two other severely retarded subjects, a niece (IV.3) and half-brother (III.9) of III.2. The half-brother was reported to have had cleft lip repair surgery. These people were not available for study. Two of the nephews of III.2 died in infancy (IV.5, IV.8), one following heart surgery (IV.5). The mother (II.2) of III.2 was karyotyped and found to have the same translocation as her son.

Discussion

In reviewing reports of trisomy 8p, the only abnormal features our patient has in common with all other cases are mental and physical retardation. Other features are seen with various trisomy 8p, but not clearly defined trisomy 8p syndrome emerges. Features such as micrognathia, hypertelorism, cardiac defects, low set ears, epicanthal folds, and carp mouth, seen in our case and other cases of trisomy 8p, are often reported with other chromosome abnormalities. The large mouth and broad nose noted by Rethore et al were not seen in our patient.

Perhaps as more cases are examined, a cardinal feature or cluster of abnormalities may be found to be associated with trisomy 8p. The variable features may be the result of partial monosomy for genetic material on the other chromosomes involved in the translocations, in our case the q25 band of chromosome 11.

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References


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Monosomy 22 with humoral immunodeficiency: is there an immunoglobulin chain deficit?

SUMMARY The cytogenetic analysis of a patient with selective deficit of IgA and decrease in IgM, IgE, and IgG is presented. Using trypsin-Giemsa banding the karyotype showed monosomy 22 (45,XX,−22). The interest of this case lies in the rarity of the illness and in the association of monosomy 22 with hypogammaglobulinaemia and selective deficit of IgA, particularly as this chromosome is known to contain genes coding for immunoglobulin chains.

Monosomy of a G group chromosome compatible with survival occurs rarely and there have been only 25 cases of partial or complete monosomy G reported. Only in three cases was the monosomy identified as a chromosome 22. Our report presents the clinical and cytogenetic findings of a female infant aged 11 years with monosomy of chromosome 22, selective deficit of IgA, and decrease in IgM, IgE, and IgG.

Case report

The proband was a female of 11 years, with a weight of 37.7 kg (25th to 50th centile) and a height of 140 cm (10th centile). The head was dolichocephalic with a flat occiput and adenoid facies. She was mentally subnormal (IQ 60) and had genu valgus and splay foot. She had recurring severe respiratory infections.

Immunoglobulins were studied with the quantitative immunoglobulin test kit with the following results (mg/100 ml): IgG 500–620 (normal range 564–1565); IgM 48 (normal range 53–375); IgA undetectable on five occasions (normal range 85–385). The IgE was studied by radioimmunoassay...
Case reports

FIGURE G banded karyotype of proband (45,XX,−22).

(Cytogenetic Findings)
In cultured peripheral lymphocytes, all 68 metaphases analysed had 45 chromosomes and were lacking a G group chromosome. Chromosome banding analysis (by immersing slides in 0.05% trypsin for 7 seconds, then in 5% bovine serum for 15 seconds, washing three times in phosphate buffer at pH 6.8, and staining with 4% Giemsa at pH 6.8 for 5 minutes) showed the missing chromosome to be number 22 (45,XX,−22) (figure). Unbanded and G banded metaphase cells from the patient’s parents, brother, and sister were normal.

Discussion
Partial monosomy of a G group chromosome was first reported by Lejeune et al17 in a child with an unusual mosaic chromosome, namely 45,XY,−G/46,XY,G minute. Up to the present there have been 25 examples of partial or complete monosomy G reported,1–4 each of whom had either three autosomes in the G group or three G chromosomes and a ring chromosome. Only in three cases1–4,5 was the monosomy for a G group chromosome identified as a chromosome 22 by banding.

Hoefnagel et al18 suggested that there were two clinical types of G deletion syndrome, and other authors8,9–11 claim to be able to separate reported cases into one or other of the two types: G deletion syndrome type I or G-1, and G deletion syndrome type II or G-2.8,9 The type I syndrome has been called ‘antimongolism’ and is associated with partial deletions of chromosome 21.8 The type II syndrome is associated with partial deletion of chromosome 22.8 Our patient has some clinical features similar to those already described by others in the G-2 syndrome8,9 (table 1).

We wish to point out the previously unreported association of monosomy 22 with humoral immuno-deficiency, expressed by selective deficit of IgA and diminution of IgG, IgM, and IgE.

In the last few years, thanks in great measure to the use of monospecific antibodies obtained by the technique of monoclonal immunoglobulin secreting hybridomas,18 it has been possible to make advances in the study of the location of the structural genes which determine human immunoglobulin molecules.

1) Using hybrid cellular clones (between mouse myeloma cells and lymphoblastoid or human myeloma cells), which secrete heavy chains of human Ig, it is possible to establish a correlation between the capacity to secrete H chains and the presence of a specific human chromosome, for

(3) Lab Pharmacia, Upsala, Sweden) and gave a result of 3 ku/l (normal 570 ku/l). Family history was negative.

