Case Report

Insulinoma — a deceptive endocrine tumour

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Abstract

Insulinoma is a deceptive endocrine tumour that can easily mislead even an astute clinician because of its bizarre and nonspecific symptom complex. A 45 year old woman presented with altered behaviour, seizures and spells of coma and was being treated as a case of hysterical neurosis. Biochemical and radiological investigations revealed fasting hypoglycaemia, endogenous hyperinsulinism, and a pancreatic parenchymal lesion. Removal of the pancreatic lesion resulted in abrupt restoration of euglycaemia and complete disappearance of patients' symptoms.

Keywords: Insulinoma, Neuroendocrine tumour, Hyperinsulinism, Hypoglycemia, Neuroglycopenia.

Introduction

Insulinoma is a quintessence of an elusive, but curable neuroendocrine tumour. It causes marked degree of hypoglycaemia, especially during fasting, exertion, excitement and other stressful conditions due to excessive and impulsive outpouring of insulin (endogenous hyperinsulinism).[1] Historically speaking, the first precise association between fasting hypoglycaemia, endogenous hyperinsulinism and pancreatic islets tumour was established by Wilder (1927).[1] Allen Oldfather Whipple proposed the classic clinical criteria for diagnosis of insulinoma (eponymously known as Whipple's triad) and Graham (1929) successfully removed insulinoma.[1,2] Its unpredictable symptoms like irrational behaviour, unexpected onset of epileptiform seizures and spells of coma are extremely frightening and distressing not only to the patients but also to the relatives and friends. Because of its deceptive, disguising and nonpathognomonic symptomatology, insulinoma can pose a diagnostic dilemma even to a shrewd clinician and

remain undiagnosed for years. More often than not, it is wrongly diagnosed and treated as a neuropsychiatric illness. This study reports a case of a similar patient of insulinoma who was misdiagnosed as "hysterical neurosis" and treated with antipsychotic drugs. The aim of reporting this case is to create clinical awareness among the healthcare professionals in order to avoid occurrence of a serious mistake in the diagnosis and treatment of insulinoma.

Case Report

A 45 year old non-diabetic woman was brought to the hospital in comatosed state. On arrival to the emergency department, her routine biochemical profile revealed profound hypoglycaemia (random blood sugar = 25 mg/dl). The patient was quickly revived by IV administration of 25% glucose followed by infusion of 10% dextrose-water. Actual history of the patient dated back to 5 years when she started to have dizziness, vertigo, blackouts, fatigability, poor work performance, sweating, tremors, palpitation and extremes of hunger. With the passage of time, she developed altered behaviour, epileptiform fits and episodic loss of consciousness. Her symptoms were characteristically precipitated by fasting, exertion and excitement and alleviated by intake of sugars, sweets, fruits and juices. After failure of spiritual, household and homeopathic remedies, she was mistakenly labeled as a case of hysterical neurosis and treated accordingly with antipsychotic drugs. The patient's condition worsened due to intolerable adverse effects of antipsychotic medications. Systemic inquiry revealed no co-morbid states. She denied history of alcoholism and prolonged drug intake or abuse. The patient's general, systemic and abdominal examinations were unremarkable. Keeping in view the fasting hypoglycaemia, an endocrinological workup was done which demonstrated a low fasting blood glucose (25 mg %), raised fasting serum

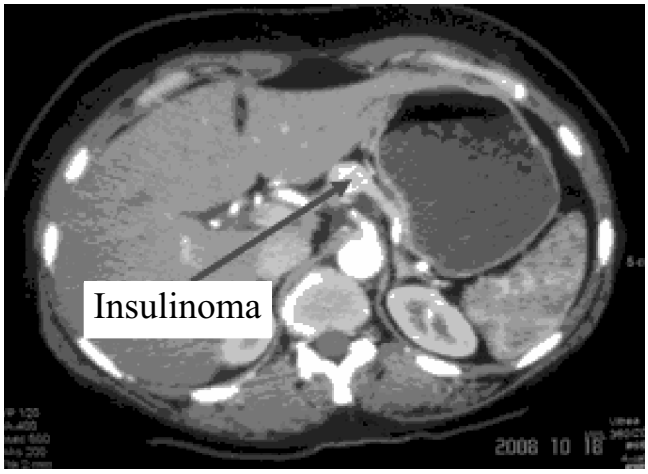

Figure-1: CT scan showing insulinoma.

