TABLE  Summary of clinical findings in three cases of trisomy 9q.

<table>
<thead>
<tr>
<th></th>
<th>Turleau et al1</th>
<th>Faed et al2</th>
<th>Present case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomic segment</td>
<td>q11→q33</td>
<td>q12→q32</td>
<td>q12→q32</td>
</tr>
<tr>
<td>Pregnancy (wk)</td>
<td>40</td>
<td>36</td>
<td>37</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>2300</td>
<td>1730</td>
<td>2300</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>50</td>
<td></td>
<td>44</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>32.5</td>
<td></td>
<td>29</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>Asphyxia or neonatal problems</td>
<td>+</td>
<td>+</td>
<td>—</td>
</tr>
<tr>
<td>Microdolichocephaly</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Slender face</td>
<td>+</td>
<td>(+)</td>
<td>+</td>
</tr>
<tr>
<td>Hypotelorism</td>
<td>+</td>
<td>(Wide set)</td>
<td>(Borderline)</td>
</tr>
<tr>
<td>Horizontal palpebral fissures</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Epicanthic folds</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Strabismus</td>
<td>+</td>
<td>+</td>
<td>—</td>
</tr>
<tr>
<td>Nose</td>
<td>Beaked</td>
<td>Beaked</td>
<td>Beaked</td>
</tr>
<tr>
<td>Mouth</td>
<td>Small</td>
<td>Small</td>
<td>Small</td>
</tr>
<tr>
<td>Lips</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Micrognathia</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Abnormality of the thumbs</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hip joint</td>
<td>Flexion contracture</td>
<td>Unilateral dislocation</td>
<td>Normal</td>
</tr>
<tr>
<td>Feet</td>
<td>Long toes with abnormal implantation</td>
<td>Ventricular septal defect</td>
<td></td>
</tr>
<tr>
<td>Internal malformation</td>
<td>Poor</td>
<td>Poor</td>
<td>Poor</td>
</tr>
<tr>
<td>Thriving</td>
<td>Poor</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Natural history</td>
<td>Alive at 5 years</td>
<td>Alive at 4 years</td>
<td>Alive at 2 years</td>
</tr>
</tbody>
</table>

Discussion

As far as we are aware, there have been only two reported cases of trisomy 9q in which most of the long arm is involved (table). The clinical features common to all three cases are: low birth weight, failure to thrive, mental retardation, narrow face, epicanthic folds, beaked nose, small mouth, micrognathia, and good life expectancy during infancy. These similarities should make it possible to recognize this abnormality on the basis of clinical findings. It is remarkable that the presence of such a large extra segment has a relatively mild effect on the patient.

The authors are grateful for technical assistance to Mr T Yokochi, Shizuoka Children's Hospital.

References


Correspondence and requests for reprints to Dr Y Nakahori, Department of Human Genetics, National Institute of Genetics, Yata 1, 111 Misima, Sizuoka-ken, 411 Japan.

Familial centric fission of chromosome 4

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SUMMARY A centric fission of chromosome 4 is described in the proband and his mother, both phenotypically normal. In addition, partial monosomy for the long arm or the short arm or both of chromosome 4 may have been present in two of the proband’s sibs who died in infancy and childhood, respectively.

Centric fission of a chromosome consists of a break in the centromeric region, which results in the

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separation of the centromere into two portions, and consequent formation of two stable telocentric chromosomes. Such an event, well known in animals, was first described in humans by Sinha et al.\(^1\) Other cases of centric fission in man have been reported by Hansen,\(^2\) Fryns et al.,\(^3\) and more recently by Janke.\(^4\)

The only case of centric fission of chromosome 4 reported so far was described by Dallapiccola et al.\(^5\) in the mother of two patients with trisomy 4p.

**Case report**

A couple requested genetic counselling because of familial infertility. A pedigree analysis, which was uninformative for the wife, indicated, however, consanguinity in the husband's family, his parents being first cousins (fig 1). In addition, the sibship of the husband's mother (IIIA) included three spontaneous abortions and two deaths in early childhood, and the husband's sibship (IVB) also included two spontaneous abortions and two deaths (IV.11 and IV.15).

Chromosome analysis showed a normal karyotype for the wife and a 47,XY,cen fiss 4 complement for the husband. As a result, the proband's parents were also examined. The father (III.7) had a normal karyotype, while the mother (III.8) was found to have a centric fission of chromosome 4.

The clinical data regarding the dead children, IV.11 and IV.15, were based on the mother's report and on examination of photographs (table 1).

![Family pedigree](http://jmg.bmj.com/)

**FIG 1** *Family pedigree.*

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>IV.11</th>
<th>IV.15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Growth</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Psychomotor retardation</td>
<td>Severe</td>
<td>Severe</td>
</tr>
<tr>
<td>Delay in walking</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Delay in language development</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Convulsions</td>
<td>Frequent</td>
<td>Frequent</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>Not identified</td>
<td>Present</td>
</tr>
<tr>
<td>Glabella</td>
<td>Normal</td>
<td>Prominent</td>
</tr>
<tr>
<td>Palpebral fissures</td>
<td>Mongoloid slant</td>
<td>Not identified</td>
</tr>
<tr>
<td>Strabismus</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Nose</td>
<td>Wide and flat bridge</td>
<td>Beaked</td>
</tr>
<tr>
<td>Ear abnormality</td>
<td>Pointed</td>
<td>Large, low set</td>
</tr>
<tr>
<td>Micrognathia</td>
<td>Doubtful</td>
<td>Present</td>
</tr>
<tr>
<td>Hypoplasia of mandible</td>
<td>Moderate</td>
<td>Present</td>
</tr>
<tr>
<td>Cardiac defects</td>
<td>Not identified</td>
<td>Present</td>
</tr>
<tr>
<td>Age at death</td>
<td>6 months</td>
<td>12 years</td>
</tr>
</tbody>
</table>
Case reports

