

De novo deletion (2) (p11.2p13): clinical, cytogenetic, and immunological data

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Abstract

We report a case of a boy with a de novo interstitial deletion of chromosome (2) (p11.2p13). Clinical features included dysmorphism of the face, genital region, and limbs, psychomotor retardation, and vitiligo. A reduced ratio of immunoglobulin (Ig) light chain expression (κ/λ ratio: 0.7) was found, compatible with deletion of one Igk allele on chromosome 2p12. The patient had no clinical or laboratory signs of immunodeficiency.

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Ten cases of chromosomal deletions involving the short arm of chromosome 2 have been described.¹⁻¹¹ Only two of them included bands 2p11, 2p12, or 2p13 in the deleted segment.^{2,4} We describe a boy with a de novo interstitial deletion (2) (p11.2p13), causing multiple dysmorphic features, psychomotor retardation, vitiligo, and disturbed distribution of immunoglobulin (Ig) light chain expression without clinical or laboratory signs of antibody deficiency or other immune disorders.

Case report

The male proband was the second child of healthy, non-consanguineous parents. Maternal and paternal ages at his birth were 33 and 35 years, respectively. Their first son is healthy. The family history showed no significant problems. The pregnancy was complicated by third trimester intrauterine growth retardation. After birth at term, the baby (length 46 cm, < -2 SD,¹² weight 2500 g, length related to weight, -1 SD¹²) was admitted to the neonatal ward because of hypothermia and aspiration of amniotic fluid. Later feeding difficulties also occurred. Dysmorphism of the face, genitals, and feet was noted and blood was taken for chromosomal analysis.

On three occasions, at the age of 3 months, 1 year, and 4 years, we saw the proband and his parents in the Department of Clinical Genetics. The following dysmorphic features were noted: very short stature, bushy hair, large fontanelle with delayed closure, high sloping forehead, prominent occiput, rectangular facies, short, downward slanting palpebral fissures, ptosis, telecanthus, highly arched eyebrows, broad nasal bridge, broad nose with anteverted nostrils and bulbous tip of the nose, short philtrum, small mouth with a thin upper lip, posteriorly rotated and low set ears, and a

broad short neck (fig 1). There was also clasped thumb position, short distal phalanges, oedematous pads on the dorsum of the feet, pes equinovarus with a transverse plantar crease, and prominent heels. Urogenital system abnormalities included a small penis, coronal hypospadias, and undescended testicles. Growth followed a curve below the 3rd centile for age related height and a curve between the 50th and 75th centile for height related weight¹³; head circumference followed a curve just above the 10th centile.¹³ From the age of 2.5 years onwards, vitiligo developed in the genital region and subsequently on the trunk, face, and limbs. The boy has a conductive hearing impairment (40 dB) and myopia (4D). Developmental milestones included turning over at 3 months, sitting at 8 months, standing at 1.5 years, walking alone at 3.5 years, and until 4 years of age only speaking some isolated words. The boy has some bronchial hyper-responsiveness but no clinical or laboratory signs of a compromised immune system. Hormonal investigations at the age of 3 months (luteinising hormone, 8 mU/l; follicle stimulating hormone, 4 mU/l; testosterone, 5.4 nmol/l; dehydroepiandrosterone sulphate, 0.6 μ mol/l; and steroid hormone binding globulin, 148 nmol/l) were normal.

CYTOGENETIC STUDIES

Chromosomal studies on peripheral blood lymphocytes and cultured fibroblasts showed a deletion of chromosome 2 (p11.2p13) with GTG and R banding (fig 2). The length of the deleted segment was estimated to be 8.6% of the length of chromosome 2 and about 0.7% of the haploid human genome. The parents had normal karyotypes, 46,XX and 46,XY, respectively, in their peripheral blood lymphocytes. A cell line of the patient is available and banked in the Department of Clinical Genetics, Rotterdam, The Netherlands (identification number 87RD0573).

