urine is a major source of amniotic fluid AFP, urethral obstruction alone would result in a low amniotic AFP level, as in disorders associated with renal dysgenesis. The raised amniotic fluid and maternal serum AFP is most probably caused by regurgitation of bile and gastric contents into the amniotic fluid due to intestinal atresia. Transudation of fetal serum as a result of the gross abdominal distension is unlikely. In omphaloceles with exposure of blood vessels, easy transudation of fetal serum will result in increased amniotic fluid AFP (Nevin and Armstrong, 1975; Weiss et al., 1976), but when the exomphalos is covered with skin amniotic fluid AFP is normal.

Fortunately, in most instances where a high AFP level has been found in the absence of a neural tube defect, the fetal abnormalities have been so serious as not to compromise the validity of termination of the pregnancy because of the high AFP value.

N. C. NEVIN, A. RITCHIE, F. MCKEOWN, AND G. ROBERTS

Departments of Medical Genetics, of Midwifery and Gynaecology, and of Pathology, Institute of Clinical Science, The Queen's University of Belfast, and the Department of Biochemistry, The Royal Victoria Hospital, Belfast, Northern Ireland

Primary hypogonadism in the Borjeson-Forssman-Lehmann syndrome

SUMMARY A 28-year-old man with mental retardation and multiple congenital malformations was found to have the classical features of Borjeson-Forssman-Lehmann syndrome. Endocrine evaluations showed primary hypogonadism as the underlying endocrine abnormality rather than hypopituitarism as suggested in earlier reports.

Borjeson et al. (1962, 1963) described 3 related males with an X-linked recessive syndrome characterised by profound mental retardation, microcephaly, peculiar facies, and hypogonadism. Findings in an isolated case (Baar and Galindo, 1965) and in one of the original patients (Brun et al., 1973) suggested hypopituitarism as the basic endocrine abnormality.

We report here the clinical and endocrine findings in an individual with this syndrome.

Case report

The patient is a 28-year-old man who has resided in an institution for the retarded since age 11. Information on his past history is scanty as we have been unsuccessful in reaching any of his relatives. According to the records, there are no similar cases or mental retardation in the family. He was born with a weight of 2.6 kg to a 15-year-old primigravida. Bilateral inguinal herniorrhaphies were performed at age 3 months, but the operative reports are not available. He sat unsupported at 3 years of age, stood alone at 34 years, and walked at 4 years. By 4 years of age he was capable of some speech, but this has remained limited to the utterance of several phrases.

When admitted to the institution at age 11 years, his height was 127 cm (50th centile for 8 years) and his weight, 27.4 kg, was 5th centile for age. Major motor seizures occurred three times in the next seven years and at age 18, sodium pentobarbital was prescribed intermittently because of increased frequency of seizures. Diphenylhydantoin, 32 mg orally, t.i.d., was started at age 20 and has been given regularly to this time. Seizures have been adequately controlled since age 23 when primidone, 100 mg, t.i.d. was added to this therapeutic regimen.

He has been admitted to hospital with cellulitis of the lower extremities on several occasions. Recurrent otitis media with bilateral tympanic membrane perforations necessitated a tympanoplasty at age 23. His

References


Requests for reprints to Dr N. C. Nevin, Department of Medical Genetics, The Queen's University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ.
IQ has been estimated repeatedly in the range of 10 to 30.

At age 28 his standing height, 138 cm (supine length 141 cm), was at the 50th centile for a 10-year-old; his head circumference, 53.5 cm, was at the 3rd centile for an adult. He had soft puffy cheeks, large normally formed ears, bilateral palpebral ptosis, depressed nasal bridge, and synophrys. The mean palpebral fissure length as measured from inner canthus to outer canthus was 2.65 cm according to the method of Smith (1976). The mean palpebral fissure length over the age of 5 years is 2.5 cm. Heart, chest, and abdominal examinations were normal with the exception of bilateral herniorrhaphy scars. His entire body was soft and flabby with a mild fatty gynaecomastia. The skin had a velvety texture. Genu valgum was present and his first and second toes were wide-spaced bilaterally while his hands appeared normal. The phallus was small measuring 2 cm in length and the scrotum and inguinal canals were devoid of testes by palpation. A few short, straight, faintly pigmented hairs were present on the mons pubis.

Fig. 1  *Patient at age 26 years.*

Fig. 2  *X-ray films of right hand and forearm, at age 26, showing open epiphysial growth plates, shortened metacarpals and phalanges, and diminished muscle mass.*
Case reports

LABORATORY EVALUATION

All parameters of an automated SMA-12 (Technicon Corporation, Terrytown, New York) serum chemical analyses were normal and a karyotype showed a 46 XY chromosomal constitution. A propranolol-glucagon stimulation test of growth hormone secretion using 20 mg/m² of propranolol and 1 mg of glucagon produced a normal increase in growth hormone to 17 ng/ml (Ruanqwit et al., 1972).

Serum T₄ was 7–5 μg/dl (normal 4–6 to 10–7 μg/dl) and resin T₃ uptake was 10–6% (normal 10–0 to 14–6%).

A random morning cortisol was 10 μg/dl (normal 5 to 20 μg/dl). A morning cortisol of 2 μg/dl followed an 11 p.m. oral dose of 2 mg of dexamethasone showing the expected suppression (Cryer, 1976).

