CASE REPORT

JIACM 2024; 25 (4): 232-35

Sheehan's Syndrome

Maniesh Kumar K, Kiruthika J**, Sukanya N***, Kalpana Ramanathan****, Chandrasekar Selvaraj******

Abstract

Sheehan's syndrome, after severe post-partum haemorrhage, is now less commonly encountered with the advent of modern care, but occurs frequently in developing countries. Initial presentations include hyponatraemia, asthenia and weight loss. It can have a gradual onset of partial to complete pituitary insufficiency over months to years. The diagnosis of this rare disease is often delayed because the symptoms are vague and the pituitary dysfunction is insidious in nature. This case report deals with a patient who had repeated admissions for hyponatraemia, hypotension and eventually was diagnosed as Sheehan's syndrome.

Introduction:

Sheehan's syndrome classically described after severe post-partum haemorrhage is now less commonly encountered with the advent of modern obstetric care, but it occurs much more frequently in developing countries[1]. Patients present with a range of symptoms occurring due to reduced secretion of pituitary hormones like GH, LH, FSH, TSH, ACTH, and PRL. Such symptoms include breast atrophy, weight loss, amenorrhoea, failure of lactation, weakness, dry skin, loss of axillary and pubic hair and psychiatric disturbances[2]. The presentation varies from acute development of hypovolaemic shock resulting in adenohypophyseal vessel vasospasm and pituitary necrosis to the gradual onset of partial to complete pituitary insufficiency over months to years. Due to its delayed diagnosis, clinical presentation (which usually impairs quality-of-life) and potentially life-threatening complications, (e.g., coma or death), Sheehan's syndrome still remains an important entity among pregnant women, clinicians and public health services around the world.

Case report

A 46-year-old lady came to the emergency department with complaints of giddiness, vomiting, easy fatiguability and loss of weight and appetite. Patient was a known case of hypothyroidism for the past 15 years for which she was on Thyroxine for 9 years. Her initial thyroid function test reports were not available. She stopped taking drugs for the past 6 years. Patient was a known case of Hepatitis C related chronic liver disease for the past 6 years for which she was treated with sofusbuvir and velpatasvir for 6 months in view of high viral load. Her latest HCV RNA PCR had no detectable levels of viral RNA. For the past 4 years she had recurrent admissions for complaints of giddiness and easy fatiguability during which she was found to have hypotension and hyponatraemia. She was treated symptomatically and discharged during those admissions. Her obstetric history was significant because of post-partum haemorrhage following the third delivery for which she received multiple blood transfusions and hysterectomy was also done. She also had a history of lactation failure following the third delivery.

On examination, her GCS was 15/15 with general examination showing pallor, breast atrophy and loss of axillary and pubic hair. Her blood pressure was 80/50 mmHg which improved to 90/60 mmHg following a 20 mL/kg fluid bolus of normal saline. Further investigations showed normocytic normochromic anaemia, hyponatraemia, a low free T4 with low normal TSH (Table I) and ultrasound abdomen showed altered liver echoes. Her Echocardiogram was normal. In view of recurrent admissions for hyponatraemia and hypotension alongwith evidence of central hypothyroidism, possibility of adrenal insufficiency was considered. Her 8 A.M. serum cortisol and serum ACTH were low (Table I) thereby confirming the diagnosis of secondary adrenal insufficiency. With a history of post-partum haemorrhage in the third delivery followed by lactation failure, and secondary hypoadrenaltim along with regression of secondary sexual characteristics, the possibility of pan-hypopituitarism was considered. Pituitary profile showed low levels of serum FSH, LH and prolactin (Table I). MRI brain showed hypoplastic pituitary (Fig. 1, 2, 3 and 4). She was treated with physiological doses of thyroxine and steroids and is currently on follow-up.

**Post-Graduate Resident, **Senior Resident, ***Assistnat Professor, ****Professor, *****Professor and Head, Department of Medicine, Government Stanley Medical College and Hospital, Chennai - 600 001, Tamil Nadu.*

Corresponding Author: Dr Sukanya N, Assistant Professor, Department of Medicine, Government Stanley Medical College and Hospital, Chennai - 600 001, Tamil Nadu. Tel: 9884510540, E-mail: drnsuki@gmail.com

Table I: Hormonal profile of the patient.

