STREAK GONADS IN RELATION TO PRIMARY AMENORRHOEA

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SUMMARY

One hundred and eighty cases of primary amenorrhoea were thoroughly investigated. Streak gonad was found in 62 (34.44%) cases. Different varieties of gonadal streaks included—classical Turner's Syndrome—37 cases, atypical Turner's Syndrome—9 cases Pure Gonadal Dysgenesis—11 cases and other rare varieties like Turney's phenotype with breast development, 45 XO without physical abnormality, 45 RO/46 XX mosaicism with delayed menarche, unilateral gonadal dysgenesis etc. in 5 cases. Phenotype—genotype relationship is not an all or none phenomenon. Neither all patients with chromosomal aberration do possess streak gonad nor all streak gonad patients have some chromosomal abnormality. Contrary to previous belief pure gonadal dysgenesis is not a rare disease.

Introduction

Primary amenorrhoea is an important problem to the gynaecologists because of its difficulty in proper diagnosis as well as treatment. It has a wide range of etiological factors of which primary ovarian failure due to streak gonads is possibly the commonest one.

Turner (1938) described the tetrad of sexual infantilism, webbing of neck, cubitus valgus and short stature in 7 girls aged 15-23 years. Later discovery showed the presence of streak ovaries and absence of one X chromosome in such patients—they are known as classical Turner's Syndrome. At present with better facilities for biochemical and cytogenetic studies it has been possible to identify a wide variety at chromosomal aberration with gonadal streaks. Presence of two normal X chromosomes are essential for development of a functioning ovary. Genes are present in both short and long arms of X chromosomes. If one X chromosome is totally absent or any of its arms is deleted primordial germ cells cannot organise gonadal tissue to differentiate into pregranulosa cells and subsequent follicle formation. Germ cells quickly die away and the gonad turn into a streak fibrosed one. But streak gonads also occur in normal genotype female (46 XX) or even male (46 XY) person known as Pure Gonadal Dysgenesis.

Material and Methods

All primary amenorrhoea patients attending out patients department in our unit of Obstetrics and Gynaecology during the period 1982-86 have been investigated. History taking and clinical examination

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was done in the standard protocol. Buccal smear was routinely taken after cleansing the mouth with plain water. Smear was fixed in alcohol-ether solution, stained and examined for presence or absence of Barr body.

Specific investigation was done according to the guideline obtained from history and examination. Gonadotrophin assay, laparoscopy and karyotyping were done in suspected cases of streak gonads (Amenorrhoea with hypoplastic uterus and underdeveloped secondary sex characters with or without short height and physical stigmas). Karyotyping was done from blood leukocytes after processing and adding Colchicine (to halt cell division at metaphase stage) and staining with giemsa. Microphotography was cut, arranged in Denver's system and studied for any abnormality. Laparotomy and gonadal biopsy was done in selected cases. Gonadectomy was done in patients having Y Chromosoms.

Results

Two hundred and forty seven primary amenorrhoea cases were included in the series. 67 patients did not turn up in subsequent visit/s to complete the investigations. So a total of 180 cases were accounted out of which 62 (34.44%) had streak gonads.

Different types of streak gonads are shown in Table I. Classical Turner's Syndrome with sexual infantilism, short stature, webbing of neck and one or more was found in 37 (59.67%) cases. Atypical Turner's Syndrome was found in 9 (14.50%) cases—8 were mosaic Turner's Syndrome with 45 XO/46 XX and one patient had short arm deletion (46 XXp-, Fig. 1) in karyotyping report. Pure gonadal dysgenesis occurred in 11 (17.74%) cases—7 had normal female (46 XX) and 4 had normal male (46 XY) chromosomal patterns. Other rare and interesting varieties of gonadal dysgenesis was found in 5 (8.10) cases as follows—(a) One case of Turner's phenotype with breast development and no other secondary sex characters, karyotype being 45 XO. (b) One case with streak gonads and without any physical stigmas. (c) One case of 45 XO/46 XX mosaicism (Fig. 2) having normal height, scanty pubic and axillary hairs and some breast development (Fig. 3). While under investigation she had spontaneous menarche at the age of nineteen and half. Her ovarian biopsy showed the presence of scattered immature and atretic follicles. (d) Two cases of

TABLE I
Types of Streak Gonads

	Diagnosis	No. of patients	Percentage
1.	Classical Turner's Syndrome (45 XO)	37	59.67
2.	Atypical Turner's Syndrome (with other types of chromosomal aberration)	9	14.50
3.	Pure gonadal dysgenesis	11	17.74
4.	Other varieties	5	8.10
	Turner's phenotype with breast development (45 XO)	1	
	Turner's genotype without physical abnormality	1	
	Mosaicism (45 XO/46XX with ovarian follicles & menstruation	1	
	Unilateral gonadal dysgenesis	2	

unilateral gonadal dysgenesis with delayed puberty. One of them showed unilateral breast development.

