Persistent hyperinsulinemic hypoglycemia of infancy: long-term follow-up after surgical treatment

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**Aim** The aim of this study was to investigate the long-term outcome of six children with persistent hyperinsulinemic hypoglycemia of infancy (PHHI) after pancreatectomy who have been followed since 1990 at the Riyadh Military Hospital, Riyadh, Kingdom of Saudi Arabia.

**Patients and methods** Data from six patients were retrospectively analyzed from chart review. PHHI was diagnosed on the basis of having high-insulin levels and low-glucose levels and a high insulin-to-glucose ratio. Lactate, pyruvate, ammonia, and urinary organic acid levels were recorded and tandem mass spectrometry screening was performed. The patients were assessed radiologically by MRI of the brain and by ultrasound examination of the abdomen. Patients who failed medical therapy underwent near-total pancreatectomy.

**Results** Hypoglycemic convulsion was the most common presenting complaint. None of the patients responded to medical treatment and thus underwent surgery. Two patients still had hypoglycemic episodes after surgery, requiring medical treatment. However, they underwent subsequent surgery because of unresponsiveness to medical therapy. Three patients developed diabetes. None of them had malabsorption, and two patients later developed epilepsy.

**Conclusion** The earlier the age at diagnosis, the better the neurological outcome. Delayed surgery might be associated with higher risk of development of diabetes. Near-total (90–95%) pancreatectomy is the treatment of choice for PHHI not responsive to medical treatment. *Ann Pediatr Surg* 7:123–125 @ 2011 Annals of Pediatric Surgery.

**Keywords:** Near-total pancreatectomy, outcome, persistent hyperinsulinemic hypoglycemia of infancy

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17 years (median age: 8 years). Age at diagnosis ranged from a few hours after birth to 2½ months. Age at surgery ranged from 1 to 6 months (median: 3 months) (Table 1).

Hypoglycemic convulsion was the most common presenting complaint. All patients had inappropriately elevated levels of insulin during episodes of hypoglycemia ranging from 12 to 125 mU/ml. The insulin-to-glucose ratio was high for all patients, and all patients required glucose infusion rate greater than 15 mg/kg/min. All patients had normal growth hormone, cortisol, and thyroid hormone levels. Lactate, pyruvate, and ammonia levels were also normal. Urinary organic acid screening and tandem mass spectrometry screening were negative for all patients. MRI of the brain was significant for two patients who later developed epilepsy. Ultrasound examination of the abdomen was unremarkable. All patients were started on diazoxide, octreotide, and glucose infusion. In addition, glucagon was given (as required) PRN. The medical treatment was considered a failure when patients, despite undergoing maximum treatment, had hypoglycemic episodes. All patients required surgery after failure of medical treatment. Three patients underwent 95% pancreatectomy, two patients underwent 90% pancreatectomy, and one patient underwent 70% pancreatectomy. Two patients (one who underwent 90% pancreatectomy and another who underwent 95% pancreatectomy) had repeated hypoglycemic episodes that required medical treatment after surgery, which later required a second surgery. Obvious overgrowth of the remaining pancreas was observed during the second surgery of the patient who underwent 95% pancreatectomy, which was performed 4 months after the first surgery.

Three patients developed diabetes: two at 10 years of age, including one who had 70% pancreatectomy, and one at 1 year of age. None of the patients had exocrine insufficiency or developmental delay. Two patients developed epilepsy later (Table 2). There was no mortality. All patients continue to be followed at the clinic. Histology for all patients revealed diffuse nesidioblastosis.

**Discussion**

We have presented the clinical outcome of six patients with PHHI who underwent surgery after failure of medical treatment with a mean follow-up of 8.25 years. Most of the cases are sporadic. However, in our series we had four patients from the familial group (66.6%) and two from the sporadic group (33.2%). Insulin-dependent diabetes developed in three out of six (50%) treated children (two at the age of 10 years and one at the age of 1 year). Other investigators have found that diabetes develops in 56% of children having near-total pancreatectomy [9]. We found that older age at surgery leads to greater risk of diabetes, in agreement with previous studies [10]. This finding relating age at surgery and development of diabetes needs confirmation with larger case series before they can be generalized. Two children were hypoglycemic after surgery, requiring medical treatment, which later required second surgery. One patient underwent 90% pancreatectomy during the first surgery and the other underwent 95% pancreatectomy. Overgrowth of the remaining pancreas was observed in one patient who underwent 95% resection. Postpancreatectomy pancreatic regrowth in four infants with PHHI has also been documented in other studies [9,11]. Postpancreatectomy regrowth is well documented in experimental models [12]. The patient who underwent 70% pancreatectomy (the first case in our series) was operated upon by a general surgeon who was covering the service of pediatric surgery at that time. This might explain the underestimation of the actual percentage of the pancreatectomy in this case, which did well postoperatively.

All patients were developmentally normal and two patients (33.3%) were diagnosed with epilepsy after a

### Table 1 Patients’ age, birth weight, and age at presentation, diagnosis, and surgery

<table>
<thead>
<tr>
<th></th>
<th>Familial cases</th>
<th>Sporadic cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at last follow-up visit</td>
<td>17 years</td>
<td>8 years</td>
</tr>
<tr>
<td>Age at presentation</td>
<td>5 days</td>
<td>First day</td>
</tr>
<tr>
<td>Birth weight</td>
<td>3.3 kg</td>
<td>3.8 kg</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>75 days</td>
<td>First day</td>
</tr>
<tr>
<td>Age at surgery</td>
<td>6 months</td>
<td>1 month</td>
</tr>
</tbody>
</table>

### Table 2 Type of surgery and long-term outcomes

<table>
<thead>
<tr>
<th></th>
<th>Familial cases</th>
<th>Sporadic cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of surgery</td>
<td>70%</td>
<td>90% followed by 95%</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>No</td>
<td>Following first surgery</td>
</tr>
<tr>
<td>Age at development of diabetes</td>
<td>10 years</td>
<td>None</td>
</tr>
<tr>
<td>Exocrine insufficiency</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Neurological abnormality</td>
<td>Epilepsy</td>
<td>Epilepsy</td>
</tr>
</tbody>
</table>
few years as compared with 64% of patients with developmental delay in another series [13], possibly associated with delayed treatment.

In our cases, age at diagnosis ranged from a few hours after birth to 2½ months (median age, few hours). This is because most of our patients were from the same family and had been admitted soon after birth to the Neonatal Intensive Care Unit for workup.

**Conclusion**

The earlier the age at diagnosis, the better the neurological outcome. Delayed surgery might be associated with higher risk of development of diabetes. Pancreatectomy 90–95% is the treatment of choice for PHHI not responsive to medical treatment.

**Acknowledgements**

**Conflicts of interest**

There are no conflicts of interest.

**References**