IMMUNOLOGICAL STUDIES

At the three visits to our department, at the ages of 3 months, 1 year, and 4 years, blood samples were taken from the proband and his parents for immunological investigations, since the Igk gene is located in the region of the deletion (2)(p11.2p13).¹⁴ Serum Ig levels of the patient were within the normal range for age and immunological marker analysis of mononuclear blood cells showed normal relative and absolute numbers of CD19⁺/CD20⁺ B lymphocytes, CD3⁺/CD4⁺ T lymphocytes,

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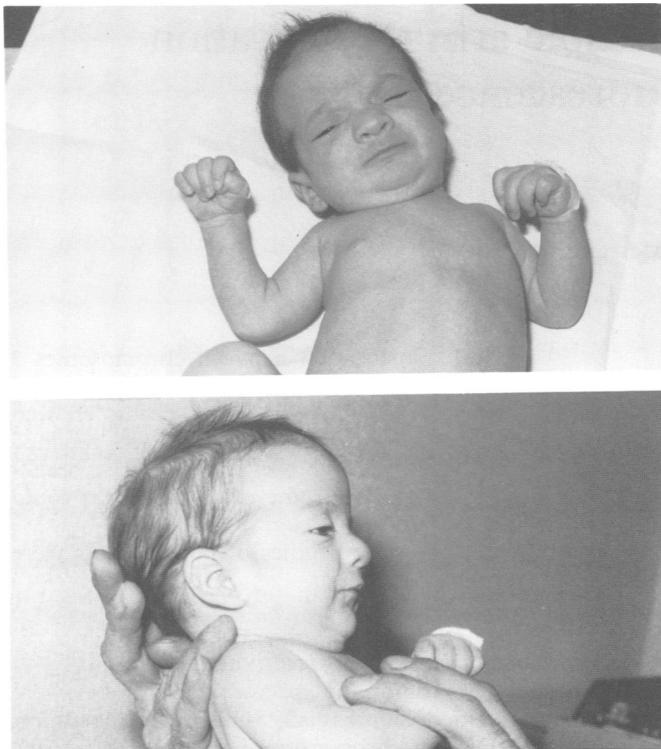


Figure 1 The patient at the age of 3 months.

and CD3⁺/CD8⁺ T lymphocytes.¹⁵ However, the distribution of Igκ and Igλ chain expression in the B lymphocytes was decreased in the patient on all three occasions (κ/λ ratio: 0.7) as compared to the mother (κ/λ ratio: 1.3), the father (κ/λ ratio: 1.5), and healthy controls (range of κ/λ ratio: 1.0 to 1.9; mean: 1.4). The decrease in the κ/λ ratio in the patient is in line with the loss of one of the chromosome bands 2p12, which contains the Igκ gene.

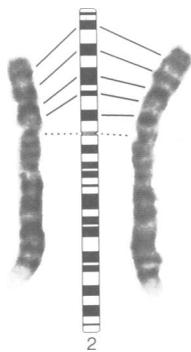


Figure 2 Partial karyotype of the proband (GTG banding). Right, normal chromosome 2; left, chromosome 2 with de novo deletion (2)(p11.2p13).

Discussion

Our patient is the eleventh reported case of an interstitial deletion of chromosome 2p. A number of dysmorphic signs such as short stature, developmental delay, deafness, rectangular facies, prominent occiput, high sloping forehead, small head circumference, broad nasal bridge and nose with bulbous tip, downward slanting palpebral fissures, low set ears, and foot abnormalities are shared by some patients with deletions in bands 2p23 to pter³⁶⁷¹¹ or in bands 2p11 to 2p21.²⁴⁵ Deletions in bands 2p21 to 2p23 are associated with a different phenotype featuring holoprosencephaly.⁸⁹¹⁰

The loss of one of the bands 2p12, contain-

ing the Igκ gene, resulted in our patient in a significantly reduced Ig κ/λ ratio. No further immunological aberrations or clinical signs of immunodeficiency were found.

Vitiligo has been suggested to have multifactorial or polygenic recessive inheritance involving four unlinked diallelic loci.¹⁶¹⁷ Immunogenetic factors may also be associated with the disease.¹⁸ Of special interest with respect to the hypothesis of polygenic inheritance is the finding of linkage of acid phosphatase (ACP₁), located in 2p25,¹⁴ with vitiligo.¹⁶ The presence of vitiligo in our patient suggests that chromosome 2p is involved in this disease, although the distance between 2p12 and 2p25 is considerable.

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