CASE REPORT

Recurrent hypoglycaemia: a delayed presentation of Sheehan syndrome

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SUMMARY

Sheehan syndrome is a rare but potentially serious complication of postpartum haemorrhage. The diagnosis can often be delayed by many years as symptoms may be subtle. We report the case of a 45-year-old woman who presented to the medical emergency unit with acute onset altered sensorium. On further evaluation she was found to have severe hypoglycaemia which was corrected by giving intravenous dextrose. On detailed clinical evaluation, she had a history of agalactia and amenorrhoea following her last pregnancy which was 15 years ago. She had a history of excessive postpartum bleeding during her last delivery. MRI of the brain showed empty sella and hormonal evaluation revealed adeno-hypophyseal insufficiency as evident from decreased levels of cortisol, thyroid-stimulating hormone, triiodothyronine, free thyroxine, follicle-stimulating hormone, luteinising hormone and prolactin. Based on clinical, radiological and laboratory parameters her final diagnosis was Sheehan syndrome with hypoglycaemia.

BACKGROUND

Sheehan syndrome or postpartum pituitary necrosis is characterised by varying degrees of anterior pituitary hormone deficiency due to postpartum ischaemic necrosis of pituitary gland occurring as a result of hypovolaemia secondary to excessive blood loss during or after the delivery.¹ This rare complication of postpartum haemorrhage was first described in 1937.² Sheehan syndrome usually presents with failure of lactation and amenorrhoea. Other symptoms and signs of this syndrome are dry, pale and light coloured skin, wrinkled face, loss of axillary and pubic hair, anaemia and asthenia.³ Hypoglycaemia due to adrenocorticotrophic hormone (ACTH) deficiency is an unusual presentation of Sheehan's syndrome.

CASE PRESENTATION

A 45-year-old woman presented to the medical emergency with a history of drowsiness for 2 days. There was no history of fever, headache, seizure or any drug intake. On physical examination, she was found drowsy with a pulse rate of 84/min, blood pressure 90/60 mm Hg and respiratory rate 16/min. Her skin was dry and pale and the face was wrinkled. Systemic examination including neurological examination was unremarkable except altered sensorium and delayed ankle jerk relaxation. She was clinically evaluated in detail for the causes of hypoglycaemia such as drug intake, infection/sepsis and other systemic diseases. On detailed questioning, her relatives disclosed that she was not

able to breastfeed her child following the last delivery, 15 years ago. She was also amenorrhoeic since then. She had a history suggestive of postpartum haemorrhage that required seven units of blood transfusion. She was also having asthenia and ill-health for the last few years.

INVESTIGATIONS

Blood glucose level of the patient was 37 mg/dL at presentation in the emergency. On complete investigations, she had a haemoglobin level of 96 g/L, total leucocyte count $7.70 \times 10^9/L$ and platelet count $175 \times 10^9/L$. Peripheral smear showed normocytic normochromic anaemia. Her serum electrolytes were within normal range with a sodium concentration of 137 mmol/L (135–145) and potassium concentration 4.8 mmol/L (3.5–5). Her arterial blood gas analysis, chest roentgenogram, ECG, echocardiography and CT of the abdomen were normal. She had a C peptide value of 0.1 nmol/L (0.17–0.83), insulin level 6.95 pmol/L (14–140) and glycated haemoglobin level 5.7%. Her hormonal profile was suggestive of panhypopituitarism with low levels of serum cortisol 12.97 nmol/L (140–690), triiodothyronine 0.02 pmol/L (2–7), free thyroxine 6.18 pmol/L (12–30), follicle-stimulating hormone 3.51 IU/L (1–100), luteinising hormone 0.85 IU/L (1–104) and prolactin 37.39 pmol/L (165–1010). Her thyroid-stimulating hormone level was normal with a value of 1.2 mIU/L (0.4–4.2) and an MRI of the pituitary gland showed empty sella (figure 1). In view of a very low level of serum cortisol and multiple pituitary hormone deficiency, stimulation test such as ACTH stimulation test was not performed.

DIFFERENTIAL DIAGNOSIS

- Pituitary hypofunction
- Sepsis
- Hyperinsulinaemic hypoglycaemia (insulinoma)

TREATMENT

The patient was given intravenous 25% dextrose in the emergency to correct her hypoglycaemia. After the diagnosis of Sheehan syndrome was made, the patient was started initially on injectable hydrocortisone and then switched on to prednisolone as the replacement dose. Once the patient was stabilised on hydrocortisone, she was also started on 50 µg thyroxine per day which was up titrated to 100 µg after 6 weeks.

OUTCOME AND FOLLOW-UP

Sensorium of the patient improved immediately after giving intravenous dextrose in the emergency. She also had few episodes of hypoglycaemia in the

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Figure 1 Sagittal T1-weighted (A) and T2-weighted (B) MRI of the sella reveal empty sella with atrophic anterior pituitary gland (short arrow) and herniation of the optic chiasm into the sella (long arrows). Incidental note was made of sphenoid sinusitis.

ward, as observed on glucose monitoring in the initial few days. Hypoglycaemia was not observed after starting hormone replacement. Currently, the patient is asymptomatic on essential hormone replacement and under regular follow-up for the last 6 months after the diagnosis.

DISCUSSION

Sheehan syndrome is postpartum hypopituitarism caused by ischaemic necrosis of the pituitary gland secondary to the extended shock resulting from postpartum haemorrhage. Pregnant women may be predisposed to develop this condition due to a twofold physiological increase in pituitary volume during pregnancy which may be compressing its supporting blood vessels.⁴ The anterior pituitary gland is more susceptible to damage compared with the posterior pituitary. Symptoms and signs of Sheehan syndrome are generally due to varying degrees of hypopituitarism, ranging from selective deficiencies to panhypopituitarism.⁵

Presentation of Sheehan syndrome can be acute or chronic; acute presentation being even rarer.³ The diagnosis of Sheehan syndrome is often delayed by many years, may be up to 15–20 years, because other signs of adeno-hypophyseal insufficiency are often delayed and subtle.^{3 6} In such cases the features of hypopituitarism, for example, secondary hypothyroidism or secondary adrenal insufficiency become evident following some stressful event in the form of severe sepsis or surgery, years after the delivery. Failure to lactate and amenorrhoea are common presenting symptoms of this syndrome. Hypoglycaemia is a rare presentation of this syndrome in acute and delayed cases. In our case, diagnosis was made 15 years after the last obstetric event. There was delay of 3 years in making diagnosis in a case who presented with hypoglycaemia.⁷ The delay in making diagnosis was 16.3 ± 4.7 years in a series of 20 cases of Sheehan syndrome.³

Hypoglycaemia is commonly caused by an overdose of insulin or other hypoglycaemic agents. Other causes of hypoglycaemia are rare and include alcohol overdose with decreased oral intake, excessive exercise, insulin-secreting tumour (insulinoma), adrenal cortex insufficiency and hypopituitarism.⁸ In healthy-looking patients repeated episodes of hypoglycaemia are usually due to hyperinsulinaemic hypoglycaemia such as insulinoma. On the other hand, in admitted and sick-looking patients recurrent hypoglycaemia is usually due to sepsis, liver or kidney failure, pituitary dysfunction and adrenal insufficiency. Hypoglycaemia can rarely be the presenting symptom in the case of Sheehan syndrome. In Sheehan syndrome, it is caused by combined deficiency of the growth hormone, ACTH and other counter-regulatory hormones. Our case presented to the emergency with

hypoglycaemia. In a patient suffering from Sheehan syndrome presenting with coma, the causes can be hypothyroidism, adrenal insufficiency, hypoglycaemia and hyponatraemia either in isolation or in combination.³ In a series of 20 cases of Sheehan syndrome published by Ozkan and Colak³, seven patients presented to the emergency with coma of whom three (15%) patients had hypoglycaemia, three (15%) had hypothyroidism and one (5%) patient had hyponatraemia. In a series of 19 patients with Sheehan syndrome by Goswami *et al*,⁹ only 1 patient presented with hypoglycaemia along with hyponatraemia. Hyponatraemia is the most common electrolyte abnormality seen in Sheehan syndrome and it is present in 33–69% of total cases.¹⁰

MRI of the pituitary is the investigation of choice. Empty sella (70%) or partially empty sella (30%) are the main radiological findings of the MRI. Initial patchy central ischaemic necrosis of pituitary is followed by atrophy which is seen on MRI as empty sella.¹⁰ Treatment of Sheehan syndrome includes replacement of deficient hormones. In patients with secondary hypothyroidism and adrenal insufficiency, glucocorticoid is replaced first followed by thyroid hormone replacement because thyroid hormone replacement can precipitate adrenal crisis by increasing the rate of metabolism of glucocorticoids. Gonadotropin deficiency also requires treatment with hormone replacement but the status of growth hormone replacement in adults is controversial. Growth hormone may be given in a patient who has psychological disturbance and asthenia even after replacement therapy with steroid and thyroid hormone.

Learning points

- ▶ Hypopituitarism should be kept in differential diagnosis while working up a case of severe or recurrent hypoglycaemia.
- ▶ Postpartum haemorrhage can cause spontaneous infarction of the pituitary gland which may not be recognised for many years.
- ▶ There should be a high index of suspicion for this syndrome in any female patient in such an age group who presents with hypoglycaemic coma.

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Competing interests None.

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