Deletion of the Long Arms of Chromosome 18 (46,XX,18q−) Associated with Absence of IgA and Hypothyroidism in an Adult

Case Report

The patient (Fig. 1) is a female aged 21. No details of her birth are known beyond the fact that her mother was aged 35 years and died 8 years later of lung cancer. There is no information about the father.

The patient was admitted to a mental deficiency hospital at age 8 years. She was thought to suffer from atypical Down's syndrome.

On examination at the age of 21 years her height was 142 cm with a sole to pubis measurement of 69 cm and a span of 137 cm; head circumference was 51 cm. She weighed 62.14 kg. Her face showed midfacial hypoplasia and a carp mouth. There were bilateral epicanthic folds and an internal, alternating strabismus. Her hair, which was fair in colour, had normal female distribution although her head hair was receding slightly at the temples. Her fingers were short and all had unlar loops.

She had generalized muscular hypotonia. Specialist investigations showed the eyes to have normal refraction. She had 50% perceptive deafness. The external meati and petrous bones were normal. The patient was hypotensive (BP 100/50). A soft systolic murmur was present following exercise and was best heard at the apex.

The heart was enlarged on x-ray and an ECG showed probable right ventricular hypertrophy. There were no physical signs of heart failure, and no goitre.

Her intelligence fell into the group of mild mental retardation (International Classification of Diseases).

Protein Studies

Serum total protein was 7.9 g/100 ml. Electrophoresis on cellulose acetate was normal with the exception of a moderately increased γ-globulin level (2.0 g/100 ml).

The serum immunoglobulins were examined on 4 occasions. At no time was IgA detectable by immunoelectrophoresis (Grabar and Burtin, 1964) on agar gel against specific antiserum (Behringwerke AG, Marburg-Lahn, Germany). The IgG and IgM arcs appeared qualitatively normal. The serum concentrations of immunoglobulins were measured by single radial immunodiffusion (Mancini, Carbonara, and Heremans, 1965) in agar gel containing specific rabbit antiserum against human immunoglobulins (Wellcome Reagents Ltd, Beckenham, England). The Wellcome antiserum to IgA appeared to be specific as it gave, on immunoelectrophoresis, a single arc with normal human serum.

The results of the immunodiffusion measurements are shown in the Table. The IgA concentration (measured

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References


Reprints from K.-M. G. at Med. Univ. Poliklinik, 7a, Robert Koch Strasse, D-3550 Marburg, Germany.
on undiluted serum) was very low or undetectable. The concentration of IgG was raised. This increase in IgG was noted in one of the IgA-deficient patients of Hobbs (1968) and might represent an antibody response to infections to which the IgA deficiency made the patient more susceptible. Indeed, during the period in which our patient's immunoglobulins were being estimated she had superficial or middle ear infections on several occasions and in October 1970 had an appendicectomy for acute appendicitis. This may also be relevant to the observed rise in IgM concentration although this remained within normal limits.

### TABLE

**IMMUNOGLOBULIN CONCENTRATION IN THE SERUM (μg/100 ml)**

<table>
<thead>
<tr>
<th>Date</th>
<th>IgG</th>
<th>IgA</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/70</td>
<td>2540</td>
<td>&lt;2</td>
<td>40</td>
</tr>
<tr>
<td>6/70</td>
<td>2530</td>
<td>&lt;2</td>
<td>90</td>
</tr>
<tr>
<td>12/70</td>
<td>3000</td>
<td>10</td>
<td>130</td>
</tr>
<tr>
<td>5/71</td>
<td>2720</td>
<td>5</td>
<td>200</td>
</tr>
<tr>
<td>Normal</td>
<td>800–1800</td>
<td>90–450</td>
<td>60–250</td>
</tr>
</tbody>
</table>

### Thyroid Studies

The serum protein-bound iodine (Riley and Gochman, 1964) was reduced at 2.5 μg/100 ml, on 2 occasions. This low result was not the consequence of a deficiency of a thyroxine binding globulin because a T₃ resin uptake (Gimlette, 1967) was in the hypothyroid range at 0.028. There was no evidence of auto-antibodies to the thyroid from the complement fixation test (Roitt and Doniach, 1958) or from the tanned red-cell haemagglutination test (Fulthorpe et al, 1961).

