X/XYq – mosaicism and mixed gonadal dysgenesis

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SUMMARY A non-fluorescent Y chromosome was observed in a phenotypic male with 45,X/46,XYq– mosaicism and mixed gonadal dysgenesis. Q-banding of the father's chromosomes showed a normally fluorescent Y. Measurements of the Y chromosomes in the father and the patient showed a significant difference in length. Evidence for translocation of the Y fluorescent segment to another chromosome was lacking in the present case.

Since the procedures for chromosome banding were introduced, many examples have been found of deletion of the bright fluorescence of the distal two-thirds of the long arm of the human Y chromosome. In most of the cases this has been caused by simple deletion of this chromosome segment, in others to Y autosome translocations, and in a small number of cases the lack of fluorescence appears to have a biochemical explanation.

We have studied a child with abnormalities of sexual development, a mixed gonadal dysgenesis, and X/XYq– mosaicism. Only one other similar patient has been reported (Conen *et al.*, 1961).

Case report

The patient, C. D. (born 12 March, 1971), a 4-year-old phenotypic male was studied because of abnormal external genitalia. He was the product of a normal pregnancy and is the second child of a 24-year-old mother and 33-year-old father. Their first child is a normal female. The family history is unremarkable. Physical examination showed an active boy with normal height, weight, and head circumference. He had a biphid scrotum and scrotal hypospadias was present (Fig. 1). The penis (32 mm length) presented a chordee which was surgically treated. A mass was palpated in the right scrotum but the left side was empty. The urogram was normal and urethrocystography revealed the existence of a vagina and a rudimentary uterus.

An exploratory laparotomy confirmed the presence of a vagina and uterus, and showed a Fallopian tube and 'streak gonad' on the left side; the mass present in

the right side was found to be a normal testis. Histological sections confirmed these findings.

Dermatoglyphs of the proband and his parents are shown in Table 1. The patient's buccal smear showed no X chromatin and no Y fluorescent body. Chromosome analysis was done on cultures of peripheral leucocytes as well as on skin and testicular fibroblasts. Routine karyotype analysis showed 45,X/46,XY mosaicism. The Y chromosome was identified by its morphological characteristics though it appeared shorter than usual. The frequency of 46,XY cells was 70% in two leucocyte cultures and 56% in fibroblast cultures. Q banding showed that the cells with 46,XY had no bright fluorescence in the long arm of the Y chromosome which appeared deleted. The rest of the chromosomes were normal, without evidence of translocation (Fig. 2). G banding after

Fig. 1 External view of the proband's genitals. See the biphid scrotum and the scrotal hypospadias.

Table 1 Dermatoglyphic data

Subject	Hand	Digital patterns					Total ridge count	'atd' angle (degrees)	Ta-Tb ridge count
		I	II	III	IV	V			
Proband	Right	W	W	UL	UL	UL	149	48	47
	Left	UL	W	UL	UL	UL		45	49
Father	Right	W	W	W	W	UL	207	40	40
	Left	W	W	W	W	UL		40	53
Mother	Right	UL	W	UL	UL	UL	152	37	36
	Left	UL	UL	UL	UL	UL		33	43

Fig. 2 Q-M stained metaphases of the proband (a) and his father (b). The arrows show the abnormal Yq— and the normal Yq chromosomes.

Fig. 3 G banding karyotype of the proband. The Y chromosome is smaller than usual.

trypsin treatment showed a normal pattern except that the Y chromosome was smaller than usual (Fig. 3).

Chromosome analyses were also carried out on the parents; the father's karyotype showed a normal Y chromosome and there was no evidence of abnormalities in any of the other chromosomes (Fig. 2). The mother's karyotype was also normal.

Comparison of the father's Y chromosome and the proband's Y chromosome was made by measuring 20 metaphases using a lens with a scale of 0.2 mm graduation. The Y chromosomes of the father and the patient showed a significant difference in length with a P value of between 0.001 and 0.01 (Fig. 4 and Table 2).

Blood group tests (Table 2) and the striking resemblance of the proband to his father (Fig. 5) are against illegitimacy in this case.

Fig. 4 Partial karyotypes of G and Y chromosomes of the proband (right) and his father (left). Conventional staining for the G chromosomes and Q-M banding for Y chromosomes.

Table 2 Mean of Y chromosome length in patient and his father

Y	Patient	Father
Mean	2.46	3.21
SD	0.501398	0.500545
N = 20		
t = 3.350862		
0.001 < P < 0.01		

Tests to evaluate testicular function showed that plasma testosterone levels were raised from a basal determination of 20 ng/ml to 188 ng/100 ml after dexamethasone and HCG were administered.

Discussion

Mixed gonadal dysgenesis has been reported frequently (Davidoff and Federman, 1973) associated with different types of mosaicism, from the classical

Fig. 5 Facial appearance of the proband and his father. Note the resemblance between them.

X/XY to the X/XY/XYY constitution (Yunis *et al.*, 1974) and X/XY dic (Hayek and Yunis, 1975). A very similar condition to the one presented here, both in clinical picture and chromosome constitution, was reported previously (Conen *et al.*, 1961). Consideration of non-fluorescent Y chromosomes has come about since Caspersson *et al.* (1971) described one case with X/XY mosaicism and 3 cases with X/XY XYY mosaicism always lacking the intense fluorescence seen in the distal two-thirds of the Y chromosome. Even though in only one of the cases was a translocation between the short arm of a No. 2 and the long arm of the Y demonstrated, Caspersson suggested that X/XY mosaics with a non-fluorescent Y might often represent translocations. Curto *et al.* (1972) and Hsu *et al.* (1974) reported 2 cases of non-fluorescent Y chromosomes with X/XY mosaicism, in which the father's Y chromosome was normally fluorescent. They also reported no significant difference in the size of the Y chromosome; this allowed Hsu *et al.* to suggest that DNA-protein interaction, caused either by altered protein or DNA configurations, could be the possible mechanism involved in the production of such abnormal chromosomes.

Translocation of the distal portion of the Y chromosome is excluded in our case because the rest of the chromosomes do not show any extra segment. Such a translocation would be evident because in human Y-autosome translocations the bright fluorescence is preserved (Noel *et al.*, 1971; Bühler, 1971; Develing *et al.*, 1973). Lack of fluorescence

Table 3 Blood grouping tests of CD family

	O	D	C	E	c	e	K	Fy	Le	M	N	S	s	Kidd	P
Father	+	-	-	-	+	+	-	a-	a+	+	-	+	-	a-	+
Mother	+	+	+	+	+	+	-	a+	a+	+	-	-	+	a-	+
Proband	+	+	-	+	+	+	-	a+	a+	+	-	+	+	a-	+

with a normal sized Y chromosome is also discarded because the length of the Y chromosome in the patient and his father showed a significant difference, with a P value of between 0.001 and 0.01 (Table 1).

Therefore, the present case is an example of X/XYq- mosaicism with a clinical picture of mixed gonadal dysgenesis, one well-developed testis, and good testicular function as evidenced by the hormone response to HCG stimulation. In addition, this case gives strong support to the concept that there are no genetic loci for testicular differentiation in the heterochromatic and fluorescent portion of the long arm of the Y chromosome.

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