CASE REPORT

Hypoglycemia due to an adult-onset nesidioblastosis, a diagnostic and management dilemma

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ABSTRACT

We describe a case of a 40 year old patient with recurrent severe fasting and postprandial symptomatic hypoglycemia that occurred 6 years after gastric bypass surgery. The hypoglycemia was associated with increased insulin and C peptide but all diagnostic modalities for localizing an insulinoma were negative. Medical management failed to control symptoms and the patient underwent subtotal pancreatectomy. Surgical tissue examination confirmed the diagnosis of noninsulinoma pancreatogenous hypoglycaemia syndrome (NIPHS) or nesidioblastosis. Initially after surgery the patient had full remission but after 6 months hypoglycemia recurred. However, this time it was well-controlled with octreotide treatment.

Key words: Hypoglycemia, nesidioblastosis, gastric bypass surgery, noninsulinoma pancreatogenous hypoglycaemia syndrome, NIPHS

INTRODUCTION

Hypoglycemia not caused by diabetes mellitus treatment is uncommon and can present diagnostic and management challenges.[1] The majority of hyperinsulinemic hypoglycemia cases are caused by insulinoma and only less than 5% are caused by noninsulinoma pancreatogenous hypoglycaemia syndrome (NIPHS) or nesidioblastosis.[2,3] Here we report a case of uncontrolled symptomatic hypoglycemia due to nesidioblastosis in a patient with history of gastric bypass surgery. The patient failed medical management and had to undergo subtotal pancreatectomy.

CASE REPORT

Our patient is a 40 year old female with past medical history of morbid obesity who underwent Roux-en-Y gastric bypass for weight reduction purposes 6 years before presentation. The patient had no major complications after surgery and no alcohol or drug use. She presented to our hospital with recurrent right upper quadrant pain, nausea and vomiting, and was found to have blood glucose of 15 mg/dl during an episode of dizziness, diaphoresis, and weakness. These symptoms resolved with dextrose solution administration; however, the patient had multiple similar episodes of both fasting and post-prandial symptomatic hypoglycemia that required starting dextrose solution drip. She was never diagnosed with diabetes and denied taking insulin or oral hypoglycemic medications. Upon further questioning, she admitted having similar episodes at home. During one of the fasting hypoglycemic episodes, glucose, insulin, and C-peptide levels were 25 mg/dl (normal range: 70- 100), 153.0 mcu/ml (normal range: 2-23), and 13 ng/ ml (normal range: 0.9-4.3), respectively. Insulin antibodies were negative. Urine sulfonylurea screen was negative. The patient was diagnosed with endogenous hyperinsulinemic hypoglycemia (insulinoma versus nesidioblastosis). Other endocrine disorders that can cause hypoglycemia, such as hypothyroidism and adrenal insufficiency, were ruled out.

To differentiate between insulinoma and nesidioblastosis, abdominal CT scan and endoscopic ultrasound were performed but failed to detect a pancreatic mass. An octreotide scan was done and did not show focal abnormality to suggest insulinoma –the test used radiolabeled somatostatin analogs to detect neuroendocrine tumors like insulinoma that have receptors for somatostatin-. Another specialized test called selective arterial calcium stimulated pancreatic venous

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sampling (SACST) was done to help localize the area(s) of the pancreas that was over-secreting insulin; this test uses calcium gluconate injections, an insulin secretagogue, into arteries supplying the pancreas with subsequent sampling of the hepatic vein to test for insulin. The SACST revealed a 6-fold increase for the superior mesenteric artery injection compared with a 3-fold increase for the splenic artery. The hepatic artery injection produced no change. Based on the results insulinoma was less likely because the increase of insulin secretion was reported in two different pancreatic artery injections. This diffuse pattern of insulin secretion favors nesidioblastosis.

The patient was started on octreotide 50 mg injections in order to control hypoglycemia; it was titrated up to 300 mg three times daily without much improvement. She was tried on diazoxide, but it was discontinued due to side effects of fluid retention and nausea. The patient was also started on nefidipine. Despite these medical therapies, she continued to have recurrent symptomatic hypoglycemia.

Since none of the imaging studies showed focal lesion(s), and the patient failed medical management, she underwent subtotal 80% distal pancreatectomy.

Histopathology examination of the excised pancreatic tissues showed diffuse islet cells hypertrophy, Islet cell pleomorphism and Ductal insular complex. These features are typical for nesidioblastosis [Figures 1-3].

Our patient did well postoperatively and was hypoglycemia free for about six months, but her hypoglycemic episodes recurred. She then responded well to medical therapy with octreotide subcutaneous injections with close follow ups.

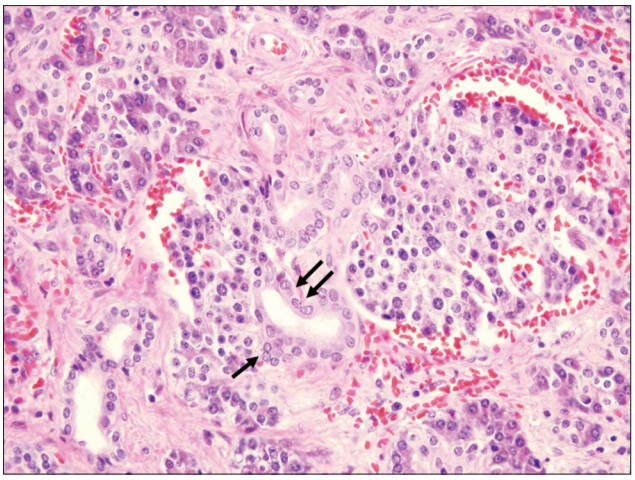

Figure 1: Ductal insular complex. Islet cells (single arrow) entering into the duct (double arrows) (×40)

