A HUNGRY TUMOR AS A RARE PRESENTATION OF CARCINOID SYNDROME

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Abstract:

Introduction: Carcinoid syndrome is a constellation of symptoms that results from biologically active peptides such as serotonin that bypass the first-pass metabolism in the liver and enter the systemic circulation. It is most commonly seen in well-differentiated neuroendocrine tumors (NETs) arising from the midgut region that metastasizes to the liver, which is normally responsible for inactivating these bioactive products. The incidence is rare with 0.5-2 new cases/10^6 population/year and with greater frequency in African-Americans.

Case Description: A 71-year-old African American male was admitted with symptoms of shortness of breath, fatigue, chronic diarrhea and findings of new-onset ascites and bilateral pleural effusions. Patient also had recurrent asymptomatic hypoglycemic episodes on admission that persisted despite the administration of dextrose. Computed tomography of abdomen & pelvis showed innumerable hyperdense and calcified liver lesions throughout the hepatic parenchyma. Carcinogen embryonic antigen along with alpha-fetoprotein levels were obtained to rule out pancreatic or liver primary malignancy and they were negative. Workup for insulinoma was not pursued due to absence of Whipple’s triad criteria. Troponins were elevated to 1.04 and brain natriuretic peptide was 404 raising suspicion for heart failure. An echocardiogram revealed severe tricuspid regurgitation leading to enlarged right atrium. The biopsy of the liver lesion revealed a well-differentiated metastatic neuroendocrine tumor, grade 1 type. Immunohistochemical stains showed positivity for synaptophysin, chromogranin, and CDX2. The positive CDX2, although not entirely specific, suggests GI/colorectal origin. His 24-hour urine 5-hydroxyindoleacetic acid (5-HIAA) was elevated at 269.5 mg/24 hour, which is highly indicative of a carcinoid tumor.

Discussion: Given the evidence of elevated 24-hour urine 5-HIAA in addition to clinical findings of right-sided heart failure with severe tricuspid regurgitation and chronic diarrhea, the diagnosis pointed to carcinoid syndrome. Tumor induced hypoglycemia (TIH) in islet cell tumors is related to insulin secreting pancreatic neuroendocrine tumors (pNETs) otherwise known as insulinomas. TIH has been also been observed in non-islet cell tumors due to release of insulin-like growth factor 2 (IGF2) or its high-molecular-weight precursor (big IGF2) which inhibits gluconeogenesis, glycogenolysis and peripheral uptake of glucose by skeletal muscle. Other causes include IGF1 tumor secretion, insulin autoantibody, secretion of GLP1 or massive tumor burden. The extensive liver tumor burden with rapid consumption of glucose is likely the explanation for his repetitive hypoglycemic episodes however, the role of IGF-2 cannot be excluded. Patient was started on octreotide injections which not only improved his symptoms of diarrhea but the frequency of hypoglycemia too. Octreotide is known for its inhibitory effect on IGF-1 and IGF-2. Its anti-neoplastic effect also helps decrease progression of tumor burden. The ideal management to minimize the occurrence of hypoglycemia is tumor resection or palliative debulking. It is important to realize that patients with carcinoid tumors can initially present with tumor induced hypoglycemia along with the classic
symptoms of diarrhea and carcinoid heart disease. A proper workup to explain hypoglycemia is imperative as it will guide the therapy and management.