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# Sheehan's syndrome: case report

## *Síndrome de sheehan's: relato de caso*

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**ABSTRACT**
Sheehan's Syndrome (SS) results from severe postpartum hemorrhage, causing pituitary necrosis and hormone deficiencies. While usually chronic, acute SS is rare and requires immediate management. Symptoms like hypotension, tachycardia, hyponatremia, and hypoglycemia suggest acute SS. A case involved a 32-year-old woman with severe hypotension and tachycardia postpartum, diagnosed with SS based on MRI findings. Acute SS stems from anterior pituitary infarction due to reduced blood flow, often following childbirth. Risk factors include multiparity and induced labor. Diagnosis relies on history, symptoms, and imaging. Acute cases may lead to circulatory collapse. Treatment involves hormone replacement therapy, with levothyroxine for thyroid dysfunction and estrogen-progesterone for gonadotropin deficiency. GH replacement is debated. Early diagnosis and therapy are vital to improve outcomes. This case underscores the importance of initiating levothyroxine and outpatient monitoring for SS. Increasing awareness is crucial for timely intervention, enhancing patients' quality of life and reducing morbidity and mortality.

**Keywords:** Hypopituitarism; pituitary insufficiency; postpartum hemorrhage.

**RESUMO**
A Síndrome de Sheehan (SS) resulta de hemorragia pós-parto grave, causando necrose hipofisária e deficiências hormonais. Embora geralmente crônica, a SS aguda é rara e requer tratamento imediato. Sintomas como hipotensão, taquicardia, hiponatremia e hipoglicemia sugerem SS aguda. Um caso envolveu uma mulher de 32 anos com hipotensão grave e taquicardia pós-parto, diagnosticada com SS com base nos achados da ressonância magnética. A SS aguda decorre de infarto da hipófise anterior devido à redução do fluxo sanguíneo, geralmente após o parto. Os fatores de risco incluem multiparidade e parto induzido. O diagnóstico se baseia no histórico, nos sintomas e nos exames de imagem. Os casos agudos podem levar ao colapso circulatório. O tratamento envolve terapia de reposição hormonal, com levotiroxina para disfunção da tireoide e estrogênio-progesterona para deficiência de gonadotrofina. A reposição de GH é debatida. O diagnóstico e a terapia precoces são vitais para melhorar os resultados. Este caso ressalta a importância de iniciar a levotiroxina e o monitoramento ambulatorial da SS. O aumento da conscientização é fundamental para a intervenção oportuna, melhorando a qualidade de vida dos pacientes e reduzindo a morbidade e a mortalidade.

**Palavras-chave:** hemorragia pós-parto; hipopituitarismo; insuficiência pituitária.

## INTRODUCTION

Sheehan's Syndrome (SS) is a rare condition caused by severe postpartum hemorrhage that leads to ischemic pituitary necrosis and thereafter to pituitary hormone deficiency. SS is characterized by lipid, glucose and coagulation abnormalities, increased body fat, insulin resistance, increased leptin concentration, low-grade inflammation and endothelial dysfunction that may incline to cardiovascular diseases. [1]

SS commonly presents as a chronic manifestation, mostly diagnosed many years after postpartum hemorrhage. Thus, acute Sheehan's syndrome is rare and must be quickly and effectively treated to avoid negative outcomes. [2] Symptoms such as persistent hypotension and tachycardia simulate hypovolemia and shock. However, hyponatremia and persistent hypoglycemia may suggest SS. [3] As acute SS is a rare condition and there are only few cases reported on current literature, we present this case to support future research about this syndrome.

Most often, women at postpartum with acute SS develop agalactorrhea, in other words, they are unable to lactation and breastfeeding the newborn. [3] Although, symptoms such as hypotension, tachycardia, hypoglycemia, extreme fatigue, nausea, and vomiting are common at this syndrome. While, on chronic SS manifests symptoms like mild nonspecific weakness, fatigue, anemia, amenorrhea, adrenal insufficiency, and hypothyroidism. Moreover, in rare cases, chronic SS can lead to diabetes insipidus. [4]

We report here our experience with a case of this rare type of Sheehan syndrome and present a review of the literature on this condition. This study was approved by the Human Research Ethics Committee of the Hans Dieter Schmidt Regional Hospital - Joinville/SC, under opinion nº 6.022.996, on April 26, 2023, CAAE – 68353023.0.0000.5363. The patient who agreed to participate in the study signed a free and informed consent form in accordance with resolution no. 466 of 2012 of the National Health Council.

