Tetrasomy 9p: confirmation by enzyme analysis

SUMMARY A 4-day-old Caucasian male presented with midline defects of the skull and face and extensive skeletal malformations. Chromosome analysis of peripheral blood lymphocytes showed tetrasomy 9p (47,XY,+i(9p)) with no evidence of mosaicism. Confirmation of the cytogenetic interpretation was obtained from the assay of the enzyme galactose-1-P uridyl transferase, the locus for which is on 9p, which showed twice the normal activity.

Tetrasomy 9p was first described by Ghymers et al.1 Four more cases have been described since.2-5 These patients all differ in their phenotypic presentation and although all of them have the extra apparent isochromosome 9p, the amount of chromosome material between the short arms of the isochromosome is variable. In three instances mosaicism was present in the tissue or tissues sampled,1 3 4 and in two cases in which chromosome analysis was done on peripheral blood lymphocytes only no mosaicism was found.2 5

Case report

The patient was the product of a non-consanguinous mating; the mother was 19 and the father was 24 years old at the time of the patient's birth. The pregnancy was full term and uncomplicated. Labour and delivery were normal and the Apgar scores were 4 at 1 minute and 3 at 5 minutes. Birthweight was 2600 g and multiple congenital anomalies were noted at birth.

Findings at 4 days of age (fig 1, 2) included widely patent metopic and sagittal sutures extending to the posterior fontanelle, flattening of the posterior of the skull, soft consistency of the skull, head circumference of 33.5 cm (25th to 50th centile), hypertelorism (inner canthal distance of 3 cm), bilateral cleft lip and palate, micrognathia, anteriorly rotated but normally placed ears with reduced cartilage on palpation, preauricular skin tag on the left, short neck, no cardiac murmur or organo-
megalgy, bilateral cryptorchidism, sacral dimple, shortened limbs with an arm span of 40 cm compared to total body length of 45.5 cm with upper to lower segment ratio of 2, contractures of the interphalangeal joints with each finger having only two phalanges and a single crease, hypoplastic to absent nails, limited abduction of the hip joints with hyper-extensible knee joints and bilateral varus deformity, increased mobility of the elbow and wrist joints suggesting joint dislocation, hypoplastic scapulae with kyphosis of the spine, and short pelvis. Muscle tone was decreased and the cry was weak. Dermatoglyphs showed bilateral simian lines with hypoplastic dermal ridges.

Radiological studies showed a small anterior cranial fossa, hypoplastic facial structures compared with the remainder of the skull, midline cleft face, hypertelorism, dislocation of the hip, knee, and elbow joints, bilateral varus deformity, and absent or poor ossification of the sternum, carpal bones, and phalanges of the hands.

The infant was later placed in a foster home where he developed apnoeic spells and died at 2 months of age. Because of circumstances, necropsy and further studies could not be performed.

The father of the patient had had numerous x-ray exposures during the past few years after injury to his face requiring extensive reconstructive surgery which was further complicated by seizures. The mother had had an induced abortion of her first and only other pregnancy which was by another man. The mother is of German extraction and the father's natural parents are said to be of American Indian-French origin. The remainder of the family history is otherwise unremarkable.

Cytogenetic Studies
Peripheral blood lymphocytes of the patient were analysed by Giemsa banding and all 60 cells counted showed an XY pattern with an extra chromosome similar in size and appearance to a number 16 chromosome, but with a banding pattern consistent with an isochromosome of the short arm of chromosome 9 (fig 3). This aberrant chromosome appeared to have only one positive C banding area, which suggests that there is probably no extra chromosome

![Fig 3](http://jmg.bmj.com/ on May 29, 2017 - Published by group.bmj.com)
Case reports

material present in the centromeric region. Both parents have normal chromosomes.

ENZYME STUDIES
Assay for the enzyme galactose-l-P uridyl transferase (EC 2.7.7.12) was performed using the UDPG consumption assay of Beutler and Baluda. Normal red blood cell enzyme activity with this method is 18.5 to 28.5 units. The patient’s red cell activity was measured twice on the same sample and gave 47.7 units (average of 46.7 and 48.7) which is about twice the mean of the control values. An NN electrophoretic pattern for the enzyme was found in the patient’s red blood cells by the method of Sparkes et al. Both parents had normal red blood cell enzyme activity and an NN electrophoretic pattern.

