Simultaneous partial monosomy 10p and trisomy 5q in a case of hypoparathyroidism

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Abstract

We report a case of monosomy for the distal region of the short arm of chromosome 10 (p13→ter) associated with trisomy for the terminal region of the long arm of chromosome 5 (q35.2→ter) that had originated from adjacent 1 segregation of a maternal reciprocal balanced translocation (5;10)(q35.2;p13).

We review the clinical findings of previously reported cases of both partial monosomy for 10p and of partial trisomy for 5q, but to our knowledge there are no previous reports of the effects of these two chromosome anomalies together. Clinically our patient showed features typical of partial monosomy for 10p (including hypothyroidism) rather than partial trisomy 5q.

At least 24 cases of partial deletion of the short arm of chromosome 10 have been previously reported,¹ with the breakpoint occurring most frequently in the segment 10p13,^{2,3} the majority (80%) having arisen de novo. The number of cases of distal trisomy 5q is small. To our knowledge, only 10 cases have been discovered that carry a duplication of the segment distal to band 5q31.⁴

Case report

The proband (fig 1) was born to non-consanguineous Caucasian parents at 35 weeks' gestation. The mother was a 37 year old primigravida and the father was 40 years old. The pregnancy was uneventful and no amniocentesis or scan was performed. At birth the baby was flat and required intubation for two and a

half minutes. She was small for her gestational age, her weight being 1910 g (between the 3rd and 10th centile), and her head circumference was 33 cm (3rd centile).

The following dysmorphic features were noted at birth: round head, thin lips, prominent eyes, downward slanting palpebral fissures, low set ears, depressed nasal bridge, high arched palate, simian crease on the left hand, short and curved fingers, and overlapping of the fingers and the third and fifth toes. There was also a rockerbottom abnormality of the feet with some valgus deformity. Her fontanelle was normal, there was no evidence of respiratory distress, and she was found to have a grade 1/6 systolic murmur. The infant was thought not to have any specific features of a documented syndrome.

At 5 weeks of age she was referred to hospital with vomiting and was diagnosed as having pyloric stenosis. On admission to hospital she was found to be hypocalcaemic with a calcium level of 1.45 mmol/l (normal range: 2.20 to 2.75 mmol/l) and a magnesium level of 0.53 mmol/l (normal range: 0.58 to 1 mmol/l). Her phosphate level was normal at 1.72 mmol/l (normal range: 1.30 to 2.00 mmol/l).

There had also been an upper respiratory tract infection for two weeks and during an x ray examination the baby had a respiratory arrest that required emergency resuscitation. She was treated with antibiotics and IV calcium gluconate and at 7 weeks of age she underwent pyloromyotomy after which the vomiting appeared to resolve. After the operation her serum calcium levels increased to 2.5 mmol/l. She was discharged from hospital but readmitted one week later with poor feeding, respiratory difficulties, generalised convulsions, and oral candidiasis. She was severely hypocalcaemic with a calcium level of 0.44 mmol/l. Her parathyroid hormone level was low at 8 ng/l (normal range 10 to 65 ng/l). She was treated with IV calcium gluconate and magnesium supplement. Vomiting recurred and she was found to have a persistent gastro-oesophageal reflux. Her immunology was normal with normal IgG, IgA, IgM, and T cell subsets. Because of her feeding difficulties, she was fed nasogastrically.

Ultrasound examination at this time showed mild cerebral ventricular dilatation, but the liver, kidneys, and spleen were normal.

The patient was transferred to another hospital for further evaluation of presumed hypoparathyroidism. At 5 months of age, she was failing to thrive, her weight being 2880 g (well below the 3rd centile), still being fed nasogastrically, and was presenting with intermittent episodes of pyrexia, for which no cause could

Figure 1 The proband at 8 months of age.

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Figure 2 (A) Balanced reciprocal translocation found in the mother, karyotype 46,XX,t(5;10)(q35.2;p13). (B) Unbalanced translocation with derivative chromosome 10 found in the proband, karyotype 46,XX,-10,+der(10)t(5;10)(q35.2;p13).

be found. Occasionally she became tachypnoeic. Solid feeding was introduced at 8 months of age although the child was very slow to feed. At the same age she was recorded as having severely delayed psychomotor development. She could not support her head and she did not smile, although she fixed and seemed to follow with her eyes. She tried to retain objects in her hands, but did not reach for them.

