Case reports

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Complex translocation in a boy with trichorhinophalangeal syndrome

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SUMMARY We report a boy with a trichorhinophalangeal syndrome (TRP syndrome), severe mental retardation, and transient megacephaly, whose karyotype showed complex, apparently balanced, translocations with breakpoints in bands 3q13, 8p22, 8q13, 11p12, and 11q21. The fact that cases presenting with phenotypes corresponding to the TRP II syndrome and deletions of the long arm of chromosome 8 have been recently reported prompted us to report this case to help in the clarification of the possible relation between 8q chromosomal mutation and the aetiology of TRP syndromes.

In 1966 Giedion¹ described a syndrome which he called trichorhinophalangeal syndrome. It consisted of hair anomalies, pear-shaped nose, and brachyphalangy, with other skeletal abnormalities. Although in most families autosomal dominant inheritance was observed, Giedion *et al*² conceded that genetic heterogeneity might exist, since in other families autosomal recessive transmission could be postulated. In 1969, Langer³ described a new clinical entity, thoracic-pelvic-phalangeal dystrophy, that shared several symptoms with the trichorhinophalangeal syndrome, its distinguishing features being mental retardation, microcephaly, multiple exostoses, and redundant skin. Later, this syndrome was called Langer-Giedion syndrome or trichorhinophalangeal syndrome type II. Recently, several authors have described patients with TRP II syndrome in whom a deletion of the long arm of chromosome 8 was detected.^{4–10} One of these authors⁴ suggested that TRP II syndrome could be due to a deletion in 8q.

As our patient's phenotype corresponds to that of the TRP syndromes, and since he has a complex chromosomal rearrangement involving a breakpoint at 8q13, we considered this case worthy of a report.

Case report

The proband, a male, was born to a non-consanguineous mother and father, aged 18 and 31 years respectively, whose previous pregnancy had resulted in a stillborn child with ambiguous genitalia and external malformations. The patient was the product of a normal pregnancy and delivery. Birth

FIG 1 The proband. (a) Note high forehead, sparse blonde hair, and pear shaped nose. (b) Note hair and very peculiar nose which is big and pear shaped with a very depressed root, downturned tip, small nares, and hypoplastic nasal alae.

weight was 2850 g. After his birth the couple had two healthy girls. At 45 days, because of an episode of vomiting, the boy was examined by a paediatrician who noted a large head. However, no hydrocephalus could be detected. The infant was referred for genetic evaluation at 2½ years. Physical examination showed (fig 1): weight and height below the 5th centile, head circumference above the 75th centile (relative macrocephaly), open and large anterior fontanelle (4 × 4 cm), high and prominent forehead, and sparse, thin, blonde hair. His parents' hair was dark and abundant. The nose was big and pear-shaped, with a very narrow and depressed root, incurved tip, and small nostrils due to hypoplastic nasal alae. The philtrum was long and prominent and he had a very high palate. Dentition was severely retarded and anomalous; both upper medial incisors and both inferior canine teeth were absent and the erupted teeth were hypoplastic. The neck was short with redundant skin. The spine showed dorsal kyphosis and marked lumbar lordosis. The hands were normal, and the feet showed external clinodactyly of the big toes. Sweating was normal. The nails were thin and fragile. His psychomotor development was very delayed; he did not walk and his vocabulary was limited to disyllables. A further physical examination at 4 years of age showed that his height was on the 5th centile and that his hair was thin, sparse, dry, and hypopigmented. The upper central incisors were still absent, and the nails remained the same. He began to walk at 3 years of age and his vocabulary was still rudimentary. He had had several convulsive episodes since the previous examination. At 5 years his height was again below the 5th centile and his head circumference was on the 50th centile. Dentition was complete but dysplastic. At 9 years the patient showed the same physical features, although his hair and finger nails had improved. His mental retardation was severe. A dermatoglyphic study showed that there were whorls on all fingers. A very mild frontal cortical and central cerebral atrophy was revealed by a CT scan. X-ray examination showed normal spine, chest, and long bones. At 6 years, a bone age of 3 was observed, and at 9 years a further examination showed that there were striking similarities between our patient's hands and those of Langer's patient, including 'cone shaped' epiphyses, more obvious on the middle phalanges of the second to fourth fingers; in addition these were broad and short with metaphyseal cupping (fig 2).

CYTOGENETIC STUDIES

Lymphocytes from peripheral blood were cultured by standard techniques and G banded.¹¹ His karyotype was very abnormal showing a complex

translocation: 46,XY,t(3;8;11)(q13;p22q13;p12q21), or in the long form: 46,XY, t(3;8;11)(3pter→3q13::8p22→8pter;11qter→11q21::8p22→8q13::11p12→11pter;3qter→3q13::11p12→11q21::8q13→8qter) (fig 3). The rearrangement was apparently

FIG2 X-rays of hands at 9 years of age: middle phalanges are short and broad, showing 'cone shaped' epiphyses mainly on 2nd to 4th fingers.

FIG3 Partial karyotype showing the chromosomes involved in the translocations. On the left the normal homologue, on the right the rearranged chromosome.

balanced and involved breaks in bands 3q13, 8p22, 8q13, 11p12, and 11q21. Parental karyotypes were normal.

Discussion

Although our patient showed several signs of ectodermal dysplasia we cannot classify him in any of the diagnostic categories proposed by Pinsky¹² and Freire-Maia¹³ because he presented additional features (severe mental retardation and megacephaly). Nevertheless, we think the proband has most of the features of TRP and Langer-Giedion syndromes, including cone shaped epiphyses, short broad middle phalanges, and metaphyseal cupping.

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Addendum

Two previous reports of LG syndrome associated with del(8q) have come to our attention since the submission of this manuscript (Zaletaje DV, Marincheva GS. *Hum Genet* 1983;**63**:178–82 and Fryns *et al.* *Hum Genet* 1983;**64**:194–5) which add support to our hypothesis on the possible role of a structural aberration of 8q in the pathogenesis of TRP syndromes.

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Interstitial deletion of chromosome 7p detected antenatally

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SUMMARY An interstitial deletion in chromosome 7(p13p15) detected in amniotic fluid cells is presented. After termination, the fetus was noted to have an asymmetrical skull, low set ears, a flattened nose, bifid thumbs and right big toe, pyloric adenomyosis, hypospadias, and simian creases. A brief comparison is made with previously reported cases involving deletions of 7p, including those associated with craniosynostosis.

Since this paper was submitted, Mr W L Whitehouse has died.
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A review of published reports showed five previously reported cases involving the deletion of band 7p14^{1–4} and nine other cases with associated short arm deletions and translocations.² Previous cases with deletion 7p14 exhibited varying associated clinical features. To our knowledge, this is the first case of an interstitial deletion of band 7p14 encountered during antenatal screening. Common anomalies include developmental delay, flattened nose, low set ears, and abnormalities of the extremities including simian creases. Craniosynostosis was not present in our case, nor in the five others involving band 7p14 where the breakpoints were proximal to band 7p21.