Familial hypogonadism with a balanced reciprocal 1;12 translocation

Balanced reciprocal autosomal translocations have variable effects on testicular function.^{1,2} The case we report illustrates a family with severe hypogonadism and an apparently balanced reciprocal translocation.

The proband was a 37-year-old Vietnamese Chinese male with an 8-year history of primary infertility owing to azoospermia. He was hypogonadal with small testes, and his 33-year-old brother had presented independently with a similar clinical picture of 5 years' primary infertility owing to azoospermia. A third brother, aged 27 years, was single and had been operated on for bilateral hernias and probable cryptorchidism but declined to be examined. Living in Vietnam with his widowed 65-year-old mother was a 39-year-old brother who had fathered six children. Both the infertile brothers benefited from testosterone replacement therapy and the raised gonadotrophins were returned to normal with androgen treatment. Both sets of couples were referred for donor artificial insemination.

Investigations included measurement of testicular volumes with a Prader orchidometer, semen analyses, and hormone and cytogenetic studies. These were performed on specimens of peripheral blood from the three brothers who all carried an apparently balanced reciprocal translocation between chromosomes 1 and 12. The karyotype was 46,XY,t(1;12)(p32;q24) in each case and is illustrated in the figure. Hormonal studies revealed severe primary hypogonadism in all three brothers (table).

The similarity of the findings in both cytogenetic and hormonal studies strongly suggests that the same mechanism of hypogonadism is present in all three brothers. The results are most consistent with a meiotic arrest of spermatogenesis causing azoospermia and infertility in the two married brothers and suggest that the third brother is also likely to be hypogonadal and infertile. The parents and the eldest brother were not available for testing but all were apparently fertile and the reason for this difference from the three younger sibs

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FIGURE Partial G banded karyotype from the proband. The two younger brothers carried the same rearrangement.

remains unclear. It is notable that all three younger sibs migrated under highly arduous refugee conditions and additional interacting environmental factors may have been present. Some sex linkage or restriction of expression of autosomal translocations has been noted previously in mouse³ and human¹ studies of associated testicular damage.

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TABLE Results of investigations in the proband and his two younger brothers.

	Patients			Controls*	
	Proband	Brother 1	Brother 2	Normal	Klinefelter's syndrome
Age	37	33	27	31 ± 1	31 ± 3
Fertility	Infertile	Infertile	?	Fertile	Infertile
Hypogonadal	Yes	Yes	?	No	Yes
Testicular volume (ml)	4	8	?	24.9 ± 0.4	4
Sperm density (million/ml)	0	0	?	83.9 ± 5.7	0
LH (IU/l)	13.2	10.6	13.9	5.5 ± 0.2	29.2 ± 2.2
FSH (IU/l)	34.6	23.3	28.4	3.7 ± 0.2	36.1 ± 3.1
Testosterone (nmol/l)	12.5	13.2	18.7	23.8 ± 0.6	10.7 ± 1.6
Prolactin (ng/ml)	8.3	11.1	—	5.9 ± 0.3	6.3 ± 0.8

*Controls are 119 normal volunteer donors for an artificial insemination programme who had normal semen analyses and 23 men with Klinefelter's syndrome. Results are mean ± 1 SEM.