Hormone	Patient Value
Free T4	0.8 ng/mL↓
TSH	0.9 mIU/mL
Serum cortisol (8 A.M.)	1.28 µg/dL↓
Serum ACTH	6.05 pg/mL↓
LH	1.69 mIU/mL↓
FSH	8.22 mIU/mL↓
Prolactin	1.76 ng/mL↓

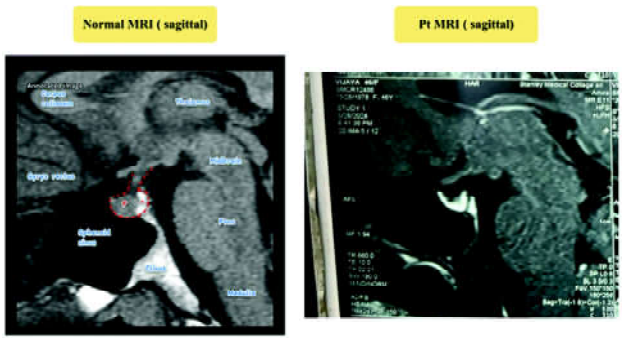

Fig. 1: *Pituitary gland measures 4.7 x 8.2 x 2.8 mm (APXTRXCC). Volume: 62 CC. No Evidence of obvious mass lesion/haemorrhage/abnormal enhancement noted.*