## CASE REPORT

A 32 years old woman have been admitted on hospital at São Francisco do Sul and have been transferred to Hospital Regional Hans Dieter Schmidt (HRHDS) at Joinville/SC due to postpartum severe hypotension (arterial pressure of 40 x 20 mmHg) and tachycardia (cardiac frequency of 140). Previously on the same day, she vaginal delivered a child and developed an intense hemorrhage. Due to the difficult of content the blooding, the medical team choose to perform a partial hysterectomy and a left salpingo-oophorectomy. She arrived at HRHDS in hypovolemic shock and using vasoactive drugs. Upon arriving in Joinville, a transfusion of red blood cells and platelets was performed. Initial laboratory tests demonstrated severe anemia (hemoglobin of 3.5 g/dl, hematocrit of 11%), thrombocytopenia (95,000 platelets per $mm^3$), blood glucose of 194 mg/dL, creatinine levels of 1.5 mg/dL and acidosis metabolic.

So, on the same day, she had an exploratory laparotomy. During the surgical procedure, blood was identified inside the abdominal cavity from the right ovarian branches, and artery ligation and right oophorectomy were performed. After 9 days in the intensive care unit (ICU), she was extubated and after 3 days she was transferred to the ward. Over the next 13 days, the patient progressively worsened with nausea, vomiting, diarrhea, asthenia, tachycardia, dry cough ventilator-dependent chest pain and dyspnea. Given these symptoms, acute lung edema was found, requiring invasive ventilation and return to the ICU.

In the ICU, an echocardiogram was requested, which showed dilated cardiomyopathy with significant left ventricular systolic dysfunction, due to diffuse hypokinesia, left ventricular ejection fraction of 37% and mitral and tricuspid insufficiency levels, in addition to mild pericardial effusion. After being extubated in the ICU, the patient returned with the same symptoms already reported. Given the above, some hormonal tests were requested. Laboratory results showed the following: adrenocorticotropic hormone (ACTH) 30.9 (reference range up to 46 pg/mL), LH 1.39 mIU/mL, prolactin 22.24 ng/mL, TSH 1.88 $\mu$IU / mL ( reference range: 0.35 to 4.94) with free T4 equal to 0.54 ng/dL (reference range 0.70 to 1.48 ng/dL), estradiol presented a value below 10 pg/mL, FSH 6.73 mIU/mL, LH 1.64 mIU/mL, prolactin equal to 17.21 ng/mL, as well as IGF-1 of 49.2 ng/mL (reference range: 71 to 234 ng/mL ) and human growth hormones less than 0.05 ng/mL (reference range up to 8ng/mL). Given these values, pan-hypopituitarism was detected, with dysfunction of the GH, ACTH, TSH, gonadotropic and prolactin axes. Thus, Sheehan`s Syndrome was suspected, and nuclear magnetic resonance imaging (MRI) of the pituitary was requested, confirming the diagnosis given the characteristic finding of necrosis of the adenohypophysis (Figure 1.). Therefore, as a form of treatment, prednisone 5 mg/day and levothyroxine 25 mcg/day were introduced. The patient presented a satisfactory clinical response, with normalization of blood pressure. Unfortunately, due to the involvement of the prolactin axis, the patient cannot breastfeed her child.

