Case Report

Hypoglycemia associated with non-islet cell neoplasia

Manash P Baruah¹, Sarojini Duttachoudhury², Nabajyoti Barman³,
¹ Consultant Endocrinologist, Excel center, Guwahati, India (formerly of Departments of Endocrinology, Gauhati Medical college, Guwahati, India)
² Departments of Endocrinology, Gauhati Medical college, Guwahati, India
³ Department of Internal Medicine, Gauhati Medical college, Guwahati, India

Email: manashbaruahinin@yahoo.co.in


Abstract

Hypoglycemia associated with non-islet cell neoplasia is a rare. Among the tumor producing non-insulin dependent hypoglycemia, adenocarcinoma of gastro-intestinal origin is rather uncommon. We report a case of metastatic adenocarcinoma presenting with hypoglycemia.

Key words: Hypoglycemia, NICTH, Tumor hypoglycemia

Introduction

Hypoglycemia in the backdrop of neoplastic disease can occur in three situations. (A) Excessive production of insulin by pancreatic insulinoma(s) or ectopic insulin-producing tumors. [B] Substrate depletion due to massive tumor infiltration of liver and adrenal glands. [C] Rather uncommonly production of substances interfering with glucose metabolism including insulin receptor antibodies (in Hodgkin’s disease and other hematological malignancies, various cytokines including tumor necrosis factor-α and interleukin-1 and 6, catecholamines (in pheochromocytomas), secretion of insulin-like growth factor (IGF)-I and solid mesenchymal tumors that secrete partially processed precursors of IGF-II (‘big’-IGF-II;).¹⁻⁷ Category [C] amongst the above is also known as non-islet cell tumor-induced hypoglycemia (NICTH).⁶

Certain varieties of non-islet cell tumors are associated with hypoglycemia. Tumors of mesenchymal origin are most commonly reported from the west.¹ Tumors of hepatic origin are more commonly implicated in the Asian countries. Production of IGF-2 like molecules by the tumor cells is implicated. Characteristically plasma insulin and C-peptide levels are suppressed.² We report a case of metastatic adenocarcinoma presenting with hypoglycemia.
Clinical Information
The patient (DT), 38 year male presented with recurrent episodes of altered behavior, increased appetite and distressful swelling of the abdomen. In the preceding months he was treated elsewhere with antitubercular drugs for abdominal tuberculosis (ascites and diffuse mesenchymal lymphadenopathy) without any sustained improvement. On his first visit to our institute he was found to have altered sensorium with low plasma glucose (45mg/dL). The episode of altered sensorium was preceded by typical symptoms suggestive hypoglycemia such as increased sweating, palpitation and tremulousness.

Biochemical Tests, Imaging and Cytology:
Venous plasma glucose during a subsequent episode of hypoglycemia was low at 33 mg/dL.

Corresponding Plasma insulin (systemic venous blood) level by 4th generation electrochemiluminescent assay was 1.00 micro U/L, which is regarded as low or suppressed in the background of such low plasma glucose. The calculated insulin:glucose ratio was 0.03. A ratio of >0.3 usually indicates insulin related hypoglycemia. Simultaneous plasma cortisol was high at 38.14 micro g/dL signifying adequate response of the H-P-A axis to the hypoglycemic stress. Hepatic, renal and thyroid profile were within normal limits.

Subsequent CECT abdomen (Fig.1) showed sheets of deposits, nodular enhancing lesions and ascites involving the peritoneal cavity and liver raising the possibility of a neoplastic lesion. Pancreas was normal. Primary site could not be identified.

Fine needle aspiration (ultrasound guided) cytology of peritoneal deposits (Fig.2) revealed acini formation and nuclear atypia indicative of metastatic adenocarcinoma cells.

Follow-up
The patient was subsequently referred to an advanced oncology center where he succumbed to the malignant process during the process of investigation. The primary site could not be determined till his death. No autopsy was performed.

Discussion
IGF-1 and IGF-2 are peptides sharing both sequence homology and some actions of insulin. Hypoglycemia may result from IGF-2 binding to insulin receptor. They have a role in tumor growth. In patients with rapidly growing tumors hypoglycemia may occur as a terminal event, due to inanition. However in great majority of cases hypoglycemia is explained by tumor production of IGF-2 or its isoforms(big IGFs). Large mesenchymal tumors, breast carcinoma, hemangiopericytomas, hepatomas, lymphomas are more commonly associated. Adenocarcinoma of gastrointestinal origin(pancreas, stomach and colon) have been encountered to a lesser extent.

Conclusion
Our case remains a rare presentation in endocrinology. Although we could not estimate the IGF-2 level in this patient, the circumstantial evidence i.e. suppressed plasma insulin level and evidence of malignancy strongly suggests hypoglycemia caused by IGF-2.
References
1. Marks V & Teale JD 1998 Tumours producing hypoglycaemia. *Endocrine-Related Cancer* **5**;111–129

**Legend1(Fig.1)**: Contrast enhanced computed tomography of abdomen shows ascites, sheets of malignant deposits and nodular enhancing lesions, One such large lesion is shown in liver (indicated by black arrow).

**Legend2(Fig.2)**: Microscopic picture of fine needle aspiration (ultrasound guided) cytology of peritoneal showing cells in acini formation(black arrow) typical of adenocarcinoma. There is marked nuclear atypia indicative of metastatic cells,(**magnification100X, H & E stain**)
Fig. 1: Contrast enhanced computed tomography of abdomen shows ascites, sheets of malignant deposits and nodular enhancing lesions, One such large lesion is shown in liver (indicated by black arrow).

Fig. 2: Microscopic picture of fine needle aspiration (ultrasound guided) cytology of peritoneal deposits showing cells in acini formation (black arrow) typical of adenocarcinoma. There is marked nuclear atypia indicative of metastatic cells, (*magnification 100X, H & E*)