CYTOGENETIC STUDIES IN PRIMARY AMENORRHOEA

By

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SUMMARY

Chromosomal aberrations (45, X0; 45, X0/46, XX and 46, XY) were detected in 7 (30.4%) of the 23 patients. Patient with sex chromosome monosomy had clinical stigmata of Turner syndrome while the patient with 46, XY chromosomal constitution had clitorial hypertrophy, lack of breast development and sparse pubic and axillary hair. In none of the 5 patients with mosaicism (45, X0/46, XX) clinical stigmata of Turner syndrome were detected except for short stature in one of them. Buccal smear examination and lack of development of secondary sex characters were found to be non-contributory as far as chromosomal consitution was concerned. This high frequency of chromosomal abnormality in an otherwise unsuspected patients of primary amenorrhoea on clinical grounds stresses the diagnostic importance of karyotyping in the evaluation of patients of primary amenorrhoea.

Introduction

Variation in the sex chromosome complement adversely affects pubertal development. In females it constitutes an imporant cause of primary amenorrhoea (Jaffe, 1978). Its incidence however, has varied from 19 to 83 per cent in different series (Philip *et al*, 1965; Jagielo *et al*, 1966; Kallio, 1973; McDonnough *et al*, 1977; Mulye *et al*, 1983; Pal, 1984). Clinically, certain somatic stigmata have been indentified to be commonly associated with such patients. Sarkar *et al* (1983) reported a close correlation between the severity of the clinical syndrome and the abnormal cell line population in Turner mosaics. Lidsten (1963) and Engel *et al* (1965) on the other hand reported lack of such correlation between abnormal chromosomal pattern and clinical features. We studied clinical and cytogenetic profiles of primary amenorrhoea patients so as to verify the incidence of chromosomally incompetent (other than 46, XX) ovarian failure and its clinical correlations.

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Material and Methods

Twenty three unselected patients of primary amenorrhoea attending the Endocrine Unit of the University Hospital were studied. The diagnosis of primary amenorrhoea was made when menarche

did not occur upto the age of 16 years (Frische, 1971). Clinical examination of these patients included anthropometric measurements, assessment of secondary sex characters and genital examination both external and per vaginal/rectal. In addition detailed systemic review and general examination for Turner stigmata were also done. Each of these patients was subjected to buccal smear examination (for sex chromation), cytogenetic studies by chromosomal culture (Bamevai *et al*, 1981) and other laboratory studies.

Observations

Clinical Profile

The age group of patients studied ranged from 16 to 26 years although majority (89.6%) of them were below the age of 22 years. Short stature (height below 5th centile for the age) was observed in 4 (17.3%) patients. Clinical stigmata of Turner syndrome in the form of short 4th and 5th metacarpals and metatarsals, webbing of neck and shield like chest were present in one patient only. Pubic hair was absent in 10 (43.4%) patients and there was lack of breast development in 9 (39.1%) patients. Genital examination revealed hypoplastic uterus in 12 (52.17%), vaginal agenesis in 3 (13.03%), transverse vaginal septum and clitorial hypertrophy in one patient each. In 9 (39.1%) patients uterus could not be felt (Table I).

TABLE
Clinical Profile of Primary Amenorrhoea Patients
(n = 23)

Parameter	n (%)
Age pattern	
Upto 18 years	9 (39.13)
19-22 „	11 (47.83)
23-26 „	3 (13.04)
Short stature (<5th percentile)	4 (17.39)
Eunuchoid Features	2 (8.69)
Broad shoulders	1 (4.34)
Turner stigmata	1 (4.34)
Lack of pubic hair development	10 (43.47)
Lack of breast development	9 (39.13)
Gynaecological Examination:	
Hypoplastic uterus	12 (52.17)
Uterus non-palpable	9 (39.13)
Transverse vaginal septum	3 (13.04)
Vaginal agenesis	1 (4.34)
Clitorial hypertrophy	1 (4.34)

Cytogenetic Studies

Buccal smear was positive for Barr bodies in 21 (91.36%) patients and was negative in the remaining 2 patients. Karyotyping of Barr body positive patients revealed 46, XX pattern in 16 (75.2%) and 45, XO/46, XX mosaicism in the remaining 5 (24.8%) patients. Of the two buccal smear negative patients, one had 45, XO and the other had 46, XY chromosomal constitution (Table II). This patient with 46, XY karyotype had clitorial hypertophy and lack of breast development while the patient with 45, XO pattern had Turner stigmata. Rest all of the 5 patients with cytogenetic abnormalities (45, XO/46, XX mosaicism) were found to have none of the stigmata of Turner syndrome except for short stature in only one of them.

