

Case Report

A rare case of recurrent hypoglycaemia

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ABSTRACT

Very often clinicians are confronted with unconscious patients; the cause being hypoglycaemia. In addition to correction of hypoglycaemia promptly, a search for the cause of hypoglycaemia must be attempted at the earliest with a stepwise approach. Here, the authors present a rare case of recurrent hypoglycaemia where a stepwise approach ultimately led to a diagnosis, but there were various reports which were misleading. The diagnosis was insulinoma which was apparent from the history and presenting features. But, the initial investigations, even though having high sensitivity, were normal, thus leading to a more invasive approach. The patient was ultimately cured by enucleation.

Keywords: Enucleation, Hypoglycaemia, Insulinoma

INTRODUCTION

Hypoglycemia is often encountered in clinical practice. Most often it occurs in patients with diabetes. In patients without diabetes, hypoglycemia is uncommon with diverse causes in which low plasma glucose concentrations lead to symptoms and signs, which resolve when the plasma glucose concentration is raised.

The approach to a patient with documented hypoglycemia, after fulfilment of Whipple's triad, should begin with proper history, physical examination and laboratory investigations. In the ill and medicated patient, hypoglycemic drugs, critical illness and hormone deficiency are the major causes of hypoglycemia while endogenous hyperinsulinism is the cause of hypoglycemia in a seemingly well individual. Insulinomas (insulin-secreting pancreatic beta-cell tumors) are the prototypical, but not the only, cause of endogenous hyperinsulinemic hypoglycemia.^{1,2}

The diagnosis of insulinoma is apparent with inappropriately high levels of insulin, C-peptide and

proinsulin at the time of hypoglycemia. Imaging like Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and transabdominal Ultrasonography (USG) detect approximately 75% of insulinomas.^{3,4} Endoscopic pancreatic Ultrasonography (EUS), with the option of fine needle aspiration of a detectable tumor, has a sensitivity of greater than 90%.^{5,6}

It is interesting that sometimes, CT fails to localize the tumor while MRI does. In other cases, MRI fails to localize the tumor while CT does. Here, authors are going to discuss about an interesting case, where USG and MRI were normal, and CT detected a tumor. In this case, even FNAC did not reveal insulinoma.

CASE REPORT

A 37-year-old female was admitted in S.M.S. Hospital, Jaipur with the history of recurrent loss of consciousness for 1 year which were preceded by diaphoresis, palpitation and dizziness. There was no history of postural dizziness or syncope. There was no history of abnormal body movements urinary or fecal incontinence

or tongue bite. There was no history of fever, headache or vomiting. Such episodes were brief in duration and with recovery after IV fluids. She was investigated by a local physician and she was found to have recurrent hypoglycemia. For further management she was referred to higher centre. So, she came to S.M.S. Hospital for diagnosis and treatment.

On examination, she was conscious, well oriented to time, place and person, her vitals were within normal limit and she was afebrile. There was no orthostatic hypotension. Neurological and other system examination was within normal limit. Her routine investigations were within normal limit. MRI Brain and EEG was also normal.

Her blood sugar was monitored every 1 hr. When her RBS (random blood sugar) went down to 42 mg/dl, blood samples were taken, IV Dextrose was started, and she was advised frequent small meals rich in carbohydrate. In that sample, her insulin level was 18.30 μ IU/ml, C-peptide was 2.95 ng/ml and cortisol were 4.63 μ g/dl. So, the cause of hypoglycemia was endogenous hyperinsulinism.

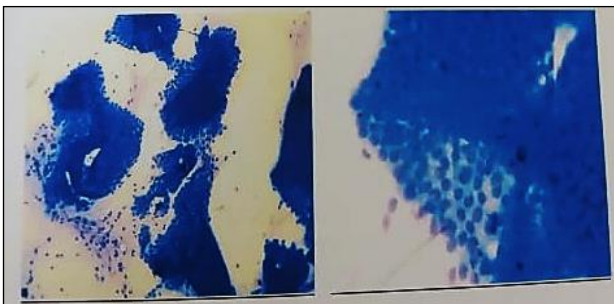


Figure 1: FNAC of pancreatic SOL.

USG abdomen was normal. MRI abdomen and pelvis revealed no significant abnormality and pancreas was also normal. Endoscopic ultrasound was done, and it revealed 1.3x0.9 cm hypoechoic/ isoechoic lesion seen at the junction of body and tail of pancreas. FNAC was taken. The cytomorphological features in FNAC were suggestive of mucinous cystic tumor of pancreas (Figure 1).

Smears show monolayered sheet of epithelial cells with focal area of honeycombing. The background show mucin. No nuclear abnormality or nucleoli seen. No speckled chromatin seen. The cytomorphological features are suggestive of mucinous cystic tumor of pancreas.

An expert opinion from surgical gastroenterologist was taken and they advised triple phase CECT abdomen. Triple phase CECT whole abdomen showed small lesion 13x14 mm in the region of neck/ proximal body pancreas - suspicious for insulinoma (Figure 2).

Small heterogeneously enhancing lesion of size approx. 13x14 mm seen closely abutting anterior pancreatic margin in the region of neck/proximal body of pancreas -

best visualized on arterial phase images forming a slightly exophytic pancreatic mass - suspicious for insulinoma. The lesion appears iso-dense to the pancreatic parenchyma on portal and venous phases.



