Partial trisomy 6p: 46,XX,−10, der(10),t(6;10)(p22;q26)pat and HLA localisation

SUMMARY A child with multiple facial anomalies showed partial trisomy 6p, 46,XX,−10,der(10), t(6;10)(p22;q26)pat. Family studies suggested that the HLA complex is probably between 6p22.4 and 6p21.05.

The HLA system had previously been localised between 6p21 and 23 and more precisely located by Berger et al above 6p21.05. We have studied the clinical presentation and the HLA system of the family of a child with partial trisomy 6p derived from a paternal translocation.

References


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Since Breuning et al collected and studied the first six known cases of trisomy 6p, 12 cases have been found with similar clinical manifestations, varying in the breakpoint and the part of 6p which was triplicated. Independent of the classification of the clinical manifestations of new syndromes, the importance of duplication-deficiency chromosomal abnormalities is determined by the localisation of gene loci. The HLA system was localised between 6p21 and 23 in 1979, and more precisely by Berger et al above 6p21.05. Our results suggest that the HLA system is below 6p22.4, the breakpoint found in the balanced translocation 6p22;10q26 of the father which produced the partial trisomy 6p22→pter of the proband.

Case report

The proband, born 6.4.75, is the second child of healthy unrelated parents with no relevant family history. The father was 37 and the mother 30. The older child is a normal 7-year-old boy. The mother has had no other pregnancies and this one was at term with a normal delivery.

At birth the child weighed 2200 g. Physical examination revealed high forehead, blepharoptosis of the left eye, bilateral blepharophimosis, convergent strabismus, high arched palate, grooved tip nose, low set ears, small mouth with thin lips, short frenula tying the tongue, bilateral clinodactyly of the 5th fingers, kyphosis, and psychomotor retardation. When she was brought to us 3 years later (fig 1), she weighed 10 kg (3rd centile) and was 79·3 cm tall (3rd centile). X-ray examination showed bilateral brachymesophalany of digits 2 and 5 and an ulnar reduction of 5 mm. Bone age was 6 months retarded for her age. Blood and urine tests, aminocids, and mucopolysaccharides were all normal. No proteinuria was detected.

![Figure 1: Face of the proband.](http://jmg.bmj.com/10.1136/jmg.a183.231)
CHROMOSOME STUDIES

Chromosome analysis was carried out on peripheral blood lymphocytes by G banding, and Q banding. The karyotype showed 46 chromosomes with an extra band in the terminal segment of the 10q chromosome. In the family study, the father and the brother had a balanced translocation (6;10)(p22; q26). The child was therefore trisomic for the segment 6p22→pter. The mother's karyotype was normal.

HLA ANTIGEN STUDIES

To detect the HLA-A, -B, -C, -B44 and -Bw6 antigens, the lymphocytes were isolated by the Boyum method and typed by the method of Mittal et al. For HLA-DR antigen typing we used

FIG 2  HLA antigens (4a=Bw4,4b=Bw6).

FIG 3  Schema and abnormal chromosomes of the proband and her father.
the method of Gutierrez et al10 for B cell separation, followed by a microcytotoxicity technique (one hour incubated with sera, 2 hours with rabbit complement). Tests were performed with all the sera of the VIII International Workshop of Histocompatibility. The results (fig 2) show the presence in the proband of one maternal and one paternal haplotype with no duplication.

COMPLEMENT AND ENZYME STUDIES

The B factor (Bf) of the alternate complement pathway allotypes was analysed by the technique of Alper et al11 and the red cell glyoxalase 1 (GLO 1) by the technique of Parr et al.17 There is a GLO/HLA crossover in one of the mother’s haplotypes that could have been received by the normal sib. These polymorphism studies were not informative.