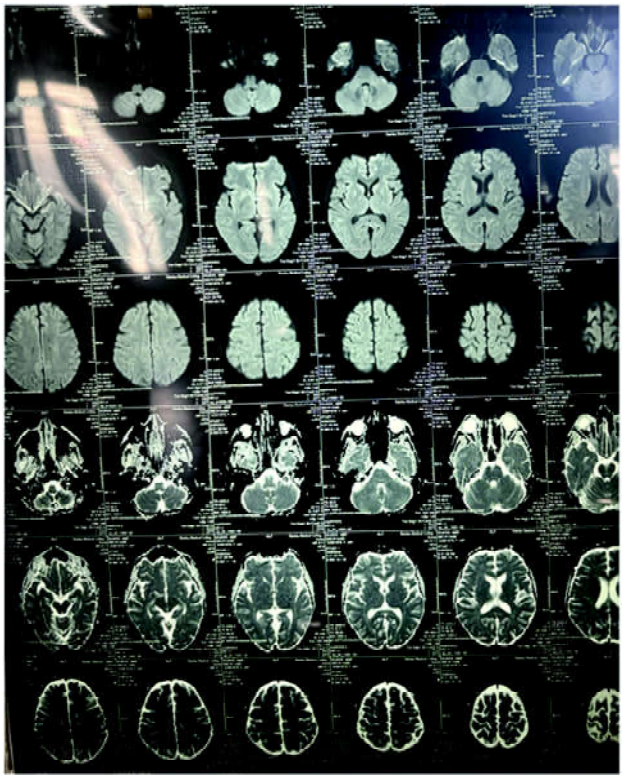

Fig. 2: *MRI brain: Axial view.*

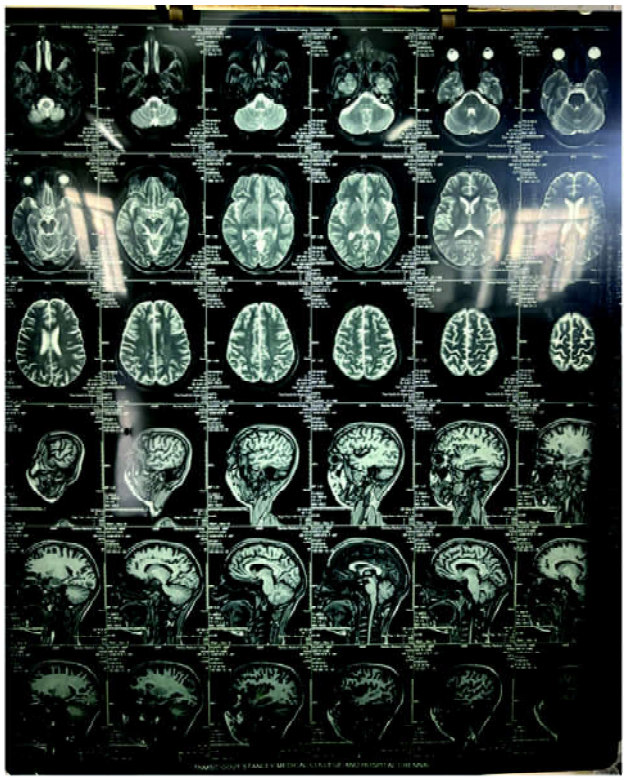

Fig. 3: *MRI brain: Axial and sagittal view.*

Fig. 3: *MRI brain: Sagittal view.*

Discussion

Even with the advent of modern obstetric care, Sheehan's syndrome is a significant cause of morbidity and mortality in developing nations[1]. An epidemiological study from India (Kashmir) has documented a prevalence of around 3.1% in adult women[3]. Normally during pregnancy, under the influence of hormones secreted by the placenta, the pituitary gland enlarges in size. At the end of pregnancy, its volume

increase by 136%. The gland enlargement is predominantly due to hyperplasia of lactotrophs within the gland. The portal vessels supplying the gland are extremely sensitive to volume and pressure changes in the systemic circulation. The anterior pituitary has a low pressure portal system in contrast to the posterior pituitary which functions at a higher pressure. Consequently, the cells of the anterior pituitary are more prone to necrosis in pregnancies complicated by significant postpartum haemorrhage[4]. Though being a post-partum event, the broad spectrum of presentation of Sheehan's syndrome serves as a major road block on the path to diagnosis. In a retrospective analysis, the mean diagnostic delay was 20.37 ± 8.34 years[5]. Presentation of the disease can be acute or chronic. In its acute form, the disease can often be fatal where the patient presents with headache, visual disturbances, loss of consciousness, failure of lactation and features of acute adrenal insufficiency such as hypotension, hypoglycaemia, extreme fatigue, nausea, vomiting and hyponatraemia[6]. Patients presenting with the chronic form on the other hand, often have non specific clinical findings. In a study by Diri *et al* involving 114 participants, 52% had non specific symptoms[7]. Secondary hypothyroidism and secondary adrenal insufficiency are among other presentations of Sheehan's syndrome, as was the case in our patient. Findings like failure to lactate, loss of axillary and pubic hair, secondary hypothyroidism and hyponatraemia have been shown to be quite common in a number of studies. In one such study by Guo-li *et al*, 85.6% had loss of axillary and pubic hair, 74.2% were unable to lactate, 70% had secondary hypothyroidism and 33.7% had hyponatraemia[8]. Hyponatraemia was a consistent and important finding in our patient, given the fact that it was the reason for her recurrent hospital admissions. The aetiology of hyponatraemia in Sheehan's syndrome is not known, but might involve increased antidiuretic hormone (ADH) release as a consequence of reduced blood pressure and cardiac output. However, a more important mechanism may be that cortisol deficiency results in increased hypothalamic secretion of corticotropin-releasing hormone (CRH), an ADH secretagogue. Hyponatraemia might even be the initial presentation of the disease[9]. With respect to radiological investigations, MRI plays a pivotal role in the diagnosis and the findings vary with the duration of disease. Early in the disease, we see an enlarged pituitary, with low T1 and high T2 homogenous signal. A ring enhancement is also a possibility during early stages of the disease. In the later stages, patients with Sheehan's syndrome can have partially (25 - 30%) or completely (70 - 75%) empty sella turcica on imaging studies[10]. In view of the varied presentations of the disease, diagnostic criteria have been proposed by Diri *et al*[7] (Box 1).

Treatment of Sheehan's syndrome is aimed at appropriate replacement of deficient hormones, though such replacement does not improve the pituitary function nor does it delay the progression of pituitary necrosis. Recombinant human growth hormone (GH) is not recommended as routine treatment for all patients with adult-onset GH deficiency, because the small clinical benefits do not seem to warrant daily injections and high cost[11]. Treatment of adrenal crisis involves IV hydrocortisone at a bolus dose of 100 mg followed by a dose of 200 mg over the next 24 hours along with treatment of the precipitating factor. For chronic secondary adrenal insufficiency, oral hydrocortisone should be given at a standard replacement dose of 10 to 20 mg on awakening and 5 to 10 mg at 3 to 6 pm[12]. For hypothyroidism, in young patients who have no evidence of ischaemic heart disease, a starting dose of 100 micrograms should be used. In older patients or patients known to have cardiovascular disease, caution should be used with an initial dose of 25 to 50 micrograms and the aim of replacement is to place the fT4 in the normal range. When hypothyroidism and hypocortisolism coexist, steroid replacement should precede the replacement of thyroxine in view of preventing an adrenal crisis[13]. Once hormone replacement is initiated and optimised, patient assessments should be on an annual basis to determine their cardiovascular risk. Constant supervision is needed to optimise the long-term outcome of patients.