(4) Using hybrid cellular clones (between mouse myeloma cells and lymphoblastoid or human myeloma cells), which secrete heavy chains of human Ig, it is possible to establish a correlation between the capacity to secrete H chains and the presence of a specific human chromosome, for
Table 1: Clinical findings in our patient and G-1/G-2 syndrome.

<table>
<thead>
<tr>
<th>Clinical signs</th>
<th>Syndromes</th>
<th>This case</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>G-1</td>
<td>G-2</td>
</tr>
<tr>
<td>Mental and motor retardation</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Downward slanting palpebral fissures</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Adenoid facies</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Epicanthal folds</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ptosis</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Brushfield spots</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Blepharochalasia</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Low set ears</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Large ears</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Flat occipit</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Flat nasal bridge</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Protruding nose</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Bifid uvula</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Micrognathia</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Dolichocephaly</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cutaneous syndactyly</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Simian creases</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Clinodactyly of the 5th fingers</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Retropositioning of the 4th toes</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Hypogammaglobulinaemia</td>
<td>IgA</td>
<td>-</td>
</tr>
<tr>
<td>Muscleoskeletal anomalies</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Other congenital anomalies</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

+ = common, − = not reported or uncommon.

example No 14, 13, 14 although these clones also preferentially retain chromosome 6, 22, and X. 14

(2) It has been postulated that the genes coding for the kappa type light chains (L chains) are found on chromosome 2. 15

(3) The genes coding for lambda type L chains were postulated to be on chromosome 22. 16 The authors, using hybrid clones between mouse myeloma cells and human B cells, preselected those that had the ability to secrete H chains of human Ig and in them they studied the expression of the human chromosome marker isoenzymes. In this way they were able to discover that the lambda chain secreting clones regularly contained chromosomes 14 and 22, but they observed that in two subclones with loss of chromosome 14 the secretion of lambda chains persisted, so they concluded that chromosome 22 is the only essential one for the formation of these chains. 16

Taking into account these data (table 2), the humoral immunodeficiency associated with monosomy 22 in our case could be in some way related to a relative deficit in the production of lambda chains. Since the homologous 22 is still presumably functional, and kappa chain production should be unaffected, the relationship of the hypogammaglobulinaemia to the deletion may be complex.

To sum up, the particular interest of our case lies firstly in the fact that it makes known the association of monosomy 22 and humoral immunodeficiency, which has not previously been described, and secondly in that it discusses whether this may partially support the hypothesis that chromosome 22 possesses the human Ig lambda chain coding genes 16 or other genes controlling rates of immunoglobulin production. Nevertheless, in order to throw light upon this last possibility, more detailed and specific immunological studies will have to be carried out.

The technical expertise of Mr J A Delgado and Mrs R Delgado and C Santamaria is greatly appreciated.

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References

Wildervanck's syndrome with bilateral subluxation of lens and facial paralysis

SUMMARY A 15-year-old female was found to have the typical features of Wildervanck's syndrome, including Klippel-Feil anomaly, abducens paralysis, retraction of the bulbi, and deafness. In addition, she had bilateral lens subluxation and facial paralysis, neither of which have been reported in patients with Wildervanck's syndrome.

Case report

The proband was a 15-year-old female, born to a 29-year-old G4, P3, A1 mother, following an uncomplicated term pregnancy with no exposure to agents known to be teratogenic. Delivery was uncomplicated and spontaneous at term. Her birth weight was 3.5 kg. In the first month, the parents noted facial asymmetry. There were no relevant problems until the age of 6 years, when a diagnosis of facial paralysis and fusion of cervical vertebrae was made. The parents were healthy and consanguinity was denied; a younger sister and brother of the patient were normal. There was no family history of any congenital malformation, deafness, or neurological abnormality. Physical examination revealed a well developed girl. She weighed 76 kg (90th to 95th centile), was 156 cm tall (10th to 25th centile), and occipitofrontal circumference was 55 cm (50th centile). She had facial asymmetry (fig 1), shortness of the neck, pterygium colli, and a low posterior hairline. Neurological examination showed bilateral abducens and right facial paralysis, but other neurological alterations, such as hemiplegia, quadriplegia, or paralysis of other cranial nerves, were absent. Ocular examination showed bilateral temporal subluxation of the lens (fig 2) and retraction bulbi. Pupillary size, shape, and reactions were normal, as were the eyelids, corneae, and fundi. An x-ray examination showed cervical scoliosis and fusion of the second, third, and fourth cervical vertebrae (fig 3). In addition, the patient had bilateral sensorineural deafness. Routine laboratory studies showed normal urine analysis and blood count and blood amino-acid analysis was also normal.

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FIG 1 Proband at 15 years of age. Note facial asymmetry.

FIG 2 Subluxation of left lens. Similar finding was present in the right eye.