Syndrome of the month

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Johanson-Blizzard syndrome

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In 1971 Johanson and Blizzard\(^1\) reported a new syndrome in three unrelated girls characterised by congenital aplasia of the alae nasi, deafness, hypothyroidism, dwarfism, absent permanent teeth, and malabsorption. Children with this syndrome had been described earlier by Morris and Fisher in 1967\(^2\) and Townes in 1969\(^3\) as examples of trypsinogen deficiency disease. Townes and White\(^4\) subsequently reviewed the patient reported in 1969\(^3\) and described the presence of additional features which confirmed the diagnosis of the Johanson-Blizzard syndrome. There have since been 22 patients reported with Johanson-Blizzard syndrome, and a further seven children related to these. The spectrum of associated features is now well documented and the inheritance of the syndrome is autosomal recessive. However, there remain many problems which make counselling difficult, in particular the degree of mental handicap and the observation that some children die from complications of the severe malabsorption despite intensive treatment. This article reviews the 22 patients previously reported and also includes details of a previously unreported boy.

Clinical features

The main features are shown in the table. The most constant signs necessary to make a diagnosis are aplasia of the alae nasi, an exocrine pancreatic defect, and unusual hair growth pattern.

In the absence of major structural abnormalities, the affected infant usually comes to medical attention because of failure to thrive. On presentation, the infant is malnourished, hypotonic, and often oedematous because of hypoproteinaemia.

**TABLE** Frequency of features in the Johanson-Blizzard syndrome

<table>
<thead>
<tr>
<th>Feature</th>
<th>Reported cases (n=22)</th>
<th>This case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoplastic alae nasi</td>
<td>22</td>
<td>+</td>
</tr>
<tr>
<td>Pancreatic insufficiency/failure to thrive</td>
<td>21</td>
<td>+</td>
</tr>
<tr>
<td>Aplasia cutis congenita</td>
<td>19</td>
<td>-</td>
</tr>
<tr>
<td>Short stature</td>
<td>15</td>
<td>+</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>13</td>
<td>Mild</td>
</tr>
<tr>
<td>Dental anomalies</td>
<td>13</td>
<td>+</td>
</tr>
<tr>
<td>Deafness</td>
<td>12</td>
<td>+</td>
</tr>
<tr>
<td>Anorectal anomalies</td>
<td>11</td>
<td>-</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>Genitourinary abnormalities</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>6</td>
<td>+</td>
</tr>
<tr>
<td>Cardiac malformation</td>
<td>3</td>
<td>-</td>
</tr>
</tbody>
</table>

**FIG 1** Our patient, a boy, aged two months. Note the small nose with aplasia of the alae nasi and the abnormal hair growth pattern, also shown in fig 3.
thin, torpedo shaped nose with large nostrils. In addition, the hair is swept up, especially frontally (fig 3), and has a patchy distribution over the scalp. Closer inspection shows areas of alopecia (fig 4) with underlying aplasia cutis congenita, which are characteristically in the midline and in the occipital region. They heal to form atrophic scars.

**MALABSORPTION**

An exocrine pancreatic defect is a constant feature of this condition. Townes\(^3\) and Townes and White\(^4\) described the abnormalities of pancreatic function. They reported an absence of trypsin, chymotrypsin, and their proenzymes, as well as carboxypeptidase and lipase, but they thought the amylase activity was normal. This was subsequently found to be a spurious result as isoenzyme studies showed that amylase was from the salivary gland. When the contribution from saliva is excluded, pancreatic amylase activity is absent. At necropsy the parenchyma of the pancreatic gland is replaced by fatty tissue.\(^5\)\(^6\) There are fewer islets of Langerhans but clinically there are no reports of impaired glucose tolerance.

The severe malabsorption caused by these enzyme deficiencies leads to hypoproteinaemia, oedema, anaemia, and failure to thrive. The treatment of the pancreatic failure is by pancreatic enzyme replacement, as in cystic fibrosis. It is a life-threatening condition and several of the children reported have died despite full medical treatment.

**SHORT STATURE**

The short stature has been attributed to hypothyroidism and malabsorption. There have been su
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Counselling

There is strong evidence for autosomal recessive inheritance. Affected sibs have been described by Moeschler and Lubinsky,8 Day and Israel,10 Helin and Jodal,15 and Bresson et al.18 Parental consanguinity has been reported by Schussheim et al.,9 Sismanis et al.,7 Mardini et al.,13 and Bresson et al.18

A more difficult problem in counselling is that of predicting the degree of mental retardation, the presence of severe structural lesions, and the success in treating the pancreatic exocrine defect. There have been no reports of prenatal diagnosis to date. At present one could offer a high resolution ultrasound scan in the hope of detecting the distinctive facial features and any structural abnormalities, such as the cardiac or urogenital lesions.

Prognosis

In the family of Mardini et al.,13 all three patients died in infancy from complications of malabsorption and failure to thrive. The girl reported by Townes3 and Townes and White4 was still alive at the age of 12 years nine months. She had short stature, no permanent teeth, a sigmoidostomy because of an imperforate anus, and she required pancreatic enzyme supplements with her meals. She had mild mental retardation. If the pancreatic malabsorption problems are overcome the child can survive infancy, but is likely to require prolonged medical supervision. Even when given the best medical attention these children may develop severe problems associated with hypoproteinaemia, namely infections and oedema, which can lead to death in childhood.

References


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