Marker chromosomes present a problem in genetic counseling because there are often no clear phenotype-karyotype correlations. We present the clinical findings in a patient who is mosaic for a supernumerary marker chromosome 20 determined by fluorescence in situ hybridization (FISH) and compare these findings to others reported in the literature. Am. J. Med. Genet. 91:171–174, 2000. © 2000 Wiley-Liss, Inc.

KEY WORDS: phenotype; aneuploidy; chromosome 20; FISH

INTRODUCTION

There is interest in clinical genetics to elucidate the phenotypic effects of marker chromosomes because of their implications in prognosis and genetic counseling. Chromosomal markers are now often identified by molecular cytogenetic methods, but limited data currently do not permit consistent phenotype-genotype correlations to be made. In addition, variations in the size and parental origin of the marker can influence outcome. The best known example of such influences exist for pseudo-dicentric chromosome 15s where a normal phenotype often results when the marker is devoid of the Angelman/Prader-Willi (AS/PWS) region and an abnormal phenotype when the marker has two maternally derived copies of the AS/PWS region [Cheng et al., 1994; Leana-Cox et al., 1994; Mignon et al., 1996]. We present the clinical findings in a child who is mosaic for a supernumerary ring chromosome derived from chromosome 20.

CLINICAL REPORT

Mother and father are a healthy nonconsanguineous couple, age 19 and 20 years, respectively. Family history was unremarkable. The patient has a healthy maternal half sister, aged 4 years. This pregnancy was normal, and a boy was born at 39 weeks gestation. His weight was 3.76 kg (50th centile), length 50 cm (50th centile) and occipitofrontal circumference (OFC) 35 cm (50th centile). The Apgar score were 9 at 1 and 5 min. At 2 years 8 months, the patient was evaluated by a geneticist because of psychomotor retardation, facial anomalies, and speech delay. His weight was 16.1 kg (50th centile), length 91 cm (50th centile) and OFC 50 cm.
cm (50th centile). He had brachyturricephaly, normal set ears with lobe creases, ocular proptosis, flat brow ridges, full cheeks and a high arched palate (Fig. 1). He had a short neck, and his chest was normal without heart murmurs. The abdomen and lower limbs were normal. Bilateral clinodactyly of the fifth finger was observed. Examination of external genitalia showed that both testes were in the inguinal canal. Electroencephalograph (EEG), skull radiographs, and results of metabolic screening were normal. A computed tomography (CT) scan was essentially normal, with a slight increase in the sella turcica size noted. A clinical diagnosis of craniosynostosis type 2 (Boston type [Warman et al., 1993]) was suggested due to the frontal orbital recession.

**CYTOGENETICS**

Lymphocytes from a peripheral blood sample were phytohemagglutinin (PHA)-stimulated, cultured by standard methods and analyzed by Giemsa banding technique (GTG). The analysis showed a ring chromosome in most cells with the karyotype 47, XY, +r/46,XY (Fig. 2). Centromere (C)-banding and nuclear organizer region (NOR)-banding were positive and negative, respectively, suggesting the chromosome had