Discussion
The phenotypic expression and the cytogenetic findings in the previously described tetrasomy 9p cases are variable. Besides the facial dysmorphic features and mental retardation, the most common congenital anomalies are high arched palate, or cleft palate or cleft lip or both, congenital heart disease, urogenital defect, strabismus, hydrocephalus, and microcephaly (table). The case reported by Wisniewski et al. appeared to be the most severely affected and similar to ours. In addition, our patient had extensive skeletal anomalies which have not been described before.

In three cases, in which one or more tissues were karyotyped, mosaicism was present, 3 4 while in three other cases, including ours, analysis was performed on peripheral blood lymphocytes only and did not show mosaicism. The morphology of the extra isochromosome in these cases also differs. Two cases were actually tetrasomic for the 9p region as well as the proximal part of 9q, band q21–22, whereas the four other cases, including ours, showed involvement of the secondary constriction to a variable degree. It is, therefore, probably not surprising that all the cases have variable phenotypic features.

The continued expansion of the human gene map now affords opportunities to confirm cytogenetic interpretations. The locus for the human enzyme galactose-l-P uridyl transferase has been mapped to 9p by somatic cell hybridisation studies. Assay for the enzyme galactose-l-P uridyl transferase in our case showed twice the normal activity in the red blood cells. This value is consistent with the presence of four genes for this enzyme based upon a gene dosage effect resulting from the tetrasomy 9p.

We thank Dr C Barrett for referring this patient. We also gratefully acknowledge the assistance of A Teng and I Klisak for the cytogenetic analysis and M C Sparkes and M Crist for the enzyme studies.

SRI J MOEDJONO, BARBARA F CRANDALL, AND ROBERT S SPARKES
Departments of Pediatrics, Psychiatry, and Medicine, Division of Medical Genetics, Child Psychiatry and Mental Retardation Program, UCLA School of Medicine, Los Angeles, California 90024, USA

<table>
<thead>
<tr>
<th>TABLE Common features* and cytogenetic findings of tetrasomy 9p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Microcephaly</td>
</tr>
<tr>
<td>Hydrocephalus</td>
</tr>
<tr>
<td>Wide open sutures and fontanelles</td>
</tr>
<tr>
<td>Hypertelorism</td>
</tr>
<tr>
<td>Epicanthic folds</td>
</tr>
<tr>
<td>Strabismus</td>
</tr>
<tr>
<td>Bulbous/beaked nose</td>
</tr>
<tr>
<td>Low set ears</td>
</tr>
<tr>
<td>Protruding/unalusual ears</td>
</tr>
<tr>
<td>High arched palate/cleft palate/lip</td>
</tr>
<tr>
<td>Micrognathia</td>
</tr>
<tr>
<td>Short neck</td>
</tr>
<tr>
<td>Congenital heart disease</td>
</tr>
<tr>
<td>Urogenital defect</td>
</tr>
<tr>
<td>Karyotype (as designated by authors) Lymphocytes</td>
</tr>
<tr>
<td>Skin</td>
</tr>
</tbody>
</table>

*Features reported in at least two cases.
References


Requests for reprints to Dr Barbara F Crandall, Neuropsychiatric Institute, 760 Westwood Plaza, Los Angeles, California 90024, USA.

Case report

A severely retarded 18-year-old boy with tertiary partial trisomy 14

SUMMARY An 18-year-old severely mentally and physically retarded boy was found to have an unbalanced chromosome complement 47,XY,+14q–. He had the characteristic facial dysmorphism, abnormal hands, and other features described previously in cases of partial trisomy 14, but appears to be the oldest case reported. His mother is a reciprocal translocation carrier, and lack of other carriers in the family is noteworthy.

Subjects with partial trisomy 14 have similar phenotypic abnormalities associated with markedly delayed motor and mental development. In the majority, a balanced translocation was present in the mothers. This report outlines another case of partial trisomy 14, in an 18-year-old boy, where the mother was a balanced translocation carrier.

Cyto genetic analysis

Chromosome analysis of standard peripheral blood cultures gave a modal number of 47 chromosomes in each of 62 cells, the extra chromosome being morphologically indistinguishable from a normal G group chromosome. G banding showed this extra fragment to be a deleted D group chromosome. All other chromosomes in the complement were normal in length and structure. Dermatoglyphic analysis showed absence of d triradius bilaterally,
Tetrasomy 9p: confirmation by enzyme analysis.

S J Moedjono, B F Crandall and R S Sparkes

doi: 10.1136/jmg.17.3.227

Updated information and services can be found at:
http://jmg.bmj.com/content/17/3/227

**Email alerting service**

*These include:*

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/