Distracting spontaneous refractory hypoglycaemia

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BACKGROUND
Spontaneous hypoglycaemia in non-diabetic individuals warrants investigation. Among the usual suspects, proinsulinoma is a more well described entity compared to the less commonly reported counterpart, proinsulin secreting neuroendocrine tumour. A series reported proinsulinoma has a 2:1 female preponderance with mean age of diagnosis at 56 years old (1). The lesion usually lies, unsurprisingly, at the body and tail of the pancreas, which signposts to the diagnosis (1–3). However, other concomitant malignancy or extra-pancreatic location may cloud the diagnosis. We herein report a case of such diagnostic conundrum.

CASE HISTORY
A 79 years old frail lady with history of dementia and hypertension presented with refractory hypoglycaemia over a period of 3 months requiring multiple admissions. During her most recent admission, intermittent ocreotide and glucocorticoid were tried but she still required continuous dextrose infusion to maintain euglycaemia.

The severe spontaneous hypoglycaemia in this non-diabetic lady, warranted a series of investigations.
- TFT excluded thyroid dysfunction
- Short synacthen test excluded hypoadrenalism
- The anterior pituitary profile including prolactin, LH, and FSH were all normal.
- Two separate samples of IGF-I was 8nmol/L and 6.2nmol/L (10-25nmol/L).
- CT scan with contrast of the abdomen and pelvis revealed a heterogeneously enhancing mass (6.6cm) arising from the lower pole of the left kidney consistent with renal cell carcinoma. Concomitantly there were extensive peripherally enhancing heterogeneous mass lesions in the liver, the largest measuring at 12cm. The pancreas was normal.
- During the event of hypoglycaemia (blood glucose 1.6mmol/L), the blood tests revealed:
  - IGF-II/IGF-I ratio less than 10, which was inconsistent with non-islet cell tumour induced hypoglycaemia (NICTH).
  - Inappropriate elevation of C-peptide 4210pmol/L (174-960pmol/L)
  - Inappropriate elevation of Proinsulin >200 (0-7pmol/L)
  - Suppressed Insulin at 12 pmol/L(0-180)

In view of multiple comorbidities, a palliative approach was taken. The post-mortem confirmed a clear cell renal carcinoma of the left kidney. Unexpectedly, the morphology and immunoprofile of the liver metastases were consistent with proinsulin secreting neuroendocrine tumour.
The immunostaining showed focal strong insulin immunoreactivity, as well as widespread CD56, synaptophysin, and chromogranin A, with negative staining for RCC.

CONCLUSION AND LEARNING POINTS
Proinsulinoma is a rare condition and can be masked by concomitant metastatic malignancy. Multiple hepatic metastases is a well-known cause of spontaneous hypoglycaemia. However, in severe intractable hypoglycaemia, coexistence of insulin secreting tumour needs to be considered to avoid missing them.

REFERENCE