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Sheehan's syndrome unveiled after decades without a diagnosis: A case report

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Abstract

Sheehan's syndrome is defined as a postpartum infarction of the pituitary gland following hypovolemic shock due to obstetric hemorrhage. Sheehan's syndrome's symptoms are often subtle, and hence it is often overlooked. In this report, we discuss a case of an 82-year-old woman who developed severe postpartum hemorrhage after her last childbirth at the age of 37, which required multiple blood transfusions. Since then, she had progressively developed malaise and lastly presented with a new onset of confusion. Basic laboratory tests detected poorly controlled hypothyroidism and severe hyponatremia, which are well-known late-presenting conditions of Sheehan's syndrome. Escaping the diagnosis for more than four decades is extremely rare and beyond what is reported previously. Despite being a rare cause of hyponatremia in the elderly, physicians should maintain a high index of suspicion and are required to look for a readily treatable and preventable cause of hyponatremia (after excluding the common causes), which may alleviate the suffering of these patients.

Keywords

Hypopituitarism, decades without a diagnosis, Sheehan's syndrome

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Introduction

Sheehan's syndrome is a condition characterized by the necrosis or damage of the pituitary gland following severe postpartum hemorrhage during or after childbirth. The case was first described in 1937 by Harold Sheehan.[1] During pregnancy, the pituitary gland naturally enlarges, making it more susceptible to low blood flow states caused by a major hemorrhage and low blood pressure. As a result, the pituitary gland can experience ischemia and necrosis. Sheehan's syndrome leads to various levels of hypopituitarism, which refers to inadequate production or release of hormones by the pituitary gland. The degree of hypopituitarism can vary, ranging from a complete loss of all pituitary hormones (panhypopituitarism) to selective deficiencies of specific hormones.[2] The long-term effects of hypopituitarism depend on which hormone is missing. For example, with growth hormone deficiency, individuals may encounter persistent tiredness, decreased energy levels and physical prowess, reduced mental agility, and a tendency towards mild obesity. In cases of secondary hypothyroidism, patients may experience tiredness, cold intolerance, constipation, weight gain, hair loss, dry skin, and slow mental processes. Anorexia, weight loss, fatigue, and recurrent hypoglycemia are features of secondary adrenal insufficiency. All of these will affect the quality of life of these patients.[3]

The clinical presentation of Sheehan's syndrome can vary widely. Initially, there may be difficulties in lactating and restoring a normal menstrual cycle, but these signs are often overlooked, either due to occurrence at the perimenopausal age or due to the focus on treating immediate postpartum hemorrhage through emergency hysterectomies.[4] Subsequent symptoms of Sheehan's syndrome may include nonspecific complaints like weakness, fatigue, headache, and pallor. As the condition progresses, severe pituitary insufficiency can occur, potentially leading to coma and even death.[5] It is worth noting that the anterior part of the pituitary gland is

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more susceptible to damage compared to its posterior counterpart.[4]

In some cases, the diagnosis of Sheehan's syndrome may be delayed for several years until features of hypopituitarism (e.g., secondary hypothyroidism or secondary adrenal insufficiency) become more apparent.[6] The mean period of diagnostic delay is variable and was found to be 20.37 ± 8.34 years on average in one of the retrospective analyses.[7] An undiagnosed woman with Sheehan's syndrome may remain relatively asymptomatic initially, but when exposed to a stressful situation that puts a strain on her thyroid and adrenal glands, symptoms may become evident.[8]

Herein, we report a case of an 82-year-old woman with Sheehan's syndrome who escaped the diagnosis for more than four decades and presented with hyponatremia, with complete recovery after starting the appropriate treatment.

Case presentation

We present an 82-year-old woman who is known to have long-standing hypertension and hypothyroidism, with complaints of general fatigue, malaise, and lack of energy for a long period with no medical encounter. Her symptoms worsened over a couple of days in the form of a new-onset confusion, for which some laboratory tests, including serum electrolytes were ordered and showed severe hyponatremia, because of which she was admitted to hospital. At presentation, vital signs showed a blood pressure of 108/62 mmHg and a pulse of 52 bpm with no orthostasis. Physical examination revealed a confused female patient but otherwise was unremarkable. The initial laboratory testing showed hyponatremia at 116 mmol/L, with normal potassium and glucose levels, and normal kidney and liver function tests. Also, her hemogram showed a leukocyte count of 5.5×10^9/L, and a neutrophil count of 4.2×10^9/L. Her hemoglobin level was 12.8 g/dL, and her platelet count was 109×10^9/L. ng/mL.

During admission, further investigation of her hyponatremia revealed hyponatremia of adrenal insufficiency (low serum osmolality at 239 mOsm/kg, high urine osmolality at 361 mOsm/kg, high urine sodium at 120 meq/L). By further questioning, she reported a history of excessive postpartum bleeding after her last normal vaginal delivery 45 years ago, which required multiple blood transfusions to correct the resultant anemia. Since then, she has had amenorrhea and failed to lactate her baby. In addition, she complained of a progressive malaise.

Suspicions of Sheehan's syndrome arose, prompting the conduct of relevant hormonal studies. The hormone profile obtained was indicative of primary pituitary insufficiency, as shown in Table 1. Furthermore, magnetic resonance imaging of the head revealed an empty sella turcica, as depicted in Figure 1, which further supported our diagnostic assessment. The confirmation of Sheehan's syndrome was based on a combination of clinical and laboratory findings, substantiated by the MRI results.[4] Treatment commenced with hormone replacement therapy, starting with a daily dose of 30 mg of hydrocortisone, followed by upgrading her L-Thyroxine dose to 50 mcg, with incremental adjustments.

Table 1. Hormonal profile using the chemiluminescent enzyme immunometric assay, before and after treatment.

