



Recurrent Hypoglycemia in Baby with Insulinoma: A Case Report

Ni Putu Sukma Sumantri Prabandari*¹, I Nyoman Wande², Ni Nyoman Mahartini³

Department of Clinical Pathology, Medical Faculty, Udayana University, Sanglah Hospital, Denpasar, Bali, Indonesia

Abstract

BACKGROUND: Insulinoma is a functional neuroendocrine tumor in the pancreas that can cause hypoglycemia due to endogenous hyperinsulinism. Insulinoma is a rare case with an incidence of 1–4 cases per million people each year. Insulinoma can occur at various ages and mostly occurs in adults with a predominance in women.

CASE REPORT: A baby boy aged 1 month 23 days was referred from Prof. Dr. W. Z. Johannes Hospital with the chief complaint was seizures. The results of the examination of blood glucose levels at Sanglah Hospital were 28 mg/dl. There were some episodes of normal blood glucose level in the patient after having some doses of glucose infusion therapy. However, it was only for a while, the blood glucose level came back low and induced the symptoms of the seizure (neuroglycopenia). The seizures stopped after having anticonvulsant therapy and blood glucose levels within normal limits. These symptoms were consistent with the Whipple triad in insulinoma. The patient has an elevated insulin level (92 IU/ml). Computed tomography scan of the abdomen with contrast showed a mass in the caudal part of the pancreas. The patient underwent a partial pancreatectomy. Histomorphology features showed pancreatic neuroendocrine tumors without metastases. Immunohistochemical results of Ki-67 showed well-differentiated neuroendocrine tumors grade 2.

CONCLUSION: Based on clinical, physical examination, laboratory, and radiology findings, the patient was diagnosed with recurrent hypoglycemia due to insulinoma and improved with partial pancreatectomy.

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***Correspondence:** Ni Putu Sukma Sumantri Prabandari, Department of Clinical Pathology, Medical Faculty of Udayana University, Sanglah Hospital, Denpasar, Bali, Indonesia. E-mail: sukmasu44@gmail.com
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Introduction

Insulinoma is a functional neuroendocrine tumor of the pancreas that can cause hypoglycemia due to endogenous hyperinsulinism. Insulinoma is rare with an incidence rate of 1–4 cases per million people each year [1]. Insulinoma can occur at any age and is mostly diagnosed in adults with a female predominance in a ratio of 1:1.4 (41% men and 59% women) [2].

Insulinoma is usually benign, measuring about 1–2 cm in size and about 10% of cases are malignant with multiple endocrine neoplasia type 1 (MEN-1) [1], [3]. The etiology of insulinoma is unknown. Insulinoma originates from pancreatic beta-cell islets with tumor manifestations in the form of insulin hypersecretion and causes hypoglycemia [4].

Case Report

A baby boy aged 1 month 23 days was admitted to Sanglah Hospital with the main complaint was seizures. The patient was a referral from Prof. Dr. W. Z. Johannes Hospital, with a diagnosis of refractory hypoglycemia. Symptoms begin with seizures

throughout the body and on examination, the patient's blood glucose level was 28 mg/dL. The patient was treated with glucose infusion and seizure medication. After the blood glucose levels came back normal, the seizures stopped. There was no history of fever, cough, runny nose, or shortness of breath. Defecation and urination were said to be normal.

The patient was born by cesarean section, the patient immediately started crying with a birth weight of 4800 g, and a body length of 53 cm. The patient's blood glucose level was said to have dropped on the 2nd day of treatment. The patient had a seizure and was treated for 3 weeks. The patient was discharged after being free of seizures and normal blood glucose levels. The patient is said to have undergone 3 times treatments due to seizures and low blood glucose levels before being referred to Sanglah Hospital.

According to the patient's mother, she said to be without complaints and had never checked blood glucose levels when she was pregnant. Family history found that the patient's grandfather was said to have diabetes. The patient is the first child. The patient was fed with breast milk for 3 weeks and then continued with formula milk. Regarding his developmental progress, at his age, the patient was able to lift his head by himself.

