THE LAURENCE-MOON-BIEDL-BARDET SYNDROME

Report of Three Cases in a Jewish Yemenite Family

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Patients are often admitted for treatment of polydactyly without the surgeon's realising that this deformity may be part of a syndrome. In this paper we present three cases of polydactyly in a family in which the manifestation was part of the Laurence-Moon-Biedl-Bardet syndrome. This syndrome was first described by Laurence and Moon in 1866 and additional cases were described by Bardet and Biedl between 1920 and 1922. The complete syndrome consists of: 1) retinitis pigmentosa; 2) polydactyly; 3) obesity of the Fröhlich type; 4) genital hypoplasia; and 5) mental retardation. The patients described here presented additional deformities.

CASE REPORTS

Case 1—A Yemenite woman aged twenty-seven years was admitted for amputation of supernumerary digits. Her maternal grandfather and paternal grandmother were brother
Case 1—The hands and feet showing the additional digits.

Figure 5—Radiograph of the hands showing a sixth digit projecting from the bifid fifth right metacarpal bone. Figure 6—Radiograph of the feet showing a thick bifid fifth right metatarsal bone from which project digits five and six. The sixth toe of the left foot arises from the head of the fifth metatarsal bone.

Figure 7—Radiograph of the pelvis showing hip dysplasia with a suggestion of subluxation on the left. There is a bilateral valgus deformity.
and sister. There was no family history of hereditary diseases or of defective vision. She had three normal brothers and one normal sister. A similar syndrome was found in one sister, aged seventeen years, and had been present in a brother who had died at the age of seventeen.

The sixth finger of the patient's left hand had been amputated with a ligature when she was a baby. Her sight had been normal until the age of twelve, when impairment of vision set in. It was first evident as night blindness and diminished visual fields which deteriorated gradually. At the time of examination she was able only to differentiate between light and dark, and to detect gross movement.

Menstruation had begun when she was sixteen; it was irregular and delayed. She attended a normal school until the age of eleven, when she was transferred to a school for retarded children. She is at present in an institution for the blind, doing handiwork.

On examination, her height was 140 centimetres, with a relatively small head, retarded facies and moderate nystagmus (Figs. 1 and 2). Her neck was short and thick and the thyroid was impalpable. The breasts and other secondary sex characteristics were well developed. She was grossly obese, particularly over the lower abdomen, flanks, thighs and buttocks. Her pelvis was wide. She had limited hip movements and moderate valgus deformities of the knees. The extremities, including the fingers and toes, were short and thick. A sixth finger was present on the right hand, and there were six toes on both feet (Figs. 3 and 4). Ophthalmoscopic examination confirmed a diagnosis of retinitis pigmentosa. Cardiovascular examination revealed a blood pressure of 170/100 millimetres of mercury and a systolic murmur was detected in the heart: radiographs showed slight enlargement of the left ventricle, but the electrocardiograph was normal. Radiographs of the hands showed the bones to be shorter and thicker than average (Fig. 5). An additional phalanx projected from the fifth right metacarpal bone. The feet showed a bifid fifth metatarsal bone from which both the fifth and sixth toes projected in the right foot (Fig. 6). In the left foot the sixth toe projected from the head of the fifth metatarsal bone. Radiographs of the skull and of the spinal column were normal. Radiographs of the hips showed dysplasia with bilateral valgus deformity (Fig. 7). Intravenous pyelography was normal. Laboratory findings were normal except for low levels of oestrogens and 17 ketosteroids (Tables I and II).

Case 2—The seventeen-year-old younger sister of the patient described has a strikingly similar history. She had normal vision which deteriorated during her early years at school. It was first manifested as night blindness, followed by a diminution of visual fields, with a gradual deterioration until she was able only to differentiate between light and dark and detect gross movements. Her menarche was at sixteen, with irregular menses.

At the age of eight years she was transferred from a normal school to a school for retarded children. At the time of examination she was at an institution for the blind, doing handiwork.

On examination she was found to be 138 centimetres tall, with a small head, low forehead and retarded facies (Fig. 8). Movement and speech were slow and she appeared mentally retarded. Her neck was short and...
thick and the thyroid was not enlarged. The secondary sex characteristics were normal. She was obese, particularly over the lower abdomen, flanks, hips, thighs and buttocks. Her pelvis was wide with limited hip movements. She too had a genu valgum deformity and short, thick extremities, including the fingers and toes. There was syndactyly of the left hand between the fifth and sixth fingers (Fig. 9), but there was no polydactyly of the feet (Fig. 10). A short systolic murmur was heard over the left parasternal area. Ophthalmoscopic examination confirmed the diagnosis of retinitis pigmentosa. A radiograph of the pelvis and hips showed dysplasia with bilateral valgus deformity. Radiographs of the skull showed a normal sella turcica and those of the spinal column were normal. The external genitalia were normal, but the patient refused to undergo vaginal examination.

