Normal Growth after Administration of Octreotide: Report on a Case of Persistent Hyperinsulinemic Hypoglycemia of Infancy Treated by Continuous Subcutaneous Injection of Octreotide

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PERSISTENT hyperinsulinemic hypoglycemia of infancy is a disease characterized clinically by persistent hypoglycemia with inappropriately high circulating insulin concentrations. Nesidioblastosis is a diffuse abnormality of the pancreas in which there is extensive, often disorganized formation of new islets, and is known to cause hyperinsulinemic hypoglycemia [1, 2]. Diazoxide can suppress hyperinsulinemia but has serious side effects [3]. Successful treatment with octreotide, a long-acting somatostatin analogue, was reported but it involves the possibility of suppression of GH [4-6]. Here we report a case of persistent hyperinsulinemic hypoglycemia in a male infant who was treated by continuous subcutaneous injection of octreotide for 4 months, and on the course of his growth and development.

Case Report

The patient was a male baby born after 38 weeks of gestation. Pregnancy and delivery were uneventful and one-min and five-min Apgar scores were 9 and 10, respectively. His birth weight was 2938 g and length 50.0 cm. There was no family history of hypoglycemia or diabetes mellitus. The body height of his father is 168 cm, and his mother 158 cm. The patient started to suck at 8 h after birth and took 10 to 25 ml of formula milk every 3 h. He was well prior to 39 h after birth, when, one hour after feeding, hypothermia and cyanosis, and then systemic tonic seizures of ten to thirty second duration suddenly occurred. His rectal temperature was 34.9 °C, heart rate 132/min, and respiratory rate 66/min. An apnea attack was detected about once every ten minutes. Excessive sweating was found on his frontal head. His crying was weak, and his lips cyanotic. The anterior fontanel was flat. Primitive reflexes and tonus of the truncal and peripheral muscles were weakened. Sun-set phenomenon was also noted. Chest auscultation and abdominal palpation revealed no abnormality. The tongue was relatively large, but no other finding compatible for Beckwith-Wiedemann syndrome was identified. Serum glucose was found to be as low as 0.06 mmol/L, but insulin secretion was maintained and its serum concentration was 12.8 μU/mL (assayed by a counting immunoassay kit provided by Sysmex Co., Ltd., Kobe, Japan) and C-peptide was 2.9 ng/mL (assayed by a RIA kit provided by Daiichi Radioisotope Co., Ltd., Tokyo, Japan). No urinary acetoacetate was found and, in addition, serum 3-hydroxybutyrate was 19 μmol/L. Plasma ammonia concentration was 50 μmol/L (normal range, less than 52 μmol/L). The clinical course is shown in Fig. 1. Immediately after hypoglycemia was observed, a high concentration of glucose solution was
administered intravenously and then prednisolone was added as an emergency measure. Because insulin secretion did not seem suppressed despite the hypoglycemia, as shown above, subcutaneous injection of octreotide was tried for its action in suppressing hyperinsulinemia and raising blood glucose after informed consent was obtained from the parents. A single injection of 1 μg of octreotide was consequently found to raise blood glucose from 2.7 to 5.2 mmol/L and was followed by four daily subcutaneous injections, and then by continuous subcutaneous injection of 0.12 μg/kg/h of octreotide, both of which also successfully suppressed hyperinsulinemia and increased the blood glucose concentration (Fig. 1). No acute side-effect of octreotide, e.g. gastrointestinal symptoms [4-6], was observed. For the continuous subcutaneous injection, Nipro SP-3HQ®, Nissho-Nipro Ltd., Osaka, Japan, was used in the same way as the insulin pump [7, 8]. The requirement for octreotide gradually increased and reached 0.38 μg/kg/h at one month of age. An accidental cessation of the injection occurred in the patient’s home at 2 months of age, and immediately caused hypoglycemia.

Because the requirement for octreotide increased gradually and almost infinitely, and because the possibility of a hypoglycemic episode without apparent symptoms could not be ruled out, subtotal pancreatectomy was performed at 4 months of age. The initial operation removed 90% of the pancreas but failed to avoid hypoglycemia. A second pancreatectomy was performed immediately and 95% of the total pancreas was removed. Histological findings obtained at the second operation are shown in Fig. 2. Focal adenomatosis was observed and the diagnosis of nesidioblastosis was confirmed. After the second operation, the patient had a normal blood glucose concentration and no symptom of hypoglycemia.

At one year and eight months of age, height was 80.0 cm, (mean – 1.14 SD) and weight was 9.4 kg.
HYPERINSULINEMIC HYPOGLYCEMIA TREATED WITH OCTREOTIDE

At 2 years 8 months, height was 88.4 cm, (mean – 1.02 SD) and weight was 11 kg. At 3 years 5 months, height was 93.8 cm, (mean – 0.95 SD) and weight was 14 kg, and mental and motor developments were within normal limits. But epilepsy and delayed myelination of the occipital lobe were found on MRI. Serum total IGF-1 was 53 ng/ml, and IGF-BP III was 1.59 µg/ml.

Discussion

In the present case, persistent hypoglycemia and an inappropriately high circulating insulin concentration were observed and histological examination of the resected pancreas revealed adenomatous islets. The excessively secreted insulin is possibly derived from adenomatous islets. Octreotide can suppress glucagon and GH. In the present case it effectively suppressed hyperinsulinemia and increased the blood glucose concentration. Continuous subcutaneous injection with an insulin pump was able to stabilize normoglycemia and to prevent severe damage to the central nervous system. In addition, at 3 years and 5 months, the patient’s growth seemed within normal limits. Octreotide itself and its use in continuous subcutaneous injection during infancy is thought to be a safe and effective measure for treating hyperinsulinemic hypoglycemia.

References