On admission, he looked lethargic, his vital signs were as follows: Pulse 120 beats/min, respiratory rate 30 times/min, body temperature 36.5°C, and

peripheral capillary oxygen saturation 96% room air, not in pain. A general physical examination has not found any abnormality. Nutritional status showed that the body weight was 5.6 kg, length 55 cm.

The laboratory result of rapid random blood glucose levels was always under 60 mg/dl. The fluctuation of rapid random blood glucose results is shown after infusion of D5% or loading dose of D10% and much more stable after the partial pancreatectomy procedures with a range 86-147 mg/dL. Other supporting laboratories evaluation includes complete blood count (CBC), blood chemistries, endocrine evaluation, and immunology profile. The CBC is shown in the normal range of values. The insulin level was high (92.1 μ U/ml). The results of the C-peptide examination were low (0.4 ng/ml). The C-peptide was examined after partial pancreatectomy in this patient, because the examination, there was not in Sanglah hospital and the patient's administration for this examination in the other laboratory, was complete after the patient underwent partial pancreatectomy. Lactate dehydrogenase (LDH) levels increased (949 U/L). Growth hormone (GH) level was within normal (13.5 ng/ml). Thyroid-stimulating hormone (TSH) and free-T4 (FT4) results were within normal (1.99 IU/ml and 1.35 ng/dl, respectively). The results of the carcinoembryonic antigen (CEA) and cancer antigen (CA) 19-9 were within normal (2.51 ng/mL and 19.75 ng/ml, respectively).

A computed tomography (CT) scan of the abdomen with contrast showed a retroperitoneal heterogeneous solid lesion whose borders were difficult to separate from the caudal part of the pancreas, accompanied by an expansion of the mass into the left retroperitoneal cavity so that it forced the left ureter and left kidney which caused a change in the left kidney axis, suggesting a caudal pancreatic mass. Figure 1 shows the CT scan abdomen result by contrast in Radiology Department at Sanglah Hospital.

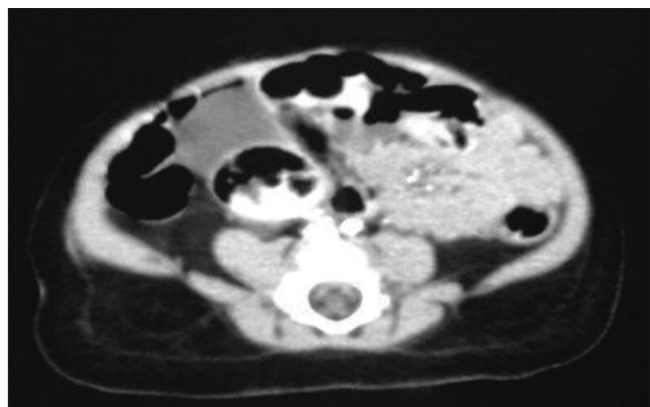


Figure 1: Computed tomography scan abdomen by contrast

Based on clinical symptoms, physical examination, laboratory, and radiological examination, the patient was diagnosed with recurrent hypoglycemia due to insulinoma. Patients were given infusion D5 1/4 NS 10 mL/hour, bolus D10% 2 ml/kg (12 ml) if blood glucose <25 mg/dl, diazepam 5 mg suppositories if

seizures, octreotide 15 mcg every 6 h subcutaneously, and formula milk 60 ml every 2 h. Curative therapy in this patient was partial pancreatectomy.

Discussion

Approaching the diagnosis of insulinoma in infants and children is a multidisciplinary challenge from pediatric endocrinology, pathology, radiology, nutritionists, and surgery. The clinical symptom that often appears is the Whipple triad which consists of a decrease in blood glucose levels, symptoms of hypoglycemia, and improvement of symptoms after correction of hypoglycemia. Symptoms during hypoglycemia may include adrenergic symptoms (hunger, palpitations, and anxiety) and neuroglycopenia symptoms (weakness, confusion or decreased concentration, drowsiness, dizziness, difficulty speaking, blurred vision, seizures, and decreased consciousness) [5], [6], [7]. This fulfilled all the criteria of the Whipple triad insulinoma, recurrent hypoglycemia, seizure due to decreased blood glucose levels and symptoms of neuroglycopenia, and hypoglycemia improved following glucose infusion.

