Case Report

Functional Localization of Adult-Onset Idiopathic Nesidioblastosis

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Nesidioblastosis is a rare pancreatic disorder involving enlarged beta cells throughout the pancreas, causing elevated insulin production. We present the case of a 53-year-old woman with the initial symptom of fasting hypoglycemia. No pancreatic lesions were indicated on computed tomography and magnetic resonance imaging scans, and an octreotide scan was negative for insulinoma. Selective arterial calcium stimulation (SACST) showed increased insulin production from the stimulation of 3 out of 5 arteries. The SACST results suggested a diagnosis of nesidioblastosis, which was confirmed by histopathology after a subtotal distal pancreatectomy. The patient has normal glucose tolerance after surgery with no further problems of hypoglycemia, indicating that this is a rare case of nesidioblastosis extending only partially through the pancreas.

1. Background

Nesidioblastosis is an extremely rare disorder; first described in infants in 1938 by Laidlaw [1], it was not found in adults until 1975 [2]. We present the first reported case of diffuse nesidioblastosis confined to the distal half of the pancreas. This case represents an intermediate form of nesidioblastosis, between highly localized focal nesidioblastosis and typical diffuse nesidioblastosis throughout the entire pancreas [3]. This distinction is clinically important as it will guide therapeutic decisions and likely prognosis for individual patients.

1.1. Case

A 53-year-old woman was referred to our clinic in 2017 with symptoms suggestive of hypoglycemia. An oral glucose tolerance test was normal. Fasting hypoglycemia was diagnosed after she underwent a 72-hour fast resulting in a low serum glucose of 3.1, with simultaneous inappropriately high insulin of 150 (NR < 95 pmol/L) and C-peptide at 1301 (NR: 325-1090). Imaging was then performed to try and determine the cause of her hypoglycemia. CT and MRI scans did not identify any pancreatic lesions or insulinomas, and an octreotide study did not show any areas of increased uptake. The patient’s symptoms intensified, with nightly hypoglycemic symptoms that resulted in an inability to
work. The patient’s symptoms could not be controlled with medical management, so further investigations were undertaken in the hope of finding a lesion that could be surgically treated.

Selective arterial calcium stimulation (SACST) with hepatic venous sampling was performed, using the methods described by Thompson et al. [4]. There was a significant relative elevation in insulin levels following the stimulation of the superior mesenteric (SMA), gastroduodenal (GDA), and splenic arteries (SA), as shown in Table 1. No elevation was seen from the stimulation of the gastroepiploic (GEA) and hepatic arteries (HA). The maximal insulin concentration was seen in response to the stimulation of the SMA, at 235 pmol/L. The response from 3 arteries in SACST strongly suggested the presence of diffuse nesidioblastosis instead of a very small insulinoma [4], and the response from the SA suggested that the nesidioblastosis would be located around the tail of the pancreas [5]. However, the lack of response from 2 arteries suggested that the nesidioblastosis did not extend through the entire pancreas.

On the basis of the SACST results, a distal pancreatectomy was performed, removing the pancreatic tail region measuring $14.5 \times 5.2 \times 2.5$ cm, and preserving the spleen and duodenum. The histopathology confirmed the presence of diffuse nesidioblastosis within the pancreatic tail, with increased numbers of islet cells (Figure 1), some of which had enlarged nuclei (Figure 2). Furthermore, when sectioned there was no evidence of discrete masses or lesions. This pathology was found to be uniformly distributed throughout all of the resected surgical specimens. While the remaining pancreas was not biopsied to prove the absence of pathological features of nesidioblastosis, we assume that there was no significant amount of remaining abnormality due to the elimination of hypoglycemia immediately postoperation.

The patient has done well postoperatively with no further hypoglycemia and normal fasting glucose tolerance for 34 months.

2. Discussion

The differential diagnosis of endogenous hyperinsulinemic hypoglycemia in adults includes insulinoma and adult-onset nesidioblastosis. Insulinoma is significantly more common than nesidioblastosis, with approximately 1 to 3 cases per million [6]. Nesidioblastosis is estimated to account for 1% to 5% of cases of adult endogenous hyperinsulinemic hypoglycemia [7]. Clinically and biochemically, nesidioblastosis cannot be distinguished from insulinomas, and insulinomas smaller than 1 cm cannot be detected using imaging techniques [8], further complicating the differential diagnosis.

Selective arterial calcium stimulation can be used to aid in distinguishing between insulinoma and diffuse nesidioblastosis; if there is a significant relative elevation in insulin with the stimulation of 2 or more arteries, then nesidioblastosis is the probable diagnosis [4]. This is likely due to the diffuse nature of nesidioblastosis, whereas insulinomas are more localized and are more likely to respond only to stimulation of one artery. This also allows for some localization of nesidioblastosis, as in this case, where arterial stimulation aided in determining that the nesidioblastosis was primarily located in the pancreatic tail. However, there is some challenge due to individual variations in pancreatic arterial perfusion and anatomy that may produce problems when attempting to localize the abnormal cells [9].

Nesidioblastosis is characterized by the presence of many beta cells with enlarged nuclei and large amounts of clear cytoplasm, in most islets throughout the pancreas [10]. Typically, no abnormalities are seen in somatostatin, glucagon, and pancreatic polypeptide cells [7, 11]. Some patients have increased numbers of beta cells and islet hypertrophy, but this is not seen in all cases [12]. Peliosis-like vascular ectasia has been seen in some cases, often when other endocrinopathies are involved [13, 14]. Increased numbers of ductuloinsular complexes are seen occasionally, although most cases lack this feature [7]. Our case did show some beta cells with enlarged nuclei, and there were also an increased number of beta cells with islet hypertrophy.
References


