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A Patient with 45XO/48XYYY Mosaicism

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Many cases of chromosomal mosaicism of the XO/XY type have been described. The phenotype of these patients has shown a wide diversity. In a recent review of 19 published cases in which the XO/XY sex chromosome pattern was established (Jackson, Hoffman, and Makda, 1966), 14 were apparently female and 5 male. The occurrence of XO/XYY mosaicism has been reported less often. Jacobs, Harnden, Buckton, Court Brown, King, McBride, MacGregor, and Maclean (1961) and Cooper, Kupperman, Rendon, and Hirschhorn (1962) each described a phenotypic female with XO/XYY mosaicism, while Trowell and Hamilton (1965) recorded a similar chromosome pattern in a phenotypic male. The present report describes a male pseudohermaphrodite who was found to have XO/XYYY mosaic sex chromosome pattern.

An XYYY sex chromosome complement has rarely been observed. Townes, Ziegler, and Lenhard (1965) reported such a pattern in a 5-year-old boy with 48 chromosomes. However, mosaicism of the XO/XYYY type has not been previously described.

Case Report

Clinical Findings. L. H. is the second child of healthy non-consanguineous parents (maternal age 24 years, paternal age 26 years). An elder sister is normal. Pregnancy was uneventful and delivery normal. At birth (February 1959) the child weighed 2834 g. (6 lb. 4 oz.) and was noticed to have a short curved phallus, with scrotal hypospadias. The testes could not be felt in the bifid scrotum. No other physical abnormalities were noted. A buccal smear taken two months after birth showed no sex chromatin, and urinary steroid excretion was normal. It was decided to bring up the child as a male.

At 4 years of age he was admitted to hospital for correction of chordee preparatory to repair of the hypospadias. A repeat buccal smear was sex chromatin negative and no drumsticks were observed in peripheral blood films. At laparotomy (January 1963) a uterus with blindly-ending Fallopian tubes was found. There was no visible left gonad, and a biopsy was taken from the right gonad which was of normal size. A sinogram performed during the operation showed that the 'urethra' communicated by an apparently normal vagina with the uterine cavity and that the Fallopian tubes were partly patent. The biopsy of the gonad showed well-formed testicular tubules; there was no evidence of ovarian stroma.

The child is apparently of normal intelligence. His height and weight are at the sixth centile, but his parents are both short (father 165 cm. (5 ft. 5 in.); mother 152 cm. (5 ft.)) and of stocky build.

Chromosome Studies. Chromosome preparations were made by a modification of the short-term peripheral blood culture method of Moorhead, Nowell, Mellman, Battips, and Hungerford (1960). The chromosome counts from two blood samples are shown in the Table. It was not possible to investigate the chromosomes in any other tissue.

TABLE

DISTRIBUTION OF CHROMOSOME COUNTS

	Date	Chromosome Number					Total
		44	45	46	47	48	
Blood culture	November 1964	5	60	3	2	15	85
Blood culture	August 1965	4	43	1	2	15	65

The cells with 45 chromosomes had 4 chromosomes in group G and 15 chromosomes in group C. The remainder of the chromosome set was apparently normal, and this cell line was interpreted as having an XO sex chromosome complement. The cell line with 48 chromosomes also had 15 chromosomes in group C, but there were 7 chromosomes in group G. Three of the small acrocentric chromosomes appeared to be different from the others in the group and had the characteristic morphology of the Y chromosome (Fig.). In view of the abnormalities in the genital system of the patient and the presence of an XO cell line, which would suggest the involvement of the sex chromosomes, it was considered that 3 Y chromosomes were present in these cells.

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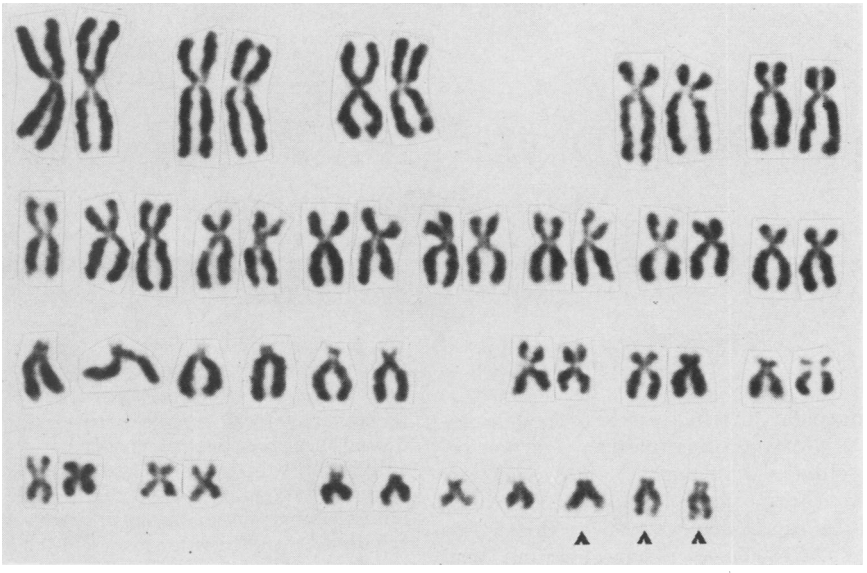

FIG. Karyotype of a cell with 48 chromosomes. The three Y chromosomes are arrowed.

There appeared to be no consistent pattern in the missing chromosomes in those cells which had counts of 44 and 46. They were interpreted as being the result of cell breakage and chromosome loss. In the first culture the cells with 47 chromosomes also showed random loss of a chromosome. However, in the repeat culture both cells with 47 chromosomes had 6 members in group G. In one of these cells, 2 Y chromosomes were apparent in addition to the normal complement of 4 small acrocentric autosomes. Thus, the existence of an XYY cell line is indicated.

Chromosome study of both parents showed apparently normal karyotypes.

Discussion

Several mechanisms could be postulated to account for the mosaic chromosome pattern observed in the patient. A simple sequence of events would involve non-disjunction of the Y chromosome in two early divisions of an XY zygote. It is quite possible that all the expected cell types are present in the patient though too infrequent in the peripheral blood for positive identification. The probability that an XYY cell line is present supports the suggestion of more complex mosaicism, and the existence of an XY cell line cannot be entirely ruled out. It may be presumed that the cells forming the testis have one or more Y chromosomes present.

The patient is concluded to be a chromosomal mosaic of the 45XO/48XYYY type, with the probability that a 47XYY cell line is also present.

Summary

A male pseudohermaphrodite with hypospadias, a uterus with blindly-ending Fallopian tubes, and a single testis on the right side is described. He is of normal intelligence and his height and weight are at the sixth centile. Chromosome analysis revealed an XO/XYYY mosaic sex chromosome pattern.

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