

## **A needs to assay Proinsulin in all suspected cases of Insulinoma: A case report**

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**Background:** Insulinomas are rare pancreatic islet cell tumors, with an incidence of 4 cases per 1 million person-years<sup>(1)</sup>. Most insulinomas are benign and small solitary tumors<sup>(2)</sup> whereas multiple insulinomas is usually associated with MEN1. Malignancy is rare with the liver and regional lymph nodes being the most common sites of metastasis<sup>(3)</sup>. Diagnosis of Insulinoma is based on the clinical, biochemical and radiological evaluation. Most patients present with characteristic symptoms such as hypoglycemia, weakness, blurred vision, diplopia, palpitations, and loss of consciousness or seizures<sup>(4)</sup>. Biochemically, the fasting plasma levels of insulin, C-peptide, and, to a lesser degree, proinsulin are elevated. Imaging techniques are then used to localize the tumor, most frequently transabdominal or endoscopic ultrasound<sup>(5)</sup>, CT<sup>(6)</sup>, MRI<sup>(7)</sup>, or somatostatin receptor scintigraphy<sup>(8)</sup>. Medical treatments of insulinomas include diazoxide<sup>(9)</sup> and octreotide<sup>(10)</sup>. Resection of insulinoma is curative in 93 to 100% of benign cases<sup>(11)</sup> but metastasis reduces survival rates by 60%<sup>(12)</sup>. Hepatic artery embolization, radioembolization, radiofrequency ablation, hepatic resection and finally liver transplantation can be tried in hepatic metastasis. Here we present a rare case of a proinsulin secreting neuroendocrine tumor with metastasis to the liver.

**Clinical Case:** A 65-year-old man with a history of ulcerative colitis, hypertension and glaucoma, presented with seizures in the setting of hypoglycemia. Workup included a CT abdomen which showed 10 hypervascular, centrally necrotic, liver masses, in both lobes of the liver, measuring up to 5.3cm, and varices at the gastric fundus. Proinsulin was 83.2 (normal<18), insulin elevated at 32.6 (normal <29), C- peptide 12 (normal <3.1), with normal cortisol and metanephrines. The patient underwent a liver biopsy, which showed moderately differentiated carcinoma (Grade G2) with polygonal cells growing in nests, suggestive of neuroendocrine origin. Immunohistostain for keratin 7, CD56, synaptophysin and chromogranin were positive. Chemotherapy treatment with everolimus was considered, however given the burden of disease it was considered to be a medical emergency and the patient underwent immediate anterior and posterior right hepatic artery embolization. The patient suffered from post embolization syndrome, which resolved and had subsequent resolution of the hypoglycemia. An octreotide scan is planned for his next visit

**Conclusion:** This unusual case of a proinsulinoma presenting in a patient with seizures underscores the need to assay proinsulin in patients with hypoglycemia and normal-mildly elevated immunoreactive insulin, and effectiveness of treatment with arterial embolization.

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