CASE REPORT

Management of Insulinoma – Our Institutional (MMC) Experience

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INTRODUCTION

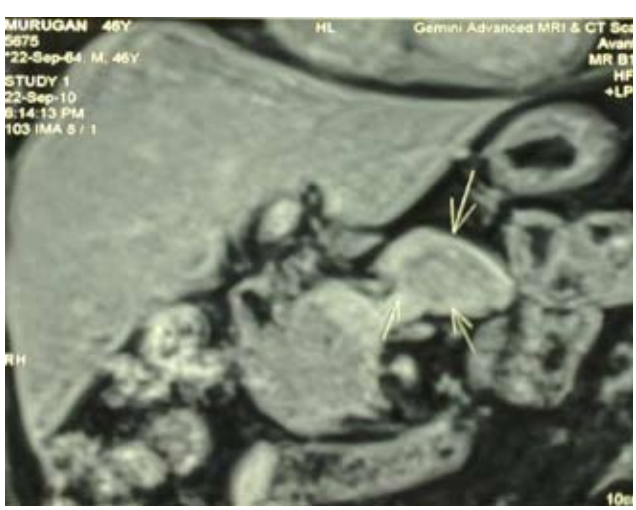
Hyperinsulinemia is a clinical syndrome with diverse etiology. Though Insulinoma is rare it is the most common functioning pancreatic islet cell tumour with annual incidence of 0.5-1 per million of the population. Insulinoma is four times more common in females[1]. They are usually sporadic but may occur as a part of MEN 1 (16%). They occur at any age but present most commonly in middle age. Median age of diagnosis is 47 years for sporadic cases and 23 years for cases associated with MEN I. Most Insulinomas are solitary (90%), small <1cm (65%), intra-pancreatic (99%) and or benign (90%). 16% are associated with MEN 1 and are often multiple, malignant in 25% of cases and have high recurrence rate[2].

Material and Methods

This is a retrospective study of cases of Insulinoma admitted from 2011-2013 in the Department of Endocrine Surgery, Madras Medical College. There were five cases, three males and two females, mean age was 33 (± s.d 16.2) range 17 to 55 years. Of which there was one case of MEN 1, female aged 28 years. The first case was operated in February 2011, the other four cases operated from March 2013 to July 2013.

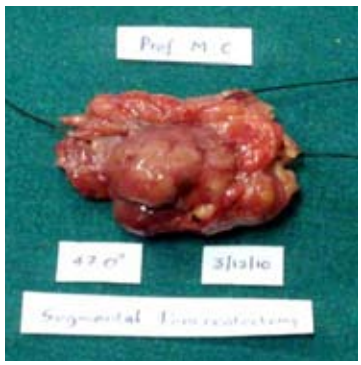
Case Report

Case No. 1 : 46 year old male presented to the hospital with history of fainting attacks on and off of one year duration, more aggravated on fasting. Patient's symptoms were relieved after taking food. He also gave history of panic attacks. Patient didn't have any symptoms suggestive of hyperparathyroidism like excessive thirst, constipation, nausea and dyspepsia or symptoms suggestive of pheochromocytoma like headache, palpitation and perspiration. Patient did not take any antidiabetic drugs. On examination patient's neurological function was normal and he didn't have any focal neurological deficit. On abdominal examination no mass lesion was present. On supervised 72 hours fast test patient developed hypoglycemic symptoms within six hours of fasting and his blood sugar was 42mg/dl. His fasting insulin was 28.6mIU/ml and C-peptide was 10.2ng/ml. Ultrasonogram abdomen showed mass in the body of the pancreas. MRI of the abdomen showed 6×3cm T2 hyperintense lesion in the body of the pancreas. Keeping Insulinoma as diagnosis, Segmental Pancreatectomy with Roux en Y Pancreaticojejunostomy was done. There was an increase in post-operative blood sugar to 156mg/ml. Histopathology report was benign neuroendocrine tumour. Patient is on 36 months of follow up without any symptoms.

