

Patterns of Presentation in Postpartum Pituitary Necrosis (Sheehan Syndrome)

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ABSTRACT

Sheehan syndrome classically presents with hypopituitarism after postpartum haemorrhage. Although the prevalence of Sheehan syndrome has decreased, it continues to be a common cause of hypopituitarism in developing countries. Disease classically presents with postpartum bleeding and a combination of anterior and posterior pituitary hormone deficiencies, although involvement of posterior pituitary is rare. Atypical presentations like cardiac or renal involvement, anaemia and psychosis are not uncommon. Prevention and aggressive management of bleeding at the time of delivery largely prevents pituitary damage.

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Until 1938 the disease postpartum pituitary necrosis was known as Simmonds hypothesised that women dying after severe postpartum bleeding had extensive anterior pituitary necrosis on autopsy due to thrombosis or bacterial emboli in hypophyseal arteries.¹ Sheehan then stated that Simmond's disease was due to necrosis of the anterior pituitary following postpartum haemorrhage.² Normally pituitary gland enlarges during pregnancy under the influence of placental hormones, mainly estrogen. The enlargement of the pituitary results in compression of small hypophyseal arteries and, in the presence of PPH, causes necrosis of the gland.^{3,4} In addition to PPH, pituitary autoimmunity and coagulation disturbances are considered risk factors for the development of Sheehan syndrome (SS).^{5,6} Rarely, SS can run in multiple generations.⁷

Typical presentations

Sheehan syndrome mainly involves the anterior pituitary and typically presents with deficiency of anterior pituitary hormones and consequent failure of target organs. Typically, SS presents with lactotroph failure (manifesting as lactation failure), gonadotroph failure (manifesting as non-resumption of menstrual cycles after puerperium), thyrotroph failure (manifesting as features of secondary

hypothyroidism), ACTH deficiency (manifesting as features of cortisol deficiency) and features of somatotroph deficiency (manifesting as features of adult growth hormone deficiency).⁸ Pituitary hormone deficiency may occur in different combinations (and order), and sometimes gonadotroph and corticotroph, may be preserved in the so-called partial SS.⁹⁻¹² Somatotroph, and thyrotroph cells are affected in all the patients and preservation, or recovery of these cell lines is exceptionally uncommon.¹³ Involvement of posterior pituitary in the form of clinical diabetes insipidus requiring treatment is extremely rare.¹⁴

Atypical presentations

Because thyroid, cortisol, sex steroid hormones, and growth hormones directly and indirectly, affect hematopoiesis.¹⁵ Pancytopenia with hypocellular marrow is not an uncommon haematological presentation in hypopituitarism.¹⁶ Anemia (normocytic and

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normochromic), leucopenia and thrombocytopenia in various combinations have been reported in women with SS. All these abnormalities completely normalise after achieving the euthyroid and cortisol state.¹⁷ Regarding the differential effect of thyroid and steroid hormones, glucocorticoids dominate hematopoiesis as against thyroid hormones.¹⁸

Cardiac abnormalities in patients with untreated hypopituitarism have not been previously studied because of the rarity of this disorder in the western world. Thyroid and steroid hormones have a profound effect on cardiac function and consequently hypopituitarism either because of the direct effect of hormone deficiencies or because of indirect effects through changes in water and electrolyte balance may lead to these abnormalities. Acute reversible presentations like heart failure due to cardiomyopathy or rhythm disturbance due to hypokalemia have been reported.^{19,20} A recent study demonstrates that treatment naïve patients with SS have many structural and functional cardiac abnormalities as seen on echocardiography. Abnormalities were seen in cardiac valves (high prevalence of mitral regurgitation), left ventricular size and mass (decreased LV end-diastolic diameter, LV volume, septal and posterior wall diastolic thickness and LV mass), and left ventricular systolic functions (decreased ejection fraction, stroke volume and fractional shortening). In addition, approximately half of the patients had pericardial effusion. These abnormalities completely disappeared after treatment with thyroxine and glucocorticoids without GH substitution. We believe that these cardiac abnormalities result from severe hypothyroidism and hypo cortisol state.^{21,22} Severe hypothyroidism in these patients can lead to neuropsychiatric manifestations, especially after treatment when even small doses of glucocorticoids can exacerbate psychosis.²³ Non-compliance to treatment can lead to hypo cortisol crisis, hypovolemia, and acute renal failure. Because these patients have small-sized organs (because of growth hormone deficiency, these can be confused with chronic kidney disease.²⁴