Discussion

Primary ovarian failure generally accounts for a sizeable proportion of patients of primary amenorrhoea (Reindollar *et al*, 1981). Such patients could be chromosomally competent (46, XX) or incompetent (other than 46, XX group). The relative incidence of this chromosomally incompetent patients in primary

TABLE II

Cytogenetic data in cases of primary amenorrhoea (n = 23)

Name	Age	Sex chromatin	Cytogenetic data							
			Chromosome count				Karyotype	Percentage		
			45	46	47	Total cell count		46, XX	45,XO	46, XX
DD	25	+ ve	25	87	0	112	45, XO/46, XX	77.68	22.32	0.0
GD	18	+ ve	0	73	9	73	46, XX	100.00	0.0	0.0
AK	18	+ ve	0	55	0	55	46, XX	100.00	0·0	0.0
NC	15	+ ve	11	27	0	38	45, XO/46, XX	71.06	28.94	0.0
SA	18	+ ve	0	50	0	50	46, XX	100.00	0.0	0.0
S	19	— ve	0	120	0	120	46, XY	0.0	0.0	100.00
S	20	+ ve	0	23	0	23	46, XX	100.00	0.0	0.0
N	18	— ve	130	0	0	130	45, XO	0.0	100.00	0.0
S	18	+ ve	0	72	0	72	46, XX	100.00	0.0	0.0
AG	19	+ ve	0	63	0	63	46, XX	100.00	0.0	0.0
SL	18	+ ve	0	42	0	42	46, XX	100.00	0.0	0.0
RN	19	+ ve	13	82	0	95	46, XX/45, XO	86.32	13.68	0.0
S	21	+ ve	0	120	0	120	46, XX	100.00	0.0	0.0
R	19	+ ve	0	45	0	45	46, XX	100.00	0.0	0.0
S	18	+ ve	32	59	0	91	46, XX/45, XO	64.84	35.16	0.0
TD	20	+ ve	0	82	0	82	46, XX	100.00	0.0	0.0
S	19	+ ve	0	92	0	92	46, XX	100.00	0.0	0.0
K	18	+ ve	0	35	0	35	46, XX	100.00	0.0	0.0
N	18	+ ve	0	22	0	22	46, XX	100.00	0.0	0.0
U	21	+ ve	0	56	0	56	46, XX	100.00	0.0	0.0
SK	19	+ ve	0	36	0	36	46, XX	100.00	0.0	0.0
SN	19	+ ve	8	69	0	77	46, XX/45, XO	89.61	10.39	0.0
VK	18	+ ve	0	38	0	38	46, XX	100.00	0.0	0.0

amenorrhoea however, has 'varied from 19 to 83 per cent in different studies (Philip *et al*, 1965; Rao, 1978; Mulye *et al*, 1983; Pal, 1984). In our patients chromosomal abnormalities accounted for primary amenorrhoea in 30.4 per cent, and amongst them chromosomal mosaicism (45, XO/46, XX) accounted for 21.7 per cent. In contrast, McDonnough *et al* (1977) reported mosaicism in 53 per cent, Philip *et al* '(1965) in 9 per cent and Kallio (1973) in 2 per cent of their patients. Mulye *et al* (1983) observed mosaicism in 22.2% of their patients which is similar to our observations.

Sex chromosome monosomy in our patients was detected in only one of them. Clinically she had the stigmata of Turner syndrome. Mulye *et al* (1983) observed sex chromosome monosomy in 38.9 per cent, Protuondo *et al* (1984) in 19.7 per cent, Philip et al (1983) in 12 per cent and Kallio (1973) in 9 per cent of their patients. Similarity, 46, XY' chromosomal pattern, possibly representing gonadal dysgenesis, was also detected in only one of our patients. She had clitorial hypertrophy and lack of breast development and sparse pubic and axillary hair. She was of normal stature. In other reports the incidence of 46, XY gonadal dysgenesis has also been variable. It has ranged from zero to 18 per cent (Jagiello *et al*, 1966, Philip *et al*, 1965; Mulye *et al*, 1983). These variabilities in the incidence of the various chromosomal abnormalities in patients of primary amenorrhoea perhaps seems to be related to differences in the criteria of patient selection and the sample size studied.

Clinically, only 2 of the 6 patients with either 45, XO/46, XX or 45, XO constitution were short statured and the stigmata of Turner syndrome were present in only one of them who had sex chromosome monosomy while in other reports all the 100 per cent of patients with abnormalities of sex chromosome (both monosomy and mosaicism) have been reported to have one or the other stigmata of Turner syndrome (Portuondo *et al*, 1984). Sarkar *et al* (1983) and Mulye *et al* (1983) reported a correlation between the serverity of clinical syndrome and the relative frequency of abnormal cell population, however, we could not observe such a correlation. We also did not observe any correlation between development of secondary sex characters and the sex chromosome constitution of the patient. Lidsten (1963) and Engel *et al* (1965) have also made similar observations.

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