

Case Report

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Importance of Selective Arterial Calcium Stimulation with hepatic venous sampling in management of a patient with multifocal insulinoma

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Abstract

Insulinoma is a rare neuroendocrine tumour arising from beta cells of pancreatic islets of Langerhans. We report a case of insulinoma presented with vague manifestations, which were undiagnosed for 2 years. The diagnostic evaluation revealed endogenous hyperinsulinism and imaging showed a pancreatic head lesion for which she underwent the surgery. Due to persisting symptoms, Calcium arterial stimulation and hepatic venous sampling was later performed and it localized an occult insulinoma that was not visible during the radiological or surgical assessment. Diagnosis of occult insulinomas remains a clinical challenge. Selective arterial calcium stimulation and venous sampling is a reliable pre-operative procedure for the positive diagnosis of insulinoma.

Keywords: *Insulinoma, Selective arterial calcium stimulation and hepatic venous sampling*

INTRODUCTION

Pancreatogenic hyperinsulinism is manifested as recurrent hypoglycemic episodes in an otherwise healthy individual. Commonly it is caused by insulin-producing beta cell tumour, insulinoma, or rarely due to diffuse hyperplasia of the pancreas, nesidioblastosis (1). Nearly 90% of insulinomas are solitary and benign tumours, while 10% can be multifocal, malignant, and familial (2,3).

Surgical excision is the curative treatment of choice in the management of insulinoma (4). Accurate pre-operative localization of the insulinoma remains challenging due to its small size (5). Conventional imaging studies such as

ultrasonography, Computed Tomography (CT), and Magnetic Resonant Imaging (MRI) often fail to reveal tumours less than 2 cm (6). Selective Arterial Calcium Stimulation Test (SACST) with hepatic venous sampling is identified as a highly sensitive test for localization of the insulinoma in the current practice (6).

CASE PRESENTATION

A 30 years old woman presented with recurrent episodes of faintishness, tremulous movements, and diaphoresis for 2 years. Initially, the episodes were brief and settled spontaneously within few minutes, but later had prolonged episodes with



brief tonic-clonic fits. She experienced these symptoms mainly in the mornings but got occasionally in the afternoons when she missed her lunch. Her appetite was increased significantly over the recent past and had gained 15kg of weight within 6 months. Her past medical history, obstetric history and drug history were unremarkable and there was no significant family history of endocrine disorders.

Examination revealed an obese lady (BMI-30) without significant abnormal physical findings. On admission, her capillary blood sugar was measured which was recorded as 56mg/dl even though she was completely asymptomatic. Her blood glucose series showed a fasting sugar value of 47 mg/dl. A prolonged fasting test was arranged but had to abandon the procedure due to faintishness with a blood sugar of 36mg/dl which responded to oral glucose. Her fasting Insulin Level was significantly high at 185 uIU/mL (Reference range-<25 uIU/mL)

and C- Peptide level was measured as 1.42nmol/L (Reference range 0.26-1.03) which was suggestive of hyperinsulinemic hypoglycemia.

The basic hormone profile of the patient revealed a low GH Level of 0.16ng/ml (reference range 2-5 ng/ml) and IGF 1 level of 305ng/ml. (reference range 89-290 ng/ml). All other hormone levels including FSH, LH, TSH, PTH, ACTH, fT4, and electrolyte profile including calcium and phosphate values were normal. With the suspicion of insulinoma, the patient underwent CECT abdomen which revealed a well-defined poorly enhancing focal area in the pancreatic head region measuring 11 * 10 cm in size (Fig. 1). There were some peripheral calcifications, but the rest of the pancreas was normally enhanced. MRI brain was arranged to exclude any pituitary lesions which could be associated with insulinoma and was found to be normal.

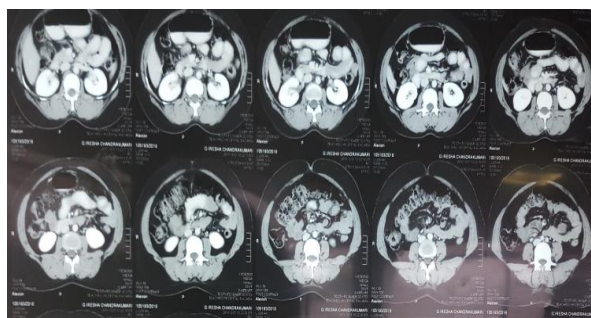


Figure 1 – CT Abdomen showing pancreatic head neoplasm

With these clinical grounds, the patient underwent spleen-preserving central pancreatectomy which was uncomplicated. During the surgery, a 2cm nodule at the lower border of the neck of the pancreas and a larger multicentric nodule at the upper border of the head of the pancreas were detected by palpation. The histopathological assessment revealed a multifocal pancreatic neuroendocrine tumor with immunohistochemical evidence of insulinoma. All the specimen margins were free of tumor.

Following the surgery, the patient was observed at the ward for a few days and her blood sugar series was satisfactory without significant hypoglycemic episodes and hence discharged from the hospital on post-op day 7. One week after discharge, the

patient presented back with similar hypoglycemic symptoms and was found to have low blood sugar values as the previous episodes. The prolonged fasting test was positive again and the fasting insulin level was found to be high, with a value of 998pmol/L (with a RBS of 40mg/dl). Repeat CECT Abdomen was not showing any residual tumours. Since the patient was having significant biochemical and clinical evidence of hyperinsulinemia, she was referred to an interventional radiologist for SACST with hepatic venous sampling for localization of an occult insulinoma.

