Received: 29 March 2021 | Revised: 21 May 2021 | Accepted: 31 May 2021

DOI: 10.1002/ccr3.4519

CASE REPORT

Clinical Case Reports Open Access WILEY

Recurrent hypoglycemia and a slowly rising hemidiaphragm: A case report

Vincent Simpson[1] | **Andrew McGovern**[2]

[1]Internal Medicine, Royal Devon and Exeter Hospital, Exeter, UK

[2]Specialist in Diabetes and Endocrinology, Royal Devon and Exeter Hospital, Exeter, UK

Correspondence
Vincent Simpson, Internal Medicine, Royal Devon and Exeter Hospital, Exeter, UK.
Email: vincent.simpson@nhs.net

Funding information
The case study wasn't funded, however, Exeter Quality Improvement Academy are paying for the publication costs

Abstract

Non-islet cell tumor hypoglycemia should be considered in unexplained recurrent non-insulin-dependent hypoglycemia. Where surgery is not possible steroids may be effective, even at low dose, at managing hypoglycaemia.

KEYWORDS

fasting hypoglycemia, hypoglycemia, insulin-like growth factor-2, nondiabetic hypoglycemia, non-islet cell hypoglycemia

1 | CASE REPORT

A 92-year-old man presented to the hospital with a fall. On arrival of the ambulance crew at his home, he was found to be hypoglycemic (1.8 mmol/L; reference range 4·0–6·0 mmol/L) and drowsy. He was treated with intravenous glucose and was GCS 15 on arrival in the emergency department. He reported several falls over the preceding few weeks, usually occurring in the morning. He could not recall whether he had eaten breakfast in the morning before admission. He had no other symptoms and no preceding history of increased hunger or weight change. His past medical history included chronic obstructive pulmonary disease, ischemic heart disease, and chronic lymphocytic leukemia but not diabetes. He was not prescribed any glucose-lowering medication. His complete blood count demonstrated a mild chronic normocytic anemia (hemoglobin 114 g/L; 130–180 g/L) but was otherwise unremarkable. Serum electrolytes, liver function tests, thyroid function tests, and C-reactive protein were all normal. His chest x-ray showed a chronically raised right hemidiaphragm. He was kept overnight for observation and glucose monitoring. At 05:00, he had a further hypoglycemic episode (venous glucose 1·9 mmol/L). The simultaneous measurement showed an appropriately low c-peptide (<94 pmol/L; 370–1470 pmol/L) and low insulin level (<2·8 pmol/L; 17·8–173·0 pmol/L). A short ACTH test (250 μg IM) excluded adrenal insufficiency. An echocardiogram done for a new ejection systolic murmur showed moderate-to-severe aortic stenosis but also showed right atrial compression raising the suspicion of a large mass. We suspected a "big" insulin-like growth factor-2 (IGF-2) producing tumor and requested IGF levels, a beta-hydroxybutyrate level, and a CT thorax-abdomen-pelvis. Pending test results, he was

started on a modest dose of hydrocortisone (10 mg at night) and an evening snack. His IGF-1 was at the lower end of the reference range (8·2 nmol/L; 4·6–23·4 nmol/L), with an increased IGF-2: IGF-1 ratio (17·2; <10 [IGF-2 140·7 nmol/L]) in keeping with non-islet cell tumor hypoglycemia. A beta-hydroxybutyrate level was low (0.03 mmol/L) and his CT showed a large heterogeneous mass (18.3 × 15·7 cm) with central calcification above the right hemidiaphragm with associated partial superior vena cava obstruction and liver displacement (Figure 1). Retrospectively reviewing his chest x-rays, the mass was evident as a steadily rising right hemidiaphragm over 10 years (Figure 2). Once the diagnosis was confirmed, he was switched to 10 mg prednisolone once a night (hydrocortisone equivalent 40 mg). Low-dose prednisolone was chosen to balance the risk of steroid side effects against the risk of further hypoglycemic events. He experienced no further hypoglycemia on the low dose of prednisolone, and therefore this was not increased. Due to his age and comorbidities, this conservative treatment was considered the optimal treatment option. Subsequent home measurement of his morning capillary blood glucose levels suggested good prevention of hypoglycemic events (ranging 6·1–7·1 mmol/L; 4·0–6·0 mmol/L).

Non-islet cell tumor hypoglycemia is a rare cause of hypoglycemia and caused by IGF-2 secretion from large tumors usually arising from the mesenchymal origin (41%), though it can arise from any cell line.1, These tumors produce high molecular weight "big" IGF-2 which acts similarly to insulin, inhibiting glucose release from the liver and increasing skeletal muscle uptake.2, In turn, this suppresses growth hormone, insulin, IGF-1, and glucagon release thereby increasing the risk of hypoglycemia. Treatment is either with resection of the tumor or, where this is not possible, high-dose steroids (eg, 30-60 mg prednisolone) with either a somatostatin analogue or growth hormone.[1,2]

This case demonstrates the importance of considering non-islet cell tumors in patients presenting with non-insulin-mediated hypoglycemia as well as the importance of reviewing serial x-rays for more insidious slow-growing tumors. Successful suppression of hypoglycemic events in non-islet cell tumor hypoglycemia can be achieved with relatively low doses of prednisolone (here prednisolone 10 mg orally taken at night) although other reports suggest higher doses are usually needed.[1,2]

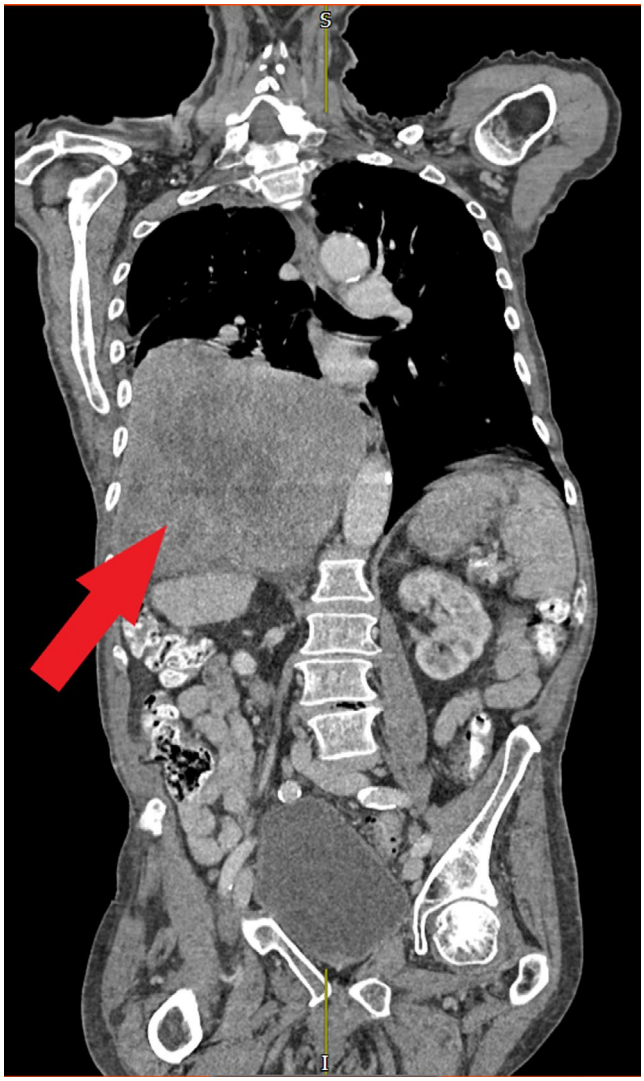

FIGURE 1 CT thorax-abdomen-pelvis with a large mass. The large heterogeneous mass measured 18.3 × 15.7 cm and is indicated by a red arrow. The mass was above the right hemidiaphragm displacing his liver and compressing his vena cava