A random serum testosterone was 48 ng/dl (normal adult male: 300–1200 ng/dl). Random morning and evening determinations of luteinising hormone were 7 and 6 mIU/ml, respectively (normal less than 11 mIU/ml). Random morning and evening follicle stimulating hormones (FSH) were 24 and 15 mIU/ml (normal 4 to 25 mIU/ml). A 3-hour constant infusion of luteinising hormone-releasing hormone (LH-RH) (Ayerst) by the method of Reiter et al. (1976) resulted in appropriate increases in LH and FSH but no corresponding rise in plasma testosterone, as shown in the Table.

An encephalogram done while the patient was on primidone and diphenylhydantoin showed diffuse, low voltage slow waves with no focal or paroxysmal activity. This was judged to be consistent with diffuse organic brain disease.

RADIOLOGICAL STUDIES

X-ray studies show pronounced retardation of fusion of the epiphysial growth plates. Some fusion in the phalanges of the hand has occurred giving a bone age approximating 16 years. The hands appear otherwise normal. Pattern profile analysis (Poznanski et al., 1972) shows generalised shortening of all bones of the hands with predominant involvement of the phalanges.

The long bones are thin and moderately under-mineralised. There is slight bowing of the radius and mild coxa vara. Soft tissue shows poor muscular development, especially in the lower extremities. The pelvis is normal, with the exception of flared iliac wings.

<table>
<thead>
<tr>
<th>Time</th>
<th>FSH (MIU/ml)</th>
<th>LH (MIU/ml)</th>
<th>Testosterone (ng/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3.9</td>
<td>12</td>
<td>40</td>
</tr>
<tr>
<td>1 hour</td>
<td>14</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>2 hours</td>
<td>23</td>
<td>29</td>
<td>34</td>
</tr>
<tr>
<td>3 hours</td>
<td>21</td>
<td>29</td>
<td>34</td>
</tr>
</tbody>
</table>

*All determinations were performed at Patterson-Coleman Laboratory, Tampa, Fl, USA.*

The upper lumbar spine shows a kyphos deformity, narrowed D₁₃–L₁ interspace, and secondary deformity of these vertebrae. The ring apophyses of the vertebral bodies remain unfused.

The skull is somewhat ‘squared’ in the lateral configuration but otherwise normal. The sutures are well seen and reflect retarded development. There are numerous dental caries and the teeth are poorly developed.

Discussion

The pattern of abnormalities found in this patient closely corresponds to that originally described by Borjeson et al. (1962, 1963) in 3 related men and later by Baar and Galindo (1965) in an isolated case. Features present in all cases include: microcephaly, excessive facial fat, large ears, enlarged breasts, abundant abdominal fat, small phallus, genu valgum, minimal pubic hair, seizures, and severe mental...
retardation. After reviewing photographs of the other cases and examining our patient, we propose that \textit{lid ptosis} rather than \textit{narrow palpebral fisses} is the common eye finding.

All cases described had short stature (average height 145-7 cm, range 136 to 156 cm). Testes were tiny in the 3 cases coming to necropsy, and clinically absent in the 2 living persons. Necropsy showed a small pituitary with normal cytology in 1 case, a normal pituitary in the second, and the pituitary was not mentioned in the third. The association of short stature and hypogonadism with a small pituitary gland in 1 patient, and gonadotropin levels in the lower limits of normal, by bioassay, in 2 patients, led to the interpretation that hypopituitarism was responsible for the endocrine abnormalities (Brun et al., 1974). Endocrine studies in our patient, however, showed normal pituitary responses as indicated by normal thyroid function, normal adrenal-pituitary axis, and normal growth hormone and gonadotropin secretion. Low testosterone levels in our case are in keeping with \textit{primary hypogonadism}. We find no evidence to support hypopituitarism as a necessary part of any of the described cases.

F. Thomas Weber, Jaime L. Frias, Richard L. Julius, and Alvin H. Felman

Department of Pediatrics, University of Florida College of Medicine, Gainesville, Florida 32610

References


Requests for reprints to Dr. F. Thomas Weber, Department of Pediatrics, University of Florida College of Medicine, Gainesville, Florida 33610, U.S.A.

Waardenburg-like features with cataracts, small head size, joint abnormalities, hypogonadism, and osteosarcoma

SUMMARY A 32-year-old black man was observed with osteosarcoma and multiple anomalies including deafness, hypopigmentation, cataracts, small head size, hypogonadism, and restricted joint mobility. The birth defects may comprise a new syndrome or combination of syndromes, of which the malignancy may be a part.

Case report

The patient was ascertained in June 1976, during an aetiological assessment of sarcoma patients on a surgical service.

Gestation, labour, and delivery were normal. The parents were a 16-year-old gravida 1, para 0, black woman, and an unrelated 16-year-old black man. Birthweight was 2.4 kg, and an umbilical hernia and clubfeet were present. Motor and speech development were delayed and at 2 years hearing was found to be impaired. Educational efforts were not made until age 12 when the patient was sent to a school for handicapped children. Greying of hair began at 12 years; beard growth began at about 18 years. He currently lives at home, cares for his personal needs, and has held two manual jobs.

The father's medical and family history were unavailable; the mother had no physical or hearing abnormalities. The only birth defect or pigmentedary anomaly among 3 maternal half sibs and other maternal relatives was profound childhood deafness in an otherwise normal cousin. The maternal grandmother had an ovarian granulosa cell tumour, and a maternal aunt had uterine leiomyoma.
Primary hypogonadism in the Borjeson-Forssman-Lehmann syndrome.
F T Weber, J L Frias, R L Julius and A H Felman

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