Late diagnosis of Sheehan syndrome – a case report

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ABSTRACT

Background: Sheehan's syndrome (SS) is a rare but serious complication of severe postpartum hemorrhage, primarily resulting from ischemic necrosis of the anterior pituitary gland. It leads to varying degrees of hypopituitarism and presents with a broad spectrum of clinical manifestations. Early features typically include agalactia due to prolactin deficiency and persistent amenorrhea. As the condition progresses, patients may develop nonspecific symptoms such as asthenia, fatigue, headache, and pallor. Diagnosis is made by a triad of clinical manifestations, biochemical findings, and imaging.

Case presentation: This report describes the case of a 63-year-old woman presenting with generalized weakness and drowsiness. Laboratory evaluation revealed hyponatremia, hypoglycemia, hypocortisolism, and secondary hypothyroidism. Magnetic resonance imaging demonstrated a partially empty sella.

Conclusion: The average delay in diagnosis of SS has been estimated at nearly two decades, likely due to the high prevalence of vague and nonspecific symptoms in affected women. Increased clinical awareness is essential to improve outcomes and prevent long-term complications associated with this condition. This case underscores that SS can present decades after delivery and that timely hormone replacement is lifesaving.

Keywords: Sheehan's syndrome, postpartum pituitary necrosis, hypopituitarism, empty sella, secondary hypothyroidism.

Type of Article: CASE REPORT **Specialty:** Internal Medicine

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Background

Infarction of the pituitary gland following postpartum hemorrhage is a well-recognized cause of hypopituitarism that results from ischemic necrosis of the anterior pituitary gland after childbirth, and is referred to as Sheehan's syndrome (SS) [1]. In developed countries, its incidence has decreased significantly due to advancements in obstetric care [2]. Conversely, in resource-limited settings, where limited access to adequate medical care, skilled professionals, and emergency obstetric services contributes to higher rates of postpartum hemorrhage, SS remains the most common cause of hypopituitarism [3].

The pathophysiology involves infarction of the physiologically enlarged anterior pituitary lobe, which becomes hypervascular and hyperplastic due to elevated estrogen and prolactin levels in pregnancy. Given this enlargement, the gland becomes more susceptible to hypoperfusion during intrapartum or postpartum events, which may precipitate ischemic injury [4].

Clinical presentation varies from panhypopituitarism to isolated hormonal deficiencies. The most common early symptoms are agalactia and/or amenorrhea [5]. In rare cases, the condition may present acutely with life-threatening complications such as circulatory collapse, severe hyponatremia, diabetes insipidus, hypoglycemia, congestive heart failure, or psychosis [5,6]. In some patients, diagnosis occurs only years later when signs of chronic hypopituitarism, such as secondary hypothyroidism or adrenal insufficiency, emerge in the context of a remote postpartum hemorrhage [5]. The mean diagnostic delay was 19.7 years, likely related to the predominance of vague initial symptoms [5].

The purpose of reporting this case is to illustrate a significantly delayed diagnosis and to emphasize the need for heightened clinical awareness to reduce the risk of missed or late recognition of SS.

Case Presentation

A 63-year-old woman presented to the emergency medicine department with generalized body weakness, lethargy,

and anorexia for 3 days. Her past medical history included dyslipidemia, chronic kidney disease, and lumbar degenerative pathology. No other relevant past medical history.

On examination, the patient was pale and presented a blood pressure of 117/55 mmHg, a heart rate of 58 beats per minute, temperature of 37.8°C, pulse oximetry of 94% on room air, and a point-of-care blood glucose of 30 mg/dl. Laboratory findings showed the following: white blood cell count 7,700 cells/µl, hemoglobin 11.1 g/dl (mean corpuscular volume 86.5 fl), normal liver and renal function tests, sodium 130 mEq/L, and c-reactive protein of 8.11 mg/dl. Basic metabolic panel, lipase level, and urinalysis are within normal range.

Cerebral and supraaortic vessels angio-computed tomography (angio-CT) was performed, excluding an acute ischemic or hemorrhagic event and carotid dissection, identifying no significant atherosclerosis at the carotid bifurcation.

A lumbar puncture was performed, revealing cerebrospinal fluid (CSF) with a pH of 7.0, elevated protein concentration (58.5 mg/dl), normal glucose level (55 mg/dl), and pleocytosis (13 cells with a predominance of mononuclear cells).

The patient was hospitalized for further evaluation, and empiric treatment for presumed viral encephalitis was initiated with intravenous acyclovir, and a CSF viral polymerase chain reaction (PCR) panel was requested to identify potential neurotropic pathogens.

