

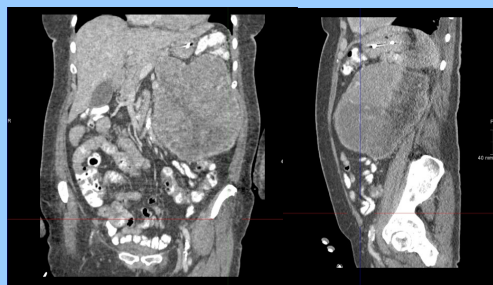
Decreased conscious level and a renal mass

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Initial Presentation

- MS, a 70 year-old retired lady found on kitchen floor by her husband having "fits"
- Later observed tonic-clonic seizures
- Past Medical History
 - Hypothyroidism
 - Hypertension
 - Ischaemic Heart Disease
- Drug History
 - Levothyroxine
 - Folic acid
 - Losartan
 - Simvastatin
 - Paracetamol
 - Aspirin
 - Bendroflumethiazide
 - Doxazosin
 - Atenolol
- Blood Pressure was 245/110. She was admitted to the intensive care unit.
- MRI brain showed subcortical oedema with subarachnoid bleed in the left temporal parietal region.



- Investigation for malignant hypertension showed a solid mass measuring 17×17×11 cm completely replacing the left kidney on CT scan
- She was discharged home on sodium valproate for seizures with a plan for a radical left nephrectomy

Further Progress

- 2 months later, found unresponsive but no seizure activity was witnessed.
- The paramedic team found her to be hypoglycaemic (near patient blood glucose reading of 1.4 mmol/l).
- Two days later, found confused, sweating with incomprehensible speech. Also had haematuria on this occasion.
- Her blood glucose was 1.8 mmol/l. She was admitted for further investigations.
- She experienced spontaneous hypoglycaemia during the night and in the morning and blood samples were taken for insulin and C-peptide levels.

Blood Results

Laboratory glucose 1.8 mmol/L (3.3 to 6.0)

Insulin <2.0 mIU/L (4.4 to 26)

C-peptide <33 pmol/L (298 to 2350)

Urine Sulphonylureas - NEGATIVE

Further investigations

IGF-I 6.6 nmol/L (4.8 to 21.6)

IGF-II 105.3 nmol/L

IGF2:IGF1 16 (<10)

Human Growth Hormone 0.6 ug/L

- This overproduction of IGF2 supports a diagnosis of non-islet cell tumour hypoglycaemia (NICTH)

Resolution

- She was provided with a glucometer and given dietary advice on how to avoid hypoglycaemia
- Following left nephrectomy episodes of hypoglycaemia resolved
- No evidence of further disease in patient

Histological Findings

- Underwent a radical left nephrectomy
- Macroscopically the tumour was a large 220 x 140 x 100 mm, lobulated, white mass, showing focal necrosis.
- Immunohistochemistry shows that the cells are positive for CD99, BCL2 and Vimentin
- Suggestive of a solitary fibrous tumour.
- Behaviour of extrathoracic solitary fibrous tumours is currently unpredictable, but mostly benign

Previous Case Reports

Previous case reports have described Non-Islet Cell Tumour Hypoglycaemia (NICTH) due to paraneoplastic syndrome predominantly in patients with solid fibrous tumours in the kidney,¹⁻³ but also adrenocortical carcinomas, pleural mesotheliomas and in retroperitoneal leiomyosarcomas and hemangiopericytomas.¹⁻³

Most case reports describe tumours associated with paraneoplastic IGF-2 production, however NICTH has also been reported to be associated with insulin receptor antibodies, tumour necrosis factor, interleukin 1 or 6 and paraneoplastic production of IGF-1.³

Discussion

- IGF-II gene located on chromosome 11¹
- Overproduction of which results in stimulation of the insulin receptors
- NICTH fasting hypoglycaemia and hypoinsulinaemia
- Decreased hepatic glucose production, diminished lipolysis and increased peripheral glucose consumption
- Inappropriately low levels of IGF1, with an increase in IGF2:IGF1 ratio (over 10) suggestive of diagnosis

Treatment

- Complete removal of the tumour or reduction of tumour main aspect of treatment
- Tumour selective chemotherapy or embolisation can have a role where unable to remove tumour²
- Glucocorticoids can help by stimulating glycogenolysis and gluconeogenesis and can help shrinkage of tumour²
- Short term beneficial effect can be achieved with parenteral glucose or dietary guidelines¹
- Somatostatin analogues do not help as somatostatin receptors in tumour likely non functional

Summary

- NICTH is a rare but serious complication of malignancy and should be considered in patient with recurrent hypoglycaemia and hypoinsulinaemia

References

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- 3 - Khowaja A, Johnson-Rabbett B, Bantle J, Moheet A. Hypoglycemia mediated by paraneoplastic production of Insulin like growth factor-2 from a malignant renal solitary fibrous tumor - clinical case and literature review. *BMC Endocr Disord*. 2014 Jun 17;14:49.