Discussion

Of the 12 cases reported, eight show the breakpoint in 6p21, three in 6p22, and one in 6p23. Bernhein et al13 made a resumé of seven 6p21 cases whose main features were: psychomotor retardation, hypotrophy, low birthweight, high and prominent forehead, close set eyes, blepharophimosis, blepharoptosis, nystagmus, high nasal bridge, small mouth, low set ears, sacral dimple, congenital heart malformation, small kidneys, and proteinuria. The remaining five cases have almost the same clinical manifestations although the breakpoints are different. Our case has the facial dysmorphism of most of those reported, particularly the grooved tip nose and the short frenula, but no cardiac or renal malformations. Our breakpoint is in 6p22-4 (fig 3)14 with the break band in p22 in both chromosomes 6 and 10. According to Berger et al,8 the HLA system is localised above 6p21.05. In our case with the breakpoint in 6p22.4, we are almost sure that the HLA antigens in the father are coded for by genes situated in the non-translocated chromosome region. The translocated segment in his daughter does not have the information to codify these antigens. However, as the father is homozygous for locus A (A2) and the sequence of loci are pter-A-C-B-Bf-D/DR-GLO-cent, it could be that the breakpoint occurred between the HLA-A and -C loci, the daughter then being disomic for A2.

The claim by Berger et al8 that 6p21.05 contains the HLA complex should not be taken as conclusive. They rest their claim on the fact that their trisomic cell responded in mixed lymphocyte culture to the mother cell which gave two of the three haplotypes. Since locus D is mostly responsible for the mixed lymphocyte reaction in normal cells (but not completely; cf Festenstein and Demant15), it was concluded that the trisomic cell was not trisomic for HLA-D and that the breakpoint was between HLA-D and -B. However, other possibilities should be considered before accepting this theory.

1) HLA-D alleles should be typed in the family for a positive demonstration of HLA-D disomy or trisomy in the proband’s cell.

2) Testing should be carried out to ascertain whether HLA trisomic cells behave as normal cells in the mixed lymphocyte reaction. There are also other loci, HLA and non-HLA linked,15 that may vary the normal mixed lymphocyte reaction response in this particular cell.

Moreover, HLA-DR typing does not support the hypothesis that the breakpoint is between D and B, because D and DR go together in the families studied16 and B/DR segregation in the family of Berger et al8 is as expected if the breakpoint is outside the HLA complex and more towards the centromere.

The only possibility that the HLA-B and -C antigens might be on the translocated segment is if the genetic polymorphism of the histocompatibility systems is for the control of whichever of the genes is expressed. Then the genome of each subject would have all the possible histocompatibility genes.17 There is evidence to support this hypothesis.18 If that were so in our case, the ‘structural’ genes could be in the translocated region and the adjacent specific depressor genes in the non-translocated segment. Thus, in the proband, the antigens of haplotypes A2, Bw44, and Cw5 would not be expressed because of the absence of the neighbouring specific depressor genes that were not translocated, not because there was a lack of the structural genes codifying for these antigens in her genome.

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References

Case reports

An infant with ring 17 chromosome and unusual dermatoglyphs: a new syndrome?

SUMMARY A case of ring 17 chromosome in a 5-month-old male infant is investigated and compared with five previously reported cases. The findings commonly observed in these patients include mental and motor retardation, seizures, short stature, muscular hypotonia, and microcephaly among others. Dermatoglyphic studies showed an increased number of ulnar loops. More interestingly, bilateral transverse hypothenar creases were noted. Two of the reported cases also had unspecified genital abnormalities. The variation in clinical findings among these patients may be explained by a difference in the breakpoints on chromosome 17.

To the best of our knowledge this is the third report of a liveborn child with ring 17 chromosome without mosaicism confirmed by banding. We present here the clinical findings in our patient compared to those observed in other cases with and without mosaicism as described in published reports.

Case report

The proband (fig 1) was the first child of non-consanguineous parents born after an uncomplicated 42 week pregnancy. The birthweight was 1290 g. The mother was 32 and the father was 34 years old.

The patient was seen at 5 months of age with a weight of 4432 g, head circumference 36·6 cm, and length 53·3 cm (all below the 3rd centile). Inner canthal distance was 30 mm and outer canthal distance was 76 mm (below the 97th centile). Anterior fontanelle size was 5·5 cm (greater than the 97th centile). The forehead was flattened and he had unruly hair. The nasal bridge was broad and depressed with anteverted nostrils. The palpebral fissures had a downward slant with epicanthic folds. He had a disconjugate gaze and an alternating esotropia. The ears were low set, with the left ear being larger than the right. Flattening of the helix,