AN INTERESTING CASE OF PURE GONADAL DYSGENESIS (JOST'S SYNDROME) — XY FEMALE

by

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The Gonadal dysgenesis is a relatively rare condition and individual experience of these cases is limited. A case with certain features and problems which have not been previously encountered is reported.

Case Report

Mrs. L. M. aged 25 was admitted on 20th May, 1968, with the history of primary amenorrhoea, inability to have sexual intercourse since her marriage ten months ago and attempted suicide resulting from depression consequent to marital disharmony. In her family the elder sister was happily married and a mother of three children and there was no history of delayed menarche in her family. Nothing significant was noted in her past medical history.

General Examination: Attired in Sari her phenotype was female with natural feminine type of shyness evident during interrogation. Her nutritional status was good. Her height was 5 ft. (152 cm) and there was no facial hirsutism. Breasts were ill-developed (Fig. 1 and 2). Pubic and axillary hairs were scanty. The cardiovascular, respiratory and the nervous systems were normal. Abdominal examination did not reveal any abnormality and there was no swelling in the groin.

Vulvo-vaginal Examination: Labia majora and minora were ill-developed. The clitoris was enlarged to about 2 cm (Fig 3). The urethra opened well away from the clitoris in the anterior part of a shallow depression about 2 cm in diameter and 1 cm depth representing the vaginal orifice. The lining of the depression was rather thin and reddish, the top of which was blind. Rectal examination did not reveal the presence of the uterus.

Special Examination: The chromosomal sex determined from the buccal mucosa, was chromatin negative. The karyotype was 46 XY. There was no structural abnormality in the cells. Intravenous pyelogram was normal. X-ray examination revealed bone age compatible to her chronological age. A search was made to exclude the possibility of undescended testes in the groin or vulval area.

Operation at laparotomy there was no uterus, ovaries or any gonad from the lumbar area down to the pelvis. The adrenals felt normal. The inguinal canal area was also explored to exclude the possibility of undescended testes. Fibrous tissue streaks representing gonads were selected for biopsy examination. The histology revealed only fibrous tissue and there was no evidence of any primordial follicle or epithelial element. The diagnosis was pure gonadal dysgenesis in chromatin negative karyotype male individual (XY Female).

Management: Since the individual was married and willing to have marital relationship as a female, the clitoris was amputated and an artificial vagina was created in the space between the bladder and the rectum. She was placed on intermittent oestrogen therapy, ethinyl oestradiol 0.05 mg daily. The patient was discharged from the hospital after a month, and nothing was heard from her since.

Discussion

The case described is one of pure gonadal dysgenesis, chromatin negative with karyotype 46 XY.

Bishop (1966) discussed the special type of ovarian dysgenesis, "Pure Gonadal dysgenesis", in which the failure of

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the ovaries to develop with the accompanying lack of secondary sexual development is the only manifestation of the syndrome. The stature is not short, in fact these women may actually be tall and there are no congenital anomalies like Turner's syndrome. Brogger and Strand (1965) collected 38 cases from the literature and Bishop in 1966 could find only 23 examples of pure gonadal dysgenesis out of 282 cases of gonadal dysgenesis largely from Polani's series from the Guy's Hospital, London. Of these 23 cases, 7 were chromatin negative and 16 were chromatin positive, only 6 being XY. 9 were XX and the rest were mosaics. The ovarian streaks from chromatin negative XO cases consisted of non-functional fibrous or connective tissue, whereas streaks from other cases showed some epithelial cells. In the XY case reported here the streak gonad contained only fibrous tissue. The XY cases are interesting and Kinch *et al* (1965) suggest that these are really cases of gonadal agenesis which are, however, genetically male. Jost (1947) showed removal of gonads of a rabbit foetus in early embryonic life before gonadal differentiation will result in the birth of a rabbit with female phenotype even though it may have been destined genetically to be a male. This is because it lacks the male evocator, nor does the foetal ovary produce oestrogen, so that if the gonads are ovaries or are absent, the phenotype is female. These XY cases of gonadal dysgenesis (agenesis) might therefore be described as Jost's syndrome. Judd *et al* (1970) reported a case of pure gonadal dysgenesis with progressive hirsutism in an individual with bilateral streak gonads with 46 XY chromosome constitution and believe that oestrogen deficiency caused increased gonadotrophin production which in turn stimulated excessive androgen production by hilus cells and perhaps also the luteinised stromal cells found in the gonadal streaks in their case. Out of 4 cases of XY female reported by Dewhurst (1967), there was only one case, with neither recognizable testicular tissue nor a uterus, and the clitoris was almost normal in size. The author quoted the references of 14 patients of predominantly male phenotype who were examples of anorchism although their karyotype was not known (Burns *et al*, 1963), in addition there have been reports of 6 patients of female phenotype in whom no gonad could be found, one of these was known to be XY chromosomal structure (Dewhurst, Paine and Blank 1963), and the rest to be chromatin negative.