Diagnosis

In an area where the disease is common, diagnosis is not difficult. Hypopituitarism in the context of childbirth associated with PPH, makes the diagnosis of Sheehan highly likely. MRI reveals empty sella in almost all the

patients. In the present context, documentation of one or more anterior pituitary hormone deficiencies and the presence of complete or partial empty sella on MR imaging is sufficient to diagnose SS. Diri et al. recently has revised the criteria for the diagnosis of SS (Table 1).

Table 1. Diagnostic criteria for Sheehan syndrome²⁵.

Essential Criteria
1. Typical history of severe postpartum uterine bleeding, particularly at last delivery.
2. At least one pituitary hormone deficiency.
3. A partially or completely empty sella turcica on a CT or MRI scan.
Suggestive Criteria
1. Severe hypotension or shock at index delivery.
2. Postpartum amenorrhea.
3. Failure of postpartum lactation.

Differential diagnosis

In the context of childbirth, hypopituitarism could also result from lymphocytic hypophysitis. The features favouring lymphocytic hypophysitis are the presence of headache, absence of postpartum haemorrhage, presence of central diabetes insipidus and hyperprolactinemia. MRI reveals diffuse enlargement of the pituitary gland, thickened pituitary stalk, with absent posterior pituitary bright spot, intense and diffuse contrast intake on gadolinium administration and presence of a dural tail.²²

Treatment and follow up.

Both glucocorticoids and thyroxine are essential for survival in these patients. Theoretically, both should be started at the same time to prevent the hypocortisolism crisis. Women under 40 years should also be given estrogen and progesterone until the usual age of menopause (up to the age of 50). Adverse metabolic effects have been demonstrated on follow up in such patients. These include metabolic syndrome, insulin resistance, low-grade inflammation and a high risk of coronary artery disease.^{26,27}

REFERENCES

1. Sheehan HL. Postpartum necrosis of anterior pituitary J Pathol Bacteriol 1937; 45:189-214.
2. Sheehan HL. Simmond's disease due to postpartum necrosis of anterior pituitary. QJM 1939; 8:277-309.
3. Laway BA, Mir SA. Pregnancy and pituitary

