

Multiple Insulinomas, a Rare Clinical Problem, Possible Case of Occult MEN I

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Abstract

A 22 years old under graduate with recurrent hypoglycemia was found to have an insulinoma after investigations. Diagnosis of insulinoma had been made by elevated C-peptide and insulin concentration with simultaneous hypoglycemia with blood glucose 35 mg/dl. Preoperative computed tomography localized a single tumor (7 mm x 7 mm x 7 mm) in the body of pancreas. On surgical exploration with intraoperative ultrasound localization a tumor was found in the body of pancreas and enucleated. Repeat intraoperative ultrasonography showed no residual disease, but palpation localized a second lesion in the body of pancreas and that was enucleated. Patient made a complete recovery. Screening for MEN I indicated that patient has several features of MEN I which remains occult at present. This case highlights a rare clinical problem of multiple insulinomas and also importance of intraoperative palpation.

Keywords: Hypoglycemia, multiple insulinomas, localization.

INTRODUCTION

Insulinomas are the most commonly found functioning endocrine tumor of pancreas. The incidence of insulinomas is 1/250,000 patient years. They are benign in most cases (85-99%), are single (93-98%), and have diameter less than 2.5 cm.¹ There is slight female preponderance with mean age of occurrence at 45 years.² In patients with insulinoma, MEN I should be suspected when multiple lesions are found. Approximately 4 to 10% of patients with hyperinsulinism will have MEN I.³

CASE HISTORY

A 22 years old undergraduate presented with loss of consciousness early in the morning and drowsiness of 4 months duration. She also had blurring of vision, weakness, palpitations, sweating in the morning. Her symptoms improved with meals and recurred on exertion. Her appetite was good and she gained considerable amount of weight. She did not have fits, abdominal pain or vomiting polyuria or double vision. She did not have family history of similar illness. Physical examination was unremarkable. Investigations results that confirmed diagnosis are given in Table 1. A hypodense lesion measuring 7 mm x 7 mm in size is seen in the body of the pancreas posterior to the main pancreatic duct in the arterial phase of the contrast enhanced CT (Fig. 1).

Based on the above investigations, a diagnosis of insulinoma was made. The patient underwent surgery.

Table 1: Diagnostic investigations of insulinoma

Investigation	Results
Fasting blood sugar	36 mg/dl
Insulin	24.7 μ u/ml (2.6-24.9)
C peptide	2 ng/ml (0.7-0.9)
Insulin/glucose ratio	0.68 (< 0.3)

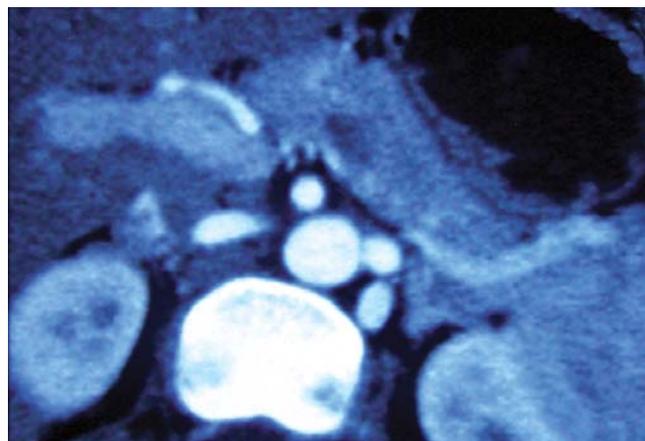


Fig. 1: Contrast enhanced CT abdomen showing hypodense lesion in the body of pancreas in arterial phase

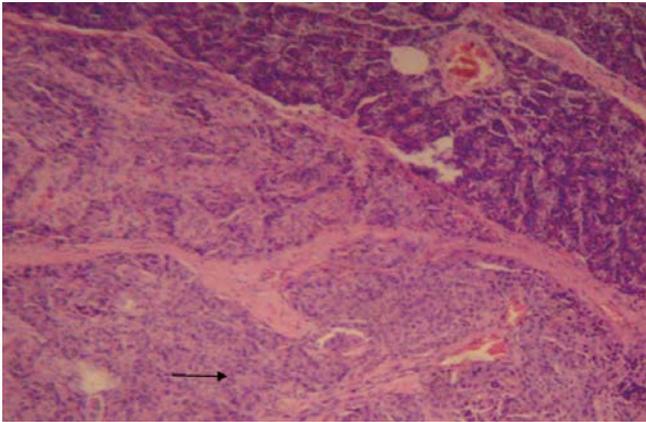


Fig. 2: Microscopic features of insulinoma. Tumor cells (arrow) arranged in nests and gyriform pattern (H and E stain; x 200)

Intraoperative ultrasound located tumor in the body of pancreas posterior to main pancreatic duct and enucleated. Repeat intraoperative ultrasound showed no residual tumor. Palpation identified a second tumor in the body of pancreas close to the first. Second tumor was enucleated. Patient made an uneventful recovery. Histology of both lesions confirmed insulinoma (Fig. 2).

In view of multiple insulinomas screening for MEN I syndrome was done (Table 2).

Table 2: Screening investigations for MEN I

Investigation	Results
Ionized calcium	1.13 mmol/l (1.12-1.32)
TSH	1.6 μ iu/ml (0.3-4.2)
Serum prolactin	434.4 mu/l (30-400)
Serum cortisol	327 nmol/l (140-700)
Serum parathyroid hormone	120 pg/ml (6-40)

CT brain and parathyroid scintigram were normal. Prolactin was marginally elevated and parathyroid hormone was elevated. As patient was asymptomatic and she did not wish to proceed with further investigations or invasive procedures, she is being followed up in the clinic every 6 months.

DISCUSSION

Insulinomas are the most common cause of hypoglycemia related to endogenous hyperinsulinism. Criteria for diagnosis of insulinoma include a serum insulin concentration of more than 6 mU/ml, a detectable concentration of serum C peptide, and a high proinsulin concentration, concomitant with symptoms of hypoglycemia and blood glucose concentration of less than 45 mg per deciliter during fasting² and insulin (mU/ml) to glucose (mg/dl) ratio > 0.3. This patient had fulfilled diagnostic criteria.

MEN I is defined as occurrence of tumors in two or more main MEN I related endocrine organs; parathyroid, pancreas, pituitary.⁴ When the lesion is multiple and occurring in younger

patients (< 30), MEN I should be suspected in patients with insulinoma and they most likely to harbor MEN I mutations.⁵ This patient is young and had two insulinomas, elevated parathyroid hormone level and marginally elevated prolactin level. Therefore this is a possible case of MEN I. Imaging studies did not reveal any parathyroid or pituitary tumors. Patient is asymptomatic despite elevated parathyroid and prolactin hormone levels. Therefore this patient can be considered to have occult MEN I at present.

Successful surgery requires adequate exposure accurate localization. A negative imaging study cannot rule out the presence of insulinoma. Sensitivity of detecting insulinoma with ultrasonography and CT scan have been reported as 9 to 63%^{6,7} 16 to 72%,⁶ respectively.

Intraoperative palpation and ultrasound are the gold standard for localizing an insulinoma with a reported success rate of 96-100%.³

The intraoperative ultrasound and contrast enhanced CT scan failed to detect the second lesion albeit due to its small size and close proximity to the other lesion. Some believe that the hands of the skilled surgeon can find the tumor better than any imaging techniques.⁷ The complimentary nature of the two is amply demonstrated in this patient. It also highlights the need to palpate the pancreas for other lesions despite negative imaging.

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