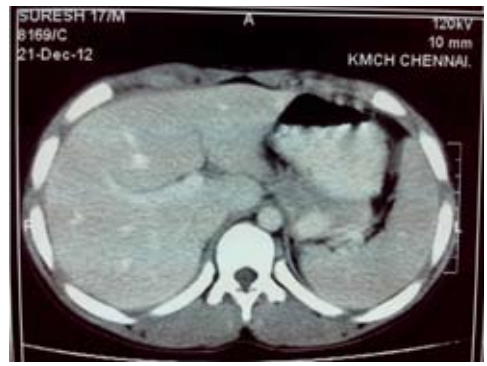


Case 1 : 46/M-MRI abdomen – 6×3cm Segmental pancreatectomy T2 hyperintense space occupying lesion body of Pancreas

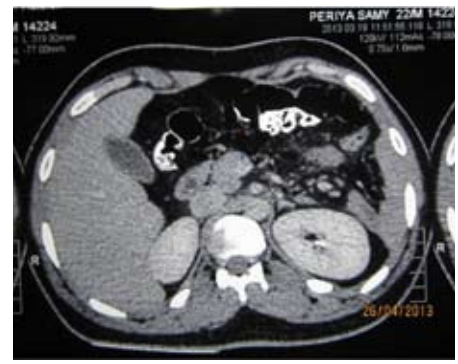
Case No.2 : 17 year old boy presented with history of fainting attacks of 6 months duration, more in the early hours of the day which was relieved when midnight meal was taken. There were no other symptoms suggestive of either hyperparathyroidism or pheochromocytoma. On clinical examination abdomen didn't reveal any mass. He developed hypoglycemic symptoms within four hours of fasting and his blood sugar was 48mg/dl. His fasting insulin was



Segmental pancreatectomy



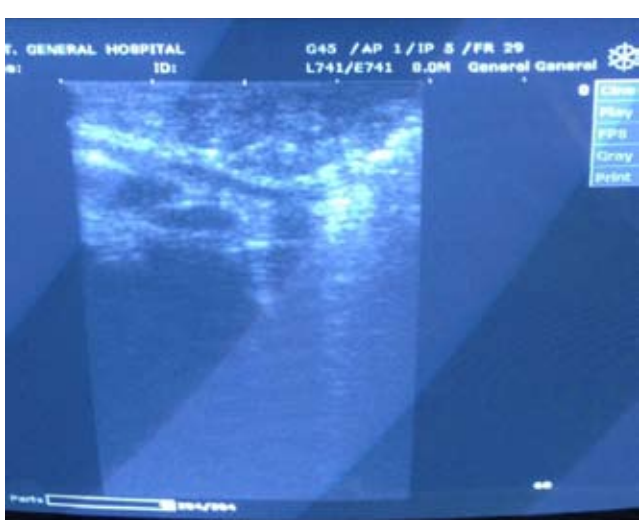
Case 2 : 17/M-CT abdomen–1.7×1.2cm Intraoperative Ultrasound lesion distal body pancreas.



Case 3 : 22/M-CT abdomen–small area of Enucleation with Roux en Y Pancreaticojejunostomy enhancement near cut edge of pancreas.

19.66mIU/ml and C-peptide was 6.36ng/ml. CT of the abdomen showed 1.7×1.2cm lesion in tail of pancreas. Intraoperative ultrasound confirmed the lesion in the distal pancreas. Distal Pancreatectomy with Splenectomy was done. His postoperative blood sugar shot up to 300mg/dl and he was treated with insulin for three days. His histopathological report was benign endocrine tumour pancreas. Patient is now euglycemic for the past 17 months and he is on follow up.