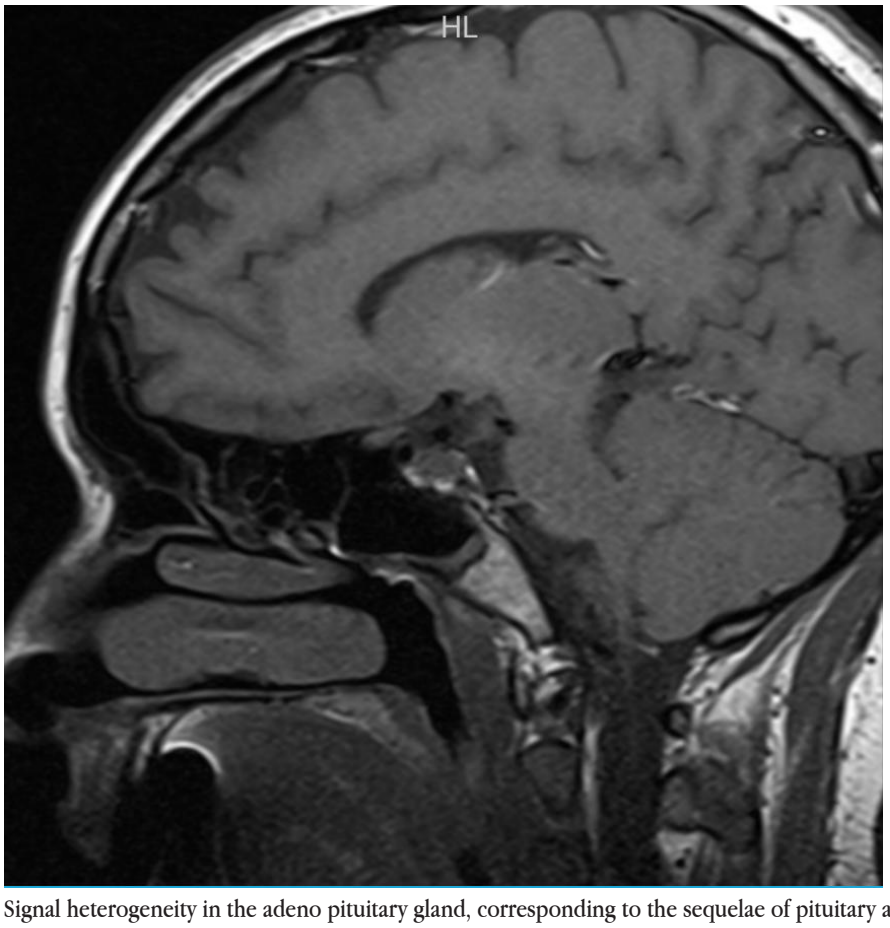


**Figure 1.** MRI - Signal heterogeneity in the adeno pituitary gland, corresponding to the sequelae of pituitary apoplexy (pituitary necrosis)

**DISCUSSION**

In the context of the present case report, acute Sheehan's syndrome is a rare occurrence. Sheehan's syndrome is a cause of hypopituitarism, first reported in 1937 by Harold Leeming Sheehan. [5] The pathophysiological aspect of this condition is not currently fully elucidated. According to Kovac K, this syndrome arises from infarction of the pituitary gland, primarily affecting the anterior lobe due to reduced blood flow, which may be secondary to vasospasm, thrombosis, or vascular compression. [6] The increased susceptibility to postpartum ischemia is believed to be attributed to the physiological enlargement of the gland during pregnancy, increasing by approximately 120-136% by the end of gestation. [7] Autoimmune causes cannot be ruled out in this syndrome, but due to the unclearly established component, in-depth investigations are required, as described by Karacas in 2016. [8]

The most common risk factors include multiparity, polyhydramnios, chorioamnionitis, twin pregnancy, induced labor, instrumental delivery, among others. However, predicting which women will experience postpartum hemorrhage is challenging, as some women may not have these common risk factors, as described by Tavares. [9]

Furthermore, the diagnosis is based on classic criteria, including a history of postpartum hemorrhage, severe shock requiring blood transfusion, absence of breastfeeding, menstrual disturbances (amenorrhea), partial or total hypopituitarism, and detection of a partially or totally empty sella on computed tomography or magnetic resonance imaging. [9] However, in most cases of Sheehan's syndrome, the pituitary sella size is within the normal range. [10] In the present case, in addition to the magnetic resonance imaging of the pituitary demonstrating ischemia of the anterior pituitary, the early and critical deficiency of prolactin corroborates and explains the failure in lactation, which is the most frequent and characteristic symptom. Gonadotropins are often unaffected, and there are cases of Sheehan's syndrome where women maintain regular menstrual cycles and even experience spontaneous pregnancies. [9]

