Case reports

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Extra Yq and partial monosomy 12p due to a Y;12 translocation in a boy with features of the 12p deletion syndrome

E ORYE, M CRAEN, G LAUREYS, R VAN COSTER, AND
B VAN MELE

Laboratory of Cytogenetics, Department of Pediatrics, Ghent State University, Ghent, Belgium.

SUMMARY A Y;12 translocation, resulting in extra Yq material and partial monosomy 12p, was found in a 7½ year old boy. He showed growth and mental retardation and several of the congenital anomalies seen in the 12p deletion syndrome. LDBH activity, the gene for which is located at 12p12, was normal in serum, in accordance with the suspected 12p13 deletion in the patient.

In a review of human Y;autosome translocations, Smith *et al*¹ concluded that, when the autosome involved was an acrocentric, the translocation was generally an accidental finding and unrelated to phenotype or fertility. When, however, a non-acrocentric chromosome was involved, the aberration was commonly associated with infertility. Y; autosomal translocations associated with anomalies more or less typical for a particular autosomal syndrome have been described infrequently.^{2,3}

We describe here a Y;12 translocation found in a boy with clinical features of the 12p deletion syndrome.

Case report

The proband was the second child of healthy, non-consanguineous parents, who were both 23 years old at his birth. An older child, a girl, was normal. Family history was negative. The mother had had no previous miscarriages and the pregnancy was unremarkable. Vaginal bleeding was noted until the fourth month. The delivery was normal and vertex at 39 weeks. Birth weight was 2500 g.

The history of the proband revealed diarrhoea at 1 week and at 3 years of age, incipient rickets at 5 months, and pneumonia at 3 years 5 months. The

most outstanding features, however, were psychomotor retardation, anorexia, and failure to thrive. The boy smiled at 4 months, could sit upright without support at 15 months, could walk at 26 months, and started to say simple words at the age of 4 years. At that age the boy was seen for the first time in our Pediatric Department. Length was 93.5 cm (<3rd centile), weight 10.6 kg (<3rd centile), and head circumference 46.5 cm (<3rd centile).

Because of periods of fatigue, anorexia, and fever the boy was seen a second time at the age of 7½ years. His height was 108 cm, weight 13.9 kg, and head circumference 47.5 cm (all <3rd centile). Psychomotor evaluation at that time revealed dysarthria and an intellectual level of at most 5½ years (IQ=80).

At physical examination, a very slender boy with dwarfism, a marfanoid body configuration (arm span of 116 cm), and a lipodystrophic aspect was seen (fig 1). Except for the corpus of Bichat, there were no fat deposits. When standing upright, a straight vertebral column was noted. The following

FIG 1 General view (left) and facies (right) of the proband at 7½ years.

congenital anomalies were noted: antimongoloid slanting eyes, slight epicanthus of the right eye, large but normally implanted ears with undivided upper antihelix, broad and anteverted nostrils, long upper lip, high arched palate, bifid uvula, irregular implantation of the teeth, and receding chin. Webbing of the neck was present and the nipples were somewhat widely set. The extremities showed extremely dystrophic musculature, big first toes, and long and slender fingers, except for short fifth fingers with clinodactyly. Normal male genitalia were present. Heart auscultation and abdominal palpation revealed no abnormalities.

Audiometry, ophthalmological examinations, intravenous pyelography, electrocardiography, and radiography of the skull and total skeleton were all normal. The interorbital distance on sinus roentgenography was 2.65 cm. An electroencephalogram was slightly too slow for his age group and showed an increased frequency of theta waves.

Laboratory investigations revealed a normal blood film and serology, except for a low total lipid (3.45 g/l). The lipidogram, however, was normal, as was the analysis of faeces and urine, the figlu test, the dosage of growth hormone, and other endocrinological investigations (bone age, thyroid hormone, plasma cortisol level, and urinary steroids).

LDHB activity, the gene for which is known to be localised on the short arm of chromosome 12, was normal in serum. Since the parents refused further investigations, other markers of chromosome 12 (triosephosphate isomerase and glyceraldehyde-3-phosphate dehydrogenase) could not be studied.

CYTOGENETIC INVESTIGATIONS

Mitoses of the proband and his parents were obtained from PHA stimulated blood cultures. GTG banding revealed a 46,XY chromosome constitution and a chromosome 12 with an elongated short arm in the proband (fig 2). CBG and QFQ banding showed that the distal short arm region of the 12p+ chromosome was comparable to the distal long arm region of the free Y chromosome. Two Y bodies were present in interphase nuclei. Apparently, long arm material of a Y chromosome was translocated onto the short arm of chromosome 12. The 12p+ chromosome of the proband could be the result of a Y;12 translocation, having arisen during spermatogenesis in the father, or it could be due to a de novo translocation, occurring early in the development of an XYY zygote. In the last instance the XYY cell line would be lost, as well as the short arm and centromere segment of the second Y in the cells with the translocation. In both instances some material of the distal short arm of chromosome 12

(p13) would also be lost. Breaks occurred most probably at 12p13 and Yq11.

