It Must be an Insulinoma! Case of Possible Non-Islet Cell Tumor Hypoglycemia

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Background

Hypoglycemia (glucose <70mg/dL) is uncommon in patients not being treated for diabetes melitus. Patients who satisfy Whipple's triad merit further evaluation and treatment. Triad includes documentation of hypoglycemia, presence of symptoms consistent with hypoglycemia, and relief of symptoms when plasma glucose is corrected.

Case Presentation

80-year-old male with a past medical history significant for remote Roux-en-Y gastric bypass surgery, hypertension, and hypothyroidism who was admitted after ground level fall resulting in subdural hematoma. No history of diabetes.

Patient endorsed intermittent dizziness episodes, generalized malaise, and 12 pounds of weight loss over 6 months. Patient persistently hypoglycemic en-route to the hospital per EMS.

Laboratory data on presentation significant for:
-Plasma glucose 62 mg/dL (nl 70-99)
-Lactate 13.6 mmol/L (nl <2)
-Uric acid 10.8 mg/dL (nl 3.7-8.0)
-Hemoglobin A1c 3.7% (nl <5.7%)

CT Multiphase pancreas and pelvis (see Figure 1): **Three arterially enhancing lesions within the pancreas**, cirrhotic liver morphology and marked thickening of the peritoneum, omentum, and numerous enlarged nodules.

Workup

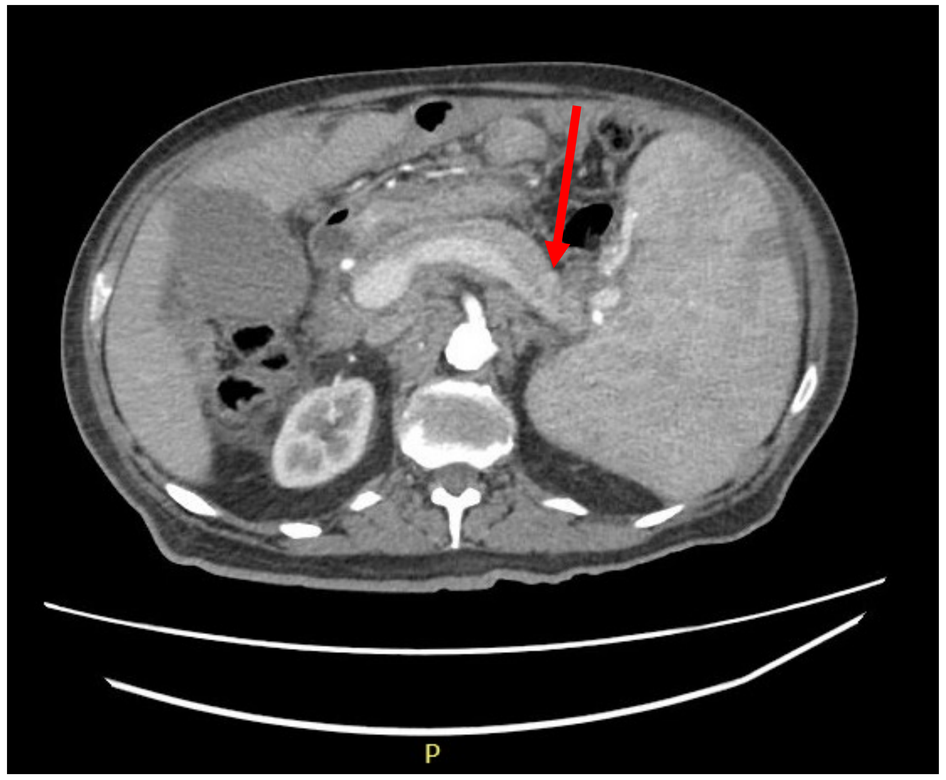
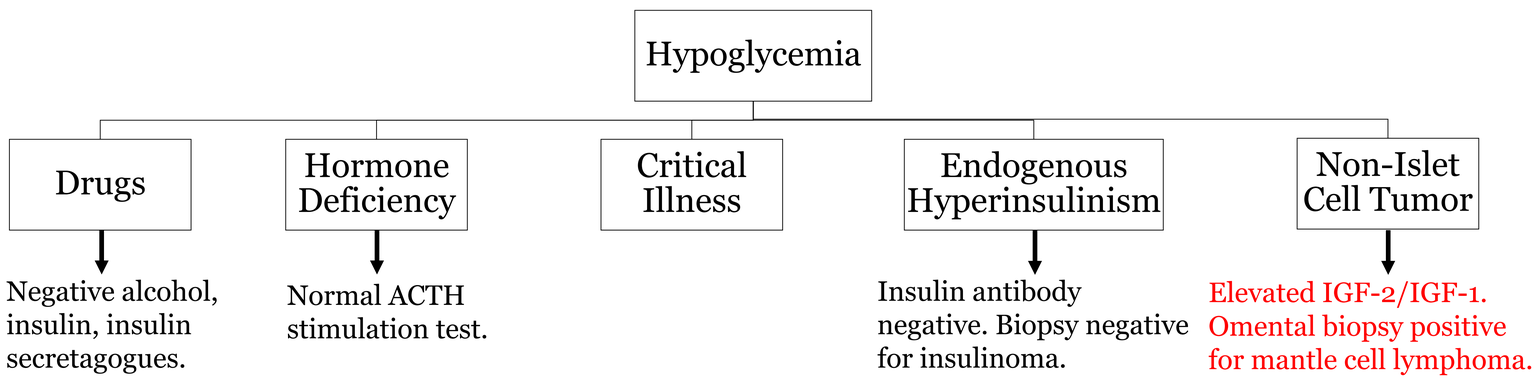