Height of the patients was shown in Table II. As people of this subcontinent are comparatively shorter in height, length below 145 cm was taken as short height. There was 47 short statured, 14 medium statured and one lanky patient. Later was 167 cm. tall and eunuchoid. She was ultimately proved to be a case of pure gonadal dysgenesis by karyotyping. Mean height of the Turner's Syndrome cases was 136 cm and that of pure gonadal dysgenesis was 155 cm.

TABLE II
Physical Heights of the Patients

Height	No. of patients	Percentage
Below 145 cm	47	75.80
145—160 cm	14	22.58
Above 160 cm	1	1.62

Secondary sex characters were mostly underdeveloped. None reached Tanner's stage 5 of puberty development (Table III).

TABLE III
Secondary Sex Characters (As per Tanner 1969)

Stages of development	No. of patients	Percentage
P 1 and 2	57	91.93
P 3	3	4.84
P 4	2	3.23
P 5	Nil	—

P = Puberty.

Different physical stigmas included—increased carrying angle in 9 patients, webbing of neck in 4 patients, coarctation of aorta with hypertension in 2, shield chest in 1, horse-shoe kidney in 1 and short 4th toe in 1 patients. Mental deficiency was suspected in 3 cases of Turner's Syndrome and 1 case of pure gonadal dysgenesis. Serum FSH value ranged from 28-117 mIU/ml (Normal adult value upto 30 mIU/ml).

Discussion

Incidence of streak gonad among primary amenorrhoea patients was 34.44%. According to different authors it is 33.18% by Gum *et al*, 1978, 43.0% by Riendollar *et al*, 1981 and 35.4% by Pal, 1984. Out of 62 cases of streak gonads 46 (74.2%) presented with Turner's Syndrome and 16 (25.8%) had other type of abnormalities mostly pure gonadal dysgenesis. Among 46 patients with Turner's Syndrome 37 (80.4%) had 45 XO karyotyping. According to Jones (1984) two thirds of Turner's Syndrome possess 45 XO karyotyping.

XO karyotype does not necessarily mean Turner's Syndrome with classical tetrads of sexual infantilism, short stature, webbing of neck and physical stigmas. There was one case with breast development and another case with normal height and no other stigmas of Turner's Syndrome. Jacobs (1969) stated that genes responsible for normal development of physical structures are situated in the short arm of the X chromosomes and that short arm of both X chromosomes must be present in the female for normal development. Above mentioned two cases donot tally with this theory. There may have some other extra-chromosomal factor modulating the physical development.

Mosaic chromosomal pattern was found in 11 cases. Among different possibilities all were 45XO/46XX. Eight patient presented as mosaic Turner's Syndrome, two as unilateral gonadal dysgenesis and one with scattered follicles in both ovaries and

delayed menarche. Presence of XX chromosomes in mosaic karyotyping tends to deviate classical Turner's picture towards normal female (Ferguson-Smith, 1965).

Another interesting group is pure gonadal dysgenesis or chromosomally compatent ovarian failure (C.C.O.F.)—where there is no chromosomal abnormality. Karyotype is of normal female (46XX) or male (46XY) type. As all patients with chromosomal aberration donot possess streak gonads (even pregnancy is reported in 45XO patient by King *et al*, 1978), likewise all patients with gonadal streaks not necessarily have some chromosomal abnormality. In pure gonadal dysgenesis pathology is beyond chromosomal level e.g. environmental damage to the gonads during embryogenesis by infection (specially viral one), drugs etc. Similarly damage by autoimmunity may be a possibility. Absence of H-Y antigen explains most of the patients with 46XY chromosomes (Wachtel, 1979). Besides 46XX dysgenesis may be a genetic disorder carried by autosomal recessive gene (Simpson, 1972)—thus it may run in families. Whatever may be the cause if gonads are damaged before the stage of gonadal differentiation development will be along female line (Jost's Theory of Neutral Sex). Contrary to previous belief pure gonadal dysgenesis is not a rare disease. In the present series it was found in 11 (17.74%) cases—4 having normal male and 7 having normal female chromosomal pattern. There was one familial pure gonadal dysgenesis (46XX) involving first and third sibling. Unlike Turner's Syndrome they were normal or tall statured and possessed no stigma. Karyotyping finally decided. Normal female karyotyping may lead one to think in favour of hypogonadotrophic hypogonadism which was differenciated by plasma gonadotrophin assay. In all the four patients with 46XY karyotyping streak gonads were removed by laparotomy to exclude the chance of malignancy.

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See Figs. on Art Paper I