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Sheehan's Syndrome: A Diagnostic Challenge in Postpartum Hypopituitarism – Case Report and Review of Pathophysiology and Management

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Abstract **Case Studies**

Background: Sheehan's syndrome is a rare but serious form of hypopituitarism resulting from ischemic necrosis of the anterior pituitary gland, typically triggered by severe postpartum hemorrhage. Its clinical presentation is often nonspecific and insidious, leading to delayed diagnosis and irreversible complications. This case report highlights the diagnostic challenges and the importance of early hormonal evaluation in at-risk patients.

Case Report: A 43-year-old female presented with secondary amenorrhea and persistent headaches two years after a complicated delivery marked by severe postpartum hemorrhage and agalactorrhea. Endocrine evaluation revealed panhypopituitarism, with deficiencies in corticotropic, thyrotropic, gonadotropic, somatotropic, and lactotropic axes. Magnetic resonance imaging (MRI) confirmed pituitary atrophy with empty sella turcica, consistent with Sheehan's syndrome. Hormone replacement therapy (HRT) was initiated, including glucocorticoids, levothyroxine, and estrogen-progestin, with plans for growth hormone replacement and bone health monitoring.

Discussion: This case underscores the critical need for a high index of clinical suspicion in women with a history of postpartum hemorrhage and lactation failure. Early recognition and prompt initiation of HRT can prevent long-term complications such as adrenal crisis, osteoporosis, and impaired quality of life. Multidisciplinary collaboration between obstetricians, endocrinologists, and radiologists is essential for optimal management.

Conclusion: Sheehan's syndrome remains underdiagnosed due to its subtle and nonspecific symptoms. Heightened awareness among healthcare providers, especially in the context of postpartum hemorrhage, is crucial for timely intervention. Lifelong hormonal monitoring and individualized HRT are key to improving outcomes in affected patients.

Keywords: Sheehan Syndrome; Hypopituitarism, Postpartum; Hemorrhage, Postpartum; Hormone Replacement Therapy; Empty Sella Syndrome; Diagnostic Errors; Hypopituitarism.

Introduction

Sheehan's syndrome is a leading cause of postpartum hypopituitarism, resulting from ischemic necrosis of the anterior pituitary gland, typically triggered by severe postpartum hemorrhage [1]. The hemorrhage leads to a state of hypotension and reduced blood flow to the pituitary gland, which in turn induces reflex vasoconstriction and vasospasm in the vessels supplying the pituitary tissue [2]. This ischemic insult, if prolonged, results in irreversible necrosis of the anterior pituitary lobule, leading to a deficiency in multiple pituitary hormones.

In classic presentations, the diagnosis of Sheehan's syndrome can be straightforward, particularly when it is characterized by the absence of lactation (agalactorrhea) and persistent secondary amenorrhea in the context of a hemorrhagic delivery [3]. In some cases, the clinical picture may be overt, with symptoms of panhypopituitarism such as fatigue, weight loss, hypotension, and hypoglycemia, facilitating early recognition.

However, the clinical manifestations of Sheehan's syndrome are often nonspecific and insidious, which frequently results in delayed diagnosis [4]. This delay can span several months to even years, as the symptoms may be misattributed to postpartum exhaustion, depression, or other more common conditions [5]. The lack of pathognomonic features underscores the importance of maintaining a high index of clinical suspicion, especially in women with a history of significant obstetric hemorrhage, in order to initiate timely hormonal evaluation and prevent long-term complications [6].

Methods

Patient Presentation

A 43-year-old female was admitted to our department for evaluation of secondary amenorrhea and persistent headaches. The clinical history revealed a significant postpartum hemorrhage two years prior, complicated by the absence of lactation (agalactorrhea) two weeks following delivery. These findings raised clinical suspicion for Sheehan’s syndrome, a condition characterized by ischemic necrosis of the anterior pituitary gland following severe obstetric hemorrhage [1].

Clinical Evaluation

A comprehensive endocrine assessment was performed, including a detailed history and physical examination. The clinical examination revealed signs consistent with corticotropic and gonadotropic deficiencies, such as fatigue, hypotension, and reduced secondary sexual characteristics. Laboratory investigations were initiated to assess anterior pituitary function.

Hormonal and Imaging Studies

- **Hypophysiogram (Dynamic Endocrine Testing):**
  A comprehensive pituitary function panel was conducted, including stimulation tests for:
  - Corticotropic axis: ACTH stimulation test to assess adrenal reserve.
  - Gonadotropic axis: GnRH stimulation test to evaluate gonadal function.
  - Thyrotropic axis: TSH and free T4 levels.
  - Somatotropic axis: IGF-1 levels and, if indicated, a growth hormone stimulation test.
  - Prolactin levels to rule out hyperprolactinemia.
- **Magnetic Resonance Imaging (MRI):** A hypothalamic-pituitary MRI was performed to evaluate structural abnormalities, including pituitary atrophy, empty sella syndrome, or signs of prior ischemic insult [7]. The protocol included T1-weighted and T2-weighted sequences, with and without contrast enhancement.

