Turner's Syndrome in a Phenotypic Male with XO/XY Mosaicism and Autosomal Aberrations

ALIDE M. C. URMENYI, MYRA K. BEATTIE, and M. R. MIRZA

From the Department of Pathology, Area Laboratory at West Park Hospital, Epsom, Surrey, and Brookwood Hospital, Surrey

In a recent review of 307 reported cases of Turner's syndrome, Ferguson-Smith (1965) noted 22 phenotypic females and male pseudo-hermaphrodites with XO/XY karyotype. Only 11 cases of phenotypic males were found and all of these had an XY karyotype. Heller (1965) in a review of 43 recorded cases noted that only 7 cases of phenotypic males with testicular maldevelopment had been analysed, and of these only one showed abnormal chromosome complement, 46/47-XX/XXY, chromatin positive. In a study of 5 new cases of Turner's syndrome in phenotypic males he found one case with aberration of autosomes in the C group and an extra chromosome in G group.

The purpose of this paper is to report a phenotypic male with XO/XY mosaicism who also showed aberrations of chromosomes in C and E groups and breaks and gaps in A and B groups (Fig. 1-4, Tables I and II).

Case Report

A phenotypic male was admitted to Brookwood Hospital as a certified patient in November 1924, suffering from delusions of a sexual nature. His age on admission was 33 years. He was single, height 5 ft. 6½ in. (170 cm.), weight 118 lb. (49 kg.), and he was a butler by occupation. Physically he was rather thin but in fair health. Both testicles were 'undescended' and the penis was puerile; the neck was webbed, pubic hair was scanty, and his voice was unbroken. He was simple and childish, disconnected in conversation, and unable to give a reliable account of himself. He was diagnosed as 'feeble-minded individual with dementia praecox'.

Personal history. He was illegitimate and there were no sibs. His early childhood is not known. He reached 7th standard at school; and joined the army during 1914-1918 war, being invalided out after 16 months of service. He went to America and spent two years in a mental hospital. He was repatriated, and

within a few days of arrival was admitted to Brookwood Hospital where he remained for 41 years.

Family history. The mother, now aged 96, was originally an employee of the father, probably as a domestic. The father was aged 40 at the time of the birth of the child. The mother later married another man, and there were no offspring of this union.

Progress. His mental condition remained unchanged apart from deterioration with ageing. He was found to have an enlarged heart and irregular heart sounds in 1951 (previously normal). The blood pressure was not recorded. Chest X-rays showed generalized cardiac enlargement. About the same time gynaecomastia and 'barrel shaped' chest were noted, and attacks of congestive failure developed. In June 1965, following an attack of cerebral embolism which caused Jacksonian epilepsy and right hemiplegia, he was seen by Dr. Oliver Garai who noted the stigmata of Turner's syndrome. The blood count was normal. ESR 64 mm./hr. (Westergren). Buccal smears were chromatin negative. Chromosomes were cultured from blood (Tables I and II). Skin culture was negative. Urinary steroids—17-ketosteroids 1.1 mg./24 hr.; 17 OH-corticosteroids 4.1 mg./24 hr. Although he partially recovered from the effects of right hemiplegia, his heart condition became progressively worse, and he died of congestive cardiac failure on September 8, 1965, at the age of 73 years.

Post-mortem findings. Necropsy was carried out 39 hours after death, by M. K. Beattie.

Body of an obese elderly male; height 5 ft. 4 in. (162 cm.); arm span 5 ft. 6 in. (167 cm.). There was oedema of the legs; hypoplastic genitals; scanty pubic hair; shield chest; webbing of neck; low-set ears. The skull bones and meninges were normal. The brain weighed 1362 g. There were two areas of cortical damage consistent with cerebral embolism noted in left frontal and parieto-occipital lobes. There was no evidence of poly-microgyria or other congenital defect reported by a neuropathologist (Dr. J. B. Brierley). The pituitary gland was enlarged, weighing 960 mg. In the thorax there was copious free fluid in the pleural

FIG. 1. Propositus. Above, metaphase plate containing 46 chromosomes; below, karyotype of the same cell XY.

