She was advised labial correction before marriage to prevent refusion of labia and was under follow-up.

At 22 years, she underwent labial correction, 3 months prior to marriage. A vertical incision was taken at the fused part of labia majora, vaginal verge sutured together with perineal edge (Fig. 2). Normal coitus was possible following surgery.

She seeked medical help 1 year after marriage as she did not conceive. She conceived with one cycle of ovulation induction with clomiphene citrate 50 mg. Serial follicular monitoring done from day 11 showed two dominant follicles. Ultrasound done in early pregnancy showed dichorionic diamniotic twins. She continued taking prednisolone 7.5 mg in pregnancy. Antenatal period was otherwise uneventful. Elective LSCS was done at 37 weeks due to previous genital reconstructive surgery. She delivered a pair of twins—a male and a female baby weighing 1.99 kg and 2.2 kg, respectively. She was given hydrocortisone injection 100 mg, 8 hourly postoperatively. Day 3 hormonal assay of both the babies was found to be normal. Lactation was adequate.

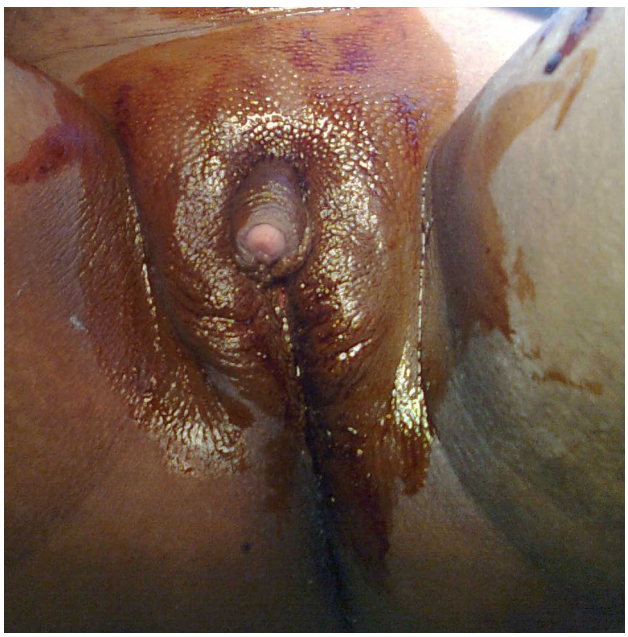

Fig. 1 Clitoral hypertrophy

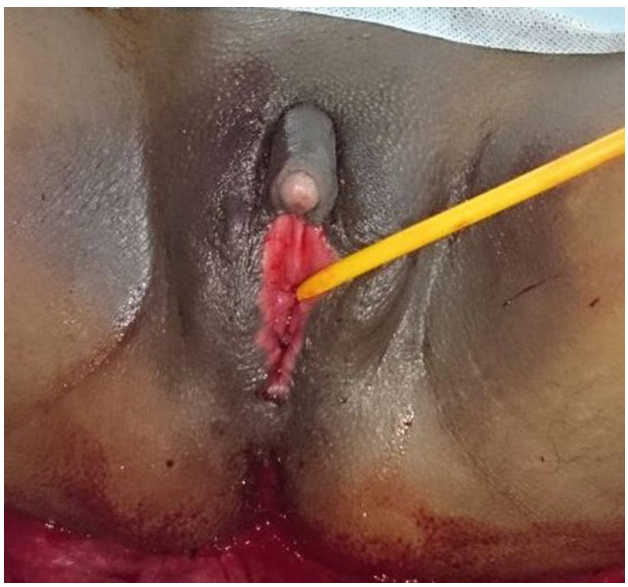

Fig. 2 Genitalia of the patient postsurgery

Discussion

CAH is a group of disorders caused due to enzymatic defect in the adrenal hormone synthesis pathway. This leads to varying levels of impairment of glucocorticoid and mineralocorticoid production and resultant excessive androgen synthesis. Lack of negative feedback by cortisol leads to an increased hypothalamo pituitary adrenal axis activity that causes adrenal hyperplasia. Elevation of 17 hydroxy progesterone is the hallmark of CAH and is used for diagnosis and follow-up of treatment [1].