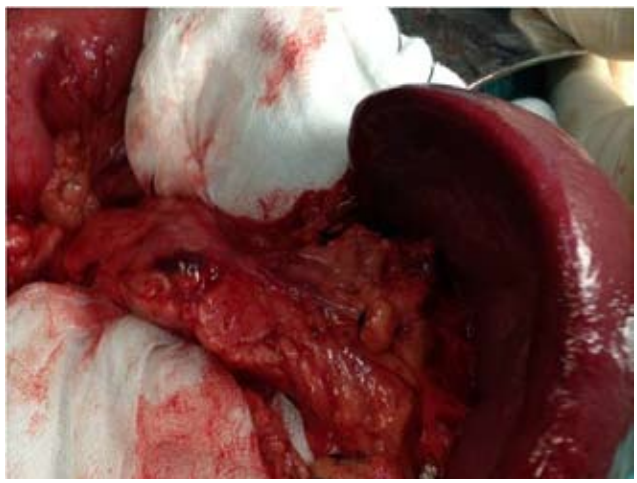
Case No. 3 : 22 year old male with symptoms of giddiness on and off and fainting episodes of 3 months duration suddenly developed inability to use all four limbs, aphasia and was admitted in a private hospital in semi conscious state. He was investigated and diagnosed to have hypoglycemic encephalopathy. His CT abdomen revealed Insulinoma in the distal pancreas for which Distal Pancreatectomy with Splenectomy was done. Because of persistent symptoms he was referred to our hospital and investigated. His fasting blood sugar, insulin and C-peptide level were 46mg/dl, 18.1mIU/ml, and 2.96ng/ml respectively. CT abdomen showed lesion near the cut edge of previously operated site. But intraoperative ultrasound showed 2×2cm lesion in the posterior part of uncinate process of pancreas. Enucleation of the tumour with Pancreaticojejunostomy was done. His postoperative blood sugar shot up to 357mg/dl for which he was treated with insulin for five days. His histopathological report confirmed benign endocrine tumour pancreas. Patient's neurological symptoms improved and he is euglycemic for the past 8 months.



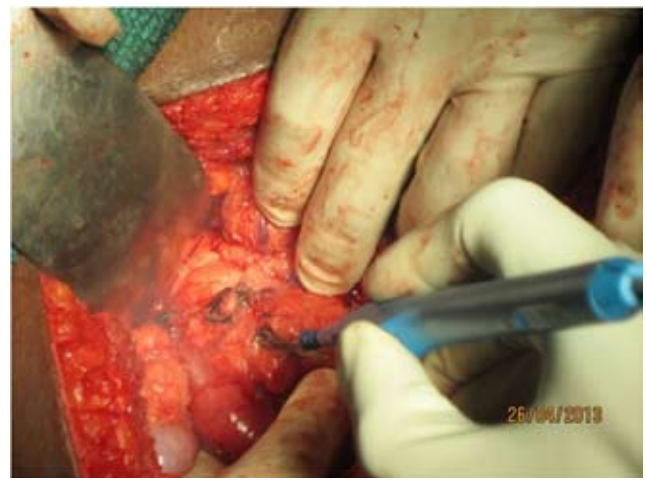
Intraoperative Ultrasound

Case No. 4 : 28 year old lady on thyroxine presented with history of early morning giddiness of 2 years duration which was relieved by taking sugar. She was earlier diagnosed as case of MEN 1 and had undergone Subtotal parathyroidectomy with transcervical thymectomy. Her blood sugar was 48mg/dl within four hours of fasting, insulin was 20mIu/ml and C-peptide was 4.28ng/ml. Serum Prolactin, IGF 1, PTH, and Serum calcium were normal. MRI brain showed Pituitary microadenoma. CT abdomen showed multiple lesions in pancreas, 0.9×0.9cm in head, 1.2×1.2cm in body, 0.8×1.8cm in the tail of pancreas. Intraoperative ultrasound confirmed the lesions and Subtotal Pancreatectomy with Roux en Y Pancreaticojejunostomy with Splenectomy was done. Post operative blood sugar was 247mg/dl and her histopathological report confirmed benign endocrine tumour pancreas. Since patient has become diabetic she is on insulin for past 5 months.