- disorders: Challenges in diagnosis and management. *Indian J Endocrinol Metab* 2013; 17:996-1004.
4. Karaca Z, Laway BA, Dokmetas HS, Atmaca H, Kelestimur F. Sheehan syndrome. *Nat Rev Dis Primer* 2016; 2:16092.
 5. Zargar AH, Singh B, Laway BA, Masoodi SR, Wani AI, Bashir MI. Epidemiologic aspects of postpartum pituitary hypofunction (Sheehan's syndrome). *Fertil Steril* 2005; 84:523-8.
 6. Goswami R, Kochupillai N, Crock PA, Jaleel A, Gupta N. Pituitary autoimmunity in patients with Sheehan's syndrome. *J Clin Endocrinol Metab* 2002; 87:4137-41
 7. Laway BA, Ramzan M, Mir SA. Sheehan's syndrome in two generations. *Indian J Endocrinol Metab* 2016; 20:884-885.
 8. Zargar AH, Masoodi SR, Laway BA, Shah NA, Salahuddin M, Siddiqi MA, Kour S. Clinical spectrum of Sheehan's syndrome. *Ann Saudi Med* 1996; 16:33841.
 9. Laway BA, Mir SA, Gojwari T, Shah TR, Zargar AH. Selective preservation of anterior pituitary functions in patients with Sheehan's syndrome. *Indian J Endocrinol Metab* 2011; Suppl3: S238-241.
 10. Laway B, Misgar R, Mir S, Wani A. Clinical, hormonal and radiological features of partial Sheehan's syndrome: An Indian experience. *Arch Endocrinol Metab* 2016; 60:125129.
 11. Laway BA, Ganie MA, Bashir MI, Kotwal SK, Mir SA, Gojwari T, Zargar AH. Sheehan's syndrome with hyperprolactinemia. *Turk JEM* 2010; 14:47-49.
 12. Laway BA, Mir SA, Zargar AH. Recovery of prolactin function following spontaneous pregnancy in a woman with Sheehan's syndrome. *Indian J Endocrinol Metab* 2013 (Suppl 3): S 696-699.
 13. Laway BA, Sumji S. Preservation of Thyrotroph Function in Sheehan's Syndrome. *Indian J Endocrinol Metab* 2017; 21:931-932.
 14. Laway BA, Mir SA, Dar MI, Zargar AH. Sheehan's syndrome with central diabetes insipidus. *Arq Bras Endocrinol Metabol* 2011; 55:1714.
 15. Laway BA. Pituitary marrow connection- Evidence based but less understood. *Austin J Endocrinol Diabetes* 2014; 1: 1-2.
 16. Laway BA, Bhat JR, Mir SA, Khan RSZ, Lone MI, Zargar AH. Pancytopenia in patients with Sheehan's syndrome, complete reversal after hormone replacement (case series and review). *Annals of Hematology* 2010; 89:305-8.
 17. Laway BA, Mir SA, Bashir MI, Bhat JR, Samoon J, Zargar AH. Prevalence of hematological abnormalities in patients with Sheehan's syndrome - response to replacement of glucocorticoids and thyroxine. *Pituitary* 2011; 14: 39-43.
 18. Laway BA, Mir SA, Bhat JR, Lone MI, Samoon J, Zargar AH. Response of pancytopenia to glucocorticoids in patients with Sheehan's syndrome. *Pituitary* 2012; 15:184-7.
 19. Laway BA, Mir SA, Jan VM, Bhat MA, Farooqi KJ. Recurrent ventricular tachycardia in a patient of Sheehan's syndrome. *Turk JEM* 2015; 19:28-30.
 20. Laway BA, Alai S, Gojwari T, Ganie MA, Zargar AH. Sheehan's syndrome with reversible dilated cardiomyopathy. *Annals of Saudi Med* 2010; 30:321-324.
 21. Laway BA, Ramzan M, Allai MS, Wani AI, Misgar RA. Cardiac structural and functional abnormalities in females with untreated hypopituitarism due to Sheehan syndrome: Response to hormone replacement therapy. *Endocr Pract* 2016; 22:1096103.
 22. Laway BA, Baba MS. Sheehan syndrome. *J Pak Med Assoc.* 2021; 71:1282-1285.
 23. Laway B, Shah T, Bashir M, Dada A, Zargar A. Acute onset psychosis following steroid replacement in Sheehan's syndrome. *Acta Endocrinol (Buc)* 2010; 6:533-8.
 24. Bhat MA, Laway BA, Allaqaband FA, Kotwal SK, Wani IA, Banday KA. Acute renal failure: A rare presentation of Sheehan's syndrome. *Indian J Endocrinol Metab* 2012; 16:306-9.
 25. Diri H, Tanriverdi F, Karaca Z, Senol S, Unluhizarci K, Durak AC, et al. Extensive investigation of 114 patients with Sheehan's syndrome: a continuing disorder. *Eur J Endocrinol* 2014; 171:3118.
 26. Bhat MA, Laway BA, Shah ZA, Wani AI, Mubarik I.

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Insulin resistance, metabolic syndrome and chronic low-grade inflammation in Sheehan's syndrome on standard replacement therapy: a case control study. Pituitary 2015; 18:3128.

Lipid and Leptin concentrations in patients with Sheehan Syndrome Indian J Endocrinol Metab 2018; 22:466-468

27. Mir SA, Shah T, Singh H, Shabir I, Laway BA. Serum