

## Houssay phenomenon: a rare case of diabetes remission

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 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<sub>1c</sub> 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. He had a low serum sodium of 120mmol/L. His early morning cortisol level was low at 56nmol/L, with an ACTH of 2.8pmol/L. With 250µg of intramuscular Synacthen injection, the cortisol level rose to 632nmol/L at 60 minutes, indicating adequate adrenal response to ACTH stimulation. Notably, the hyponatraemia resolved following the administration of Synacthen. A complete pituitary hormone profile showed other features consistent with pituitary dysfunction, i.e. secondary hypothyroidism and hypogonadotropic hypogonadism. This, together with a mildly elevated prolactin level, suggested the presence of a sellar lesion causing pituitary stalk compression.

His hypoglycaemia and gastrointestinal symptoms resolved with 5mg of prednisone. He was also started on thyroxine and testosterone replacement, and recommenced on his previous dose of metformin, without the



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

need for insulin. An outpatient pituitary MRI (Figure 1) revealed a cystic intra- and suprasellar lesion that displaced the pituitary stalk and abutted the optic chiasm. The appearance resembled a Rathke's cleft cyst. The pituitary gland was flattened within the floor of the sella. He later suffered an episode of severe central headache that was thought to be related to the cyst and was 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. Hypopituitarism is often associated with ACTH, cortisol and growth hormone deficiency, leading to severe hypoglycaemia in a diabetic patient on insulin.<sup>1</sup> Cortisol deficiency is associated with increased ADH secretion, thus the presence of unexplained hyponatraemia should alert the clinician to this possibility.<sup>2</sup> Anorexia associated with chronic cortisol deficiency can result in glycogen depletion, increasing the risk of hypoglycaemia in this setting. Hypothyroidism also contributes to the development of hypoglycaemia.<sup>3</sup>

In type 1 diabetic individuals with unexplained hypoglycaemia, cortisol deficiency from Addison's disease should be excluded. In type 2 diabetes, cortisol deficiency from any cause, including a pituitary origin, should also be considered. Recurrent

hypoglycaemic episodes, in a diabetic patient, resulting from hypopituitarism have been termed the 'Houssay phenomenon' after the Argentinian Nobel laureate who demonstrated in 1931 that diabetes in pancreatectomised dogs could be ameliorated by removal of the anterior pituitary.<sup>4</sup> A destructive lesion of the pituitary gland with amelioration of the diabetic state is rare.<sup>5</sup>

Most cases of Rathke's cleft cysts remain silent during the patient's lifetime and are found post-mortem.<sup>6</sup> Pituitary dysfunction is the most common feature in symptomatic cases, occurring in 50–69.3%<sup>6,7</sup> of the patients, followed by visual acuity and field disturbance in 14.3–55.8%, and headache in 49.0%.<sup>7</sup> Little is known about the natural history of this benign lesion and they can rarely spontaneously resolve.<sup>8</sup> Sometimes, endocrine dysfunction can occur suddenly, often initiated by intracystic haemorrhage and rupture of the cyst which induces inflammation of the cyst wall.<sup>7</sup> The surgical approach in managing these cysts is performed transsphenoidally, and 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, especially in those using insulin or other oral hypoglycaemic agents. The presenting features may include persistent hyponatraemia, hypotension, and gastrointestinal symptoms. Rathke's cleft cysts are an uncommon cause of pituitary dysfunction.

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