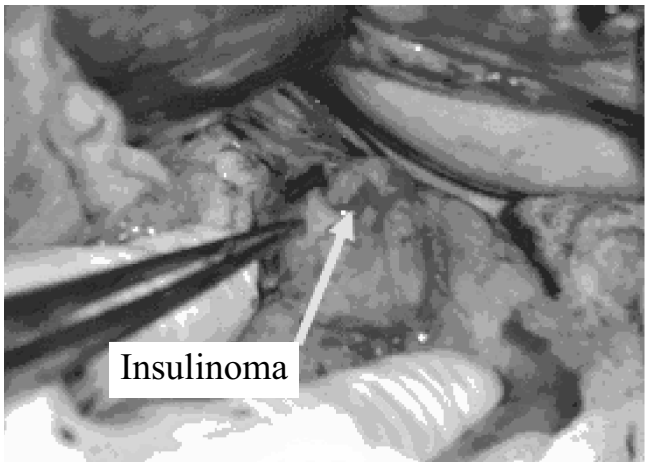

Figure-2: Insulinoma (intraoperative view)

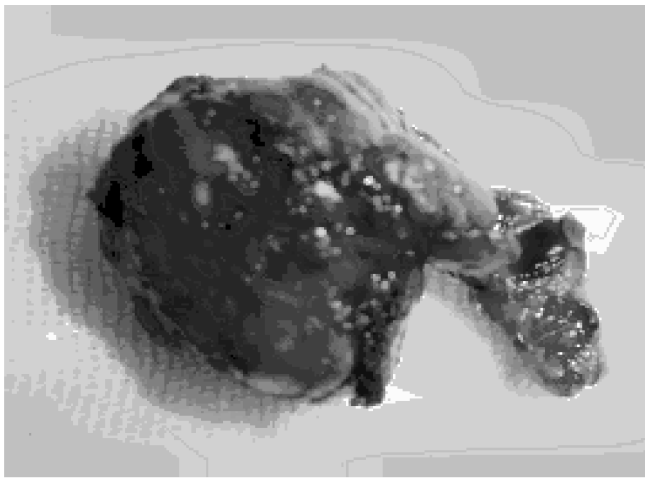

Figure-3: Resected specimen of insulinoma.

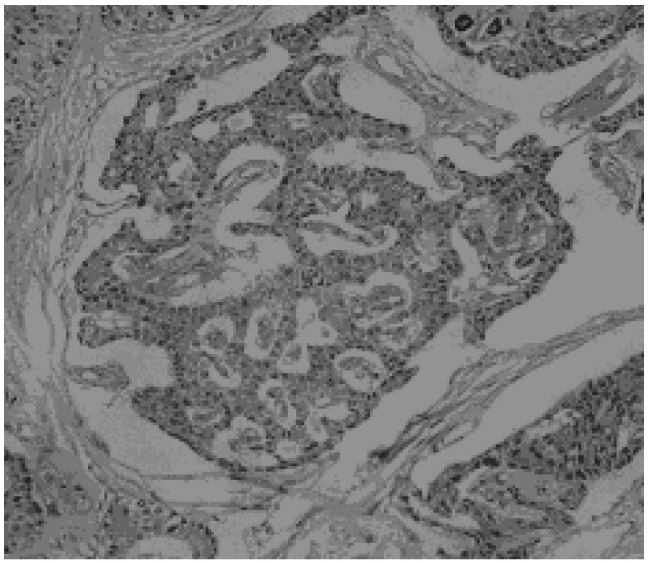

Figure-4: Histonathology of insulinoma.

