Short reports

Three cases of 16q duplication

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Complete or partial duplication of 16q has been described in 20 cases.¹⁻⁴ We have recently diagnosed a further three patients.

Case 1 was delivered by Caesarean section at 32 weeks' gestation because of intrauterine growth retardation (<3rd centile), oligohydramnios, and fetal distress. Dysmorphic features included a high forehead, beaked nose, long philtrum, micrognathia, simple ears, a simian crease on the right hand, anteriorly placed anus, and micropenis. The infant died on day 18. Necropsy findings were: head circumference 29 cm, crown-heel length 42 cm, absent fontanelles, hydrocephalus with aqueduct stenosis, bicuspid aortic and pulmonary valves, patent ductus arteriosus, anomalous origin of the left subclavian artery, absent gall bladder, and hydrocephalus secondary to aqueduct stenosis. Chromosome analysis showed a paternally derived unbalanced 10;16 translocation: 46,XY,-10,+der(10),t(10;16)(q26.3;q21)pat (figure).

Case 2 was born to a 29 year old mother with one previous normal child and four first trimester miscarriages. Birth weight was 1800 g and head circumference 31 cm at 38 weeks' gestation. Low set ears, choroidal coloboma, transposition of the great arteries, ventricular septal defect, arthrogryposis, and hypospadias were apparent. He died at 3 months of age. Chromosome analysis showed a maternally derived unbalanced 3;16 translocation: 46,XY,-3,+der(3),t(3;16)(p26;q23)mat (figure).

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Case 3 was referred at 19 years of age for fragile X testing. He was severely retarded with no speech, autistic features, large ears, large nose, and hyperextensible joints. Head circumference was 55 cm (50th centile). Chromosome analysis showed a maternally derived unbalanced 16;22 translocation: 46,XY,-22,+der(22),t(16;22)(q24;q13.3)mat (figure).

All reported cases of 16q duplication have resulted from a parental translocation so that critical analysis of the clinical features of 16q duplication is made difficult by the concomitant autosomal monosomy. Nevertheless, growth retardation and mental handicap are inevitable and a high forehead, beaked nose, long philtrum, and micropenis in males are frequent findings. Hahn *et al*¹ have proposed an association between the extent of 16q reduplication and the presence of visceral abnormalities such as congenital heart disease and gastrointestinal defects, including malrotation and anorectal abnormalities, and an inverse relationship between extent of reduplication and longevity. Our data are broadly consistent with this as case 3, who is the oldest patient yet reported, had the smallest reduplication. However, severe visceral abnormalities can occur in patients with duplication of 16q21→qter, and the extent of the concomitant monosomy is also relevant.

Parental translocations have most frequently involved chromosomes 9 (n=3), 11 (n=2), 15 (n=4), 18 (n=2), and 22 (n=2).¹⁻⁴ Chromosomes 3 (case 2) and 10 (case 1) have not been reported previously. Francke⁵ described a patient with an unbalanced 16;22 translocation with duplication of the distal third of 16q and partial 22q monosomy. Her patient, who had more extensive 16q duplication than case 3, had intrauterine growth retardation, prominent forehead, generalised hypotonia, and a large patent ductus arteriosus, and died during the first year of life.

1 Hahn SYE, Chitayat D, Iqbal MA, Cho S, Nitowsky HM. Partial duplication 16q: report of two affected siblings resulting from a maternal translocation and literature review. *Clin Genet* 1987;31:343-8.

2 Lessick ML, Israel J, Wong PWK, Szego K. Partial trisomy 16q secondary to a maternal 9;16 translocation. *J Med Genet* 1989;26:63-4.

GTG banded partial karyotypes observed in cases 1, 2, and 3 for balanced translocation carrier parent and unbalanced translocation child. Full details of karyotypes are in the text. The ideogram of chromosome 16 shows the breakpoint on chromosome 16q for each case.

- 3 Dowman C, Lockwood D, Allanson J. Familial translocation $t(9;16)$. *J Med Genet* 1989;26:525-8.
- 4 Nyan WL, Mascarello J, Barshop B, Doroski D, Hirschhorn K. Duplication of 16q and deletion of 15q. *Am J Med Genet* 1989;34:183-6.

- 5 Francke U. Quinacrine mustard fluorescence of human chromosomes: characterization of unusual translocations. *Am J Hum Genet* 1972;24:189-213.

4

Cutting GR, Kasch LM, Rosenstein BJ, *et al*. A cluster of cystic fibrosis mutations in the first nucleotide-binding fold of the CFTR protein. *Nature* 1990;364:366-9.

5

Feldman GL, Williamson R, Beaudet AL, O'Brien WE. Prenatal diagnosis of cystic fibrosis by DNA amplification for detection of KM-19 polymorphism. *Lancet* 1988;ii:102.

6

Rosenbloom R, O'Brien WE, Beaudet AL. DNA amplification for detection of the XV-2c polymorphism linked to cystic fibrosis. *Nucleic Acids Res* 1989;17:7117.

7

Voss R, Ben-Simon E, Avital A, *et al*. Isodisomy of chromosome 7 in a patient with cystic fibrosis: could uniparental disomy be common in humans? *Am J Hum Genet* 1989;45:373-80.

8

Lerer I, Cohen S, Chemke M, *et al*. The frequency of the $\Delta F508$ mutation on cystic fibrosis chromosomes: correlation of CF haplotypes in Jewish communities and Arabs. *Hum Genet* 1990;85:416-7.

9

Lemna WK, Feldman GL, Kerem B, *et al*. Mutation analysis for heterozygote detection and the prenatal diagnosis of cystic fibrosis. *N Engl J Med* 1990;322:291-6.

10

Tsui LC. Population analysis of the major mutation in cystic fibrosis. *Hum Genet* 1990;85:391-445.

11

Cremonesi L, Ruocco L, Seia M, *et al*. Frequency of the $\Delta F508$ mutation in a sample of 175 Italian cystic fibrosis patients. *Hum Genet* 1990;85:400-2.

12

McIntosh I, Curtis A, Lorenzo ML, *et al*. The haplotype distribution of the $\Delta F508$ mutation in cystic fibrosis families in Scotland. *Hum Genet* 1990;85:419-20.

13

Santis G, Osborne L, Knight R, Ramsay M, Williamson R, Hodson M. Cystic fibrosis haplotype association and the $\Delta F508$ mutation in adult British CF patients. *Hum Genet* 1990;85:424-5.

14

Balassopoulou A, Loukopaoulos D, Kolia P, *et al*. Cystic fibrosis in Greece: typing with DNA probes and identification of the common molecular defect. *Hum Genet* 1990;85:393-4.

15

Vidaud M, Fanen P, Martin J, Ghanem N, Nicholas S, Goossens M. Three point mutations in the CFTR gene in French cystic fibrosis patients: identification by denaturing gradient gel electrophoresis. *Hum Genet* 1990;85:446-9.

Correction

In the paper by Maher *et al* in the November 1991 issue of the Journal (*J Med Genet* 1991;28:801-2), we regret that two chromosomes were missing from the partial karyotype. The correct figure is reproduced below.

GTG banded partial karyotypes observed in cases 1, 2, and 3 for balanced translocation carrier parent and unbalanced translocation child. Full details of karyotypes are in the text. The ideogram of chromosome 16 shows the breakpoint on chromosome 16q for each case.