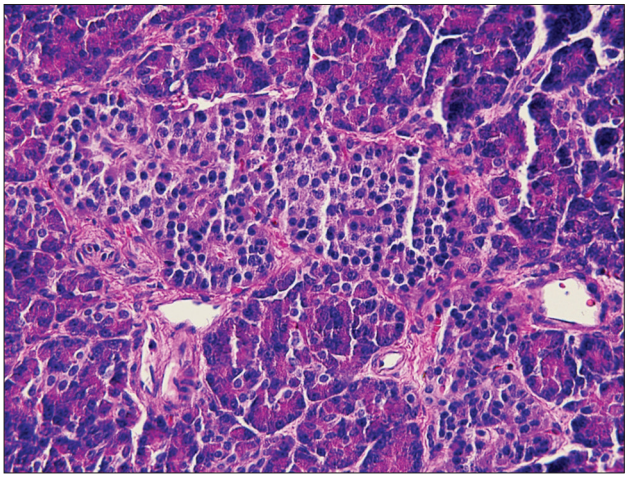

Figure 2: Irregular shaped hypertrophied islets (×40)

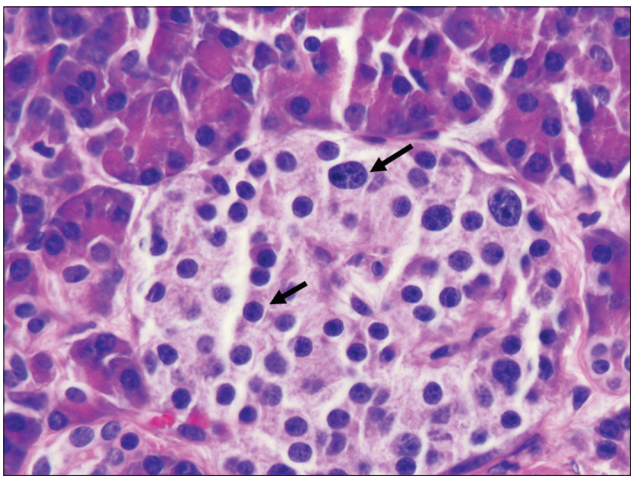

Figure 3: Islet cell pleomorphism. Marked difference in size of cells within same islet (×100)

DISCUSSION

Nesidioblastosis was first reported in infants by George F. Laidlaw in 1938.[4] He described nesidioblastosis as neoformation of Langerhans islets from the pancreatic ductal epithelium, and it is now known to be the primary cause of persistent hyperinsulinemic hypoglycemia in infants.[5] In Adults, hyperinsulinemic hypoglycemia is mainly caused by insulinomas, other causes are rare and usually due to adult-onset nesidioblastosis, which was first described in 1975.[6] Since then fewer than 100 cases have been reported but it seems to be increasing in frequency.[7]

The cause of adult-onset nesidioblastosis is unknown, but there seems to be an association with gastric bypass surgery.[8] Our patient underwent gastric bypass surgery about 6 years before presentation. The distinction between insulinoma and nesidioblastosis preoperatively can sometimes be difficult ,as the clinical presentation might be similar, and imaging studies can be equivocal.[1,9] In patient with nesidioblastosis symptoms occur mainly postprandially and only rarely while fasting. In contrast, most patients

with insulinomas have fasting hypoglycemia.[2,8] Moreover, radiological localization studies, such as CT scan, endoscopic ultrasound, octreotide scan, and selective arterial calcium stimulation test (SACST) with hepatic venous sampling, can be performed to distinguish between a focal abnormality (insulinoma) and a diffuse process (nesidioblastosis).

Other possible etiologies of hyperinsulinemic hypoglycemia include drug induced hypoglycemia, gastric dumping syndrome and exogenous insulin administration. Our patient had both fasting and post-prandial symptomatic hypoglycemia. We have documented inappropriately high insulin levels while hypoglycemic during fasting periods, which goes against dumping syndrome. Drug induced hypoglycemia was considered and ruled out by urine screening for Sulfonylurea. In addition High C-peptide levels seen in our patient should not be seen with exogenous insulin administration.

The patient was tried on aggressive medical therapy including Octreotide injections (to suppress the secretion of insulin), Diazoxide (a potassium channel blocker that can decrease insulin secretion), and Nifedipine (a calcium channel blocker that can decrease insulin secretion). Despite this medical management, the patient continued to have symptomatic hypoglycemia. Since medical management deemed ineffective, she underwent subtotal 80% distal pancreatectomy.

Although there is limited data regarding the efficacy of pancreatectomy for nesidioblastosis, successful resolution of hypoglycemia has been reported after partial or subtotal pancreatectomy.[10] On the other hand, recurrent hypoglycemia has also been reported that may require total pancreatectomy.[11]

Histopathology descriptions of excised pancreatic tissue include islet cell hypertrophy with enlarged and hyperchromatic nuclei, increased periductular islets ,and β-cells budding off ductular epithelium.[12,13]

CONCLUSION

Adult-onset nesidioblastosis is the main cause of noninsulinoma hyperinsulinemic hypoglycaemia and should be considered in patients with previous history of gastric bypass surgery; subtotal distal pancreatectomy could provide clinical benefit in refractory cases.

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