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Ambiguous Genitalia in an adult female due to classic virilising Adrenal Hyperplasia – A Rare case report

Gynaecology

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ABSTRACT

Congenital Adrenal Hyperplasia is a rare autosomal recessive disorder in which there is virilisation of the female foetus due to production of androgenic hormones, cause being an enzymatic defect in steroidogenesis. According to National Organization of Rare Disorders (NORD), USA, CAH is a rare disease and in Asian region the incidence is about 1:45000 live births. Usually this condition is diagnosed in new born or in children. I am presenting this case because the disease remained undiagnosed in the patient till the age of twenty six years. Patient came in the outpatient department with the complaints of primary amenorrhea and abnormal genitalia. On examination the patient had a pseudo phallus with the masculine appearance of the glans and the persistence of the fusion of the labia majora to resemble a scrotum. Phenotype was male. Vaginal length was normal. USG showed that uterus and adnexa were normal. 17 OH Progesterone was high and Karyotype was 46 XX. Diagnosis of CAH was made. Clitoroplasty was done and postoperatively oral steroids were started. Patient has started menstruating regularly. This case is presented here because it is rarely seen in adults. It enhances knowledge for the treatment options for such patients so that they can lead a happy sexual life and if possible any fertility options that can be offered to them .

Introduction

Ambiguous genitalia have always kept the attention of humanity. Along history of human kind, image of hermaphroditism has been seen from abhorrent to mythologically divine.

The term Congenital Adrenal Hyperplasia (CAH) encompasses a group of abnormal recessive disorders, each of which involves a deficiency of an enzyme involved in the synthesis of cortisol, aldosterone or both(1).Deficiency of 21- hydroxylase, resulting from mutation or deletion of CYP21 A, is the most common form of CAH, accounting for more than 90% of cases.

Classic virilising adrenal hyperplasia is a rare disorder giving rise to ambiguous genitalia. The purpose of the study is to find treatment options for this chronic condition because it affects the patients medically, psychologically and socially.

Case Report:

A 26 year old patient presented in the outpatient department as a case of primary amenorrhoea and abnormal genitalia . Her external body appearance was male type with good muscular development, broad shoulders, prominent thyroid cartilage and male distribution of hair. She was short statured, her height being 151cm. She dressed as a female.On examination the breasts were absent. For the genital organs, the pt. had a pseudophallous, with the masculine appearance of the glans and the persistence of fusion of labia majora to resemble a rudimentary scrotum. Urethra was separate. The vaginal length was normal. Uterus was anteverted and anteflexed and normal in size.

Figure 1:
A: phenotypically male
B: Absent breasts
C:Pseudophallous with prominent glans
D: Urethra and vagina are separate

The patient came from a rural background, lived in abject poverty, was married off by her parents at the age of 16 years, but was abandoned by the husband as he did not find her suitable enough. Her family history showed that she had a younger sister who also had the same problem, that is of primary amenorrhoea, abnormal genitalia, and absent breasts but she had a happy married sexual life with her husband who was a widower and a father, so she refused for any treatment whatsoever. The patient had three brothers, all of whom were normal.

The Complete blood count, blood sugar ., liver functions, renal functions, thyroid function tests, were within normal limits. Serum LH – 14.91ng/ml, S. FSH- 2.99ng/ml, S. Prolactin-19.01ng/ml, S. Insulin-16.6ng/ml, S. Testosterone-186.42ng/ml and 17-hydroxy Progesterone was 231ng/ml. USG upper abdomen including adrenals were normal. Trans Vaginal Sonography showed that the uterus was 4cm × 3cm × 1.8cm. Right ovary was 30mm × 19mm. Left ovary was 30mm × 19mm. MRI whole abdomen was normal. Karyotype was 46 XX. Progesterone challenge test was negative. But she responded to an oestrogen + progesterone combination given for 20 days and had induced menses.

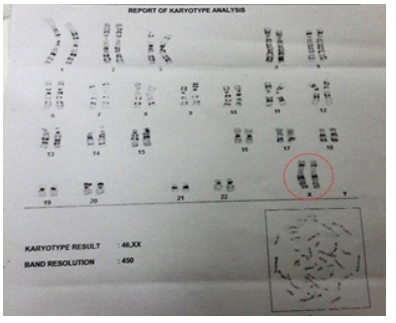

Figure 2 46 XX Karyotype

Diagnosis of Congenital Adrenal Hyperplasia was made based on virilism, high 17-hydroxy progesterone, high serum Testosterone, 46 XX karyotype and normal uterus, tubes and ovaries. Surgery

was planned for correction of the enlarged clitoris resembling a pseudophallus .The corpora cavernosa of the clitoris was removed but important neurovascular attachments were conserved in order to maintain sexual gratification. The method of clitoroplasty involved separating the pseudoglans from the paired erectile tissues and reducing it in size to simulate that of a woman's clitoris.

