

CLINICAL VIGNETTE

Technologic Assistance to Establish an Elusive Diagnosis

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Case

A 66-year-old female with well controlled ulcerative colitis and stage 1 triple negative breast cancer reports symptoms of possible low blood glucose (BG) for two years. The diagnosis of hypoglycemia was established during an office visit when she became confused and disoriented and was found to have BG of 39 which responded to oral glucose. Previous symptoms during included palpitations and generalized anxiety. She denied seizures or loss of consciousness. These symptoms were attributed to panic attacks, though fruit juice and candy helped alleviate them. Prior evaluation included normal serum insulin and C-peptide, co-syntropin, and thyroid function. Her previous endocrinologist suspected an insulinoma and a 72-hour fast was planned.

The patient established care with UCLA endocrinology, during the pandemic. Continuous glucose monitor (CGM) as well as 72-hour fast were initially deferred. She was offered a personal intermittently scanned Freestyle Libre CGM with a monitor. Due to lack of insurance coverage for CGM hypoglycemia technology, multiple clinic samples were obtained. Almost 48% were in hypoglycemic range (normal <1%).

Patient returned to the office for fasting testing. DEXCOM G7 rtCGM was placed the day prior and was connected to an office phone, for real time monitoring with hypoglycemia alerts. She had significant low BG levels overnight as well during the early morning. Most BG were in the 60s to 70s range on DEXCOM from 8 AM to noon, but started dropping significantly in the afternoon, which was confirmed with fingerstick BG testing as well as patient symptoms. Venous blood was drawn twice at a laboratory in the same building and corresponded to low BG on fingerstick check. Insulinoma was diagnosed with a serum BG of 46 mg/dl (<55 mg/dl), beta-Hydroxybutyrate of 2.3 mmol/dl (should be >2.7 mmol/L), insulin of 3 microU/ml. Non-suppressed insulin ≥ 3 microU/ml suggests insulin-mediated cause of hypoglycemia; c peptide was not suppressed at 1.3 ng/ml (<0.6 ng/ml), and sulfonylurea screen was negative.

A DOTATATE scan did not localize any pancreatic lesion. After tumor board discussion, endoscopic ultrasound was performed by gastroenterology. EUS revealed a 12 x 8 mm round, hypoechoic, well-demarcated lesion in the uncinate pancreas, suggestive of a neuroendocrine tumor. She subsequently underwent surgical resection. Pathology confirmed low grade, well-

differentiated neuroendocrine tumor, consistent with insulinoma.

Discussion

Insulinoma typically presents clinically with fasting hypoglycemia and recurrent episodes of neuroglycopenic symptoms that may or may not be preceded by sympathoadrenal (autonomic) symptoms. Whipple's triad supports the presence of pathologic rather than physiologic hypoglycemia. Whipple's triad is as follows:

1. Symptoms of hypoglycemia
2. Concomitant low serum BG level, measured by laboratory assay
3. Resolution of symptoms when BG is raised

When clinical suspicion for an insulin or insulin like growth factor (IGF) mediated hypoglycemic disorder is based on home BG monitoring a supervised fasting test is scheduled to document Whipple's triad and possibly determine the etiology of hypoglycemia.¹ Laboratory tests during a documented hypoglycemic episode can determine etiology. The setting supervised fast depends on patient characteristics and institutional resources. Our patient reported consistent symptoms after a short fasting period of 8-12 hours. Observation in the outpatient clinic after an overnight fast was likely to result in symptomatic hypoglycemia and avoid the challenges of an inpatient fast. CGM was used to time fingerstick BG checks, to minimize patient discomfort.

CGM technology has rapidly evolved and become more accurate for assessing BG levels. It measures interstitial glucose and is broadly classified into isCGM (for frequent use) and rtCGM (for continuous use). This diabetes technology is typically used for patients with insulin dependent diabetes. Use has recently expanded to include automated insulin delivery (AID) systems like connected insulin pumps and pens, which modulate insulin delivery based on CGM-informed algorithms.² Less is known about the use of these devices for diagnosis and management of hypoglycemia, partly due to lack of insurance coverage in patients without diabetes. Several case reports dating as far back as 2008 used CGM to detect hypoglycemia in the setting of insulinoma.³⁻⁷ Presence of trend arrows and associated alarms makes CGM devices more advantageous than fingerstick BG levels.⁸ These arrows are

based on interstitial glucose variation over the previous 15 minutes and estimate rate of glucose rise or decline over the next 30-60 minutes.⁹

This case demonstrates that CGM technology can be utilized during an outpatient supervised fast, for timed fingerstick BG as well as other laboratory tests necessary for diagnosis of this rare condition.

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