Both parents had normal chromosomes.

Discussion

In the proband extra Yq material and a partial deletion of 12p13 were present. In view of the dysmorphic features of our patient and the chromosome findings, an XYY syndrome seems unlikely. Indeed, the XYY constitution is found in males with normal or increased height, normal or borderline intelligence, and infrequently with undescended testes or hypogonadism. Other congenital anomalies are generally absent.⁴

The dysmorphism of the proband, however, is most likely the result of a partial 12p deletion. Although only a limited number of patients with a 12p deletion syndrome are known,⁴ the following characteristics have been noted: failure to thrive, mental retardation, microcephaly, antimongoloid slanting eyes, large nose, microretrognathia, large

FIG 2 Several examples of the GTG banded chromosomes 12 and the normal Y chromosome (first and second row), as well as the CBG banded 12p+ and Y chromosomes (third and fourth row). A partial QFQ banded mitosis showing the 12p+ and Y chromosome, and a quinacrine mustard stained interphase nucleus with two Y bodies are also shown (below).

and low set ears, clinodactyly and other abnormalities of fingers and toes, and cryptorchidism or micropenis or both.

In most cases with 12p- syndrome a larger deletion than in our patient was present, mostly including band 12p12. It is quite clear, however, that our proband has several features in common with the 12p deletion syndrome. Patients with a ring chromosome 12 have also been reported.^{5,6} They have several features in common with the 12p deletion syndrome and with our patient. The clinical features in these patients are⁵: failure to thrive, mental retardation, epicanthus, 'cupped', low set ears, ogival palate, short webbed neck, low hairline, and cryptorchidism. In the ring chromosome cases a partial deletion of 12p13, similar to that in our patient, is present.

Regarding the enzyme lactate dehydrogenase B (LDHB), no reduction in activity was noted in our patient. Decreased activity was found in the 12p deletion cases⁴ but not in the ring chromosome 12 case of Zuffardi *et al.*⁶ This seems to be in accordance with the gene localisation of LDHB at 12p12 and points to a similar 12p deletion in our

patient as in the ring chromosome 12 case of Zuffardi *et al.*⁶

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Correspondence and requests for reprints to Dr E Orye, Laboratory of Cytogenetics, Department of Pediatrics, Ghent State University, De Pintelaan 185, 9000 Ghent, Belgium.

Interstitial deletion of the long arm of chromosome 11

J M KLEP-DE PATER, H F DE FRANCE, AND J B BIJLSMA

Clinical Genetics Centre, PO Box 18009, 3501 CA Utrecht, The Netherlands.

SUMMARY A girl with an interstitial deletion of the long arm of chromosome 11 is described. The patient was mildly mentally retarded and showed some facial dysmorphic features, including hypertelorism, ptosis, and cleft palate.

Since Jacobsen *et al.*¹ reported a family with a terminal deletion 11q, about 30 other cases have been published. These cases were all severely mentally retarded and presented with characteristic craniofacial anomalies: trigonocephaly, epicanthus, ptosis, flat nasal bridge, short bulbous nose with anteverted nostrils, triangular shaped mouth, retrognathia, and low set malformed ears. In all but one of the reported cases a de novo deletion of 11q, with loss of at least the terminal region q24→qter, was present. De novo interstitial deletions of the long arm of chromosome 11 have been reported in four infants by Taillemite *et al.*² Sørensen *et al.*³

McPherson and Meissner,⁴ and Bateman *et al.*⁵ Two of these cases were mildly mentally retarded and had trigonocephaly, hypertelorism, short bulbous nose, and high and narrow palate. In three cases low set ears were also present. In the case of Bateman *et al.*⁵ who presented with Peter's anomaly, neither mental retardation nor dysmorphic signs were noted.

We report a girl with only mild mental retardation and some of the above mentioned phenotypic features in whom an interstitial deletion of the long arm of chromosome 11 was found.

Case report

The proband was the only child born to a young woman, who was reported to take drugs and drank alcohol in unknown quantities throughout pregnancy. The proband was removed from the custody of her mother and placed under the care of the juvenile court. According to the rules of this organisation no further information on the mother can be published