**Letter to editor**

**Insulinoma of Pancreatic Head Localized by Intra-Arterial Calcium Stimulation with Hepatic Venous Sampling**

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**Abstract**

Hypoglycemia is a common medical emergency. Insulinoma, a rare pancreatic endocrine tumour is the most common cause of hypoglycemia in patients without systemic illness. Most insulinomas are small, solitary and benign, which can be treated effectively by surgical removal of the tumour. Diagnosis is based on clinical features, laboratory tests and radiological investigation to localize the tumour. However, small size of this tumour leads to difficulty in localization of the disease, especially in occult insulinoma. Intra-arterial calcium stimulation with hepatic venous sampling can be utilised for preoperative localization of the tumour. We hereby present a case of a 33-year-old woman presenting with history of recurrent hypoglycemic symptoms and morbid obesity. A thorough history, clinical examination and laboratory investigation including prolonged fasting test were conducted and diagnosis of insulinoma was made. Intra-arterial calcium stimulation with hepatic venous sampling was carried out and revealed localization of insulinoma at pancreatic head.

**Keywords:** Insulinoma; preoperative localization; intra-arterial calcium stimulation with hepatic venous sampling

**Introduction**

Pancreatic insulinoma is a relatively rare endocrine tumour with an estimated annual incidence of four in every one million persons¹. It is female predominance, with mean age of presentation being fifth decade of life. Most insulinomas are solitary and small, with 90% being less than two cm². Although 90% of these tumours are benign², they have the potential to produce profound morbidity and risk of fatal hypoglycaemia. Insulinoma can be treated effectively by surgical excision. Hence, preoperative localization of the tumour is essential. Although a variety of non-invasive imaging modalities, such as transabdominal ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) have been highly favoured, preoperative localization fails 10–27% of the time, particularly in the case of occult insulinoma³. Occult insulinoma refers to a biochemically proven tumour with indeterminate anatomical site before operation. Intra-arterial calcium stimulation with hepatic venous sampling (ASVS), an invasive modality, is highly accurate in the preoperative localization of insulinomas and has been shown to be superior to non-invasive localization techniques³,⁴.

**Case report**

A 33-year-old woman was admitted to emergency...
Obesity is also a frequent feature in patient with insulinoma as patient tends to increase frequency of food intake to avoid hypoglycemic symptoms\(^4\).
Our patient experienced typical neuroglycopenic and sympathetic overdrive symptoms, and she also gained weight excessively within the two years of hypoglycemic episodes.

Diagnosing insulinoma accurately requires clear clinical observation and laboratory tests. Clinically, insulinoma is diagnosed by presence of Whipple’s triad which consists of hypoglycemic symptoms provoked by fasting, plasma glucose level less than 50 mg/dL (2.8 mmol/L) during the appearance of symptoms, and relief of symptoms after glucose administration. Measurement of plasma glucose, pro-insulin, insulin, and C-peptide during a 72-hour fast has been gold standard for biochemical diagnosis of insulinoma for over 80 years. The rationale of this prolonged fasting test is to establish inappropriately high pro-insulin, insulin and C-peptide concentrations in the setting of low fasting plasma glucose concentration. According to Endocrine Society clinical practice guideline, the findings of hypoglycemic symptoms, signs, or both with fasting plasma glucose concentration < 55mg/dL (3.0 mmol/L), pro-insulin ≥ 5.0 pmol/L, insulin ≥ 3.0 μU/mL (18 pmol/L), and C-peptide ≥ 0.6 ng/mL (0.2 nmol/L) establish endogenous hyperinsulinism.

Our patient displayed characteristics typical for insulinoma, including presence of Whipple’s triad and endogenous hyperinsulinism established by 72-hour fasting test. Pro-insulin level was not measured as the test was not available in our hospital.

Once clinical and biochemical diagnosis of insulinoma is established, investigation to localize the tumour is carried out to aid management decision. Pre-operative localization aids in differentiation of solitary from multiple lesions and thus allows simple enucleation of a solitary tumour rather than unnecessary blind resection of the pancreas, attribute to higher operative success rate and reducing operative morbidity and mortality. Non-invasive imaging modalities such as US, CT and MRI are highly preferred, but are often unsuccessful in insulinomas less than 2 cm in diameter. When non-invasive modalities fail to localize the tumours, invasive modalities such as endoscopic ultrasonography (EUS), angiography, transhepatic portal venous sampling, and ASVS are utilized. Comparing these two modalities, invasive ones have higher sensitivity compare to non-invasive ones, particularly ASVS technique which is reported to be the most sensitive technique with sensitivity of over 90% (range 87.5-100%) in localization accuracy.

ASVS was introduced by Doppman et al. in 1991, whereby localization of pancreatic insulinoma is based on release of insulin from islet cell tumour after stimulation by secretagogue (calcium). The success of ASVS relies on few assumptions, including that the tumour has a dominant feeding artery, that calcium stimulates a characteristic release of insulin granules from tumour cells, and that the remain beta cells are suppressed from the chronic insulin hypersecretion. However, it should be noted that this regionalization instead of exact localization, as the lesion is not visually identified precisely, but is identified according to its increased insulin secretion. An additional advantage of ASVS is to aid in distinguishing functional from non-functional tumour in MEN-1 patients with multiple lesions. As in this case, attempts to localize patient’s insulinoma with CT, MRI and pancreatic angiography were unsuccessful, but ASVS showed that the insulinoma was located at the pancreatic head region.

Insulinoma can be treated surgically or medically. Surgical excision is curative in most cases and hence is the treatment of choice. Medical management generally is recommended to high-risk candidates for surgery, those unwilling for surgery, those who have undergone unsuccessful surgery with persistent symptoms and when surgery is technically impossible. It includes dietary modification and pharmacological treatment with diazoxide, calcium channel blockers and somatostatin analogues.

Insulinoma is an uncommon neuroendocrine tumour, mostly benign, but can be life-threatening in causing fatal hypoglycemia. Biochemical diagnosis is obtained by 72-hour fast followed by imaging modalities to confirm the diagnosis and to localize the tumour. Preoperative localization remains challenging especially in the case of occult insulinoma as in this case. ASVS has been shown to be highly sensitive and accurate in localization of insulinoma which aid in patient’s treatment planning.

Acknowledgements: None
Funding: None
Conflict of interest: None
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References:


