Localisation of occult extra-pancreatic insulinoma using Glucagon-Like Peptide-1
receptor molecular imaging.

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Figure 1 - Localisation of an occult insulinoma using GLP1 molecular imaging.tiff

We report a case of an occult insulinoma and the use of glucagon-like peptide-1 (GLP1) receptor molecular imaging for tumour localisation.

A 64-year old woman with type-2 diabetes mellitus presented to emergency with frequent symptomatic hypoglycaemia. Her local doctor had previously advised cessation of metformin monotherapy and home blood glucose level (BGL) monitoring in the context of hypoglycaemia and improved glycaemic control (HbA1c 5.4%) despite 20kg weight gain. However she recommenced monitoring due to transient impaired conscious state and noted hypoglycaemia (1.7mmol/L) prompting this admission.

On examination the patient was obese (132kg) with central adiposity (BMI 52kg/m²), Glasgow Coma Score 15 and BGL 9.4mmol/L. She became diaphoretic and anxious 5 hours after presentation. Investigations confirmed hypoglycaemia (2.0mmol/L) concurrent with inappropriately elevated insulin (46mIU/L), pro-insulin (99.9pmol/L, reference range (RR) <13.3) and c-peptide (2.54nmol/L, RR 0.30-2.30) with a suppressed β -hydroxybutyrate (0.3mmol/L, RR <0.5), negative insulin antibodies and a negative sulfonylurea screen consistent with insulinoma. HbA1c was 4.4%, other biochemistry were normal.

Contrast-enhanced abdominal computerised tomography (CT) demonstrated a normal pancreas with a 1cm splenic hilum nodule consistent with a splenunculus. The patient's abdominal girth precluded further investigation

with magnetic resonance imaging. ⁶⁸Ga-exendin-4 positron emission tomography (PET)/CT clearly identified a solitary insulinoma at the site of the reported splenunculus (Figure 1). The patient underwent laparoscopic resection and histology revealed a 15x10x10mm neuroendocrine tumour abutting the pancreatic margin. Immunohistochemistry stained positive for synaptophysin, chromogranin, insulin and Ki-67 proliferation index was <1%. Postoperative hyperglycaemia (15mmol/L) was managed with Metformin 2g plus Gliclazide MR 60mg daily.

Hypoglycaemia due to insulinoma in patients with diabetes is rare¹. The majority of insulinomas are solitary and intra-pancreatic; <1% are ectopic and <10% are malignant or multifocal². Surgical resection is required for cure and preoperative localisation is preferable but limited by small tumour size. Reported accuracy varies widely but a contemporary study³ demonstrates sensitivity of abdominal CT (64%) and MRI (75%). Endoscopic ultrasound (65%) and intra-arterial calcium stimulation testing (IACST, 63%) are highly operator dependent and the latter particularly invasive. Extra-pancreatic location and typical enhancement pattern of the apparent 'splenunculus' in this case confounds localisation by conventional imaging and IACST likely would have been misleading. Notably a similar insulinoma masquerading as a splenunculus was identified post-mortem in a patient who died despite multiple localisation attempts by conventional imaging, venous sampling and repeat laparotomy⁴.

Sensitivity of somatostatin receptor (SSTR) imaging is limited by SSTR Type-2 expression in 69% of insulinomas. However dense GLP1 receptor expression is present in nearly all insulinomas⁵ and rapidly emerging experience with ⁶⁸Ga-exendin-4 PET/CT demonstrates confident localisation of up to 97.7% insulinomas⁶. GLP1 negative cases are typically avid on SSTR imaging^{5,6}.

Halo reconstruction artefact (i.e. suppression of background activity adjacent to regions of intense uptake) is a known limitation of PET 'scatter correction' algorithms. Whilst this may theoretically limit detection of small lesions in the pancreatic tail, it does not appear to have reduced the high sensitivity of ⁶⁸Ga-exendin-4 PET/CT in this case or published trials⁶. Recently updated scatter correction protocols have reduced this problem, but if observed it can be resolved through re-processing PET data without use of 'scatter correction'.

In our patient initially reported to have a normal pancreas on CT, ⁶⁸Ga-exendin-4 PET/CT effectively localised an insulinoma at the splenic hilum enabling a curative laparoscopic resection. This case highlights the role of functional imaging with ⁶⁸Ga-exendin 4 PET/CT for preoperative insulinoma localisation.

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FIGURE LEGEND

Figure 1.

Contrast-enhanced CT (A) demonstrates typical enhancing appearance of apparent 'splenunculus' (arrow), subsequently clearly characterized as extra-pancreatic insulinoma with focal intense uptake on fused ^{68}Ga -exendin-4 PET/CT (B) and PET maximum intensity projection (C). Note reduced background tracer uptake adjacent to intensely avid kidneys due to 'halo' reconstruction artefact.

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