Table I shows that routine laboratory examinations were normal in both patients, but some endocrine findings were abnormal (Table II).

**Case 3**—According to the parents, the brother who died at the age of seventeen was also obese, had six digits on all extremities and at the age of five his vision had begun to deteriorate until he was almost blind. At first at a normal school, he was later transferred to one for retarded children. During adolescence he had suffered from a renal disease which was the cause of his death.

**DISCUSSION**

The Laurence-Moon-Biedl-Bardet syndrome is a rare hereditary recessive condition. About 400 cases have been described in the literature since Laurence and Moon's four cases reported in 1866. The full syndrome was found in only a small proportion of these cases. According to the investigation made by Warkany and Weaver (1940) only twenty-four of 102 cases showed the complete syndrome. Reilly and Lisser (1932) found that twenty-five of the seventy-seven cases which they investigated had the complete syndrome.

In addition to the five main features of the syndrome (retinitis pigmentosa, polydactyly, obesity, genital hypoplasia and mental retardation) many other disturbances have been described (Table III). Both of our cases had the full syndrome, with in addition a deformity of the hips.

Obesity and polydactyly are most often found (Reilly and Lisser 1932; Warkany, Frauenberger and Mitchell 1937; Warkany and Weaver 1940). Some authorities state that if polydactyly and a Fröhlich-type obesity are found in children, the Laurence-Moon-Biedl-Bardet syndrome should be considered (Lisser and Escamilla 1957). The polydactyly is usually
### TABLE I
**Laboratory Examinations**

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
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</thead>
<tbody>
<tr>
<td>Urea (milligrams per cent)</td>
<td>20</td>
<td>26</td>
</tr>
<tr>
<td>Glucose (milligrams per cent)</td>
<td>98</td>
<td>105</td>
</tr>
<tr>
<td>Calcium (milligrams per cent)</td>
<td>9.6</td>
<td>10</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>3.8</td>
<td>3.9</td>
</tr>
<tr>
<td>Cephalin</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Thymol turbidity</td>
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<td>Normal</td>
</tr>
<tr>
<td>Alkaline phosphatase (Bessey-Lowry units)</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Total protein (grammes per cent)</td>
<td>8.3</td>
<td>—</td>
</tr>
<tr>
<td>Albumin</td>
<td>5.2</td>
<td>—</td>
</tr>
<tr>
<td>Globulin</td>
<td>3.1</td>
<td>—</td>
</tr>
<tr>
<td>Urinary amino-acids</td>
<td>Normal</td>
<td>Normal</td>
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</table>

### TABLE II
**Endocrine Findings**

<table>
<thead>
<tr>
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<th>Case 1</th>
<th>Case 2</th>
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<tbody>
<tr>
<td>Protein bound iodine gamma (per cent)</td>
<td>7</td>
<td>6.6</td>
</tr>
<tr>
<td>Urinary 17 ketosteroids (milligrams per 24 hours)</td>
<td>2.6*</td>
<td>6</td>
</tr>
<tr>
<td>Urinary 17 hydroxy corticosteroids (milligrams per 24 hours)</td>
<td>7.9</td>
<td>17.1</td>
</tr>
<tr>
<td>Urinary oestrogens (micrograms per 24 hours)</td>
<td>5.1‡</td>
<td>7.9‡</td>
</tr>
</tbody>
</table>

* Low level (normal range in our laboratory 20 per cent less than total 17 hydroxy cortico-steroids).

† High levels (normal range 4 to 16 milligrams per 24 hours). These high levels do not prove a disturbance of the hypothalamo-pituitary-adrenal axis, because they may also occur in otherwise normal but obese persons.

‡ Low levels (normal range 10 to 50 micrograms per 24 hours depending on the stage of the cycle).

### TABLE III
**Additional Disturbances Described in Reported Cases of the Laurence-Moon-Biedl-Bardet Syndrome**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syndactyly</td>
<td>Deafness</td>
</tr>
<tr>
<td>Dwarfism</td>
<td>Dental anomalies</td>
</tr>
<tr>
<td>Mongolian facies</td>
<td>Kidney anomalies</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>Anal atresia</td>
</tr>
<tr>
<td>Microphthalmus</td>
<td>Diabetes insipidus</td>
</tr>
<tr>
<td>Cataracts</td>
<td>Valgus of knees</td>
</tr>
<tr>
<td>Convergent strabismus</td>
<td>Ataxia</td>
</tr>
</tbody>
</table>
non-symmetrical. Syndactyly may occur with or without polydactyly. The obesity resembles that of Fröhlich’s disease (adipo-genital dystrophy), with a typical distribution of fat over the lower abdomen, hips, buttocks and also of the breasts, especially in male adolescents.