Box 1: Diagnostic Criteria for Sheehans's syndrome as proposed by Diri *et al*.

Essential criteria for the diagnosis:	Criteria that are not essential, but, if present are strongly suggestive of the diagnosis:
• Typical history of severe post-partum uterine bleeding, particularly at last delivery	• Severe hypotension or shock at index delivery
• At least one pituitary hormone deficiency	• Post-partum amenorrhoea
• A partially or completely empty sella turcica on a CT or MRI scan in the chronic phase	• Failure of postpartum lactation

Conclusion

Hypopituitarism is a rare, chronic disease associated with considerable morbidity and reduction in life span. Though the incidence of Sheehan's syndrome has declined in the past few decades as a result of modernised obstetric care in the developed world. The syndrome has been increasingly recognised as one of the leading causes of hypopituitarism in developing countries. The clinical impact of hypopituitarism can be variable and is determined by the age at which the condition occurs, its rapidity of onset, the gender of the patient, the underlying cause, and the pattern of hormone deficiencies. Non-specific symptoms being a common presentation, affect the quality-of-life, especially because of long diagnostic delay. In such instances, patients often remain undiagnosed or misdiagnosed for a long time and receive inappropriate treatments. This was the case in our patient where non-specific symptoms and recurrent hyponatraemia led to her diagnosis almost 15 years after her initial insult of post-partum haemorrhage. Increased awareness of this condition can facilitate earlier diagnosis and prompt treatment, hence improving the quality-of-life and lowering morbidity and mortality.

References

1. González G, Gerardo J, Almaguer B *et al*. Sheehan's Syndrome Revisited: Underlying Autoimmunity or Hypoperfusion? *Inter J Endocrinol* 2018; 8415860: 8.
2. Feinberg EC, Molitch ME, Endres KK *et al*. The incidence of Sheehan's syndrome after obstetric haemorrhage. *Fertility and Sterility* 2005; 84 (4): 975-9.
3. Zargar AH, Singh B, Laway BA *et al*. Epidemiologic aspects of post-partum pituitary hypofunction (Sheehan's syndrome). *Fertil Steril* 2005; 84 (2): 523-8.
4. Schury MP, Adigun R. Sheehan's Syndrome. [Updated 2023 Sep 4]. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459166/
5. Gokalp D, Alpagat G, Tuzcu A *et al*. Four decades without diagnosis: Sheehan's syndrome, a retrospective analysis. *Gynecol Endocrinol* 2016; 32 (11): 904-7.
6. Roberts DM. Sheehan's syndrome. *Am Fam Physician* 1988; 37: 223-7.
7. Diri H *et al*. Extensive investigation of 114 patients with Sheehan's syndrome: a continuing disorder. *Eur J Endocrinol* 2014; 171: 311-8.
8. Du GL, Liu ZH, Chen M *et al*. Sheehan's syndrome in Xinjiang: Clinical characteristics and laboratory evaluation of 97 patients. *Hormones (Athens)* 2015; 14 (4): 660-7.
9. Schrier RW. Body water homeostasis: clinical disorders of urinary dilution and concentration. *J Am Soc Nephrol* 2006; 17: 1820-32.
10. Gokalp D *et al*. Four decades without diagnosis: Sheehan's syndrome, a retrospective analysis. *Gynecol Endocrinol* 2 June 2016 (epub ahead of print).
11. Frohman LA. Controversy about treatment of growth hormone-deficient adults: a commentary. *Ann Intern Med* 2002; 137 (3): 202-4.
12. Bornstein SR, Allolio B, Arlt W *et al*. Diagnosis and Treatment of Primary Adrenal Insufficiency: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2016; 101 (2): 364-89.
13. Toogood AA, Stewart PM. Hypopituitarism: Clinical Features, Diagnosis, and Management. *Endocrinology and Metabolism Clinics of North America* 2008; 37 (1): 235-61.