insulin level; 24.80 mU/ ml (N = 3-20 mU/ml), and raised serum C-peptide level; 10.80 ng/ ml (N = 1.1-5.0 ng/ml). Thyroid function tests, serum calcium, cortisol and prolactin levels were within normal range. On the basis of biochemical results, a presumptive diagnosis of insulinoma was made. Transabdominal ultrasonography depicted an ill-defined hypoechoic pancreatic mass. Dynamic CT abdomen confirmed the existence of a partly exophytic, hypervascular, ovoid mass (1.8 x 2.04 cm) in proximal part of body of the pancreas, abutting the coeliac trunk and splenic vessels (Figure-1). The patient was explored through Mercedes-Benz incision and a tan-coloured, hard, oval mass (1.5 x 2.0 cm) was enucleated from proximal part of the body of the pancreas (Figure-2 and 3). Removal of the pancreatic lesion resulted in prompt restoration of euglycaemia with altogether vanishing of the symptoms. Her biochemistry at the time of discharge was; normal blood glucose (110 mg %), normal insulin level (4.70 mU/ ml) and normal C-peptide level (1.40 ng/ml). On first follow-up visit after a fortnight, patient's fasting blood glucose level was 98 mg/dl with no episode of hypoglycaemia and coma during that period. Histopathology of the resected specimen showed a well-encapsulated benign insulinoma (Figure-4).

Discussion

Insulinoma is a rare neuroendocrine tumour arising from beta cells of islets of Langerhans with an overall incidence of 4 cases per million per year. About 90% of insulinomas are solitary, benign, intrapancreatic and sporadic while 10% are multiple, malignant, extrapancreatic and familial. The familial insulinomas have a special predilection for occurrence in association with MEN-1 and von Hippel-Lindau disease.[1-3]

Under physiological circumstances, the pancreas secretes equimolar quantities of insulin and C-peptide from a common precursor (proinsulin). Contrarily, insulinoma predominantly secretes insulin (insulin-flooding) and causes hypoglycaemia, especially but not exclusively in the fasting state. Hyperinsulinaemic hypoglycaemia presents with two types of symptoms; 1) neuroglycopenic symptoms; dizziness, diplopia, blurring of vision, amnesia, obtundation, irrational behaviour, seizures and coma and 2) adrenergic symptoms due to sympathetico-adrenal stimulation; anxiety, tremors, sweating, palpitation and hunger. The symptoms are classically precipitated by fasting, exertion and excitement and ameliorated by intake of sugars, sweets, fruits, and juices.[4,5,8] Clinical diagnosis of insulinoma is suggested by the presence of Whipple's triad; 1) occurrence of neuroglycopenic symptoms in the fasting state, 2) documentation of low blood glucose level (< 45 mg %) during the attack, and 3) dramatic alleviation of the symptoms on glucose administration. The biochemical hallmark of diagnosis of insulinoma is the fasting hypoglycaemia in the face of inappropriately raised serum insulin and C-peptide levels and exclusion of surreptitious intake of exogenous insulin or oral hypoglycaemic agents.[5-7]

After confirmation of biochemical diagnosis, the exact preoperative anatomic localization of insulinoma with modern imaging modalities like ultrasonography (abdominal / endoscopic), CT-scan or MRI is absolutely mandatory before embarking upon a major pancreatic surgery.[2,3,5,8]

Surgery is the only curative treatment of this potentially lethal condition. The nature of surgery depends upon the size, location and resectability of insulinoma. Simple enucleation is the most favoured option for solitary insulinoma, especially if not abutting a main pancreatic duct or a major blood vessel while distal pancreatectomy with or without splenectomy is preferred for multiple insulinomas occurring in the body and tail of the pancreas. Pancreatoduodenectomy (Whipple's procedure) becomes indispensable for a non-enucleable insulinoma in the head and neck regions of the pancreas.[6,9,10] After removal of one insulinoma, a comprehensive digital exploration of the remaining pancreas by a skilled surgeon is imperative to exclude the presence of additional insulinoma(s). Peroperative failure to locate the insulinoma necessitates the usage of intraoperative ultrasonography which plays an instrumental role in unveiling the impalpable insulinoma with 100% success rate.[1,6,7,9] Although technically demanding, laparoscopic resection of insulinoma is undoubtedly being done in many advanced laparoscopic centres with minimal morbidity and mortality.[10] Combination chemotherapy with or without radiotherapy is being used for the patients who are unfit or unwilling for surgery and for those who have malignant, irresectable, residual, recurrent or metastatic insulinomas.

To conclude, because of its elusive and deceptive nature, insulinoma can pose a diagnostic challenge even to an experienced clinician. Accurate biochemical diagnosis and precise preoperative anatomic localization of insulinoma are highly desirable to avoid blind subtotal distal pancreatectomy.

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