

Sporadic Insulinoma In A 16-Yr-old Girl: A Rare Case Report and Review of Literature

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Abstract: Insulinoma is rare pancreatic islet cell neuroendocrine tumor typically sporadic, solitary and benign. We report the case of sporadic insulinoma in 16-year-old girl who presented with chief complaints of loss of consciousness episode daily since 7 month associated with palpitation, tremors, and diaphoresis. Clinical examination and laboratory investigation suggestive of pancreatic insulinoma, then patient admitted for further workup. A fasting test of 48-hour was done and ceased within 3 hours due to occurrence of hypoglycemic symptoms. During the episode, blood was drawn and results showed low blood glucose level and high insulin, pro-insulin and C-peptide levels.

The hypoglycemic symptoms were relieved by glucose administration and Whipple's triad for insulinoma was achieved. Triple phase computed tomography scan whole abdomen showed mass lesion with of approx. 13×12 mm noted in neck of pancreas. Fat planes with adjacent structures maintained. Patient underwent laparoscopic enucleation of pancreatic tumor. Histopathological and immuno-histochemical examination of the pancreatic mass has confirmed neuroendocrine tumor (insulinoma). A post-operative 6-month follow-up showed resolution of hypoglycemic symptoms, normalized blood glucose, insulin, pro-insulin and C-peptide levels, and no evidence of recurrence.

Keywords: insulinoma; whipples triad; pancreas

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I. Introduction

Insulinoma is very rare neoplasm with incidence of approximately four cases per million individuals per year[1]. Most insulinoma are sporadic in origin(90%) but it may be a part of multiple endocrine neoplasia type 1 (MEN-1) (10%). It is more common in women than men[2]. Sporadic insulinomas is usually present at the age of 45-50 years[1,2,3,4,5]. We report the rare case of sporadic insulinoma in a young 16-year-old girl who presented with chief complaints of loss of consciousness episode daily since 7 month associated with palpitation, tremors, and diaphoresis. It is diagnosed by clinical, biochemical, and imaging investigations. The curative treatment is surgical resection (enucleation).

Case Report

A 16-year-old girl presented to surgery OPD with chief complaints of loss of consciousness episode daily since 7 month associated with palpitation, tremors, and diaphoresis. These symptoms were episodic in nature, worsened by fasting and exercise, and relieved by food and juice intake. Past medical history and past surgical history was not significant. Laboratory investigations showed low blood glucose (64 mg/dL; reference range: 70-100 mg/dL), high blood insulin levels (6.42 µU/mL; reference range: 0-5 µU/mL) and C-Peptide level(2.74ng/ml). Rest all endocrine hormone like GH level (0.419), ACTH level (32.7), IGF-1, basaline cortisol level (13.03), dexamethasone suppression cortisol level (2.12) parathyroid hormone level (14.56pg/ml), prolactin level (7.07ng/ml), LH (3.17mIU/ml), FSH (4.50mIU/ml) T4 level (0.96ng/dl), TSH level (1.48uIU/ml) were normal. Clinical findings and laboratory investigations were suggestive of pancreatic insulinoma. Patient was admitted for further workup. A fasting test of 48-hour was done and ceased within 3 hours due to occurrence of hypoglycemic symptoms.

During the episode, blood was drawn and laboratory results showed low blood glucose level (40 mg/dL), and high blood insulin (22.9 µU/mL), pro-insulin (16.2 pmol/L; reference range: 2-6 pmol/L) and C-peptide (809 pmol/L; reference range: 0-200 pmol/L) levels. The hypoglycemic symptoms were relieved by glucose administration and Whipple's triad for insulinoma was achieved.

(Triple phase CT-mass lesion in neck of pancreas)

A triple phase contrast-enhanced computed tomography scan whole abdomen showed heterogeneously enhancing soft tissue density mass lesion with well defined margins of approx 13×12 mm noted in neck of pancreas. Fat planes with adjacent structures maintained. Patient was scheduled for Laparoscopic enucleation. Histopathological examination: the cells had centrally located oval-shaped nuclei, stippled (salt and pepper) chromatin and scant finely granular eosinophilic cytoplasm. There was no evidence of mitosis, vascular and perineural invasion. Surgical resection margins were tumor-free. Immunohistochemical examination: tumor cells stained positive for chromogranin A, synaptophysin, insulin and Ki-67 (6%). Tumor cells stained negative for somatostatin. Based on the clinical, laboratory, imaging, histopathological and immunohistochemical study, a final diagnosis of benign insulinoma neuroendocrine tumor. Post-operative radiotherapy or chemotherapy was not required due to the benign nature of insulinoma. Follow up after 6 month showed resolution of hypoglycemic symptoms, normalized blood glucose (108 mg/dL), insulin (1.8 μU/mL), pro-insulin (2.5 pmol/L) and C-peptide (175 pmol/L) levels, and no evidence of recurrence.