Ballester *et al* (1970) reported familial gonadal dysgenesis in 3 sisters of normal stature, aged 28, 17 and 14 with primary amenorrhaea and sexual infantilism. All had a positive buccal smear with normal 46 XX karyotype. These girls had deafness and speech defect without any congenital deformity, such as webbing of the neck or coarctation of the aorta. Of the 39 cases found, a normal XX pattern was found only once in a girl of short stature, but in almost half of these with normal and tall stature.

In view of the varied cytogenetic pattern in gonadal dysgenesis ranging from a normal XX pattern to all sorts of mosaicism it is rather difficult to postulate the cause of failure of ovarian development. In fact, the cause is not really known. The suggestions are that it is faulty genetic or gonadal development, it could be either or both. Dewhurst (1967) described cases of XY female and observed that those without any visible masculine features will probably be examples of pure gonadal dysgenesis due to complete testicular failure in the very early embryo resulting in total failure of masculinization and

of inhibition of Mullerian structures, and in patients with evidence of masculinization of the external genitalia less early or less complete testicular failure will permit some male differentiation and may have a greater or lesser effect on Mullerian inhibition. Ballaster *et al* (1970) believe primary interference in ovarian histogenesis may be a possible aetiologic factor. Jones *et al* (1958) explain cases with normal XX chromosomes as missing mosaic pattern in which an abnormal chromosome component is present only in those cells of the embryo which give rise to the primitive germ cells. Surprisingly, Carr, Haggar and Hart (1968) demonstrated the presence of germ cells in gonads from abortuses with a chromosomal component of 45 XO. Furthermore, on histological sections of the XO and XX gonads from abortuses, they did not find any significant histologic difference between them upto 3rd intra-uterine month. The presence of germ cells in the gonad of the XO foetuses is in contrast to their absence in XO adults. Grumbach *et al* (1958) suggest that gonadal dysgenesis might be a primitive disturbance affecting the germ plasm between the 8th and 10th week due to a deleterious environmental agent of unknown aetiology. The occurrence of fimilial gonadal dysgenesis amongst sisters suggests that the condition is genetically determined (Ballister *et al*, 1970). Single gene mutation or minute chromosomal deletions may also be responsible for this malady.

The normal karyotype found in our case (46 XY), chromatin negative genetically male harbouring streak gonads with fibrous tissue, does not rule out the possibility of mosaicism. The special feature of this case was that the individual had an enlarged clitoris with heterosexual female instinct, and since she was already married, the clitoris was amputated, a vagina was created. Jeffcoate (1958) rightly believes that these intersexed individuals are not strongly sexed in either direction.

Summary

A case of pure Gonadal dysgenesis in a married phenotype female individual with chromosomal chromatin negative 46 XY is reported. A brief review of the literature is made and the problems of management is discussed. The patient had streak gonads consisting of fibrous tissue only on microscopical examination. The individual had an enlarged clitoris with heterosexual instinct and since she was already married, the clitoris was amputated and an artificial vagina was created.

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See Figs. on Art Paper VI-VII