Case No. 5 : 55 year old female with history of fainting attacks of 6 months duration, relieved on taking meal was admitted to our hospital. Her blood sugar was 38mg/dl in four hours of fasting



Distal Pancreatectomy with Splenectomy



Enucleation with Roux en Y Pancreaticojejunostomy

and insulin and C-peptide levels were 58.1mIu/ml and 12.76ng/ml respectively. MRI abdomen showed 1.1x1cm T1 hypointense lesion at junction of head and uncinate process of the pancreas. Intraoperative ultrasonogram showed another lesion in the body of the pancreas. Enucleation of both the lesions were done. Postoperative blood sugar was 150mg/dl. Histopathological report came as benign endocrine tumour pancreas. Patient is on follow up for past 5 months.

Results

In this study we had five patients with endogenous hyperinsulinemic hypoglycemia. Three were male and two were female. Mean age of presentation is 33 (± s.d 16.2) range 17-55 years. One patient was diagnosed as a case of MEN 1. In hypoglycemic state all of them had palpitation, hunger and giddiness and one patient presented with hypoglycemic encephalopathy and seizures. Inspite of taking additional meal none of them had weight gain. Four of the five patients were diagnosed as cases of Insulinoma within one year of onset of symptoms.

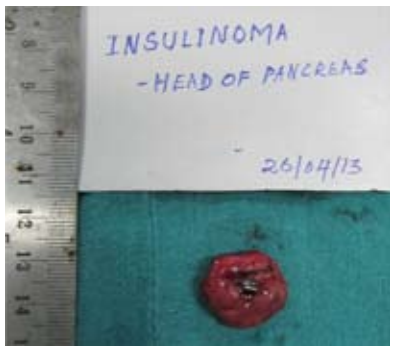
Biochemical Diagnosis : Correct diagnosis of Insulinoma is dependent on the clinical symptoms -Whipples triad. All patients had symptoms of hypoglycemia, food intake or glucose transfusion alleviated the symptoms and fasting serum glucose was less than 45mg/dl at the onset of symptoms. All patients had high fasting insulin and serum C peptide values.

Localisation : CT abdomen was performed in three patients and MRI abdomen was done for two patients. CT abdomen identified the lesion correctly in two out of three patients. In the patient with hypoglycemic encephalopathy the fibrous reaction around the cut edge was mistaken for Insulinoma but intraoperative ultrasonogram identified the exact lesion in the uncinate process of pancreas. In one of the patients for whom MRI was done, MRI revealed only one lesion while intraoperative ultrasound picked up a second lesion.

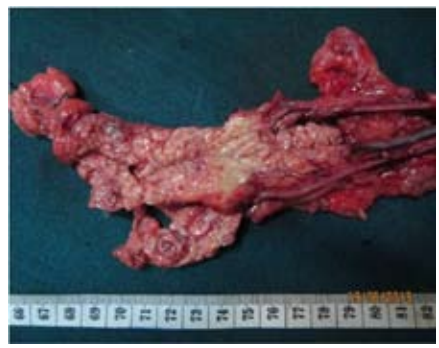
Operative Procedures : Enucleation, Segmental Pancreatectomy, Subtotal Pancreatectomy and Distal Pancreatectomy were the various procedures performed. Two cases had single lesion while rest had multiple lesions (two cases had two lesions, one case had three lesions). Mean size of tumour was 1.4cm (± s.d 0.75) range 0.5 to 2.5cm. The patient with MEN 1 in whom the Subtotal Pancreatectomy was done become diabetic and she is on Insulin. Mean follow up is 9.6 (± s.d 12) range 31 months to 2 months.

Discussion

Insulinoma is generally considered as a rare entity with an incidence of 0.5 to 1 per million people. Virtually all Insulinomas are intrapancreatic in location. The median age at presentation is 47 years and more common in female with female to male ratio of 1.4:11. In our study mean age presentation was 33 years (± s.d 16.2) range 17 to 55 years. Most are solitary and 10% are multiple. In our study two cases were solitary, two cases had two lesions and one case had three lesions in the pancreas. Patients with Insulinoma present with symptoms of hypoglycemia secondary to excessive and uncontrolled secretion of insulin. Symptoms are often nonspecific, episodic, varies among individuals and can differ from time to time in the same individual. Hypoglycemic symptoms can be divided into neuroglycopenic and neurogenic symptoms[3]. In our study in hypoglycemic state all patients had palpitation, hunger and giddiness and one patient had hypoglycemic encephalopathy and seizures.