TABLE I
NUMBERS OF METAPHASES COUNTED AND ANALYSED

	44	45	46	47	48	Polyploid	Total	Analysed
Propositus	1	9	19	1		2	32	12
Mother	1	3	11	1	1	1	18	6

TABLE II
ABNORMALITIES FOUND ON ANALYSIS

	A	B	C	DEF	G	X	Y
Propositus	1 break	2 gaps	3 monosomy; 1 trisomy; 1 very small	E 16: 4 small; 2 short arm deletion E 16: 1 monosomy; 1 trisomy; 3 small	—	1 break in small arm	3 missing
Mother	—	—	1 monosomy		1 small	3 Deletions in long arm	—

FIG. 2. Propositus Above, metaphase plate containing 45 chromosomes; below, karyotype of the same cell XO. Note small E 16.

cavities; the lungs were oedematous. The heart was enlarged, weight 695 g. Both atria and ventricles were dilated and hypertrophied. There was old infarct of the left ventricle; and mural thrombi in both ventricles. The aorta was 2 cm. in diameter. Examination of the abdomen revealed that apart from massive congestion and oedema all the organs were normal except the left kidney which was situated low in the abdomen. In addition to hydronephrosis and a few minute stones in the pelvis, several cysts, apparently congenital in origin, were seen. No testicles were found in the scrotum or in the inguinal canals. A small fibrocystic structure, which

appeared to communicate with the vas deferens, was found at the left internal abdominal ring: this was taken for section. Seminal vesicles and vasa deferens were present; the prostate was small. The adrenals, thyroid and parathyroid were normal.

Histological studies. *Fibrocystic structure at internal abdominal ring:* on serial sections no testicular tissue or interstitial cells were found. Vas deferens was only found along with cystic structure lined by endothelial cells, ? cystic remnant of processus vaginalis.

Pituitary. Large pituitary weighed 960 mg. Pars

FIG. 3. Propositus. Above, metaphase plate containing 45 chromosomes; below, karyotype of same cell XY. Note small arm deletion of E 16 and deletion of one chromosome of ? 11 or 12.

anterior showed deeply staining basophilic cell hyperplasia invading the pars posterior.

Prostate. This was small. There was hypoplasia of acinar and muscular tissue.

Adrenals, thyroid, parathyroids. Normal histology.

Left kidney. In addition to a large cystic area, small cysts lined by cubical epithelium were seen in the cortex unconnected with the renal pelvis. A few small renal stones were present. The remnant of renal tissue at the periphery showed evidence of chronic pyelonephritis. The appearances suggested simple cysts of anomalous development, in addition to secondary pyelonephritis and hydronephrosis.

Right kidney. Glomeruli appeared larger than normal suggesting hypertrophy. There was arterio- and arteriolar-sclerosis.

Chromosome Studies in the Mother. At the time of death of the propositus it became possible to obtain

blood from his mother but only a small number of metaphases were found suitable for counting (18 in all); 3 deletions were noted in the long arm of the X (the propositus had shown one break in the short arm). The autosomes in Group C and E were abnormal in the mother (as in the son) (see Fig. 3, 5, and 6, and Table II).

Discussion

The case described is an example of XO/XY mosaicism in a phenotypic male. This is a rare condition; one case with hypospadias, retention of right gonad, and obesity has been reported by de la Chappelle and Hortling (1963). The fact that the vas deferens was persistent may be taken as an indication of the presence of foetal testicular hormones. It is generally believed that during foetal

FIG. 4. Propositus. *Above*, metaphase plate containing 47 chromosomes; *below*, karyotype of same cell XY. Note trisomy of C group ? 11 or 12.

FIG. 5. Mother. Karyotype of cell, XX, 45 chromosomes. Monosomy of C group and deletion of long arm of X.

Fig. 6. Mother. Karyotype of cell, XX, 45 chromosomes. Monosomy of E group and deletion of long arm of X.

life the male hormones prevent the mesonephric duct from degenerating, and at the same time inhibit the normal development of the paramesonephric or Müllerian duct, from which the female genital ducts and uterus develop. Streak gonads were not found in this case, but by the age of 73 complete atrophy of the rudimentary gonads might well be expected. The basophilic cell hyperplasia observed in the pituitary and the very low urinary ketosteroid could be explained by the absence of circulating testicular hormones.

In addition to the absence of Y in a proportion of cells of the propositus, chromosome analysis revealed a variety of abnormalities in both son and mother, C and E groups being involved in both, and it is of some interest in Heller's case that abnormalities of chromosomes in the C group were also present. Deletion of the long arm of the X in 3 cells of the mother might be of significance, so that maternal transmission is a possibility to be considered.

Summary

An elderly phenotypic male is described with Turner's syndrome, anorchia, congenital cysts of the kidney, mental subnormality with schizophrenic overlay, XO/XY karyotype, and aberrations of chromosomes of the C and E groups. Examination of a limited number of metaphases cultured from the mother's blood suggested the possibility of maternal transmission.

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