XY GONADAL AGENESIS SYNDROME: OCCURRENCE IN A CHILD

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INTRODUCTION

In a fetus with XY karyotype, normal sex differentiation is mediated by the fetal testes, which is responsible for Wolffian duct stabilization, Mullerian duct regression, closure of the urogenital sinus and urethral groove and growth of the phallus [1].

In pregnancy, insufficient testicular hormone in the male fetus during the gonadogenesis period, leads to phallus formation without structural abnormalities of the genital tract [2], the patients are either phenotypically female or have ambiguous genitalia with 46 XY karyotype [1].

CASE REPORT

A nine years old child, reported to out patient department of Paediatrics, Military Hospital, Rawalpindi, Pakistan with ambiguous genitalia since birth. Her parents were not consanguinous but distant relatives to each other. There was no history of genital abnormalities in either family. The stretched phallus was 3.5 cm. The scrotal sac was rudimentary, not completely fused and the testes were absent (Figure). Urethral opening was present at the tip of phallus. The patient was of average height and built, lying comfortably in bed, well oriented, having blood pressure 100/70 mm of Hg, pulse 90/min and respiratory rate 26/min.The child weighed 22 kg and was 123 cm tall. No axillary or pubic hair were noted. Similarly, no breast development was found. Rest of the systemic examination did not reveal any abnormality. Radiologically, bones were normal for age. Ultrasonographic study did not show the presence of uterus or gonads. Relevent labortry investigations results are given in table.

Serum FSH and LH levels were elevated, however, rest of the hormonal profile was unremarkable. After stimulation with β human chorionic gonadotropin (β-hCG), there was no increase in the testosterone level. Chromosomal analysis revealed a normal male karyotype 46XY with no chromosomal structural defects.

Parents were given treatment options of surgical reconstruction of vagina and clitorectomy along with female steroid replacement therapy at age of puberty or male steroid replacement therapy at puberty age depending upon whether they want to continue rearing the child as female or want to rare as male respectively. parents could not decide yet about the treatment options. The child is being following up monthly in paesiatics out patient department, Military Hospital Rawalpindi for growth monitoring.

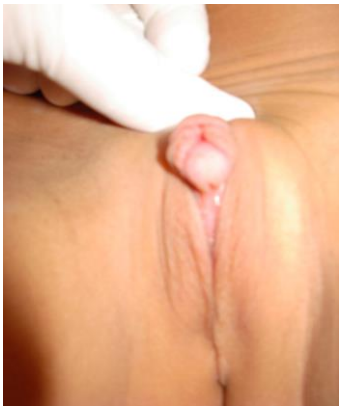

Figure: Phallus with rudimentary and partially fused scrotal sac.

DISCUSSION

XY gonadal agenesis syndrome was first defined as Vanishing Testes syndrome in 1957 [3]. In the patients with 46 XY karyotype, genital elements were absent, moreover the development of genital duct, urogenital sınus and external genitalia were heterogeneous [4].

There is a spectrum of genital anomalies as a result of cessation of testicular function between 8-12 gestational weeks. In this rare anomaly, external genitalia were ambiguous but appeared more like female genitalia, there were labial hypoplasia, small phallus like clitoris, and some degree of labioscrotal fusion. No internal gonadal tract or gonads were usually found in those cases. Mostly the children were reared as females [5]. Other

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Table: Laboratory investigations

Test	Result	Reference Range
1. Blood Hb	12.6	12 – 15 g/dl
2. ESR	8	0 – 15 mm at 1st hr
3. Serum FSH(basal)	34.2	1- 4 mIU/ml
4. Serum LH (basal)	61.6	1.4 – 7.7 mIU/ml
5. HCG stimulation Test		
Serum Testosterone (Basal)	0.02	< 1.7 nmol/l
Serum Testosterone (2 days after 1st inj of hCG (pregnyl) 1000 IU given intramuscular)	0.01	
Serum Testosterone (2 days after 2nd inj of hCG (pregnyl) 1000 IU given intramuscular)	0.01	
6. Serum DHEA-S	40.5	45 – 430 µg/dl
7. Serum E_2(Prepubertal-Basal)	33	18 –220 pmol/l
8. Serum17 OHP (Basal)	2.5	0.1-2.7 nmol/l
9. Serum Progesterone	1.65	0.3 – 4.7 mmol/l
10.Serum Prolactin	205	40 – 530 mIU/l
11.Serum Na^+	137	136 – 149 mmol/l
12.Serum K^+	4.0	3.5 – 5.0 mmol/l
13.Serum Cortisol(basal /morning)	11	5 - 25 µg/dl
14.Serum GH	18.4	0 – 14 mIU/l
15.Thyroid profile		
Serum fT4	11	8 – 24 pmol/l
Serum TSH	3.2	0.4 – 4 mIU/l

FSH: Follicle stimulating hormone; LH: Leutinizing hormone;Hb: Haemoglobin; ESR: Erythrocyte sedimentation rate; 17 OHP: 17 hydroxy progesterone; DHEA-S: Dehydroepiandrostenedione sulphate; GH : Growth hormone; E_2 : Estradiol; fT4: Free T4 ; TSH : Thyroid stimulating hormone .

variables include Swyer syndrome, rudimentary testis syndrome and anorchia [5].

In Swyer syndrome, testicular regression occurs before 8th gestational weeks, where patients have female phenotype along with vagina, uterus and fallopian tubes but the gonads are found in the form of undifferentiated streaks [5].

If testicular regression is occurring between 14th to 20 th gestational weeks, it will result in rudimentary testis syndrome and if after 20th weeks, it will result in anorchia [5], a syndrome characterized by the finding of normal male differentiation both internally and externally but no gonadal tissue [1].

In our patient, considering partial fusion of the labioscrotal folds, no internal genital tract or gonadal presence along with laboratory and imaging studies results, it appears that insult to the testes must have occurred between 8th to 12th week of gestation and the patient profile satisfies the criteria for the diagnosis of XY gonadal agenesis syndrome.

CONCLUSION

In all the cases with ambiguous genitalia, there should be early diagnosis and sex assignment so that the treatment may be started as soon as possible to make the patient fit for the society. The reconstructive surgical treatment as well as hormonal therapy may be given depending upon the assigned sex. The patient must be followed up for supportive psychological therapy if required. Prenatal screening should be performed in families with genetic predisposition.

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