Decreased conscious level and a renal mass

Jolyon Dales, Jenny Prouten, Thrasos Macriyiannis & Marie-France Kong

Department of Endocrinology, University Hospitals of Leicester NHS Trust, Leicester, UK

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.

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, but also adrenocortical carcinomas, pleural mesotheliomas and in retroperitoneal leiomyosarcomas and hemangiopericytomomas.

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.

Discussion

- IGF-II gene located on chromosome 11
- 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 tumour
- Glucocorticoids can help by stimulating glycogenolysis and gluconeogenesis and can help shrinkage of tumour
- Short term beneficial effect can be achieved with parenteral glucose or dietary guidelines
- 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


Investigation for malignant hypertension showed a solid mass measuring 17x17x11 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