The retinitis pigmentosa is a degenerative process of the retina with typical distribution of pigment as polymorphic particles, concentrated mainly on the periphery of the retina. The pigmentation progresses gradually to involve the centre of the retina as well. In the early stages the retina appears paler than normal. Clinically it manifests itself as night blindness, with the visual field gradually diminishing to near-blindness (Duke-Elder 1940, Bisland 1951). Mental retardation may range from mild to severe.

Genital hypoplasia in this syndrome is manifested in the male as cryptorchism and hypoplasia of the penis, and in the female as hypoplasia of the uterus and labia. In adolescence there may be impotence and disturbance of spermatogenesis in the male, while in the female there may be disturbances of the menses. The hypogonadism may be primary or secondary (Oettlé, Rabinowitz and Seftel 1960; Reinfrank and Nichols 1964). In our cases there was a disturbance in the hypothalmo-pituitary-gonadal axis which was evident in the low level of oestrogens and the irregularly delayed menses (Table II). We assume that there was also hypoplasia of the uterus.

The etiology of this syndrome is unknown. The features may be divided into two types: 1) those that may be genetic in origin, such as retinitis pigmentosa and polydactyly (Warkany et al. 1937, Warkany and Weaver 1940, Lurie and Levy 1942); and 2) those in which the cause is less obvious, such as obesity and genital hypoplasia. Many investigators believe that these disturbances are secondary to an abnormality in the hypothalamus (Laurence and Moon 1866, Raab 1924, Reilly and Lisser 1932, Francke 1950, Wilkins 1957) because of the resemblance to Fröhlich’s disease. However, in all the cases described in the literature there was no evidence of an abnormal hypothalamus, and in most cases the endocrinological findings were normal. Thus the obesity appears to be of a pseudo-Fröhlich type. Necropsy studies have been made in some cases but have failed to reveal any typical abnormal cerebral changes (Van Bogaert and Borremans 1936; Anderson 1941; Bisland 1951; McLoughlin, Krovetz and Schiebler 1964). The high level of hydroxysteroids in Case 2 does not prove a disturbance of the hypothalamo-pituitary-adrenal axis because this may also occur in otherwise normal but obese persons (more precise tests could not be done because of a lack of consent of the patients).

The etiology of the disease is thought to be associated with an autosomal recessive hereditary disturbance caused by a mutation of two genes within one chromosome (Durham 1960). In our cases we were unable to trace the family tree any further back than the grandparents, where consanguinity was found. Thus we assume that the genetic disturbance may have occurred in that generation. The occurrence of occasional sex chromosome aneuploidy, such as XXX, has been documented, but its significance is unknown (Bowen, Ferguson-Smith, Mosier, Lee and Butler 1965). Chromosome examinations were not done in our cases.

The syndrome appears to have a familial incidence: in 80 per cent of the cases reported in the literature there was more than one case in a family (Durham 1960). In 30 per cent of the cases there was a history of intermarriage in earlier generations (Burn 1950, Wilkins 1957). There was a high incidence of abortions and death of children at an early age in involved families (Durham 1960). It should be noted that in the family described by us the mother gave a history of two abortions, in addition to the death of the son at seventeen years.

There is no effective treatment for this syndrome. Trials with testosterone, oestrogens and ACTH (Scott and Johnson 1942, Hurxthal and Musulin 1953, Durham 1960) proved unsuccessful. Amputation of supernumerary digits provides only cosmetic relief.

It should be stressed that whenever a congenital malformation is seen, the surgeon should consider the possibility that it may be part of a syndrome. Once the diagnosis is proven, he may be able to inform relatives of the prognosis so that, as in this case, they may be made
aware of the fact that the syndrome is a progressive condition and is not cured by the amputation of supernumerary digits.

SUMMARY

1. Three cases of the Laurence-Moon-Biedl-Bardet syndrome occurring in a Yemenite family are presented. The parents were first cousins.
2. In two of the patients the complete syndrome, which comprises retinitis pigmentosa, polydactyly, obesity, genital hypoplasia and mental retardation, was found. The patients also had abnormalities of the hips.

REFERENCES