Enucleation with Roux en Y Pancreaticojejunostomy



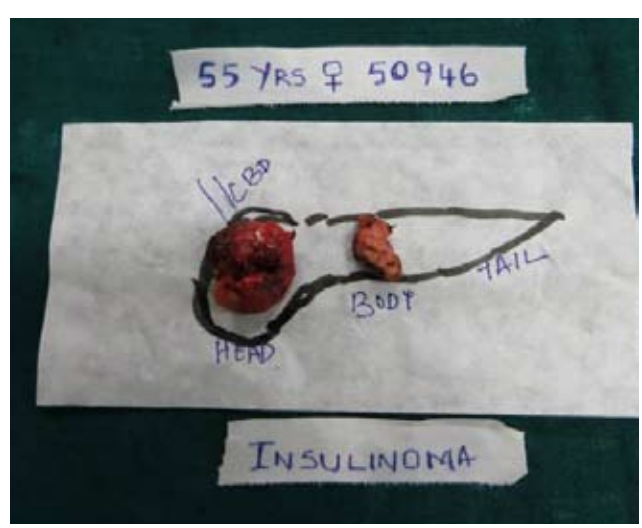
Subtotal pancreatectomy with splenectomy

Intraoperative Ultrasound

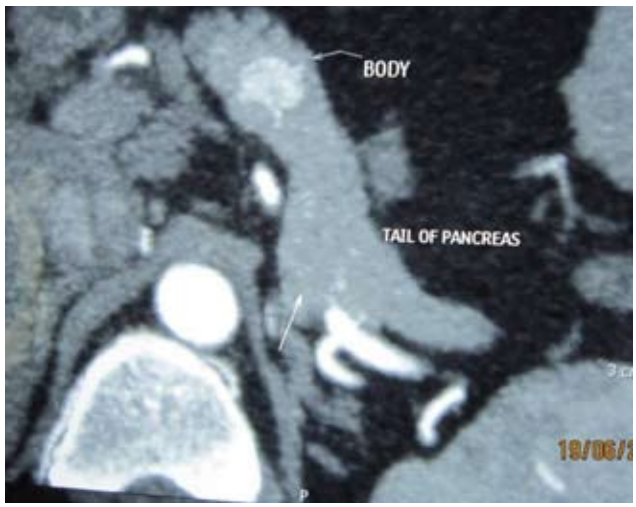
Correct diagnosis of Insulinoma is dependent on the clinical symptoms, Whipple triad. The presence of hypoglycemic symptoms with fulfillment of the following criteria is diagnostic for Insulinoma: According to the expert consensus, the diagnosis of hypoglycaemia related to endogenous hyperinsulinism can be made when serum insulin concentration is equal to or greater than 3mIU/L, serum C-peptide concentration is equal to or greater than 0.6 ng/ml (0.2 nmol/L), and serum pro insulin concentration is equal to or greater than 5 pmol/L at the time of hypoglycaemia, with venous plasma glucose concentrations less than 0.55 g/L. During a fast test, beta-hydroxy-butyrate levels of 2.7 mmol/L or less and an increase in plasma glucose of at least 0.25 g/L after intravenous glucagon indicate mediation of hypoglycaemia by insulin4. Whipples triad is the earliest evidence suggesting the existence of Insulinoma. In our study all patients had Whipple's triad and high fasting serum insulin and serum C peptide values.