Subsequent laboratory investigations demonstrated central hypothyroidism, evidenced by inappropriately normal Thyroid-Stimulating Hormone (TSH) (1.65 µIU/ml) in the presence of reduced free T4 (0.56 ng/dl), total T4 (3.88 µg/dl), and total T3 (0.30 ng/ml). Concurrently, adrenal insufficiency was identified, with a markedly low morning serum cortisol level of 1 µg/dl and suppressed Adrenocorticotropic Hormone (ACTH) (<1.50 pg/ml), consistent with secondary adrenal insufficiency. The CSF viral PCR panel was negative. Based on these findings, a diagnosis of central adrenal insufficiency was established. Acyclovir was discontinued, and the patient was started on hydrocortisone and levothyroxine replacement therapy.

During further examination of the patient's history, she reported having a significant postpartum hemorrhage, with a resulting coma, 28 years earlier. After childbirth, she had difficulty lactating and became menopausal. She also reported having had symptoms of anedonia, abulia, and weakness for several years.

Magnetic resonance imaging (MRI) of the brain was consistent with a partially empty sella (Figure 1).

The patient was diagnosed with Sheehan syndrome, which was associated with hypothyroidism and adrenal insufficiency. She was initially given hydrocortisone, 15 mg in the morning and 10 mg in the evening, which was followed by levothyroxine supplementation, 75 µg, daily started 5 days later.

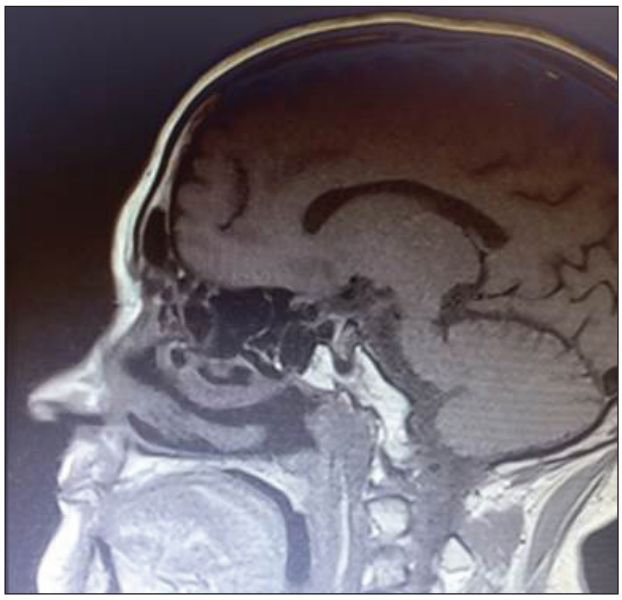

Figure 1. *Decreased pituitary gland showing an aspect of a "partially empty" sella.*

The patient demonstrated progressive and sustained clinical improvement following initiation of appropriate hormone replacement therapy. Asthenia and anorexia subsided gradually, accompanied by the resolution of orthostatic hypotension and hypoglycemic episodes. These clinical changes reflected a global improvement in metabolic and neuroendocrine status. Moreover, serial laboratory assessments showed normalization of lipid profile and previously identified normocytic normochromic anemia, reinforcing evidence of hypothalamic-pituitary-adrenal axis recovery and improved overall endocrine function.

Discussion

The incidence of SS has significantly declined in developed countries due to advances in obstetric care; however, underdiagnosis and delayed recognition remain challenges. SS is more prevalent in resource-limited settings where access to skilled obstetric care and timely transfusion is restricted [3].

During pregnancy, the anterior pituitary enlarges, becoming particularly vulnerable to ischemia in the setting of hypovolemia. The syndrome may involve partial or complete deficiencies of anterior pituitary hormones [prolactin, ACTH, TSH, Luteinising Hormone (LH), Follicle-Stimulating Hormone (FSH), and Growth Hormone (GH)] and, in rare cases, posterior pituitary dysfunction [1]. Although the initial insult is ischemic, an autoimmune or inflammatory mechanism may contribute to progressive pituitary dysfunction over time. Some patients develop autoantibodies against pituitary antigens, although this finding is not consistent across cases [7].

Clinically, SS may present acutely, subacutely, or remain latent for years. Acute presentations typically involve failure to lactate, amenorrhea, hypotension, or

adrenal crisis shortly after delivery [5]. Chronic cases are more insidious, characterized by nonspecific symptoms such as fatigue, anorexia, weight loss, cognitive impairment, or orthostatic hypotension. In many cases, these symptoms remain unrecognized until a physiological stressor, such as infection or surgery, unmasks adrenal insufficiency [8].