Elevated insulin levels support the diagnosis of insulinoma. GH examination can rule out causes of hypoglycemia due to GH deficiency [8]. This patient had an elevated insulin level of 92.1 u IU/ml (normal 3.2–28.5 μ U/ml). The GH level in this patient was normal at 13.5 ng/ml. Normal serum GH levels at the time of hypoglycemia can rule out GH deficiency. High serum insulin values indicate hyperinsulinism as a cause of hypoglycemia.

Insulinomas are usually benign, but malignant insulinomas in children have been reported. Approximately 10% of insulinoma cases are accompanied by the presence of MEN-1.

MEN-1 is an autosomal dominant syndrome that can affect the parathyroid glands, anterior pituitary, and pancreas. The parathyroid tumor is an early manifestation that can cause primary hyperparathyroidism in more than 85% of patients [6]. Thyroid function tests were performed on this patient to rule out this. Thyroid function examination results were normal in TSH (1.99 IU/ml) and FT4 (1.35 ng/dl).

Radiological examinations such as abdominal ultrasonography, CT scan, and magnetic resonance imaging may be performed to help locate the tumor [9]. The patient underwent a CT scan of the abdomen with contrast that suggested a mass at the caudal part of the pancreas.

Tumor markers are substances produced by the tumor or host in response to the presence of a tumor from normal tissue. LDH is an enzyme in the glycolysis pathway that is released due to cell damage. LDH shows a correlation with a solid tumor mass. CEA

and CA 19–9 can be elevated in pancreatic cancer, levels with increasing tumor severity [10]. This patient's LDH result was high, 949 U/L (normal 240–480 U/L). The results of CEA and CA 19–9 examination in this patient were normal, so it could give the impression that the tumor in the pancreas was benign.

Surgery is a curative measure and standard of therapy in insulinoma cases. Tumor resection can be done partially depending on the size and type of tumor. Infants with focal type insulinoma can undergo partial pancreatectomy with a small risk of developing diabetes, while octreotide is used as medical therapy to suppress insulin secretion. Administration of glucose infusion can prevent symptoms of neuroglycopenia and hypoglycemia [8], [9], [11].

This patient underwent a partial pancreatectomy and found a tumor/mass with a size of 1 cm × 1 cm in the caudal part of the pancreas. The resected part of the caudal pancreas was examined histomorphology and immunohistochemically for Ki-67 to determine the type and grade of tumor [12]. Histomorphology examination showed a pancreatic neuroendocrine tumor and none of the tumor cell metastases were found in one mesentery lymph node structure. Immunohistochemical examination of Ki-67 staining in this tumor stained ± 5% of the cell components that make up the lesion. Based on the 2017 World Health Organization (WHO) criteria, this tumor classification is well-differentiated neuroendocrine tumor grade 2.

Early detection and appropriate management can provide a good prognosis. The patient's blood sugar level was stable after tumor resection (86–147 mg/dl). Post-operative wound care is carried out until the wound heals and monitoring blood glucose levels are monitored postoperatively. The patient showed normal blood glucose levels when follow-up 3 days after discharge from the hospital. The patient returns to Kupang with his family and the family was advised to continue to do blood glucose monitoring and the patient's condition. After 2 years of evaluation, the patient grows according to his development.

Conclusion

Case of a boy aged 1 month 23 days with recurrent hypoglycemia due to insulinoma. The patient met the Whipple triad criteria and had elevated insulin levels. Radiological examination showed a mass on the caudal part of the pancreas. The patient underwent partial pancreatectomy with histomorphology results showing pancreatic neuroendocrine tumor without metastases. Based on the results of Ki-67 immunohistochemistry and 2017 WHO criteria, the classification of this tumor is well-differentiated neuroendocrine tumor grade 2. The patient's blood sugar level was stable after tumor

resection. Blood glucose levels are still evaluated after surgery.

Authors' Contributions

All of the authors were the physician who treated the patient in this report, prepared the manuscript, and participated in discussions about the manuscript also approved the final version. This case report has received ethical approval with no: 2662/UN 14.2.2.V II.14/LT/2021.

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