

## Electronic letter

### A child with bisatellited, dicentric chromosome 15 arising from a maternal paracentric inversion of chromosome 15q

EDITOR—Carriers of paracentric chromosome inversions are usually regarded as being at low risk of having offspring with an unbalanced chromosome complement.<sup>1,2</sup> Some reports have suggested that rearrangements, such as very small interstitial deletions or duplications arising from unequal crossing over at the base of the inversion loop and deletion or deletion/duplication recombinants, created by the breakage of an unstable dicentric chromosome, can arise from paracentric inversions.<sup>3-7</sup> Pettenati *et al*<sup>8</sup> reviewed 446 cases of paracentric inversions and suggested that carriers of such inversions had a 3.8% risk of having viable offspring with stable recombinant chromosomes. However, this observation has been disputed<sup>9</sup> as it is possible that so called paracentric inversions giving rise to monocentric recombinants are actually insertional translocations and the traditional view is that the resulting unbalanced

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chromosomes arising from a paracentric inversion would involve either a dicentric or acentric chromosome, and therefore be unlikely to be viable.<sup>10</sup>

We report a liveborn child with mild dysmorphic features who had a dicentric chromosome arising from a maternal paracentric inversion. To our knowledge there have only been two previous reports of this situation arising.<sup>11,12</sup>

The proband is the second child of healthy, non-consanguineous, Scottish parents. He was born at term, by spontaneous vaginal delivery, following an uncomplicated pregnancy. His birth weight was 2860 g and occipitofrontal circumference (OFC) was 33 cm (both 3rd centile). Shortly after birth he developed respiratory distress and was noted to have mild dysmorphic features, including a prominent nasal root, large prominent eyes, and micrognathia (fig 1). He also had dislocated hips, severe talipes equinovarus, and held his hands tightly clenched, although there were no contractures and his palmar creases were normal. An echocardiogram showed a large perimembranous ventricular septal defect (VSD) with a small patent ductus arteriosus but ultrasound scans of his head and kidneys were normal.

At the age of 16 weeks his VSD was repaired as he was failing to thrive and had developed symptoms of cardiac



Figure 1 The proband aged 3 months.

