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MALIGNANT INSULINOMA

Article

INTRODUCTION

Insulinomas are rare neuroendocrine tumours of the GIT with an incidence of 1-4/million1. They are the most common cause of hypoglycemia due to endogenous hyperinsulinemia. In 1927, Wilder established the association between hyperinsulinism and functional islet cell tumour2. Insulinomas have been misdiagnosed as psychiatric or seizure disorders. They secrete insulin in addition to a large no of other hormones like gastrin, ACTH and Glucagon etc. Most are benign i.e. >90%, so the malignant are even more rare. About 10 % are multiple; out of which 50% are associated with MEN 1. Most of the symptoms are due to hypoglycemia and include altered behavior/consciousness. The genetics include mutations on MEN 1 on chromosome 11 and K-ras3.

CASE REPORT

A 17 yr old boy developed sweating and loss of consciousness after hearing a bomb blast near his home. Worrisome parents took him to Rawalpindi General Hospital where he improved with treatment. Two days later he suffered from sweating and seizures and was brought to CMH Rawalpindi. He gave past history of dizzy spells and anxiety during stressful conditions. His birth and developmental history was normal. He is the youngest of three siblings who are all healthy. He was advised referral to MH, Rawalpindi for observation. Detailed examination was unremarkable. During his stay in ward he developed sweating and a generalized tonic clonic fit. Thereafter, urgent routine investigations, ECG, metabolic screen and CT scan brain were requested. Meanwhile another fit was observed to be associated with a low blood glucose random. Every time the patient dramatically improved with I/V dextrose. The Whipple's triad was justified here. Fasting levels of insulin and C-peptide were sent and he was supplemented with frequent I/V drips. His investigations showed a lowest random blood sugar of 19 mg/dl, raised serum fasting insulin and C-peptide levels, USG abdomen showed hepatosplenomegaly, multiple discrete hypoechoic foci in liver and mass pancreas, EUS with linear probe showed mass around pancreas and biopsy was undertaken. The histopathology report showed tubular structures, lined by polygonal cells and abundant eosinophilic cytoplasm suggestive of malignant insulinoma (Figure). His CT scan abdomen with contrast showed mass body and tail of pancreas, hepatic metastases and splenomegaly. Rest of his baseline, metabolic and endocrine screen were within normal limits

DISCUSSION

Malignant insulinomas are rare among rarities. The diagnosis depends on fasting hypoglycemia4. A blood glucose <40 mg/dl in an otherwise healthy person with CNS dysfunction such as confusion or abnormal behaviour merits further investigation to rule out insulinoma. Patients adapt to chronic hypoglycemia by increasing their efficiency in transporting glucose across BBB, which masks awareness that their blood glucose is approaching critically low levels. Counter regulatory hormonal responses as well as neurogenic symptoms such as tremor, sweating and palpitations are blunted during hypoglycemia. Clinically the patient manifests Whipples triad which include symptoms of hypoglycemia, documented low blood glucose levels and reversal of symptoms with I/V dextrose6. Symptoms often develop early morning, after missing a meal or occasionally after exercise. Initially it includes CNS symptoms such as blurred vision or diplopia, headache, feelings of detachment, slurred speech and weakness. Convulsions or coma may occur. The differential diagnosis include hyperinsulinemia from surreptious insulin or sulphonylureas, extra pancreatic tumours, post prandial hypoglycemia, early hypoglycemia, post gastrectomy, functional due to increased vagal tone as in late hypoglycemia (occult diabetes), delayed insulin release due to β cell dysfunction e.g. in counter regulatory deficiency or idiopathic, alcohol related hypoglycemia, immunopathological hypoglycemia and pentamidine induced hypoglycemia. An elevated insulin level in response to a prolonged fast clinches the diagnosis7. Thereafter, imaging studies like transabdominal ultrasound, endoscopic ultrasound, and multiphase CT scan should be undertaken to localize the tumour and aim for histopathology8. Medical therapy is reserved for inoperable and malignant insulinomas to reduce hypoglycemic attacks and tumour burden and includes Diazoxide and Somatostatin analogues9. Successful localization and Whipples procedure or subtotal pancreatectomy is curative in operable cases10. The complications include irreversible brain damage from severe prolonged hypoglycemia, obesity from frequent feedings and glucose drips. The prognosis remains poor. The median survival is approximately 38 months. Despite the disease reputation of being indolent, survival of patients with advanced disease remains only 2 years.

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