Del(4)(q33→qter): another case report of a child with mild dysmorphism

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SUMMARY A male child is described with some growth and developmental delay and other minor dysmorphic features. Chromosome analysis showed a de novo deletion of the q33→qter terminal segment of a chromosome 4. There has been published discussion concerning the severity of phenotypic malformations in the seven cases described so far with this particular deletion. We add details of our patient to help to delineate further features of this syndrome.

There have been many reports of terminal deletions of the long arm of chromosome 4 which have

involved deletion of the q31→qter segment.¹ Some authors suggest that these patients can be classified as belonging to 'the 4q- syndrome' on the basis of clinical findings.² Only seven cases have been described with a deletion of the more distal portion of 4q, that is, del 4q33→qter.²⁻⁷ These patients show a more varied and milder phenotype than those with the larger deletion.

Case report

The proband was born at 41 weeks' gestation after an uneventful pregnancy to a G1P0, 25 year old mother and 26 year old father. Evidence of fetal distress appeared during labour and delivery was by caesarean section. Apgar scores were 5 and 8 at one and five minutes, respectively. Birth weight was

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FIG 1 The patient at 14½ months of age. (a) Facial appearance, (b) full length, and (c) lateral view of face.

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3860 g (>50th centile), head circumference was 37.5 cm (>90th centile), and length was 56.4 cm (>97th centile). At three days of age episodes of cyanosis were observed associated with a mild degree of tachypnoea; this resolved at five days.

Physical features noted at birth were arachnodactyly, particularly involving the first and second toes, a mild degree of mandibular hypoplasia, a high arched palate, prominent ears, superfluous flesh at the back of the neck (fig 1), and a hoarse quality in the vocal element of his cry.

Subsequent development showed a mild degree of retardation. At nine months of age he started to roll over; at 11 months he started to crawl, but did not achieve the sitting position until 12 months of age. At 15 months of age he started to pull himself up to the standing position and to walk around objects with support. Length and weight measurements followed the 10th centile while head circumference was on the 50th centile.

Although babbling, he had no meaningful words at 15 months and comprehension of the spoken word was less than expected at that age. An audiological assessment showed no abnormality. While there was suspicion of an intellectual deficit he was still too young for meaningful assessment.

CYTOGENETICS

Analysis of G banded chromosomes from a peripheral lymphocyte culture using the Ibraimov harvest method⁶ showed a terminal deletion of bands q33→qter in one chromosome 4 (fig 2). Parental chromosomes were normal.

FIG 2 Partial GTG banded karyotype showing the deleted chromosome 4 on the right of each pair.

Discussion

A deletion of the q31→qter segment of chromosome 4 results in a recognisable syndrome, often with major abnormalities and reduced survival.^{1 2} While the patients display normal birth weight, those surviving the neonatal period have reduced growth rate, severe oropharyngeal incoordination, and moderate to severe developmental delay. A survey of published reports¹ showed that 16 of 18 patients had cleft palate, six having cleft lip as well. Eleven patients had cardiac defects and seven patients died in the first six months of life; two of these died at birth with major congenital abnormalities, three died in infancy of cardiac failure, and two because of oropharyngeal incoordination.

Of the seven cases reported with a deletion of the more terminal segment of chromosome 4, that is, q33→qter,²⁻⁷ and our patient, all presented with some of the above features, albeit in milder form. All eight del(4)(q33) patients survived the neonatal period and ranged in age from 17 weeks to 12 years at the time of reporting. Seven of the eight had normal birth weight, eight had micrognathia, and five had microcephaly. Most (seven) had a flattened nasal bridge, three had a cleft palate, five some hand anomalies, and six had malpositioned toes. One had the Pierre-Robin anomaly³ and one had Williams' syndrome.⁴ While four patients had cardiac defects,^{4 6 7} these were mild and not life threatening; only two^{4 6(patient 1)} had anomalies possibly associated with Williams' syndrome. Developmental delay was described as moderate to mild.

Jefferson *et al*⁴ stated that most of the patients described with this deletion have facies consistent with Williams' syndrome and, in fact, our patient could be similarly described. However, other clinical features of this syndrome, such as hypercalcaemia, have not been reported in these patients. This would seem to indicate that any connection between Williams' syndrome and del(4)(pter→q33:) may be tenuous.

Conclusions

The features of our patient seem to concur with the seven other reports of terminal 4q33→qter deletions in that there is mild dysmorphism and some developmental delay present. These features are apparently less severe than in those patients having a larger deletion of the 4q31→qter segment.

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Features of Turner's and DiGeorge's syndromes in a child with an X;22 translocation

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SUMMARY We describe the clinical and cytogenetic findings in an infant who presented with the features of both Turner's and DiGeorge's syndromes associated with a unique translocation between chromosomes X and 22.

DiGeorge's syndrome (DGS) is a rare condition in which, despite some degree of variability, the clinical features usually include neonatal hypocalcaemia, defective cellular immunity, absent or hypoplastic thymus and parathyroid glands, cardiovascular anomalies, and a typical facies. Dysmorphic features include downward slanting palpebral fissures, ear anomalies, hypertelorism, and a short philtrum. Recently DGS has been shown to be

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FIG 1 Appearance of the proband.