TESTICULAR FEMINIZATION IN THREE CASES OF PRIMARY AMENORRHEA

by

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Testicular feminization syndrome is characterized by female phenotype with XY karyotype. According to Hamerton (1971) these males have female external genitalia, normal breast development and hair distribution, absent uterus and undescended testes. This condition is considered to be due to an X-linked recessive gene. The present study deals with genetic, cytogenetic and endocrinologic aspects in 3 cases with testicular feminization syndrome originally referred to us with a complaint if primary amenorrhea.

Material and Methods

Cytogenetic analysis was carried out on metaphase figures obtained from short term leucocyte cultures. Buccal smears are scraped from each patient, fixed and stained with 2% Toluidine Blue. Two hundred intact vesicular nuclei were counted for X-chromatin frequency. The principle diagnostic endocrinological aid used in this study was the urine determination of 17-ketosteroids described by Appleby and Norymberski (1955). Ultrasonographic scan was performed to detect the abnormalities of the uterus, using ultrasonograph model EP (unirad) Ohio, U.S.A.

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Case 1:

A 24 year old female, born to non-consanguineous parents. She had 2 younger sisters. One sister attained menarche at the age of 22 years, after two months she had secondary amenorrhoea. Another sister aged 20 years also did not attain menarche. The facial appearance and body configuration of the affected were feminine. Her height was 160 cms. and weight was 50 kgs. Her breast development was positive. Axillary hair and pubic hair were absent. External genitalia were of female type. Labia majora well developed and labia minora were not developed. Clitoris was normal. Pathology report revealed that it was a case of testicular feminization syndrome. Well formed testes and epididymis were present. 24 hours urinary 17-ketosteroids were found to be 8.12 mg/24 hours. Laparotomy was performed and the results indicated the presence of testes on both sides joined by fibrous band. There were no uterus or mullerian tissue. The X-chromatin was not observed in the epithelial cells of buccal mucosa and karyotype was 46, XY.

Case 2:

A 35 year old female born to non-consanguineous and healthy normal parents. She had 3 younger sisters. One sister married and got children. Two younger sisters attained menarche. There was no history of similar illness in the family. She had 2 younger brothers and all were normal. She had eunuchoid built. She was 174 cms. in height and weight 72 kgs.

She was married at the age of 18 years but had never been conceived. Although phenotypically a female, she was slightly masculine in appearance with small underdeveloped breast. Per Vagina revealed infantile uterus and cervical length 3.6 cms. No endometrial tissue was obtained. 24 hours urinary 17—ketosteroid level was 19.6 mg. It was just above the range of a normal male. (Mean value of normal male—15 mg. 24 hours). Ultrasonographic scan showed the presence of hypoplastic uterus.

Case 3

A 21 year old female born to non-consanguineous parents. She had 1 younger sister who attained menarche at the age of 18 years. She had 6 brothers, one died after poisoning at 1½ years age. She was married at the age of 20 years. The patient was moderately built and feminine in appearance. Her height was 144.5 cms. and weight 47.2 kgs. On vaginal examination uterus was infantile, oral mucosa was negative for X-chromatin. Chromosome analysis showed 46 XY. Ultrasonographic scan revealed the presence of small uterus. 17-ketosteroid level in the 24 hours urine sample was 8.74 mg.

Discussion

Female phenotype with male karyotype is the most common observation in testicular feminization syndrome (Puck *et al* 1960; Himathonykanu *et al* 1974; Jacobs and Strong 1959). This syndrome is characterized by the presence of female external genitalia, intraadbdominal testes, well developed breasts, amenorrhea, negative X-chromatin, normal levels of follicle stimulating hormone and 17-Ketosteroids. Our patients have satisfied fully, the criteria for the testicular feminization syndrome. The laboratory fndings in these patients revealed a male karyotple (46 XY) negative for X-Chromatin and normal male range of 17-Ketosteroids. In case 1 the condition of amenorrhea seems to be familial. But we do not know the cause for this. It was not possible to carry out investigations in all the affected siblings. Cases 2 and 3 are sporadic. They have male and female and female siblings, whose sexual development is quite normal. Intraabdominal testes were present in all these cases. Thus it looks reasonable that the efficiency of masculinization of sex by Y Chromosome was undoubtable.

In usual course of embryonic development, the sexual differentiation tends to be feminine as X-Chromosome is common in either sex. But this tends to be male with the intervention of Y-Chromosome during sexual differentiation. The Y-Chromosome directs the embryonic indifferent gonads to organize testes. Thus organized testes secrete testosterone which induces all the extra gonadal masculine development. Sitteri and Wilson (1974) studied critically the testosterone formation and metabolism during sexual differentiation in the human embryos and pointed out that testosterone from the fetal testes is necessary for masculinization of the extra gonadal organs in the male fetus. In the present situation, there was no block till the organization of testes, but further development of other male genital organs was not taken up. It means there was some metabolic defect governed by autosomal or sex limited X-born recessive gene(s) which led to the female phenotype in the presence of testes. Several workers have proposed that autosomal or X-linked recessive gene or genes overcome the influence of Y-chromosome on masculinization of sex organs, thus leading to a female phenotype in testicular feminization syndrome (Phansey *et al* 1980; Puck *et al* 1960; Lubs *et al* 1959; Morris and Mahesh, 1963). Therefore, it is reasonable to conclude in the present situation that similar mode of inheritance of such gene(s) played a significant part in the sexual ambiguity of testicular feminization.

Summary

1. Cytogentic, endocrinologic and ultrasonographic investigations were carried out in three cases of testicular feminization syndrome originally referred to us with a complaint of primary amenonhea.

2. All the three cases had 46, XY karyotpye. Cells from buccal mucosa were negative for X-chromatin.

3. 17-ketosteroid level in 24-hours urine sample showed high level in one case.

4. Ultrasongraphic scan revealed the presence of hypoplastic uterus in two cases.

5. Laparotomy revealed the presence of testes in one case.

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