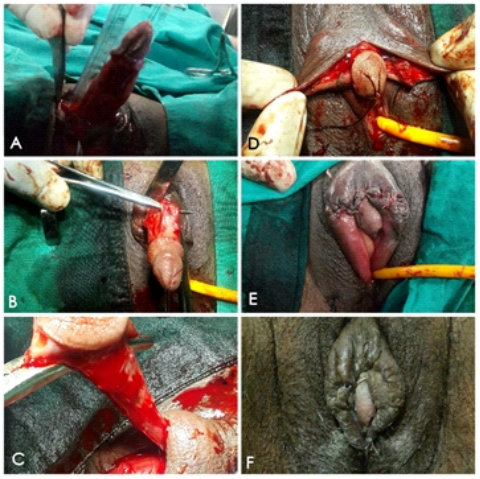

Figure 3:
(A to E): Reconstructive surgery of the pseudophallous (>6.5cm) done to simulate a woman's clitoris
F: final result one month after surgery.

As part of the treatment plan tablet Dexamethasone 0.5mg/day and tablet finasteride 1mg/day were started. Steroid therapy is to be continued lifelong. With this therapy, ovarian and uterine functions become normal and fertility is possible. Patient has started menstruating regularly after three months of therapy.

Discussion:
Ambiguous genitalia are diagnosed at birth or in children and is rarely found in adults. But in this patient due to ignorance, poverty, old belief systems and fear of society, the parents and the patient hid the problem of Virilising Congenital Adrenal Hyperplasia.

Females with severe CAH due to deficiencies of 21-hydroxylase, 11-beta-hydroxylase, or 3-beta-hydroxysteroid dehydrogenase have ambiguous genitalia at birth (classic virilising adrenal hyperplasia); genital anomalies range from complete fusion of the labioscrotal folds and a phallic urethra to clitoromegaly, partial fusion of the labioscrotal folds, or both. Internal female reproductive organs (uterus and ovaries) are normal.

Females with still milder deficiencies of 21-hydroxylase or 3-beta-hydroxysteroid dehydrogenase activity may present in adolescence or adulthood with oligomenorrhea, hirsutism, and/or infertility (nonclassic adrenal hyperplasia). (2)

Females with 21-OHD CAH have a normal 46,XX karyotype. 21-OHD CAH is inherited in an autosomal recessive manner. Most parents are heterozygous for a pathogenic variant. Approximately 1% of pathogenic variants are de novo; thus, 1% of probands have only one parent who is heterozygous. In some instances during evaluation of a proband, a parent not previously known to be affected may be found to have biallelic pathogenic variants and the non-classic form of 21-OHD CAH. At conception, if the parents of a proband are both known to be heterozygotes, each sib has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier. Carrier testing for at-risk relatives and prenatal testing for pregnancies at increased risk are possible if the pathogenic variants in the family are known. (3)In our study, both the female siblings had CAH, while the three male siblings were unaffected.

Congenital adrenal hyperplasias (CAH) are inherited defects of cortisol biosynthesis found in 1:10000 to 1:15000 live births.(4)
A very high serum concentration of 17-hydroxyprogesterone, the normal substrate for 21-hydroxylase, is diagnostic of classic 21-hydroxylase deficiency. Most affected neonates have concentrations greater than 3500 ng/dL (105 nmol/L).

In virilised females, the principal aims of surgery are to reduce clitoris/phallus size, create a vaginal orifice that will allow menstrual flow and intercourse, and to correct the urogenital sinus and vaginal pouch to prevent incontinence. In the past, the surgeons have undertaken early clitoral recession and labioscrotal reduction, followed by vaginal pull-through at 2–4 years of age. Later on, early clitoroplasty and genitoplasty were recommended, definitely by the age of 18 months and in the hands of experienced paediatric surgeons, a single-stage procedure was performed with encouraging results. (5, 6)

Today reduction clitoroplasty, where the glans is preserved and part of the erectile bodies are excised, is the most widely accepted and used technique.Clitorectomy has not been considered a reasonable option for decades. (7)

Life saving glucocorticoid treatment was introduced in 1950's and the number of adult patients is now growing. Adult patients are prescribed a variety of glucocorticoids including hydrocortisone, prednisolone, dexamethasone and combinations.(8)The patient was started with tablet dexamethasone in consultation with an endocrinologist. This has to be continued throughout life and spontaneous menses have started.

Conclusion:
I reported this case because of its rarity. The patient came for treatment in adulthood. Clitoroplasty was done. Clitoral reduction for an enlarged clitoris or pseudophlallus, especially in an adult is a rare procedure, but it provides an excellent cosmetic appearance for female patients.With the medical treatment the patient has now started having normal menses.
Compliance with Ethical Standard
Conflict of interest: There is no conflict of interest.

Disclosure:
The author has no financial disclosure related to the content of this manuscript.

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