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Karyotype (% cells with de novo ring/marker chromosome)</th>
<th>Clinical findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>This study</td>
<td>2y 8m</td>
<td>47,XY,+r/46,XY (80% lymphocytes)</td>
<td>Psychomotor retardation (PMR), brachyturricephaly, posteriorly rotated ears with lobe creases, ocular proptosis and flat brow ridge, full cheeks, high arched palate, micrognathia, short neck, clinodactyly of 5th fingers.</td>
</tr>
<tr>
<td>Callen et al., 1991 (case 10)</td>
<td>7y 10m</td>
<td>47,XY,+m/48,XY,+2m (72 and 28% of lymphocytes)</td>
<td>Normal intelligence, &lt;3rd centile for height and weight, scaphocephaly, low set ears, high palate with high-pitched voice, micrognathia, hyperextensible elbows and fingers, clinodactyly of fingers 2, 4 and 5, syndactyly of fingers 2–5; mild scoliosis.</td>
</tr>
<tr>
<td>Blennow et al., 1993 (case E)</td>
<td>4y</td>
<td>47,XY,+r/46,XY (48% lymphocytes)</td>
<td>PMR, slight growth retardation, low set ears; limited hip mobility as a newborn; abnormal behavior</td>
</tr>
<tr>
<td>Batista et al., 1995</td>
<td>1y 4m</td>
<td>47,XY,+r/46,XY (86% cord blood)</td>
<td>PMR, &lt; 3rd centile for height and weight, asymmetric face, micrognathia, high palate, short philtrum, abnormal ears, hypotonia, hyperextensible joints, and clinodactyly.</td>
</tr>
<tr>
<td>van Langen et al., 1996</td>
<td>1y 2m</td>
<td>47,XY,+r/46,XY (60% lymphocytes)</td>
<td>PMR, 25th centile for height, 75th centile for weight, coarse facies with full cheeks, deep set eyes, slightly upslanted palpebral fissures, strabismus, normal ears, short nose with antverted nares, micrognathia, normal philtrum and palate; broad neck and thorax, widely spaced nipples, broad and short hands and feet, clinodactyly of 5th fingers, slight hyperextensible elbows and knees.</td>
</tr>
<tr>
<td>Viersbach et al., 1997 (case 1)</td>
<td>1y 8m</td>
<td>47,XY,+r/46,XY (80% amniocytes; 9% cord blood)</td>
<td>Normal development, syndactyly of 2nd and 3rd toes.</td>
</tr>
<tr>
<td>Viersbach et al., 1997 (case 3)</td>
<td>4y 2m</td>
<td>47,XY,+29/48,XY,+2r/46,XY (1 and 2 rings in 25 and 17% of lymphocytes)</td>
<td>PMR, &lt;3rd centile for height and weight, cardiac anomalies, hypertelorism, low set ears, clubbed fingers, depressed root of nose, bilateral plantar furrow.</td>
</tr>
<tr>
<td>Crolla et al., 1998 (case 24)</td>
<td>1y 9m</td>
<td>47,XY,+r/46,XY (57% lymphocytes)</td>
<td>PMR, hypoplastic ala nasi, long filtrum, micrognathia, pectus excavatum; hypotonia.</td>
</tr>
<tr>
<td>LeChien et al., 1994</td>
<td></td>
<td></td>
<td>PMR, normal growth, coarse facies with full cheeks, short philtrum, epicanthal folds, short upturned nose and micrognathia, normal palate.</td>
</tr>
<tr>
<td>Grammatico et al., 1992</td>
<td></td>
<td></td>
<td>Prominent forehead, small eyes, large ears, antverted nares, short neck, heart defect, dimpled chin.</td>
</tr>
</tbody>
</table>
Supernumerary Ring Chromosome 20

characterization of the ring chromosome but the G-banding pattern and the phenotype of the patient resembles that of chromosome 20p trisomy (Table I: LeChien et al. [1994] and Grammatico et al. [1992]) not 20q trisomy (Table I: Herens et al. [1990]). The case reported by Callen et al. [1991] had many of the features in common with trisomy 20p but had normal intelligence with no psychomotor retardation. This child had a cytogenetically smaller marker chromosome (slightly larger than the centromeric heterochromatin), and presumably its size contributed to this difference.

Currently, it appears that mosaicism involving chromosome 20p trisomy in approximately 50% or greater of lymphocytes results in psychomotor retardation, craniofacial abnormalities, and clinodactyly. The effects on clinical outcome are presumably dependent on tissue distribution and genetic content of the supernumerary chromosome, although parental origin (i.e., imprinting) may also play a role for chromosome 20 [Juppner et al., 1998]. The spectrum of effects will be defined as more detailed clinical and molecular evaluations of supernumerary chromosomes are performed.

REFERENCES


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