Adult Onset Nesidioblastosis: A Diagnostic Dilemma

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Nesidioblastosis is a rare entity usually seen in the neonates. Our case is unique as this would be the only reported patient on dialysis and there are only 2 patients reported in the literature that are older than our patient. Nesidioblastosis, while exceedingly rare in adult populations, should be considered in the differential diagnosis of severe hypoglycemia. While extensive laboratory and imaging tests could not identify the pathology, ASVS test (intra-arterial calcium stimulation with venous sampling) played a pivotal role in the diagnosis by localization of the pancreatic lesion. Nesidioblastosis can often be unrecognized, and early identification and prompt treatment plays a critical role in the management of such patients.

INTRODUCTION

Nesidioblastosis is defined as diffuse proliferation of pancreatic islet cells budding from ductal epithelium. The term “nesidioblastosis,” introduced by Laidlaw in 1938, is derived from Greek language “nesidia” stands for islets and “blastos” for germ. Adult-onset nesidioblastosis associated with hyperinsulinemic hypoglycemia is a rare entity, with less than 75 published cases till date. There have been only two reported cases of nesidioblastosis in patients older than our patient; and this is the first reported case of nesidioblastosis in a dialysis patient, which makes it unique.

CASE PRESENTATION

A 79-year-old African-American patient was admitted to a tertiary care hospital with altered mental status secondary to hypoglycemia. Patient was hospitalized 3 months prior with similar presentation and her symptoms were attributed to dysphagia from deconditioning and a percutaneous endoscopic gastrostomy (PEG) tube was placed. However, the patient continued to have hypoglycemic episodes despite placement of PEG. As a result, a workup for organic cause of hypoglycemia was initiated.

Laboratory results showed a C-peptide level of 13.0 ng/ml (normal, 0.9–4.3 ng/ml), insulin level of 27 IU/ml (normal, 1.4–14 IU/ml) and the urine sulphonylurea screening test was negative. CT and MRI scans of the abdomen and pelvis did not reveal any tumors. This was followed by a complete body scan that was also unremarkable.

As a result, invasive tests were launched to find the exact cause of hypoglycemia. ASVS (intra-Arterial calcium Stimulation with Venous Sampling) test was performed by Interventional Radiology using fluoroscopy. 0.025 mEq/kg of calcium was injected in the gastroduodenal artery, superior mesenteric artery and splenic artery. Hepatic vein samples for insulin levels...
were drawn from each artery at baseline and after injection with calcium. There was a two-fold increase in insulin levels from gastroduodenal and splenic arteries after injection of calcium suggesting hyper-secretion of insulin from pancreas supplied by these arteries (Figure 1).

Based on ASVS test results, patient underwent an exploratory laparotomy and a successful distal pancreatectomy with splenectomy was performed. Intraoperative ultrasound also failed to localize the lesion. Post-operatively, patient had no further hypoglycemic symptoms. Pathology showed islet cells hyperplasia (Figure 2A and B) with immunohistochemical staining positive for chromogranin (Figure 3A and B).

**DISCUSSION**

Nesidioblastosis is usually seen in neonates. It is very infrequently described in adults as a cause of hypoglycemia with less than 100 cases were published till date.

In neonates, the pathogenesis is related to disruption of normal relationship between blood glucose level and insulin secretion due to dysfunction of adenosine triphosphate (ATP) dependant potassium channel of the beta-cells. In infants, mutation is seen in SUR1/Kir 6.2 gene complex on chromosome 11p 14–15. In adults, no such relation to SUR1/Kir is found.

Clinically, patients with nesidioblastosis have neuroglycopenic episodes exclusively after meal ingestion. For diagnostic evaluation other causes of organic hypoglycemia such as exogenous insulin ingestion, sulphonylurea use and insulinoma need to be ruled out (Table 1). As mentioned above, patients with nesidioblastosis have post-prandial hypoglycemia, and negative 72-hour fasts that helps to distinguish insulinoma from nesidioblastosis.

Nesidioblastosis has been well established in patients with gastric bypass surgery. Therefore, clinicians need to be cautious in ascribing postprandial hypoglycemic symptoms to the dumping syndrome.

Standard radiologic test like spiral CT, MRI, endoscopic ultrasound may fail to localize any pancreatic tumor and selective intra-arterial calcium-stimulation test with venous sampling should be considered (ASVS). It is considered the best diagnostic test with sensitivity of approximately 100%. In this test, a rapid bolus of calcium gluconate is administered via a catheter in the celiac axis and the splenic, superior mesenteric, and gastroduodenal arteries. Blood samples are obtained through a catheter in the right hepatic artery.

**Figure 1.** Intra-arterial calcium stimulation with venous sampling shows a two-fold increase in insulin levels from gastroduodenal and splenic arteries after injection of calcium.
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Figure 2A and B. Pathology slides of the pancreas showing islet cell hyperplasia.

Figure 3. Pathology slides of the pancreas showing positive staining with chromogranin (A) and synaptophysin (B).

vein before injection and at several intervals after the injection. These blood samples are then tested for glucose, calcium, and insulin levels. An excessive insulin response from calcium stimulation in an artery sug-

gests the site of lesion. It can also be done intra-operatively to help the surgeon in ensuring proper tumor resection depending on the arterial distribution indicating hyperfunction of the beta cells.
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On pathological slides, nesidioblastosis is characterized by diffuse hypertrophy of beta cell islets and islet-like cells budding off exocrine ducts, which stain positive for chromogranin.

Pancreatic resection is the definitive treatment, however, the extent of surgical resection is still controversial. Most surgeons perform distal pancreatectomy; however, some have treated by 90–95% pancreatectomy. Near-total pancreatectomy is associated with insulin-dependant diabetes and also with exocrine pancreatic dysfunction. If surgery fails or is counter-indicated, medication, such as diazoxide, sandostatin or verapamil, can be used.

CONCLUSION

Nesidioblastosis, a rare entity, is one of the rare causes of hyperinsulinemic hypoglycemia in adults. It is a disease usually described in neonates, but our 79-year-old patient had this unusual case of hypoglycemic events that required extensive evaluation. Nesidioblastosis can often be unrecognized, and early identification and prompt treatment plays a critical role in the management of such patients.

References