This syndrome can manifest in two ways: acute or chronic; in the reported case, it presents as an acute condition. In acute forms, clinical findings include signs of adrenocortical insufficiency such as hypotension, hypothermia, tachycardia, hypoglycemia, hyponatremia, nausea, and vomiting. Severe cases can lead to circulatory collapse, severe hyponatremia, central diabetes insipidus, congestive heart failure, and even psychosis. [9] Chronic or late presentation symptoms are more variable: amenorrhea, sterility, reduced axillary and pubic hair due to gonadotropin deficiency; asthenia, weakness, fatigue, and muscle mass loss due to thyroxine and GH deficiency; hypoglycemia, cold intolerance, and premature aging. [9] Patients commonly present fine wrinkles around the eyes and lips, signs of premature aging, dry and hypopigmented skin, breast atrophy, and thinning of axillary and pubic hair. [11]

In patients with such medical history and clinical presentation, baseline hormone level assessment, including prolactin, free T4 (T4L), TSH, ACTH, cortisol, FSH, LH, estradiol, and IGF-1, may suffice for the diagnosis of Sheehan's syndrome. However, some may require dynamic tests of pituitary function. [12] Sheehan's syndrome associated with dilated cardiomyopathy is rare, and there is no therapeutic approach described in the literature. Hormone replacement for the deficiencies presented is the main known available resource, as improvement in the described clinical cases is independent of specific therapy for heart failure with reduced ejection fraction. [13]

In the present report, due to the acute characteristics and hemodynamic instability, the patient required surgical intervention to

contain postpartum hemorrhage. The study by Matsuzaki *et al.* (2017) differs in relation to acute treatment for postpartum hemorrhage, as they successfully performed uterine embolization. [14] This demonstrates different treatments for the acute and severe form that predisposes to SS. Subsequently, noticeable changes in laboratory tests, such as ACTH, T4L and IGF-1, indicated hypopituitarism and later Sheehan's syndrome.

The treatment of Sheehan's syndrome is the same as for other causes of hypopituitarism; the deficient hormones should be adequately replaced. Thyroid dysfunction is treated with Levothyroxine, and gonadotropin deficiency is managed with estrogen-progesterone replacement, recommended in premenopausal women with central hypogonadism, provided there are no contraindications. The use of GH replacement is controversial, and there is no consensus regarding risk-benefit and cost-effectiveness.[9] In this case report, the patient's treatment was initiated with Levothyroxine 25 mcg/day, and she was discharged with outpatient follow-up by endocrinology and cardiology specialists.

The incidence of acute Sheehan's syndrome has exhibited a decline globally, particularly in highly developed nations and regions, attributed to advancements in obstetric care. Nevertheless, its prevalence remains notable in developing countries characterized by limited access to obstetric services.[15] Consequently, ensuring adequate obstetric care is imperative to promote maternal health and mitigate the occurrence of acute Sheehan's syndrome among pregnant women. This necessitates measures aimed at averting potential hemorrhagic events or shocks through the provision of comprehensive obstetric interventions. This corroborates the studies by Baggio *et al.* (2024) who finds that there is a relationship between good birth care planning and the obstetric outcome, respecting care protocols based on scientific evidence, which ensure the health of the woman and the newborn. [16]

In this sense, due to pituitary insufficiency, hormone replacement therapy is imperative to enhance the well-being of afflicted individuals and mitigate the morbidity and mortality associated with the condition. The present investigation offers practical insights by correlating this case report with the diagnosis and management of a specific pathology. Consequently, this approach contributes to the amelioration of patient quality of life while concurrently reducing the morbidity and mortality rates associated with the clinical complications of the syndrome.

## CONCLUSION

Sheehan's Syndrome, often overlooked, represents a significant etiology of hypopituitarism. Owing to its nonspecific symptoms, a substantial portion of affected individuals may endure protracted intervals without a proper diagnosis or appropriate therapeutic intervention. Consequently, it is imperative to augment awareness of this condition in order to facilitate earlier and more accurate diagnostics, along with the judicious administration of hormonal replacement therapy. This endeavor aims to ameliorate the quality of life for afflicted individuals and mitigate the morbidity and mortality linked with the syndrome.

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