Comparison of the clinical symptoms of patients with partial trisomy 10p, partial monosomy 5q, and our case.

	10p13 →pter	5q34 →qter	Our patient
Growth and mental retardation	+	+	+
Abnormally shaped skull	+		
Microcephaly		+	
Craniofacial dysplasia		+	
Olfactory bulb/tract abnormalities	+		
Short, receding forehead		+	
Flat nasal bridge	+		+
Prominent nasal bridge		+	
Anteverted nostrils	+		
Short neck		+	
Low set ears	+		+
Prominent eyes			+
Downward slanting palpebral fissures	+	+	+
Epicanthic folds	+	+	
Ptosis	+		
Hypotelorism	+		
Hypertelorism		+	
Strabismus	+	+	
High arched palate	+		+
Micrognathia		+	
Large upper lip		+	
Minor abnormalities of hands and feet	+	+	+
Simian creases	+		+
Widely spaced nipples	+		
Cardiac malformations	+	+	
Convulsions	+		+
Hypocalcaemia	+		+
Hypoparathyroidism (Di George type)	+		+
Pyloric stenosis	+		+

CYTOGENETIC FINDINGS

Cytogenetic studies in the proband and her parents were carried out on chromosome spreads obtained by blood lymphocyte culture after staining with the trypsin-Giesma banding technique. The first examination showed a normal karyotype. A month later a further chromosome study was performed and the proband was found to have the following karyotype: 46,XX,-10,+der(10)t(5;10)(q35.2;p13) (fig 2B). The father had a normal chromosomal constitution but the mother was found to be a balanced carrier of a reciprocal translocation between the long arm of chromosome 5 and the short arm of chromosome 10. Her karyotype was 46,XX,t(5;10)(q35.2;p13) (fig 2A). The proband received the der(10) through an adjacent 1 segregation from her mother and was therefore monosomic for the 10p13→pter segment and trisomic for the 5q35.2→qter segment.

The mother became pregnant again when the patient was 6 months old. A chorion villus sampling was performed in the 10th week of gestation and the fetus was shown to have a normal female karyotype. The baby was born at 25 weeks' gestation and is making good progress.

The maternal aunt was tested and found to have a normal karyotype.

Discussion

The major clinical findings exhibited by the proband described here have been compared with previously published findings reported

for both trisomy 5q34→ter and monosomy 10p13 (table).

Our proband showed retarded growth and development and low set ears, which are symptoms common to both syndromes. However, the high arched palate, flat nasal bridge, simian crease, hand and foot malformations, feeding difficulties, and pyloric stenosis are all commonly observed in monosomy 10p. Certain findings in the present case, such as hypocalcaemia and hypothyroidism which have occasionally been reported in case of monosomy 10p,^{2,5-7} are also found in the Di George syndrome. This anomaly consists of a developmental defect of the third and fourth branchial arches and is characterised by thymic and parathyroid aplasia or hypoplasia, cardiac malformations, and dysmorphic features.

Greenberg *et al*⁸ report that five out of 27 patients with features of Di George anomaly showed chromosome abnormalities, three of whom had monosomy 22q11, one monosomy 18q21.33, and one monosomy 10p13. Gencik (personal communication), Bridgman *et al*,⁵ Koenig *et al*,² Herve *et al*,⁶ and Monaco *et al*⁷ reported additional cases of monosomy 10p13 associated with features of the Di George sequence.

It would seem that the anomalies in our patient reflect to a large extent the features of a partial deletion of 10p syndrome. Our case may also be seen as a confirmation of the previously described association between 10p deletion and hypoparathyroidism similar to

that observed in Di George sequence. No immunological defect was found in our patient, but Di George sequence represents a heterogeneous entity, in which some diagnostic criteria may be absent.

It is suggested, therefore, that chromosome analysis should be performed in all cases of suspected Di George sequence, and in view of the different abnormalities that are known to occur, high resolution banding should be used and attention focused on 10p as well as on the better recognised 22q.

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