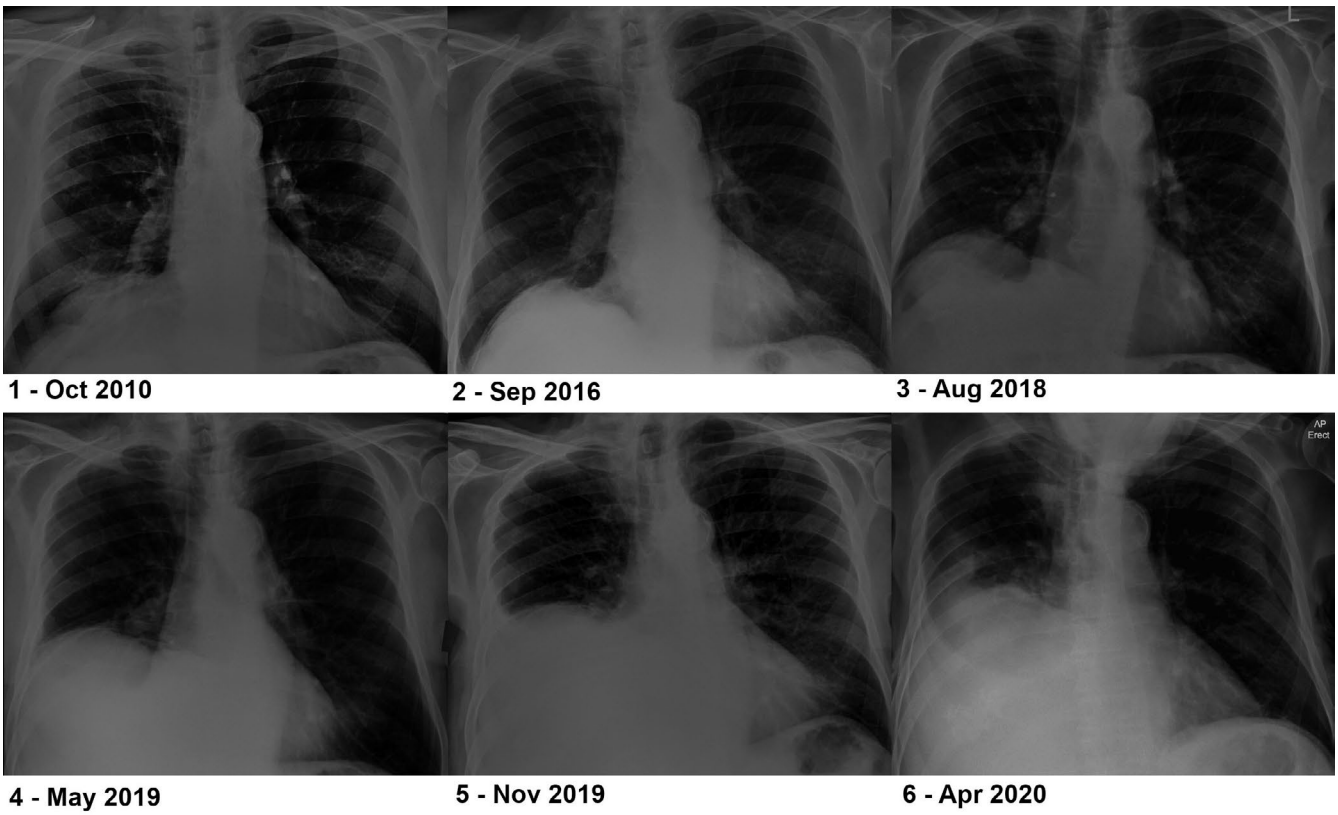

FIGURE 2 Serial chest x-rays over a 10-year period. There is a slowly rising right hemidiaphragm indicating a slow-growing mass as shown on the CT thorax-abdomen-pelvis

ACKNOWLEDGEMENTS

We would like to acknowledge the support of the Exeter Quality Improvement Academy.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

VS and AMcG were involved in the clinical care of the patient and in the preparation of the manuscript. Both authors read and approved the final submitted version. Written informed consent was obtained from the patient's next of kin as the patient had unfortunately passed away from an unrelated pneumonia at the time of writing.

CONSENT STATMENT

Published with written consent of the patient.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Vincent Simpson https://orcid.org/0000-0002-5325-0375
Andrew McGovern https://orcid.org/0000-0002-6833-9399

REFERENCES

1. De Groot JWB, Rikhof B, Van Doorn J, et al. Non-islet cell tumour-induced hypoglycaemia: a review of the literature including two new cases. *Endocr-Relat Cancer*. 2007;14(4):979-993. https://doi.org/10.1677/ERC-07-0161
2. Bodnar TW, Acevedo MJ, Pietropaolo M. Management of non-islet-cell tumor hypoglycemia: a clinical review. *J Clin Endocrinol Metab*. 2013;99(3):713-722.

How to cite this article: Simpson V, McGovern A. Recurrent hypoglycemia and a slowly rising hemidiaphragm: A case report. *Clin Case Rep*. 2021;9:e04519. https://doi.org/10.1002/ccr3.4519