In this procedure, the arteries supplying the pancreas were cannulated and intra-arterial calcium gluconate, which is a pancreatic

secretagogue, was injected. Serial blood samples were collected from the hepatic veins at time intervals of 30 seconds, 60 seconds, 90 seconds, 120 seconds, and 180 seconds (Table 1, Fig. 2). At 60 seconds of post-stimulation to the proximal

splenic artery, there was a significant surge of insulin secretion recorded as 1357microIU/ml. This finding was consistent with a residual functional tumor tissue in the body of the pancreas.

Table 1- Findings of Selective arterial calcium stimulation and venous sampling test

Site	Insulin Level (uIU/mL)					
	0 sec	30 sec	60 sec	90 sec	120 sec	180 sec
Distal Superior mesenteric artery	77.7	77.6	82.8	100.5	100.6	88.9
Hepatic artery proper	100.2	102.8	104.5	117	124.2	134.3
Gastroduodenal artery	81.2	130.8	98.3	111	118.2	120.8
Proximal Superior Mesenteric artery	77.9	145	127.6	188.7	230.1	196.1
Distal splenic artery	183.7	172.6	138	157.8	152.5	138.4
Proximal splenic artery	180.1	190.2	1357.2	1296.8	800	324.2

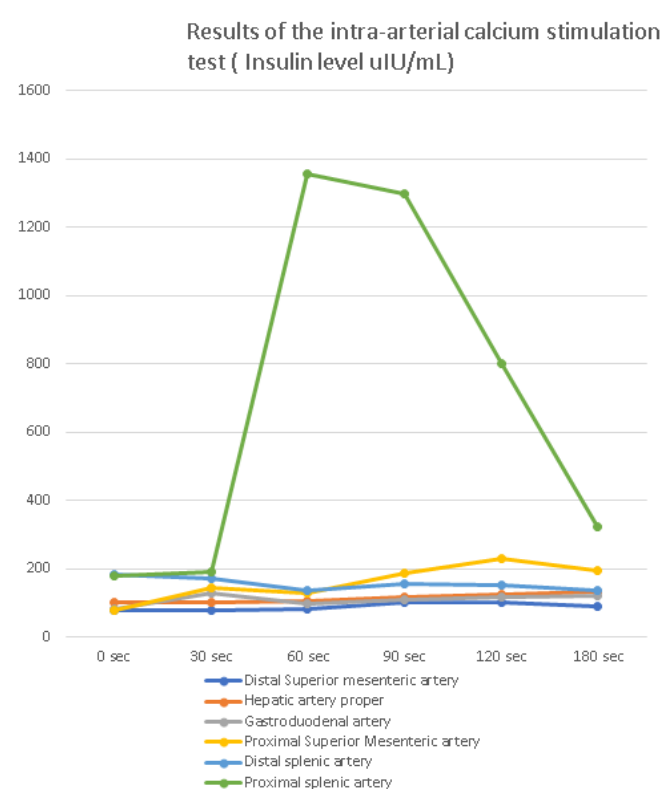


Figure 2 - Results of the intra-arterial calcium stimulation test

However, the patient was not willing to proceed with another surgery due to the risk of surgical morbidity. She agreed to be medically managed with diazoxide therapy and close monitoring of her blood sugar levels. Her diet plan was adopted to minimize the hypoglycemic episodes introducing frequent meals rich in carbohydrates, balanced

with proteins, fat and fiber. Her hypoglycemic awareness was satisfactory. Finally, she was referred to the endocrine clinic for subsequent follow-up.

6 months later, the patient was reviewed at the medical clinic. She was mildly hypoglycemic with

baseline glucose levels between 60-75 mg/dL, which she was able to manage with the given plan.

DISCUSSION

Radiological identification of an insulinoma is challenging and the symptoms usually precede the occurrence of a visible tumor (7). Even though, endoscopic ultrasound has a satisfactory accuracy in the detection of insulinoma, its use is limited in the local setting due to poor availability (8). SACST is a highly sensitive dynamic test that can localize an insulinoma with an 80%-94% of accuracy (9). It is possible to miss an occult tumor even during the surgical exploration as presented in this case. Management of patients with occult insulinomas in those with previously negative pancreatic exploration remains challenging (1). Repeated surgeries with excessive manipulation pose an increased risk of postoperative pancreatitis (1). Therefore, it is worth considering performing SACST in all patients with insulinoma before surgical exploration to pick-up the occult tumours which can co-exist with radiologically visible lesions (2).

CONCLUSION

Insulinoma is a rare tumour that can be difficult to diagnose with conventional imaging. SACST is a helpful functional study in the pre-operative localization of an insulinoma.

Abbreviations

CECT-	contrast-enhanced computed tomography
FSH –	Follicular Stimulation Hormone
LH-	Luteinizing Hormone
GH-	Growth Hormone
TSH-	Thyroid Stimulating Hormone
PTH	Parathyroid Stimulating Hormone
ACTH	Adrenocorticotrophic hormone
FT4	Free thyroxin level
BMI-	Body Mass Index
SACST	Selective Arterial Calcium Stimulation Test

Author declaration

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Authors' contributions

SU collected data, reviewed the literature, and wrote the manuscript. GP critically analyzed the manuscript. All involved in the patient care. All authors read and approved the final manuscript.

Conflicts of interest

Authors declare that there are no conflicts of interest

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None

Availability of data and material

All the data included in the manuscript is from the patient's old medical records and the investigations done during the ward stay.

Consent for participation and publication

Informed written consent was taken from the patient

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