**TABLE 2 Clinical data identified in partial aberrations of chromosome 4.**

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>4p−</th>
<th>4q−</th>
<th>4p+</th>
<th>4q+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>Low ++</td>
<td>Normal</td>
<td>Low +</td>
<td>Low +++</td>
</tr>
<tr>
<td>Growth delay</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Psychomotor retardation</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Delay in language development</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Hypotonia</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Convulsions</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Age of survival</td>
<td>17 years</td>
<td>4 years</td>
<td>Youth</td>
<td>—</td>
</tr>
<tr>
<td>CNS malformations</td>
<td>Frequent</td>
<td>Rare</td>
<td>Rare</td>
<td>—</td>
</tr>
<tr>
<td>Brachycephaly or oxycephaly</td>
<td>++</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Haemangiomas</td>
<td>++</td>
<td>Normal</td>
<td>Low hairline</td>
<td>Normal</td>
</tr>
<tr>
<td>Absence of scalp</td>
<td>++</td>
<td>Normal</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Hypertelorism</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Coloboma</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Strabismus</td>
<td>++</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Palpebral fissures</td>
<td>Antimongoloid</td>
<td>Horizontal mongoloid</td>
<td>Horizontal</td>
<td>Horizontal or slightly slanted</td>
</tr>
<tr>
<td>Glabella</td>
<td>Prominent</td>
<td>Prominent</td>
<td>Prominent</td>
<td>Prominent</td>
</tr>
<tr>
<td>Nose</td>
<td>Beaked</td>
<td>Wide and flat bridge</td>
<td>Low set, dysmorphic</td>
<td>Low set, dysmorphic</td>
</tr>
<tr>
<td>Micrognathia</td>
<td>+++</td>
<td>+++</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cleft lip and/or palate</td>
<td>+++</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hypoplasia of mandible</td>
<td>++</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cardiac defects</td>
<td>+++</td>
<td>+++</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Accessory ribs</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Vertebral malformations</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hypoplasia of pelvis</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Renal anomalies</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Abdominal anomalies</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hip dislocation</td>
<td>+</td>
<td>+</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Flexion creases of 4th finger</td>
<td>+++</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Dermatoglyphs</td>
<td>Reduced</td>
<td>Normal</td>
<td>Increased</td>
<td>Normal</td>
</tr>
<tr>
<td>Camptodactyly</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Flat or displaced feet</td>
<td>+</td>
<td>+</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Clinodactyly</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hypoplasia of external genitalia</td>
<td>+</td>
<td>+</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cryptorchidism</td>
<td>+</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

+++ severe, ++ moderate, + mild, — absent.

**FIG 2 Chromosomal pattern of the proband (GTG banding).**
Discussion

This appears to be the first published case report of transmitted centric fission of chromosome 4 so far. It is interesting to observe the particular stability of human telocentric chromosomes, which involve a high risk of transmission of non-balanced gametes.

In sibships A and B there are early spontaneous abortions which could be attributed to the unbalanced form of the aberration. Another point worthy of attention is the possible clinical interpretation of the two children of sibship B, who died at 6 months and 12 years, respectively. Their phenotype was deduced from the clinical history and the photographs.

Table 2 lists the symptoms described in cases of partial aberrations of chromosome 4 and allows a comparison with those present in the two dead children as a possible aid to a specific diagnosis.

Of the various clinical manifestations described in table 1, subject IV.11 presented with a normal birth weight, flat and wide nasal bridge, mongoloid slant, absence of strabismus, and died at 6 months. These symptoms are also found in cases of partial 4q—suggesting that partial monosomy of the long arm of chromosome 4 was present in this child.

Subject IV.15 presented with a beaked nose, pronounced micrognathia, strabismus, and marked hypoplasia of the mandible. Death occurred at 12 years. This appears to be consistent with malformations found in partial monosomy of the short arm of chromosome 4. In particular, the age of death is similar to the only case reported of survival through the first year of life in a subject with partial 4p monosomy.

We would like to thank Mr Mario Sanchioni for his help with the photographs.

References

4 Janke D. Centric fission of chromosome 7 in three generations. Hum Genet 1982;60:200-1.

Correspondence and requests for reprints to Professor Giuseppe Del Porto, Via San Calepodio 7, 00152 Rome, Italy.

Mosaic Down's syndrome with de novo 45,XX,—21,—22,+t(21q;22q)/46,XX,—21,+t(21q;21q) rearrangement

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*Department of Pediatrics, University of Tennessee Center for the Health Sciences, Memphis, Tennessee; and †the Genetics Screening and Counselling Service, Denton, Texas, USA.

SUMMARY The occurrence of mosaic Down's syndrome with two independent Robertsonian translocation cell lines is very rare. Such a patient is reported here, in whom an unbalanced Robertsonian translocation between two chromosomes 21 was detected in the majority of cells. The patient also revealed a minor cell line with a second Robertsonian translocation involving a chromosome 21 and a 22. The chromosome translocations detected in this patient were de novo in origin.

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G Del Porto, C Di Fusco, M Baldi, P Grammatico and E D'Alessandro

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