Figure 1 (above): CT multiphase with red arrow indicating arterially enhancing lesion within the tail of the pancreas

Serum evaluation:
- Plasma glucose 30mg/d
- Proinsulin 50.2 pmol/L (nl <8.0)
- Insulin 4 uIU/mL (nl 3-25)
- C-peptide 2.6 ng/mL (nl 3-25)
- GH 0.59 ng/mL (nl 0.05-3.00)
- Insulin antibodies <0.4 U/mL
- B-Hydroxybutyric acid 2.4 mg/dL (nl 0.0-3.0)
- Sulfonylurea hypoglycemia panel negative
- **IGF-1 44 ng/mL** (nl 18-184)
- **IGF-2 294 ng/mL** (nl 267-616)

Omental biopsy:
- Immunophenotype: positive for CD5, CD20, cyclinD1, SOX11
- Clonal B-cell population detected
- **Mantle cell lymphoma**

Differential Diagnosis



Discussion

- Non-islet cell tumor hypoglycemia (NICTH) is an exceedingly rare paraneoplastic syndrome caused by tumor secretion of IGF-2.
- Inappropriately low insulin levels in combination with low IGF-1 provide strong evidence in diagnosing NICTH.
- IGF-2 levels are not always elevated. IGF2/IGF1 ratios can help guide clinical reasoning towards non-islet cell tumor hypoglycemia. Ratio >10 is highly suggestive, especially if IGF-1 levels are <100ng/mL. NICTH may have contributed to this patient's hypoglycemia
- Lactic acidosis with associated hypoglycemia can be explained by the Warburg effect where glucose is rapidly consumed by tumors and fermented to lactate rather being oxidized.
- Unclear significance of elevated proinsulin levels in this case, current literature does not allude connection between lymphoma and elevated proinsulin levels.

Learning Points

- Non-islet cell tumor hypoglycemia is a rare cause of non-diabetes related hypoglycemia
- IGF2/IGF1 ratios can help guide clinical reasoning towards NICTH
- The Warburg effect can account for profound lactic acidosis and hypoglycemia in the setting of solid tumors

References

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