Diagnostic Criteria

The diagnosis of Sheehan's syndrome was considered based on:

1. History of severe postpartum hemorrhage [1].
2. Clinical and biochemical evidence of anterior pituitary hormone deficiencies [3].
3. MRI findings suggestive of pituitary necrosis or atrophy [7].

Results

Comprehensive Pituitary Function Assessment (Hypophysiogram)

The hypophysiogram revealed evidence of panhypopituitarism, characterized by deficiencies in all anterior pituitary hormones. The detailed findings are as follows:

1. **Corticotropic Axis Deficiency**
    - Serum cortisol was profoundly suppressed (below the reference range), indicating adrenal insufficiency.
    - ACTH levels were inappropriately low or undetectable, confirming secondary adrenal insufficiency due to pituitary dysfunction [8].
2. **Thyrotropic Axis Deficiency**
    - Free T4 (Ft4) was at the lower limit of normal, suggesting reduced thyroid hormone secretion.
    - TSH levels were inappropriately low, consistent with central hypothyroidism [3].
3. **Somatotropic Axis Deficiency**
    - IGF-1 levels were borderline low, indicating growth hormone (GH) deficiency.
    - Further stimulation testing (e.g., GHRH + arginine test) was not performed due to clinical constraints.
4. **Gonadotropic Axis Deficiency**
    - Estradiol levels were significantly low, consistent with hypogonadism.
    - Gonadotropins (LH and FSH) were inappropriately low, confirming hypogonadotropic hypogonadism [8].
    - Bone mineral density (BMD) assessment revealed osteopenia of the lumbar spine, likely secondary to chronic estrogen deficiency and untreated hypogonadism.
5. **Lactotropic Axis Deficiency**
    - Prolactin levels were low, indicating lactotrope dysfunction, which is typically seen in Sheehan's syndrome due to infarction of lactotroph cells [1].

Imaging Findings (Hypothalamic-Pituitary MRI)

The MRI demonstrated pituitary atrophy with an empty sella turcica, supporting the diagnosis of Sheehan's syndrome [7]. No structural lesions or pituitary adenomas were identified.

Summary of Hormonal Profile

Hormone	Result	Interpretation
Cortisol	Very low	Corticotropic deficiency
ACTH	Low/undetectable	Secondary adrenal insufficiency
Free T4	Low-normal	Thyrotropic deficiency
TSH	Low	Central hypothyroidism
IGF-1	Borderline low	Somatotropic deficiency
Estradiol	Low	Gonadotropic deficiency
LH/FSH	Low	Hypogonadotropic hypogonadism
Prolactin	Low	Lactotropic deficiency

Clinical Implications

- Hormone replacement therapy (HRT) is indicated, including glucocorticoids, levothyroxine, and estrogen/progestin [8].
- Bone health monitoring (DEXA scan) and calcium/vitamin D supplementation are recommended.
- Long-term follow-up is essential to assess treatment response and prevent complications (e.g., adrenal crisis, osteoporosis) [6].

Imaging Findings: Hypothalamic-Pituitary MRI

The hypothalamic-pituitary MRI revealed pituitary atrophy with an empty sella turcica (arachnoïdocèle), which is highly suggestive of Sheehan's syndrome [7]. These findings are consistent with post-ischemic necrosis of the anterior pituitary gland, secondary to severe postpartum hemorrhage. No structural lesions, pituitary adenomas, or other abnormalities were detected (Fig2).

Therapeutic Management

Given the patient's established panhypopituitarism and prior initiation of hormone replacement therapy (HRT), the therapeutic plan was optimized as follows:

1. **Thyroid Hormone Replacement**
    - Levothyroxine 100 µg/day was continued to maintain euthyroidism and prevent symptoms of hypothyroidism [8].
2. **Glucocorticoid Replacement**
    - Hydrocortisone 15 mg/day was administered to prevent adrenal insufficiency and avoid adrenal crisis. The dose was adjusted to mimic physiological cortisol secretion [8].
3. **Gonadal Hormone Replacement**
    - Estrogen-progestin replacement therapy was initiated to address hypogonadism, improve bone mineral density, and alleviate symptoms of estrogen deficiency (e.g., vaginal atrophy, mood disturbances).
    - Transdermal estradiol (e.g., 50 µg/day) combined with oral progesterone (e.g., 10 mg/day for 12 days/month) was considered, pending

further evaluation of bone health and bleeding risk.