The average delay in diagnosis has been estimated at nearly two decades. Lactational failure and amenorrhea are among the earliest signs but are often overlooked, particularly when the postpartum hemorrhage was not clearly documented [5]. These findings underscore the need for heightened clinical suspicion, especially when evaluating women with a relevant obstetric history and subtle endocrine dysfunction.

In this context, the patient's obstetric history demonstrated hallmark features associated with the SS diagnosis. During detailed anamnesis, she reported a severe postpartum hemorrhage complicated by coma 28 years earlier. In the subsequent postpartum period, she experienced lactational failure and amenorrhea. These historical elements were pivotal in establishing the diagnosis.

Hormonal evaluation typically reveals low levels of cortisol, thyroid hormones, estradiol, and prolactin, with inappropriately low or normal corresponding pituitary hormones, reflecting secondary endocrine failure. These deficiencies manifest clinically as adrenal insufficiency, central hypothyroidism, gonadal failure, and growth hormone deficiency. Biochemical abnormalities are also frequent, particularly hyponatremia due to impaired free water clearance. Anemia, commonly normocytic and normochromic, is multifactorial and linked to multiple hormonal deficits [9].

Imaging of the pituitary gland plays a supportive diagnostic role. In early stages, MRI may show an enlarged pituitary without signs of hemorrhage. In late stages, the classical radiological finding is an empty or partially empty sella, reflecting atrophic changes in the pituitary tissue. This feature, although not pathognomonic, strongly supports the diagnosis in the appropriate clinical context [4].

The diagnosis of SS is established based on clinical history, physical examination, laboratory confirmation of anterior pituitary hormone deficiencies, and characteristic imaging findings [10].

Clinically, SS should be suspected in women with a history of significant postpartum hemorrhage who subsequently develop lactational failure, amenorrhea, or symptoms suggestive of hypopituitarism. Biochemical evaluation of pituitary hormones is essential, as early identification of hormonal deficiencies guides timely initiation of replacement therapy. Prompt and adequate hormonal replacement is critical to prevent acute decompensation and to reduce long-term morbidity associated with delayed or incomplete treatment [1,10].

Management of SS involves long-term hormone replacement tailored to the patient's profile. Glucocorticoid replacement with hydrocortisone is initiated first to avoid precipitating adrenal crisis, particularly before the introduction of levothyroxine. The typical adult regimen is 15 mg in the morning and 5 mg in the evening. Central hypothyroidism is treated with levothyroxine, and estrogen/progesterone replacement is considered based on age, uterine status, and fertility goals. GH replacement in adults remains controversial but may be beneficial in selected cases [1].

In the present case, the patient demonstrated progressive clinical improvement following initiation of hydrocortisone and levothyroxine. Asthenia, anorexia, and orthostatic symptoms resolved gradually, and glycemic control stabilized with no further hypoglycemic episodes. Anemia corrected over time, and her lipid profile normalized, likely reflecting resolution of underlying endocrine dysfunction. These findings highlight the importance of recognizing subtle clinical features and initiating timely treatment to prevent long-term complications, including cardiovascular risk and metabolic syndrome.

Long-term prognosis in SS is generally favorable when adequate hormone replacement is maintained, although lifelong therapy and regular endocrinological follow-up are required. Patient education on stress-dose corticosteroid adjustments during illness, surgery, or trauma is essential to prevent adrenal crises and ensure safe long-term management.

What is new

Sheehan's syndrome often goes unnoticed due to its insidious onset and nonspecific symptoms.

A high index of suspicion is required when central adrenal insufficiency, hypothyroidism, and prior obstetric complications coexist.

Prompt diagnosis and hormone replacement therapy can significantly enhance quality of life and prevent life-threatening complications.

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List of abbreviations

angio-CT	Angio-computed tomography
CSF	Cerebrospinal fluid
MRI	Magnetic resonance imaging
PCR	Polymerase chain reaction
SS	Sheehan's syndrome

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication
Written informed consent was obtained from the patient for publication of their clinical history and associated data.

Ethical approval
Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	Patient (gender, age)	63 years, female
2	Final diagnosis	Sheehan syndrome
3	Symptoms	Lethargy, Anorexia, Hypotension, Hypoglycemia, Hyponatremia
4	Medications	Hydrocortisone, Levothyroxine
5	Clinical procedure	None
6	Specialty	Internal Medicine