Additional pedigree supporting the frequent origin of XYY from consecutive meiotic non-disjunction in paternal gametogenesis

SUMMARY A 48,XXYY Sardinian patient, born to a 46,XX mother heterozygous for the *Gd Mediterranean* mutant, and to a 46,XY father hemizygous for the same mutant, was found to have a mosaic distribution of G6PD(+) and G6PD(−) peripheral red blood cells. The most likely interpretation of this finding is that the propositus is an additional example of an XYY zygote derived from a consecutive meiotic non-disjunction during paternal gametogenesis.

In the course of a population study on Klinefelter's syndrome in the island of Sardinia, where the incidence of G6PD deficiency of Mediterranean type may be as high as 30% among males (Siniscalco *et al.*, 1966), we found an XYY male born to a G6PD-deficient father and to a mother who is an obligatory heterozygote for the *Gd Mediterranean* mutant.

Clinical and laboratory findings

The patient, 22 years old, had the following findings:

- (1) Bilateral atrophy of the testes (average size 8 in arbitrary units; normal values 11.86 ± 0.15).
- (2) Slender (height 176 cm, weight 73 kg; normal values $158.65 \text{ cm} \pm 0.47$ and $61.9 \text{ kg} \pm 0.52$).
- (3) High titres of FSH and LH (66.6 mIU/ml and 50 mIU/ml , respectively; normal values $7.05 \text{ mIU/ml} \pm 0.85$ and $5.06 \text{ mIU/ml} \pm 1.09$).
- (4) 40% of buccal mucosa cells were sex chromatin positive.
- (5) Of 50 metaphases from peripheral blood cultures, 48 had 48 chromosomes. Ten of these metaphases were karyotyped with quinacrine banding and found to be 48,XXYY. The presence of the extra X and of the extra Y chromosomes was confirmed by microscopical screening also in all the other metaphases which were not karyotyped. Cytogenetical studies were performed on both parents of the propositus and found to be normal.

The patient has normal sexual development, no gynaecomastia, and no apparent impairment of mental capacity and behaviour. He completed obligatory schooling with average performances and is at present working as a farmer. He is the seventh of nine children, born after a normal pregnancy, when his mother was 36 years old and his father 39. The mother had had 3 earlier spontaneous abortions. There is no consanguinity and no medical problems in the family.

Fig. Family pedigree.

Discussion

The propositus and his mother have a mosaic population of G6PD(+) and G6PD(−) peripheral red blood cells, which is characteristic of heterozygotes with the genotype *GdB/Gd Mediterranean* (Rinaldi *et al.*, 1976). This conclusion is supported by the analysis of the red cell G6PD phenotypes of all members of the pedigree (Fig.), on the basis of which the presence of other G6PD alleles, besides the ones mentioned above, can be excluded. In view of these findings, the possibility that the XXY genome of the propositus is the result of an early mitotic non-disjunction of a normal XY zygote can also be excluded, since in this case he should have been homozygous for the mutant or the normal allele. Thus, discarding the unlikely event of an independent occurrence of non-disjunction in both parents of pre-reductional type in the mother and postreductional in the father, the most likely explanation remains that both types of meiotic non-disjunction have occurred consecutively during the paternal gametogenesis. The X and the Y must have gone into the same 'spermatocyte II' during the reductional meiosis, and both Ys, but only one X (and the *Gd Mediterranean* mutant carried by it), must have segregated during the equational division in the 'spermatid' which matured into the sperm that fertilised a normal haploid egg carrying the *GdB* allele.

To the best of our knowledge, this is the third instance, among a total of 36 XXY propositi ascertained so far (De la Chapelle *et al.*, 1964; Pfeiffer *et al.*, 1966; Sanger *et al.*, 1977), in which the origin of the supernumerary sex chromosomes can be identified as the result of consecutive non-disjunction having occurred during paternal gametogenesis.

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