4. **Growth Hormone Replacement (Consideration)**
    - Given the low IGF-1 levels, recombinant human growth hormone (rhGH) therapy may be considered in the future, provided there are no contraindications (e.g., active malignancy, intracranial hypertension).
5. **Bone Health Management**
    - A dual-energy X-ray absorptiometry (DEXA) scan was recommended to monitor bone mineral density (BMD) due to the presence of osteopenia.
    - Calcium and vitamin D supplementation (e.g., calcium carbonate 1000 mg/day + vitamin D3 800 IU/day) was advised to prevent further bone loss.

Follow-Up Plan

- Regular hormonal monitoring (cortisol, TSH, free T4, estradiol, IGF-1) every 3–6 months.
- Clinical assessment for symptoms of hormone deficiency or excess.
- Annual DEXA scan to evaluate bone health.
- Patient education on the importance of adherence to HRT and recognition of adrenal crisis (e.g., stress dosing of glucocorticoids during illness) [8].

Discussion

Diagnostic Challenges in Sheehan's Syndrome

This case underscores the frequent delay in diagnosing Sheehan's syndrome, a condition often unrecognized despite its classic presentation [4]. The absence of lactation (agalactorrhea) following a postpartum hemorrhage is a highly specific early sign that should prompt immediate endocrine evaluation [3]. However, this clinical clue is frequently overlooked, leading to a diagnostic delay that may extend from months to years [5]. Such delays result in progressive hormonal deficiencies, long-term complications (e.g., osteoporosis, adrenal crisis), and reduced quality of life [8].

Pathophysiological Considerations

Sheehan's syndrome arises from ischemic necrosis of the anterior pituitary gland due to severe postpartum hemorrhage, which induces hypotension and vasospasm in the hypophyseal vasculature [2]. The selective vulnerability of lactotrophs (e.g., prolactin deficiency) is often the earliest manifestation, followed by deficiencies in other pituitary axes (corticotrope, thyrotrope, gonadotrope, somatotrope) [1]. The panhypopituitarism observed in this case reflects advanced pituitary damage, emphasizing the need for early recognition [6].

Clinical Implications and Management

The cornerstone of Sheehan's syndrome management is timely diagnosis and hormone replacement therapy (HRT) [8]. In this case, the patient was already on partial HRT (levothyroxine and hydrocortisone), but comprehensive replacement (including estrogen-progestin therapy) was necessary to address hypogonadism and prevent further bone loss. The MRI findings (pituitary atrophy and empty sella) confirmed the chronicity of the pituitary insult, reinforcing the diagnosis and guiding long-term management [7].

Preventive Strategies and Awareness

Given the potential morbidity of untreated Sheehan's syndrome, increased clinician awareness is critical [6]. Obstetricians should routinely screen for lactation failure in women with postpartum hemorrhage, and endocrinologists should maintain a high index of suspicion for pituitary dysfunction in such cases [3]. Multidisciplinary care (obstetrics, endocrinology, radiology) ensures optimal outcomes [5].

Limitations and Future Directions

This case report highlights the diagnostic challenges but lacks genetic or molecular data to explore potential predisposing factors (e.g., thrombophilias, vascular abnormalities) [1]. Future studies should focus on early biomarkers of pituitary ischemia and the role of advanced imaging (e.g., dynamic contrast-enhanced MRI) in detecting subtle pituitary damage [7].

Conclusion

This case underscores the critical importance of early recognition and long-term follow-up in women with a history of severe postpartum hemorrhage. The delayed diagnosis of Sheehan's syndrome, as illustrated here, can lead to progressive hypopituitarism, irreversible complications (e.g., osteoporosis, adrenal insufficiency), and significant impairment in quality of life [8]. A high index of clinical suspicion—particularly in the context of postpartum lactation failure—is essential to initiate timely endocrine evaluation and hormonal replacement therapy [3]. The integration of multidisciplinary care (obstetrics, endocrinology, and radiology) ensures comprehensive management, while structured follow-up mitigates long-term morbidity [5]. Ultimately, proactive screening and intervention in at-risk populations not only improve clinical outcomes but also enhance patient well-being, reinforcing the need for heightened awareness among healthcare providers [6].

Declaration of Interest

The authors declare no conflicts of interest related to this article.

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Declarations:

This study had an anonymized patient data. As the research involved no direct intervention or modification of standard patient care, formal approval from an ethics committee was not required in accordance with institutional and national guidelines for observational studies. The patient data was anonymized prior to analysis to protect confidentiality and treated according to the Algerian national guidelines

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Authors' contributions

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