Test name (unit)	Patient's value before treatment	Patient's value after treatment	Normal reference range
Prolactin (ng/mL)	3.39	7.29	5–25
FSH (mIU/mL)	2.69	7.4	25–134
LH (mIU/mL)	0.5	2.6	14–52
TSH (μIU/mL)	0.6	0.9	0.5–4.5
T3 (pmol/L)	0.46	4.2	2–7
Free T4 (pmol/L)	0.5	19	12–30
ACTH (pmol/L)	15.5	12.5	7.2–63
Cortisol AM (mcg/dL)	4.2	12.6	5–25
IGF-1 (ng/mL)	32	103	65–200

ACTH: adrenocorticotropic hormone; FSH: follicle-stimulating hormone; LH: luteinizing hormone; TSH: thyroid-stimulating hormone; T4: thyroxine, T3: triiodothyronine; IGF-1: insulin-like growth factor-1.

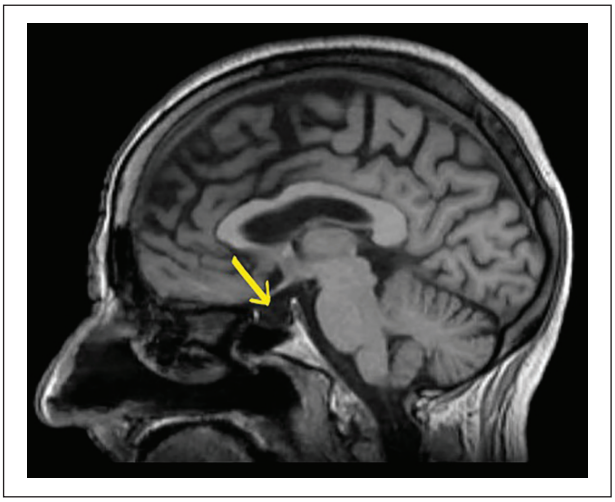

Figure 1. Sagittal gadolinium-enhanced T1-weighted MRI demonstrates an empty sella turcica (arrow).

The patient was followed up for several weeks after the hospital discharge, and we observed a full restoration of her hormonal and electrolyte imbalance within 6 weeks. Her sodium improved to the normal range (Na 139 meq/L), and this was sustained during multiple follow-up visits. In addition, her platelet count has normalized after treatment.

Discussion

Sheehan's syndrome typically needs high index of suspicion for diagnosis. This is due to the fact that the initial symptoms, such as the failure to lactate the baby or the lack of energy, may be mild and often overlooked by the affected individual. Consequently, the diagnosis may not be made until several

years or even decades after the peripartum inciting events. However, there are cases where patients may present with a sudden and severe condition, such as acute adrenal insufficiency and hypothyroidism, which can be life-threatening.[1] The initial diagnosis relies on a comprehensive clinical history and physical examination, complemented by relevant laboratory tests and imaging studies, including the assessment of anterior pituitary hormone levels and pituitary magnetic resonance imaging, respectively.[4] In addition to hormonal irregularities, other manifestations of Sheehan's syndrome encompass hyponatremia (which is primarily caused by adrenal insufficiency, hypothyroidism, or syndrome of inappropriate antidiuretic hormone secretion),[9] hematologic abnormalities, such as anemia and, in some cases, pancytopenia,[10] osteoporosis, and impaired quality of life.[5]

Here, we present this elderly female with severe hyponatremia and secondary hypothyroidism (low T4 and T3, with TSH in the lower limit of normal). After investigating the cause of hyponatremia, the diagnosis of Sheehan's syndrome was established by considering the patient's medical history of a remote severe postpartum hemorrhage and confirming it with appropriate laboratory tests and imaging studies. The delay in the diagnosis of Sheehan's syndrome has been documented in the literature, albeit not for that long period as noticed in our case. The mean delay in the diagnosis varies considerably in the reported cases of Sheehan's syndrome. One retrospective cohort study found it to be 9 ± 9.7 years.[11] In another review, the diagnosis was delayed for an average of 20.37 ± 8.34 years.[7] The mean delay in the diagnosis of our patient (of 45 years) much exceeded what has been previously reported in the literature.

The delay in the diagnosis of Sheehan's syndrome has been attributed to various reasons. One of the theories is that the symptoms of Sheehan's syndrome develop insidiously over a prolonged period, and hence may be easily overlooked by the patient and the physician. In addition, secondary amenorrhea that develops after Sheehan's syndrome (especially if it occurs in the perimenopausal period) can conceal the earliest and most important symptoms of this disorder: hypogonadotropic hypogonadism[12]

After revising the literature, all cases were treated with hormone replacement therapy (steroid and L-thyroxin hormones) with a good response. We also managed our patient with glucocorticoid (oral hydrocortisone), followed by upgrading her thyroid hormone replacement therapy with complete resolution of her symptoms and normalization of her electrolyte and endocrinologic abnormalities within 6 weeks of therapy (i.e., sodium and free T4 levels).

Conclusion

Sheehan's syndrome often presents late after the inciting postpartum hemorrhage. This is mainly because the symptoms are subtle and slowly progressive. Nevertheless, the spectrum of the presenting symptoms may not be gathering at one time and may develop insidiously over decades, necessitating a higher index of suspicion. The long time period away from the inciting delivery should not distract us from considering a reversible and readily treatable condition, which could significantly alleviate the suffering of an elderly patient.

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Author contributions

All authors contributed equally to the report (reviewing the literature, writing the case presentation, and discussing the case information). All authors reviewed the results and approved the final version of the article.

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Ethics approval

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Informed consent

Written informed consent was obtained from the patient as she has the full capacity to consent for her anonymized information to be published in this article.

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