

Interstitial deletion 2q32.1→q34 in a child with half normal activity of ribulose 5-phosphate 3-epimerase (RPE)

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SUMMARY High resolution banding analysis showed a de novo interstitial deletion, 46,XX, del(2) (q32.1q34), in a malformed and severely mentally retarded girl aged nine years. Biochemical studies showed that the proband had half normal activities of both erythrocyte isocitrate dehydrogenase (IDH₁) and ribulose 5-phosphate 3-epimerase (RPE). It is suggested that the gene for RPE is located on the segment 2q32.1→q34.

Case report

The proband was a nine year old Japanese girl, the second child born to a 26 year old mother. The father was 27 years old. The family history was unremarkable, except for the second pregnancy, which was terminated because of rubella infection. Pregnancy was complicated by vaginal bleeding at about three months. The child was born at term, birth weight 2030 g. She had feeding difficulties owing to a cleft palate and was fed via a nasogastric tube for the first three months.

Her growth and psychomotor development were considerably delayed. Physical examination at six years of age showed a malnourished and hypotonic girl with a height of 78 cm (-5.5 SD), weight of 6.0 kg (-7.4 SD), and head circumference of 41 cm (-7.9 SD). She neither sat nor spoke any meaningful words. Her face was odd looking and the following dysmorphic features were observed: a prominent forehead, sparse hair, small and downward slanting palpebral fissures, hypertelorism, long eyelashes, malformed auricles, prominent antihelix, anteverted nostrils, small mouth, high arched and cleft palate, irregular dentition, micrognathia, short neck, and arachnodactyly. Dermatoglyphic studies showed the axial triradius in the *t'* position bilaterally. Computerised tomography of the skull showed mild ventricular dilatation with some degree of cortical atrophy. Skeletal age was two years. At

present, the child is cared for by her parents at home and is totally dependent on others.

CYTOGENETIC STUDIES

Cytogenetic studies using high resolution GTG¹ and RBA banding methods on peripheral blood lymphocytes from the proband showed an interstitial deletion of the long arm of chromosome 2 (figure). The breakpoints appeared to be at 2q32.1 and 2q34, and her karyotype was interpreted as 46,XX,del(2) (q32.1q34). Both parents had normal chromosomes.

BIOCHEMICAL STUDIES

The activity of erythrocyte isocitrate dehydrogenase (IDH₁) was examined by the method of Cleland *et al*² and ribulose 5-phosphate 3-epimerase (RPE) by the method of Wood³ (table). The levels of both

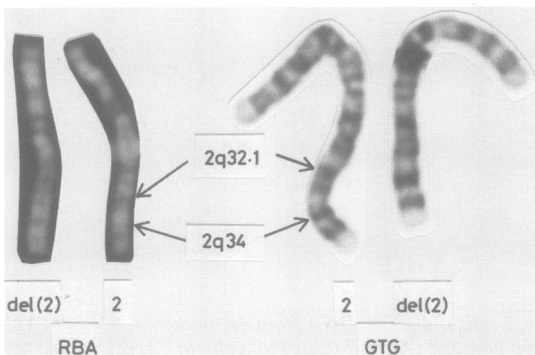


FIGURE Partial karyotypes of the proband stained with GTG and RBA banding methods. Arrows indicate breakpoints.

TABLE IDH₁ and RPE activities* in red cells of the proband.

	Normal controls [Mean (SD)]	Proband [Mean (SD)]
IDH ₁	0.880 (0.253) (n=50) (100)†	0.392 (n=3) (44.5)†
RPE	20.45 (1.90) (n=12) (100)†	8.40 (n=2) (41.1)†

*Expressed as nmol/min/mg Hb.

†The values in parentheses are percentages with respect to the normal sample.

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enzymes in the proband were significantly reduced. We concluded that the proband was a heterozygote for both IDH₁ and RPE.

Discussion

Biochemical studies showed that the proband had half normal activities of IDH₁ and RPE, suggesting that she was a heterozygote for both enzymes. The gene for IDH₁ has been assigned to sub-band 2q33.3 by Narahara *et al.*⁴ High resolution GTG and RBA banding analysis showed that the segment 2q32.1→q34 was deleted in the proband in agreement with their observations. On the other hand, the gene for RPE has been assigned to the segment 2q32→qter by Gross *et al.*⁵ using interspecific hybridisation. From the gene dosage effect, our observations suggest that the gene for RPE is located on the more proximal portion of this segment, 2q32.1→q34. Further studies of patients with similar deletions of the long arm of chromosome 2 are required to elucidate the critical band for the expression of RPE.

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Apparent monosomy 21 owing to a ring 21 chromosome: parental origin revealed by DNA analysis

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SUMMARY A three and a half year old mildly retarded boy is presented. Karyotyping showed monosomy 21 (45,XY,-21) in all 50 metaphase spreads examined from two lymphocyte cultures, and in 20% of cells examined from cultured fibroblasts; the remaining 80% of cells showed a ring 21 chromosome (46,XY,r(21)(p1q22)). Molecular studies using chromosome 21 specific DNA probes confirmed the monosomy in blood and showed that the ring 21 chromosome was paternal in origin. Parental karyotypes were normal.

In a recent review it was concluded that karyotypes with a ring 21 chromosome (46,r(21)) can be associated with three distinct phenotypes.¹ In the

classic form there is severe retardation with marked dysmorphism and a poor prognosis for long term survival. At the other end of the spectrum, some subjects with this karyotype are entirely normal, being ascertained either by chance or, in the case of males, through investigation of azoospermia. The third phenotype, documented in a total of four patients, is characterised by mild mental retardation and minor facial dysmorphism.^{1–4} We now present the clinical, cytogenetic, and molecular findings in a further patient with this 'mild' ring 21 chromosome syndrome, who was particularly unusual in that all metaphase spreads examined from lymphocyte culture showed monosomy 21 (45,XY,-21), thus providing a unique opportunity to determine parental origin using chromosome 21 specific DNA probes.

Case report

The three and a half year old male patient was the