Inverted tandem duplication of 8p12→p23.1 in a child with increased activity of glutathione reductase

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Abstract

At least 16 cases of inversion tandem duplications of the short arm of chromosome 8 have been reported. Structural rearrangements of chromosome 8 have made it possible to localise the gene for glutathione reductase (GSR) to 8p21.1. We report here on a 16 month old boy with mental retardation with partial trisomy 8 owing to a de novo inv dup(8)(p12→p23.1).

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Figure 1 The proband.

Case report

The proband, a male, was born by normal delivery at 38 weeks' gestation, weighing 2994 g, with a head circumference of 36 cm. The pregnancy was complicated by peripheral neuropathy and by polyhydramnios. At birth he had tachycardia, tachypnoea, and developed cyanosis. Initially he had difficulty in feeding. He had generalised hypotonia and also polycythaemia, which was treated by exchange transfusion.

Examination showed dysmorphic features which included dolichocephaly, hypertelorism, prominent, square forehead, micrognathia, and bilateral, low set ears (fig 1). The palpebral fissures were horizontal. The lower lip was everted and the upper lip was cupid bow shaped. The anterior fontanelle was small. There was clinodactyly of the fifth fingers and zygodactyly of toes 2 and 3 bilaterally. At 16 months he showed evidence of motor delay and mild mental retardation. He could stand only with support and was unable to raise himself from the prone position. Speech was delayed.

Chromosome analysis showed one chromosome 8 with an enlarged short arm which was interpreted as an inverted tandem duplication with duplication of the region 8p12→p23.1 (fig 2). The karyotype

Figure 2 Partial GTL banded karyotype and schematic representation of the inverted tandem duplication of 8p.

was 46,XY,inv dup(8)(p12→p23.1). Chromosome analyses in the parents showed normal chromosomal constitutions. Glutathione reductase (GSR) activity was 15.14 IU/g Hb (normal range 4.75 to 9.47 IU/g Hb). Maternal and paternal GSR activity was 5.94 and 6.35 IU/g Hb respectively.

Discussion

Our patient had partial trisomy 8p owing to an inversion duplication of the short arm p12→p23.1. A total of 16 patients with a similar chromosomal finding has been reported.¹⁻³ In 1982 Jensen *et al*¹ described two patients with an inverted duplication of 8p21→p23 and reviewed 11 other published cases. Subsequent reports include a 24 year female with severe mental retardation who had a de novo inverted duplication of 8p21.1→p22² and another adult female, also with mental retardation and dysmorphic features owing to an inverted duplication of 8p12→p23.1.³ Patients with an inverted tandem duplication 8p show marked variation of clinical features with no distinct phenotype. The most consistent clinical finding was profound mental retardation. The variation in clinical phenotype may in part be explained by the different chromosomal breakpoints and the variable deleted regions. At

present it is not possible to distinguish trisomy 8p as a separate clinical entity. It appears that the mental retardation is more pronounced than in the full trisomy 8 syndrome.² Some patients with inverted duplication 8p survive into adulthood; one reported patient was aged 20 years² and another aged 24 years.³

Gene localisation studies confirmed the partial duplication 8p in our patient. The gene for glutathione reductase (GSR) (EC:1.6.4.2.) has been assigned to the short arm of chromosome 8. Some patients with duplication of the short arm of chromosome 8 show increased levels of red cell GSR.¹⁻⁴ Indeed it has been shown that the GSR gene is localised to subband 8p21.1.¹ Our patient, whose duplication involved this region of chromosome 8, had an increased GSR activity.

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- 3 Dill FJ, Schertzer M, Sandercock J, *et al*. Inverted tandem duplication generates a duplication deficiency of chromosome 8p. *Clin Genet* 1987;32:109-13.
- 4 George DL, Francke U. Gene dose effect: regional mapping of human glutathione reductase on chromosome 8. *Cytogenet Cell Genet* 1976;17:282-6.