Classical CAH is the commonest cause of sexual ambiguity at birth such that every case of ambiguous genitalia at birth is considered CAH unless proven otherwise. Neonatal screening is done by measuring 17 OH progesterone on day 3.

In adults and adolescents after epiphyseal closure, treatment with long-acting steroids is preferred. Treatment is monitored by serial measurements of 17 hydroxy progesterone, andrestenedione and testosterone levels every 3–4 months during pubertal phase and 6 months to annually once the dose of glucocorticoids is well established. The aim is to maintain mildly elevated levels of these hormones [2]. The dosage of glucocorticoids should be increased during stressful events, labor and delivery.

Depending on the amount of exposure to androgens in utero, female fetuses can have varying degrees of clitoromegaly and labial fusion. Reconstructive surgery required may differ for each individual depending on the degree of anatomical distortion. There is a lack of consensus on the timing of surgery and the optimum surgical approach. Surgeries done in infancy or childhood have an advantage of tissue elasticity for reconstruction, but may require revision later. Newer techniques of clitoroplasty preserve innervation and clitoral sensation. Advantage of delayed reconstruction is that there is reduced risk of vaginal stenosis and subsequent dilatation. The patient can also be actively involved in decision making.

Fertility in females with simple virilizing CAH on steroid therapy is 35–60% [3]. Fertility is reduced due to chronic anovulation caused by excess androgen and progesterone production, secondary polycystic ovaries, structural anomalies of external genitalia, delayed psychosexual development and decreased sexual activity. Once pregnant, they should be screened for gestational diabetes at the initial visit and then at second trimester due to chronic steroid exposure.

Chances of a female with CAH giving birth to an infant with CAH is 1 in 120 [3]. Prenatal diagnosis by chorionic villus sampling or amniocentesis and molecular genetic analysis of CYP21A2 gene can be offered to women who are at high risk of carrying fetuses with CAH (women who have previously given birth to babies with CAH or when both partners are carriers for 21 hydroxylase deficiency). When both partners are carriers, there is 1 in 8 chance of them having an affected female baby. To prevent genital ambiguity in female fetuses, dexamethasone therapy has to be initiated by 9 weeks of pregnancy. These invasive procedures do not yield results until after genital differentiation. Hence, 7 out of 8 fetuses will have to be treated unnecessarily with dexamethasone till results from invasive testing are obtained. Use of dexamethasone in the first trimester is associated with low birth weight, orofacial clefts, poor verbal memory and poor scholastic competence in human studies [4]. More recent noninvasive prenatal diagnosis using cell-free fetal DNA from maternal plasma can be offered before 9 weeks of pregnancy, so that only affected fetuses can be treated by initiation of dexamethasone before genital differentiation [3].

However, the Endocrine Society does not recommend such treatment and suggests that it should be given only as per institutional protocols [5]. Hence, treatment should be initiated only after counseling the couple and weighing risks and benefits.

Conclusion

With prompt diagnosis, counseling and treatment of CAH, satisfactory menstrual, sexual and reproductive function can be achieved. A multidisciplinary approach is the ideal way to tackle the multiple clinical problems of a case of CAH.

Compliance with Ethical Standards

Conflict of interest Dr. Sheela Shenoy and Dr. Madhuja Gopishyam declare that they have no conflict of interest.

Ethical Statement All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed Consent Informed consent was taken from the patient.

References

1. Turcu AF, Auchus RJ. Adrenal steroidogenesis and congenital adrenal hyperplasia. Endocrinol Metab Clin N Am. 2015;44(2):275–96. https://doi.org/10.1016/j.ecl.2015.02.002.
2. Merke DP, Poppas DP. Management of adolescents with congenital adrenal hyperplasia. Lancet Diabetes Endocrinol. 2013;1(4):341–52. https://doi.org/10.1016/S2213-8587(13)70138-4.
3. Reichman DE, White PC, New MI, et al. Fertility in patients with congenital adrenal hyperplasia. Fertil Steril. 2014;101:301–9.

4. Miller WL, Witchel SF. Prenatal treatment of congenital adrenal hyperplasia: risks outweigh benefits. Am J Obstet Gynecol. 2013;208(5):354–9.
5. Speiser PW, Azziz R, Baskin LS, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010;95:4133–60.