Figure 2: Triple phase CECT whole abdomen.

On the basis of this report, the gastro surgeon did laparoscopic enucleation of the pancreatic lesion. After the operation, the patient never had hypoglycemia. The biopsy of the lesion revealed a well encapsulated cellular tumor consisting of tightly packed cells in the centre. In the periphery, the cells were loosely arranged, at places assuming a gyri form pattern. Many vessels are seen along with intervening fibrous stroma. The cells were relatively monomorphic with moderate to scant cytoplasm, stippled chromatin and inconspicuous nucleoli. Nucleolar prominence is focally noted. Mitotic count 2/10 hpf. Surrounding tissue revealed few normal acini. Overall histomorphology was consistent with neuroendocrine neoplasm. Ki-67 was advised for exact grading and serological correlation for confirmation of insulinoma. The patient refused further investigations. So, a final diagnosis of INSULINOMA was made.

DISCUSSION

Insulinomas are rare; an incidence of 1 in 250,000 patient-years has been reported.⁷ It has a slight female preponderance with median age at presentation of 50 years. Patients with an insulinoma typically present with a history of episodes of neuroglycopenia occurring in the postabsorptive (fasting) state. However, an appreciable subset of patients (6% in one series 8) report symptoms exclusively in the postprandial state. Similarly, in this case, the patient was a middle-aged female who presented with recurrent neuroglycopenic symptoms followed by loss of consciousness.

As the patient was seemingly well and non-diabetic, authors thought of endogenous hyperinsulinism as the cause of hypoglycemia. But as it is very rare, before going to a specific work up, authors did a thorough work up consisting of a proper history, physical examination and relevant laboratory investigations and all were found to be normal. Then authors monitored blood glucose hourly keeping the patient in the fasting state. When her blood glucose was 42 mg/dl, she developed neuroglycopenic symptoms (diaphoresis, palpitation, dizziness); blood samples were collected at that time and IV dextrose was started which made her comfortable (Whipple's triad satisfied).

In patient, insulin level was 18.30 μ IU/ml, C-peptide was 2.95 ng/ml and cortisol were 4.63 μ g/dl. Critical diagnostic findings are a plasma insulin concentration ≥ 3 μ IU/mL (≥ 18 pmol/L), a plasma C-peptide concentration ≥ 0.6 ng/mL (≥ 0.2 nmol/L), and a plasma proinsulin concentration ≥ 5.0 pmol/L when the plasma glucose concentration is < 55 mg/dL (< 3.0 mmol/L) with symptoms of hypoglycemia.⁹ So, according to diagnostic criteria, endogenous hyperinsulinism was present and was the cause of hypoglycemia.

As insulinoma is the most common cause of endogenous hyperinsulinism, the next step was to localize the tumor for resection.¹⁰ A number of non-invasive techniques are available for the localization of a suspected insulinoma, including transabdominal ultrasonography, CT and/or MRI. The sensitivity of transabdominal ultrasonography in the localization of insulinomas is poor (ranging from 9% to 64%).¹¹ However, insulinomas demonstrate characteristic features when imaged with both CT and MRI and the sensitivity of these techniques has been reported to be 33%-64% and 40%-90%, respectively.¹² The sensitivity and specificity of MRI is generally superior to that of CT, as is the detection of extra pancreatic extensions.³ Currently, there is strong evidence emerging for the use of MRI in the imaging of insulinomas, and investigators have shown a high sensitivity for MRI in the detection of insulinomas. In this case, the USG was normal, so authors went for MRI. Surprisingly, even after having high sensitivity, the MRI was normal in patient. As, CT and MRI were having almost similar sensitivity, the next step was to go for invasive technique.

EUS is currently the test of choice in most Western centers, with reported detection rates of 86.6%-92.3%.¹³ Endoscopic ultrasound was done in this case and it revealed 1.3 \times 0.9 cm hypoechoic/ isoechoic lesion seen at the junction of body and tail of pancreas. As suspicion of insulinoma was very high, FNAC was taken. Here also, unexpectedly, FNAC did not reveal characteristic features of insulinoma but rather of a mucinous cystic tumor of pancreas.

The Gastroscopy department decided to enucleate the tumor and they advised for a triple phase CT abdomen.

Here, after a long process, triple phase CECT whole abdomen showed small lesion 13 \times 14 mm in the region of neck/ proximal body pancreas which was suspicious for insulinoma. To date, laparoscopic resection has often been performed for insulinomas that are benign, small, and/or located in the body or tail of the pancreas.¹⁴ So, the tumor was laparoscopically enucleated, and the histopathology confirmed it to be insulinoma. The patient never had such symptoms anymore and she was cured.

So, in this study, authors found a rare diagnosis of insulinoma which is uncommon in the general population. Further, the case became interesting as authors were highly suspecting insulinoma but was not able to localize it with MRI. All these features made this case exceptional.

In a study done by Jyotsna VP et al, localization predicted by each pre-operative test was compared to localization at surgery for accuracy.¹⁵ Among non-invasive modalities, multiphasic MRI could localize insulinoma in 85 per cent whereas multiphasic CT in 79 per cent. Three patients in whom insulinoma could not be localized by CT were localized correctly by MRI. In one patient where MRI failed to localize tumor, CT localized tumors. Thus, MRI and CT are complimentary, and there is a need to repeat one if the other is negative. Multiphasic MRI yielded a better result than multiphasic CT.

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