An unusual case of hypoglycemia mediated by paraneoplastic production of insulin like growth factor-2 (IGF-2) by gastrointestinal stromal tumour

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Background

- Non islet cell tumour hypoglycaemia (NICTH) is a very rare paraneoplastic phenomenon associated with tumours of mesenchymal origin
- There is an estimated incidence of approximately one per million person-years [1]

We present a rare case of hypoglycaemia secondary to paraneoplastic non-islet cell secreting tumour

Case history

A 79 year-old female, with a background history of hypertension and ischaemic heart disease was brought by ambulance to hospital following collapse, associated with low capillary blood glucose (CBG) - 2.1mmol/L. Her regular medications include ramipril, clopidogrel and atorvastatin. She did not have a history of diabetes. While an inpatient, the majority of low capillary blood glucose (CBG) readings were late at night or in the early mornings. She had normal hypothalamic pituitary adrenal (HPA) axis, with cortisol of 747nmol/L (N<430)

Investigations at time of hypoglycaemia

- Venous glucose 1.9mmol/l
- C peptide <94pmol/l
- Serum insulin <10pmol/l

Fig. 1 Investigations at time of hypoglycaemia

There was filling defect within the inferior vena cava extending into the left common iliac vein in keeping with venous thrombosis.

Further investigations are shown below

IGF-2 79.5nmol/l
IGFBP3 2.2mg/l (2.0-5.5)
IGF-2:IGF-1 ratio 22.1 (significantly high)

This confirms a diagnosis of insulin like growth factor 2 (IGF-2) driven non islet cell hypoglycaemia.

Radiology

CT abdomen and pelvis with contrast showed an 18cm lobulated inhomogeneous pelvic mass with liver masses.

Fig. 3: CT slice showing pelvic mass

Subsequent tissue biopsy confirmed a diagnosis of gastro-intestinal stromal tumour (GIST)

Fig. 5 - Histology slide

Discussion/Conclusions

- NICTH should be considered when non-ketotic hypoglycaemia occurs in the setting of low serum insulin levels. (2)
- The number of reported cases of GIST remains low, however, it is suggested that the occurrence of hypoglycaemia prior to tumour diagnosis tends to be less common. (4-5)
- Glucocorticoids remain the first line treatment to avoid NICTH. Their use is advocated even when tumours are inoperable(2).
- However one study has shown proven effectiveness of Imatinib, even when patients have metastatic or unresectable GISTs and as such it is suggested as a first line treatment. (6)
- Due to the rarity of this condition, evidence is limited to only a few cases. Further case reports and studies are required.