### Chromosome Studies

Cells were examined from a culture of the peripheral blood and from a fibroblast culture from the skin. All cells were found to have an abnormal chromosome replacing a member of the E group. Pairing of the chromosomes from photographs after staining with quinacrine hydrochloride (Atebrin) revealed no abnormality of any other chromosome. It is also clear that it is chromosome 18 which is affected because chromosome 17 is strongly fluorescent only on the distal portion of the long arms but normally both proximal and distal portions of the long arms of chromosome 18 are bright. In this patient the distal fluorescent region is deleted from chromosome 18 (Fig. 2).

The abnormality was not found in any of the relatives examined but no first degree relatives were available.

### Discussion

Low intelligence, small stature, poor muscular tone, carp mouth, midfacial hypoplasia, and internal strabismus are all features of this patient which have been reported in other cases of the Eq—syndrome (de Grouchy et al, 1964; Lejeune et al, 1966; Wertelecki, Schindler, and Gerald, 1966; Insley, 1967; Nance et al, 1968). Her fingers, however, are short rather than long and tapered, and show a complete absence of whorl patterns (cf, Wertelecki et al, 1966), Hypothyroidism is not a characteristic of the syndrome but absence of IgA has been reported.
production appears to be active (Giblett, 1969). There is no information on how this gene repression operates but it is possible that, as in X chromosome anomalies, it is the deleted chromosome which is inactivated. If this is true, the region of the chromosome deleted is unimportant; only the gene on the complete chromosome will be active.

**Summary**

An adult female with mild mental deficiency and hypothyroidism has been found with a deletion of long arm material from chromosome 18. Unlike most of the previously reported cases with this chromosome abnormality she has short fingers without whorls. She has gross reduction in the serum immunoglobulin A; the significance of this association, of which several cases have been reported, is discussed.

We wish to thank Dr J. P. Mellon for allowing us to study his patient and Professor J. R. C. Batchelor and Dr W. W. Park for encouragement and helpful criticism. We are grateful to Dr T. E. Isles for T3 uptake measurements, to Dr D. M. Green for confirming the absence of thyroid antibodies, and to Miss June Sim for technical assistance.

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**REFERENCES**


Inherited Pericentric Inversion of a Group D (13-15) Chromosome

Pericentric inversions of autosomes have been reported infrequently in human subjects, and have been reviewed by Jacobs et al (1967), Weitkamp et al (1969), Crandal and Sparkes (1970), and Wilson et al (1970).

We report a family showing both a pericentric inversion and an unbalanced crossover segregation product from the inversion. The present family shows inheritance through two generations of a structurally abnormal D chromosome interpreted as a pericentric inversion. The carriers of inversion are phenotypically normal and show no increased frequency of congenital malformation or fetal loss. The propositus described below is the only known individual with an unbalanced crossover segregation product from the inversion.

Case Report

The pedigree of the family is shown in Fig. 1. The propositus, a male infant (III.3), was the product of a full term pregnancy born to a gravida 3, para 2 25-year-old mother. The father was 27 years old and there were two older sibs. The mother, father, brother, and sister are all phenotypically normal. There was no family history of mental retardation or congenital malformations. The parents are of Italian ancestry and non-consanguinous.

![Diagram of Pedigree](http://jmg.bmj.com/)

**Fig. 1.** Pedigree of the family.

The propositus weighed 2890 g at birth. He had some respiratory distress on the second day of life and radiographs revealed an over-inflated, hyperlucent left lung. Repeat radiological examination on the 7th day revealed equal expansion and aeration of both lungs.

The patient was first admitted to The Hospital for Sick Children at 5 weeks of age because of difficulty in breathing and diarrhoea. He weighed 4.2 kg, was 56 cm long, and lay in an opisthotonotic position. He had an unusual looking round face with slight micrognathia and somewhat low set ears (Fig. 2). There was pitting oedema of both feet. The heart, lungs, and abdomen appeared normal except for a small umbilical hernia. External genitalia were normal male and both testes were descended (Fig. 3).

The infant was treated for gastroenteritis and discharged after 20 days of hospitalization. Since then he has been hospitalized on 4 separate occasions for repeated attacks of pneumonia and respiratory distress.

He was last admitted in June 1969 at 9 months of age because of cardiac failure and severe respiratory distress. He weighed 7.5 kg (<3rd centile). A loud pansystolic murmur was heard best in the 4th left intercostal space.