II. Discussion

Insulinoma are rare functional insulin-secreting neuroendocrine tumors derived from the beta cells of pancreas [7]. They secrete endogenous insulin autonomously and independently of the blood glucose levels, resulting in a state of hyperinsulinemia. Whipples triad and inappropriately elevated blood insulin levels (greater than 5-10 μU/mL)[8] during the 48-hour fasting test[9] is sufficient for diagnosis of insulinoma. Whipple's triad includes:

- 1) Biochemical evidence of hypoglycemia (blood glucose level less than 45 mg/dL)
- 2) Clinical evidence of hypoglycemic symptoms
- 3) Reversal of the hypoglycemic symptoms when carbohydrates are administered [10].

Neuroglycopenic symptoms include dizziness, confusion, apathy, amnesia, personality and behavioral changes, visual disturbances, seizure, and coma [11] are induced by hyperinsulinemia [8]. Biochemical investigations are proinsulin levels of more than 5 pmol/L, C-peptide levels of more than 200 pmol/L and negative anti-insulin antibodies [12]. Majority of insulinomas arises from pancreas (98%)[4,6]. Most of insulinomas (90%) are benign lesions. It involves the pancreatic head, body and tail equally [1]. Malignant insulinomas (10%) are rare entity which is usually more than 3cm in diameter.

The combination of endoscopic ultrasound and triple phase computed tomography scan has 100% sensitivity in image localization of tumor [14]. Magnetic resonance imaging is used for identification of hepatic metastasis [8]. Somatostatin receptor scintigraphy is not helpful in localizing insulinoma because most of insulinoma does not express somatostatin receptor [15]. Angiography combined with arterial stimulation venous sampling, using calcium as the insulin secretagogue, is probably the most sensitive available diagnostic technique (accuracy 94% to 100%). Intraoperative manual palpation of the pancreas and ultrasonography are both sensitive methods for the detection of the site of insulinomas. Insulinomas stain positively for insulin, pro-insulin, chromogranin A, synaptophysin, neuron specific enolase, cytokeratin [16]. Distant metastasis and local invasion is diagnostic criteria for malignant insulinoma [17]. Surgery is the mainstay of management in insulinoma. Successful cure rate of surgery is ranging from 77% to 100% [4, 15]

Indication of medical treatment is

- 1) Preoperative control of blood glucose levels
- 2) Non-surgical candidates
- 3) Patient with unresectable metastatic disease [18].

Diazoxide (50- 600 mg/day) is the most effective and commonly used medical drug. It acts by directly suppressing insulin production by pancreatic beta cells for controlling hypoglycemia (50-60% symptomatic control)[19].

Mostly insulinoma (90%) are benign, solitary and small (less than 2 cm in diameter). Surgical procedure of choice is enucleation [4, 15]. Indication of pancreatectomy (partial/complete)

- 1) All lesions doubtful for malignancy
- 2) Involving large segments of pancreas
- 3) Extensively invading adjacent structures
- 4) Obstructing main pancreatic duct or invading regional lymph nodes [4].

Insulinoma (benign) have favorable prognosis. Malignant metastatic insulinomas have poor prognosis [1, 20] despite miscellaneous therapeutic modalities like surgical excision, chemotherapy (streptozocin plus doxorubicin/5- fluorouracil), hepatic artery embolization, hepatic artery chemoembolization, peptide-receptor radionuclide therapy etc.

III. Conclusion

Sporadic insulinoma should be considered in the differential diagnosis of any young individual presenting with frequent hypoglycemic symptoms (neuroglycopenic and/or autonomic nervous system symptoms). Definitive diagnosis established on the basis of clinical, laboratory, imaging, histopathological and immunohistochemical studies. Management part includes surgical resection (open/laparoscopic) and medical treatment (tab diazoxide 50-600mg/day) for selective patients who are not fit for surgery.

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