Houssay phenomenon: a rare case of diabetes mellitus remission

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Summary

Hypoglycaemia in a type 2 diabetes patient can be due to oral hypoglycaemic agent(s), in particular sulphonylureas, or insulin therapy. Pituitary dysfunction is a less common, yet important, cause of severe hypoglycaemia. Associated features include nausea, dizziness, hypotension, and hyponatraemia.

We describe a case of severe hypoglycaemia in an individual with insulin treated type 2 diabetes, secondary to panhypopituitarism from a Rathke's cyst. A brief overview on Rathke's cysts is provided.

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Key words

hypoglycaemia; hypopituitarism; Rathke's cyst

Case report

A 72-year-old man was brought into the emergency department at 2am after being found unresponsive at home. A capillary glucose level was found to be low at 2.9mmol/L. The patient regained full consciousness following correction of his hypoglycaemia with glucagon and intravenous glucose.

He was diagnosed with type 2 diabetes mellitus six years ago and had been on metformin XR 500mg and 26 units of a long-acting insulin analogue (insulin glargine) at night. His HbA_{1c} had fallen from 6.5% to 5.6% (48 to 38mmol/mol) over the past three months. Apart from a previous stroke, he had not had any other vascular complications. A month before presentation, he underwent an abdominal CT and an upper endoscopy for nausea, vomiting and abdominal pain, but no abnormalities were found.

On admission, his blood pressure was 109/60mmHg. Physical examination was unremarkable. The initial brain CT scan was reported to be normal. His blood glucose levels remained low during the admission, and thus his antidiabetic medications were stopped. His adrenal hormone, cortisol, was low at 56nmol/L. Cortisol secretion is caused by the pituitary hormone ACTH. His ACTH of 2.8pmol/L, suggested that the low cortisol is due to a pituitary defect. A complete pituitary hormone profile showed other features consistent with pituitary dysfunction. He has low thyroid hormone and testosterone, with corresponding low TSH and gonadotrophins, both of which come from the pituitary.

His hypoglycaemia and gastrointestinal symptoms resolved with 5mg of prednisone, which replaced the cortisol. He was also started on thyroid hormone and testosterone replacements, and recommenced on his previous dose of metformin, without the need for insulin. An outpatient pituitary MRI (Figure 1) showed a cystic lesion occupying the pituitary sella, and flattening the pituitary gland to the floor of the sella. The appearance of this lesion resembled a Rathke's cleft cyst. He was then referred for surgical drainage of the cyst.

Discussion

The development of hypoglycaemia in a patient with previously well controlled diabetes may be due to many causes. These include being on antidiabetic medications, reduced dietary intake or increased activity. Deficiencies in hormones that prevent or reverse hypoglycaemia, such as adrenaline, glucagon, cortisol and growth hormones, can result in hypoglycaemia. Hypopituitarism is a condition characterised by deficiency of pituitary hormones, including growth hormone and ACTH. ACTH deficiency leads to cortisol deficiency. Thus, hypopituitarism can lead to severe hypoglycaemia in a diabetic patient on insulin.[1] Cortisol deficiency is associated with increased ADH secretion, which causes hyponatraemia. Therefore, the presence of unexplained hyponatraemia should alert the clinician to this possibility.[2] Reduced intake resulting from chronic cortisol deficiency can lead to depletion of glycogen, the stored form of glucose, increasing the risk of hypoglycaemia in this setting.

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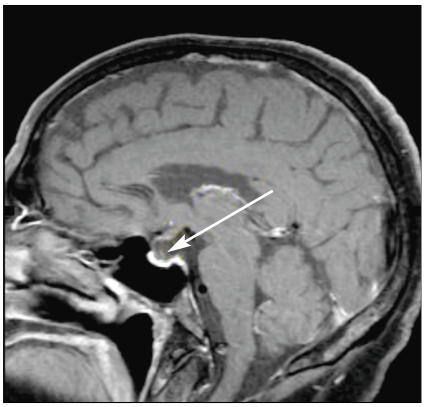

Figure 1. MRI (T1 sagittal with contrast) showing a Rathke's cleft cyst (arrowed)

In type 1 diabetic individuals with unexplained hypoglycaemia, cortisol deficiency from Addison's disease, which affects the adrenal, should be excluded. In type 2 diabetes, cortisol deficiency from any cause, including a pituitary origin, should also be considered. Apart from hypoglycaemia, cortisol deficiency can cause hypotension, lethargy, gastrointestinal symptoms, electrolyte abnormalities, etc.

Recurrent episodes of hypoglycaemia, in a diabetic patient, resulting from hypopituitarism have been termed the 'Houssay phenomenon' after the Argentinian Nobel laureate, Bernardo Houssay. He demonstrated in 1931 that diabetes in dogs that had undergone a pancreatectomy could be ameliorated by removal of the anterior pituitary.[3] However, a destructive lesion of the pituitary gland with amelioration of the diabetic state is rare.[4]

Rathke's cyst, an uncommon cause of pituitary dysfunction, arises from embryonic remnants of Rathke's pouch, which is formed during the fourth week of gestation. Most cases of Rathke's cleft cysts remain silent during the patient's lifetime and are found post-mortem.[5] Pituitary dysfunction is the most common feature in symptomatic cases, occurring in 50–69.3%[5,6] of the patients, followed by visual acuity and field disturbance, and headache.[6] Little is known about the natural history of these benign lesions and they can rarely spontaneously resolve.[7] Sometimes, hormone deficiencies can occur suddenly, often initiated by intracystic haemorrhage and rupture of the cyst.[7] The surgical approach in managing these cysts involves opening the cyst and aspirating the content, followed by partial excision of the cyst wall to prevent reaccumulation of the cyst content.

In summary, cortisol deficiency should be suspected in individuals with stable diabetes experiencing hypoglycaemic events. The presenting features may include persistent hyponatraemia, hypotension, and gastrointestinal symptoms. While this uncommon but serious cause of hypoglycaemia should be considered by medics, it is important that nurses are also aware of this condition.

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