In all our patients we performed localization technique before surgery. The sensitivity of trans abdominal ultrasonography ranges from 9-64%[5-7]. Endoscopic ultrasound has been used to improve the accuracy in recent years[8]. In our series trans abdominal ultrasonography was not much useful. The advent of helical CT scanning has improved detection compared to conventional CT. The sensitivity of abdominal CT in Gouya *et al* series is 94% and in our study CT abdomen confirmed the lesion in three out of the four patients on whom it was done[9]. Sensitivity of upto 95% is reported for intraoperative ultrasonography done with high resolution probe allowing the direct imaging of the pancreas without the interference of overlying gas or organs. In our study in all the patients except one (where investigation was not performed) intraoperative ultrasonogram identified the correct location of the lesion as well as detected new lesions.

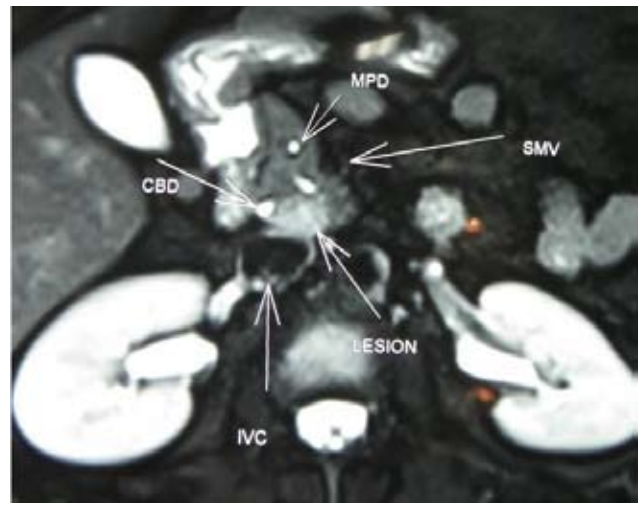
For benign Insulinoma simple Enucleation is the procedure of choice[10]. Overall cure rates of 75-95% are reported after surgery with prognosis dependent on the clinical presentation and whether complete resection was achieved. As far as surgical technique laparoscopic or open method may be used. Enucleation is indicated for small benign tumours 2-3mm away from the main pancreatic duct. Intraoperative or intraductal ultrasonography can be used to measure the distance between the tumour margin and the main pancreatic duct. Resection is indicated when the tumour abuts the pancreatic duct or major vessels or where malignancy is suspected[10]. Resection options include Pylorus Preserving Whipple procedure, Segmental Pancreatectomy or Distal Pancreatectomy depending on the site of Insulinoma. Spleen preserving Pancreatectomy is indicated for tumour in distal pancreas[11]. For tumour with complicated splenic anatomy, Distal Pancreatectomy with Splenectomy is advisable. In our study Enucleation of lesions was performed



Two lesions, 2 x 2cm head, <1cm hypointense lesion junction of head and body of pancreas



Case 4 : 28/F-CT Abdomen - 0.9×0.9 cm lesion head, Subtotal pancreatectomy with splenectomy 1.2×1.2cm body, and 0.8×0.8cm tail of pancreas



Case 5 : 55/F-MRI abdomen - 1.1×1cm T1 Intraoperative Ultrasound Two lesions, 2×2cm head, <1cm hypointense lesion junction of head and body of pancreas uncinate process.

in two cases, Segmental Pancreatectomy, Subtotal Pancreatectomy with Splenectomy and Distal Pancreatectomy with Splenectomy were each done in one case respectively. In 80% of patients with MEN 1 there are multiple tumours. In these patients 80-85% Subtotal Pancreatectomy to the level of portal vein with Enucleation for lesions in the head of the gland is recommended. In our study Subtotal Pancreatectomy was performed on the patient with MEN 1 who had multiple lesions. Blind pancreatic resection should not be performed for occult Insulinoma in the absence of preoperative and intraoperative detection of lesions in the pancreas.

Conclusion

Insulinoma has to be kept in mind with patients presenting with unexplained hypoglycemia and surgical treatment can give complete cure and immense symptom relief to these patients. The choice of surgery done depends on the nature of tumour, location, multiplicity and presence of syndromic association.

References

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