

A Novel Cause of Hypoglycaemia Secondary to Non-Islet Cell Tumour

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Introduction

Hypoglycemia is uncommon in adults who are not being treated for diabetes and may be due to varied aetiologies.

The mechanism in non-diabetic hypoglycemia may result from excessive insulin or insulin-like activity (IGF-2), reduced gluconeogenesis, disruption of hepatic glucagon metabolism, or increased glucose utilisation.

From an endocrinology perspective, causes of interest include endogenous hyperinsulinism (insulinoma, non-insulinoma pancreatogenous hypoglycaemia and autoimmune hypoglycaemia) and non-islet cell tumours¹.

This case demonstrates a novel cause of hypoglycaemia secondary to ectopic insulin secretion in association with a mixed disseminated high grade neuroendocrine carcinoma of the prostate.

Case Report

Seventy three year old male presenting with new onset of recurrent episodic symptoms consistent with hypoglycaemia (slurring of speech, sweating, agitation and confusion) and pre-hospital capillary glucose less than 1 mmol/L with resolution of symptoms after treatment with oral glucose.

The past medical history was unremarkable and no precipitating factors were found.

The finding on clinical examination was hepatomegaly with irregular edge.

Recurrent hypoglycaemia was initially avoided by high oral glucose intake with intensive blood glucose monitoring, however this was insufficient to prevent nocturnal hypoglycaemic episodes.

Investigation

- The suspicious examination finding was investigated with CT scan of thorax, abdomen and pelvis in which disseminated malignancy involving the liver, lungs and spine with no primary tumour identified .
- A significantly elevated PSA pointed towards prostate cancer as the likely primary and the elevated CA-19-9 was attributed to the hepatic metastasis (Table 1) . An elevated chromogranin A suggested a neuroendocrine element which complicated the interpretation.
- PET scan confirmed multiple bone metastasis involving the femurs and humerus. Liver biopsy was obtained in attempt to identify the primary tumour and define management plans.
- Capillary blood glucose of 1.9 mmol/L was obtained following three hours of monitored fasting with concurrent serum sample showed in table 2.



Image 1: CT Abdomen and PET scan

Initial Management

- Prednisolone was started to mitigate overnight hypoglycemia which initially controlled blood glucose levels.
- As rapid recurrent hypoglycemia ensued, continuous IV infusion of 10% dextrose was initiated with the following treatments:
 - Diazoxide (orally)²
 - Octreotide (subcutaneously)³
 - Degarelix (GnRH antagonist) was commenced for presumed advanced prostate adenocarcinoma
- In respect of patient's wishes, active treatment was withdrawn with comfort being made the priority.

Tumour Marker	Result	Reference
PSA	82.7 ug/L	0.1-6.5
CA-19-9	308 KU/L	0-35
CEA	2.5 ug/L	0-2.5
AFP	3KU/L	0-20
Chromogranin A	16.5 nmol/L	0-6

Table 1: Tumour markers

Test	Result	Reference
Serum Glucose	<0.1mmol/L	
Insulin	224.3 pmol/L	17.8-173
C-Peptide	1953 pmol/L	298-2350
IGF-1	25 ug/L	47-207
IgG Insulin autoantibodies	3.1 mg/L	0-5

Table 2: Serum levels with capillary glucose 1.9 mmol/L

Outcome

- The liver biopsy showed high grade neuroendocrine carcinoma without an obvious primary origin with negative immunohistochemistry testing for prostate specific antigen and insulin.
- Post-mortem examination revealed a large infiltrated prostate containing both adenocarcinoma (poor and well differentiated) and high grade neuroendocrine (small and non-small cell) carcinoma with extensive metastasis of the neuroendocrine carcinoma and normal pancreas and gastrointestinal tract.
- This to our knowledge is the first report of ectopic insulin secretion in association with a mixed disseminated high grade neuroendocrine carcinoma of the prostate.

References

1.Cryer, PE, Axelrod L, Grossman AB, Heller SR, Montori VM, Seaquist ER, Service FJ. Evaluation and Management of Adult Hypoglycemic Disorders: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2009; 94:709-728
 2.Goode PN, Farndon JR, Anderson J, Johnston ID, Morte JA. Diazoxide in the management of patients with insulinoma. World J Surg 1986; 10:586-592.
 3.Vezzosi D, Bennet A. Octreotide in insulinoma patients: efficacy on hypoglycemia, relationships with Octreoscan scintigraphy and immunostaining with anti-ss2A and anti-ss25 antibodies. Eur J Endocrinol. 2005;152:757-767