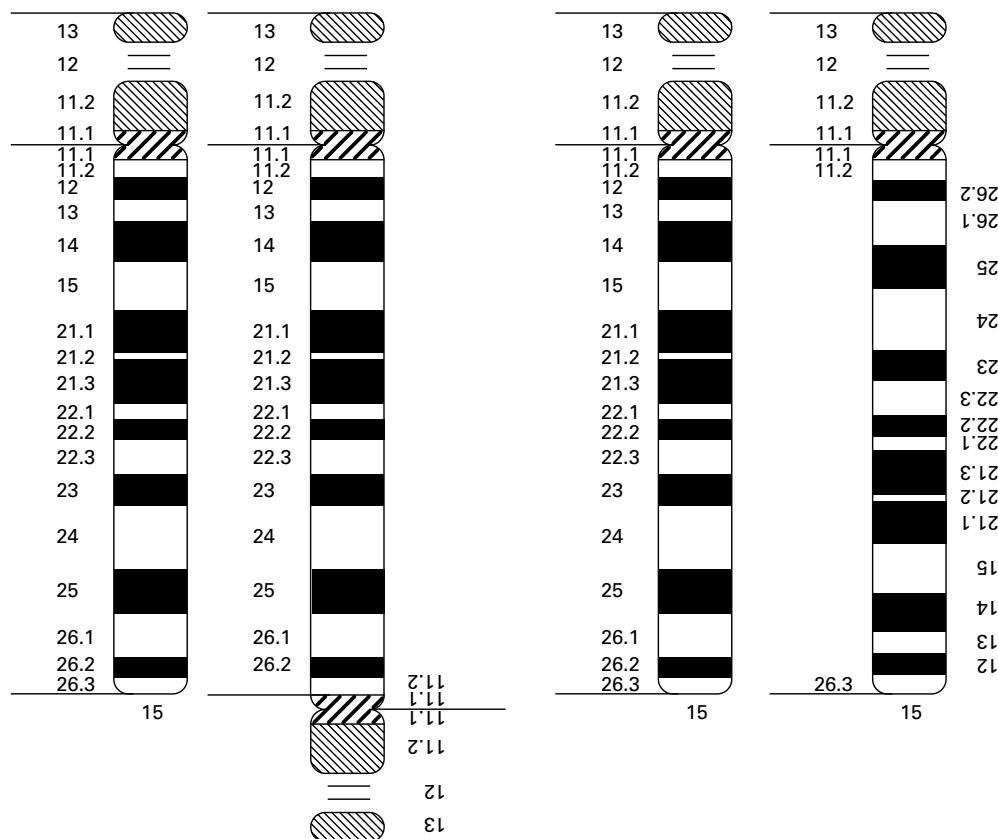


Figure 2 Chromosomes 15 from the infant (left) and his mother (right).

failure. When reviewed at the age of 13 months his dysmorphic features were less apparent but his growth parameters and OFC had fallen below the 3rd centile. He remained in a splint for his dislocated hips for 11 months and did not walk until the age of 2 years. The position of his feet remains a problem and ankle-foot orthoses are currently being considered. His general development, at the age of 35 months, is assessed to be one year behind his chronological age. He remains microcephalic with OFC less than 2 SD below the mean and weight on the 3rd centile.

Chromosome analysis of peripheral blood lymphocyte cultures from the proband showed a 46,XY chromosome complement with a bisatellited dicentric chromosome 15. This was subsequently interpreted as a 46,XY,rec(15)(pter→q26.3::q11.2→pter)inv(15)(q11.2q26.3)mat karyotype (fig 2), derived from an apparently balanced paracentric inversion of chromosome 15 carried by the proband's mother, 46,XX,inv(15)(q11.2q26.3) (fig 2). The father had an apparently normal karyotype.

This results in the proband being trisomic for 15pter→q11.2 and monosomic for the region 15q26.3→qter. This karyotype would be consistent with a crossover within the inversion loop during maternal meiosis.

This is only the third report of a liveborn child with a dicentric chromosome resulting from a paracentric inversion in one of the parents. In all cases, the distal segment of the chromosome, beyond the inversion, is small. In our report the proximal segment is also relatively small and so, therefore, is the duplication. The case report by Mules and Stamberg<sup>11</sup> concerned a child with a dicentric chromosome 14 and the duplicated segment was larger. This child died a few hours after birth.

Predicting the prognosis for the proband in this report is difficult. There have been a number of reports of patients

with a ring chromosome 15 who are deleted for the small distal segment.<sup>13 14</sup> Those with a very distal breakpoint, as with our patient, have shown mild mental handicap and relatively mild growth failure, with some phenotypic similarities to Russell-Silver syndrome. The review of patients with ring chromosome 15 by Wilson *et al*<sup>15</sup> indicated that around 25% of patients with this chromosomal abnormality also had congenital cardiac defects.<sup>15</sup> Trisomy for proximal 15q has resulted in a variable degree of mental handicap and dysmorphism, if the Prader Willi/Angelman critical region (PWACR) is included in the duplicated region and is of maternal origin, but no consistent effect on growth has been documented.<sup>16 17</sup> Unfortunately, it has not been possible to obtain a further sample from our patient to determine whether or not he is trisomic for PWACR or to assess the stability of the dicentric chromosome.

The birth of abnormal children to carriers of paracentric inversions is rare and the absolute risk must still be very small. The risk may be greater if it is a woman who carries the inversion, and is greater when the chromosome is acrocentric with a large inversion, where the distal breakpoint is close to the tip. It is therefore important that family studies and prenatal diagnosis are considered if the higher risk criteria are met. It was considered that for this family the risk would be high following the birth of an affected child and chromosome analysis has been offered to relatives of the mother. So far, only the mother's sister, who is her only sib and who has one healthy son, has been found to carry the inversion, so it has not been possible to quantify the actual risk of this type of recombination to carriers of this particular paracentric inversion.

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