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Research Paper

Medical Science

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Disorder of Sexual Development with 46XY Karyotype

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ABSTRACT

A 16-year-old, reared as female presented with complaints of genital ambiguity and primary amenorrhoea along with lack of secondary sexual characters, but without short stature and Turner's stigmata. Karyotype analysis revealed 46XY karyotype.Basal cortisol 15.64µg/dl, Luteinizing Hormone was 4.81mIU/ml and Follicle Stimulating Hormone was 11.23mIU/ml. BasalDi-hydroxy testosterone- 1032 ng/dl ,testosterone of 5.73 ng/dl and Androstenedione of 2.13 ng/ml. Ultrasonography revealed Bilateral testis which appear normal in size, echo texture and vascularity. Epididymis poorly formed. No Mullerian structures seen. No uterus found. Cystogenitoscopy revealed short urethra with normal bilateral ureteric orifices and normal bladder size and echo-texture. Pseudo vagina with separate opening for urethra was seen. Based on these results a diagnosis of 46XY Disorder of Sexual Development (DSD) with partial androgen insensitivity syndrome was made. The patient was managed with a multidisciplinary approach and fertility issues discussed with theparents.

Introduction:

A 16-year-old person, reared as female, born out of non-consanguineous marriage, Hindu by religion, commerce student of XI STD, belonging to extended nuclear family of upper lower class as per modified Kuppuswamy scale presented to our Urban Health Centre with complaints of genital ambiguity and primary amenorrhoea along with lack of secondary sexual characters for which she was referred to Endocrine OPD of our hospital for further evaluation and management in April 2012. The case was reported to health centre because her 3 year younger sister had onset of menarche and her mother became anxious for this index case for not being having any secondary sexual characteristics nor onset of menarche.Other past history, family history, antenatal history, perinatal history, and developmental history were non-contributory.

On examination, anthropometric measurements were appropriate for her age. She is thin built with height of 160cm, weight 45Kg with BMI of 17.57. She was normotensive. Tanner's Sexual Maturity Rating (SMR) was B1, P2-3 with general and systemic examinations being unremarkable. No Turner's stigmata seen.

Genital examination revealed presence of pubic hairs with phallus like structure of length of 2 cm. Bilateral testis were palpable in labio-scrotal fold (2-3cm with 6-8 cc in volume).Blind vagina seen as a perineal opening covered with thin membrane.

Investigations:

Routine biochemical and haematological like CBC, Liver function text or Renal function text were normal.

Other investigations were enlisted in table below:

Sr. No.	Parameters	Observed values	Normal values
1	Calcium	8.0	9.0 -10.5 mg%
2	Phosphorus	2.3	2.5-5.0 mg%
3	Alkaline Phosphatase	5.4	3-13 CAU
4	FSH (Follicular Stimulating Hormone)	11.23	2.5-10 mIU/ml
5	LH (Luteinizing Hormone)	4.81	2.5-10 mIU/ml
6	Testosterone	5.73	F-0.2-0.8 ng/ml M-4.0-11 ng/ml
7	Basal Cortisol	15.64	5-25 microgm/dl
8	DHT (Di Hydroxy Testosterone)	1032	24-368 pg /ml
9	Androsteindione	2.13	0.2-3.1 ng/ml

- Ultrasonography (Abdomen & Pelvis) revealed bilateral testis which appear normal in size, echo texture and vascularity. Epididymis poorly formed. No Mullerian structures seen. No uterus found.
- Cysto-Genitoscopy revealed short urethra with normal bilateral ureteric orifices and normal bladder size and echo-texture. Pseudo vagina with separate opening for urethra was seen.
- Karyotyping from National Institute of Research in Reproductive Health revealed 46XY from 20 analysed blood cells.

Discussion:

This 16-year-old normotensive person reared as a girl came diagnosed as 46XY disorder of sexual differentiation (DSD).Since the basal testosterone level was high, aromatase deficiency and partial androgen insensitivity syndrome (PAIS) were next in the line of diagnostic possibilities. Since patient was reared as female, she and her parents wanted her to be a female gender in future. But functionality of the external genital organs was not expected with absence of ovaries and uterus. So there is need for a combined decision involving the patient, her parents, Gynecologist, Endocrinologist, Social Worker and a counsellor to rule out all the possibilities and decide the feasibility to remove the male gonads and assign a female sex to the patient. Her further management related to surgeries will be taken after completion of 18 years of age.

The 46,XY disorders of sex development (46,XY DSD) are characterized by ambiguous or female external genitalia, caused by incomplete intrauterine masculinisation, and the presence or absence of Mullerian structures. Complete absence of virilization results in normal female external genitalia and these patients generally seek medical attention at pubertal age, due to the absence of breast development and/or primary amenorrhoea.[1]

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The term DSD was proposed for congenital conditions in which chromosomal, gonadal or anatomical sex is atypical. In general, factors influencing sex determination are transcriptional regulators, whereas factors important for sex differentiation are secreted hormones and their receptors. The current intense debate on the management of patients with intersexuality and related conditions focus on four major issues: 1) aetiological diagnosis, 2) assignment of gender, 3) indication for and timing of genital surgery, 4) the disclosure of medical information to the patient and his/her parents.[2]The management of this patient can be difficult as phenotypically females may need multiple staged procedures for clitoroplasty, vaginoplasty, and gonadal biopsies/ gonadectomise with hormonal treatment. These patients are at increased risk of cancer, so it is prudent to remove the non-functional gonadal tissues. [3]These patients usually need a multidisciplinary approach for management, but still long-term data on fertility and functional improvement of each approach of treatment is lacking.

Need to focus on concerns of parents:[4]

- Gender identity
- Peer reviews
- Future security & marriage
- Fertility with future parenting
- Their concern about stigma and discriminations.

Need to focus on patient's concern:

- Possibility whether she can still be reared as girl child
- Convincing about her medical conditions with future treatment outcomes
- Stigma by peer groups.
- Psychological upsets and depression about body image.

Recommendations:

- Privacy, confidentiality, and careful use of language help reduce feelings of freakishness and shyness. [5]
- Outreach teaching at local institutions so that referring Obstetric and Neonatal personnel understand the basics of DSD management.[5]
- Provide integrated care for patients, including initial support to parents.
- Develop and implement an integrated consultation system and multidisciplinary clinic with regular case conferences.
- Implement long-term follow-up of patients and their families to evaluate outcomes, to ensure quality care, and to advance team learning.[5]
- Connect with and educate Community Paediatricians and other health care professionals.
- Reach out to parents and adults with DSDs to grow a local peer support network.
- Providing a consistent liaison from the team to the family allows the family to feel anchored and builds a relationship of trust.
- There is need that these cases must be detected earlier age group so that appropriate treatment and hormonal therapy can be initiated proper time so that the psychological and social problems faced by patients and families can be reduced.

Image:

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