

# Acute renal failure: A rare presentation of Sheehan's syndrome

Manzoor A. Bhat, Bashir A. Laway, Faheem A. Allaqaband, Suman K. Kotwal, Imtiyaz A. Wani<sup>1</sup>, Khursheed A. Banday<sup>1</sup>

Departments of Endocrinology and <sup>1</sup>Nephrology, Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India

### ABSTRACT

Sheehan's syndrome occurs as a result of ischemic pituitary necrosis secondary to severe postpartum bleeding. It is one of the most common causes of hypopituitarism, characterized by variable clinical presentation. Acute kidney injury occurs rarely in Sheehan's syndrome and most of the cases have been found to be precipitated by rhabdomyolysis. We here present a case of Sheehan's syndrome with acute kidney injury where the precipitating cause was chronic hypocortisolemia. We believe this is the first reported case of Sheehan's syndrome in which acute kidney injury was precipitated by adrenal insufficiency.

**Key words:** Acute kidney injury, acute renal failure, Sheehan's syndrome

## INTRODUCTION

Sheehan's syndrome (SS) is one of the commonest causes of hypopituitarism in underdeveloped and developing countries. It occurs as a result of ischemic pituitary necrosis due to severe postpartum hemorrhage.<sup>[1-3]</sup> Although a small percentage of patients with SS may present as abrupt onset acute hypopituitarism immediately after delivery, most patients have a mild disease and go undiagnosed and untreated for years together.<sup>[4-6]</sup> The spectrum of clinical presentation of SS is extremely varied and ranges from non-specific complaints such as weakness, fatigue, and anemia to severe pituitary insufficiency resulting in coma and death.<sup>[1,5,6]</sup> As in other types of hypopituitarism, hormonal deficiency ranges from loss of single tropic hormone to classical panhypopituitarism. Failure of postpartum lactation and menstruation is the most common presenting

feature of SS. Other clinical presentations include secondary hypothyroidism and adrenal insufficiency.<sup>[6,7]</sup> Other associations include anemia, pancytopenia, and cardiac abnormalities like cardiomyopathy.<sup>[8-10]</sup> SS presenting as acute kidney injury (AKI) is rare. Only few cases have been reported in the literature and most are precipitated by rhabdomyolysis.<sup>[11-13]</sup>

We report a case of AKI in a middle-aged female with SS who recovered dramatically after being started on intravenous steroids and volume replacement. Our case suggests that besides hypothyroid myopathy leading to rhabdomyolysis and consequently compromised renal function and AKI, chronic adrenal insufficiency can also predispose to the risk of AKI.

## CASE REPORT

A 56-year-old woman was referred to our hospital with a 4–5 day history of nausea, two episodes of vomiting, and few episodes of loose motions, followed by oliguria at home. She denied any history of fever, dysentery, abdominal pain, trauma, muscle pain, or change in color of urine. She also denied history of any drug intake. On enquiring, the patient gave history of longstanding ill health in the form of generalized weakness, easy fatigability, cold intolerance,

### Access this article online

#### Quick Response Code:



Website:  
www.ijem.in

DOI:  
10.4103/2230-8210.93777

**Corresponding Author:** Dr. Bashir Ahmad Laway, Department of Endocrinology, Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India. E-mail: drlaway@gmail.com

constipation, hair loss, and weight gain starting after her last child birth some 22 years back. Last delivery was a full-term normal delivery conducted by a local midwife at her home. She denied any history of profuse bleeding or blood transfusion during her last peripartum period. However, she had lactation failure and had menstrual cycles for a few months before complete cessation of menses after her last delivery. Physical examination revealed an ill-looking, dehydrated patient with pulse of 54 beats/minute, blood pressure of 90/60 mm Hg without any postural drop, respiratory rate of 18/minute, and oral temperature of 97.6°F (36.4°C). The patient had mild pallor, dry tongue, coarse and dry skin with non-pitting edema of the lower extremities. Hypopigmented area was seen around right nasal orifice and there was loss of lateral eyebrows. Thyroid gland was not palpable and there was no lymphadenopathy. Her breasts were atrophic and sparse axillary and pubic hair was noticed. Chest, cardiovascular, and abdominal examinations were non-contributory. Central nervous system examination revealed slow mentation in the form of delayed response to verbal commands. Examination of motor system did not reveal any focal neurodeficit, but deep tendon jerks were markedly delayed.

Laboratory evaluation revealed normochromic normocytic anemia. Liver function tests were normal except for low albumin. Kidney function test was deranged with initial urea of 71 mg/dl (normal value 20–40 mg/dl) and serum creatinine of 4.5 mg/dl (normal value 0.5–1.5 mg/dl). Muscle enzymes were slightly elevated with creatine phosphokinase (CPK) being 168 IU/l (normal value 10–70 IU/l) and lactate dehydrogenase (LDH) was 983 U/l (normal value 200–450 U/l). Arterial blood gas and electrolyte analysis revealed pH of 7.31, PCO<sub>2</sub> of 27 mm Hg, bicarbonate of 13 mmol/l, serum sodium 130 mmol/l, and potassium of 3.6 mmol/l. Plasma glucose was only 38 mg/dl. Chest X-ray was normal and 12-lead ECG revealed sinus bradycardia with low-voltage QRS complex. Routine urine examination revealed pus cells 4–5, RBCs 2–3, absent albumin and casts. Renal ultrasound revealed relatively small-sized kidneys (right 8.5 × 3.2 cm, left 8.7 × 3.4 cm) with increased echogenicity, with maintained corticomedullary differentiation bilaterally. Her hormone profile revealed panhypopituitarism [Table 1]. The diagnosis of panhypopituitarism most likely secondary to SS associated with acute renal failure was made on the basis of her past medical history of failure to lactate post her last child birth with gradual cessation of menses, peripheral signs and symptoms of hypothyroidism, and abnormal biochemical and hormone profile.

The patient was given intravenous fluids in the form of dextrose normal saline with close monitoring of urine output, replacement therapy in the form of intravenous

**Table 1: Basal anterior pituitary hormones and serial kidney function tests during admission**

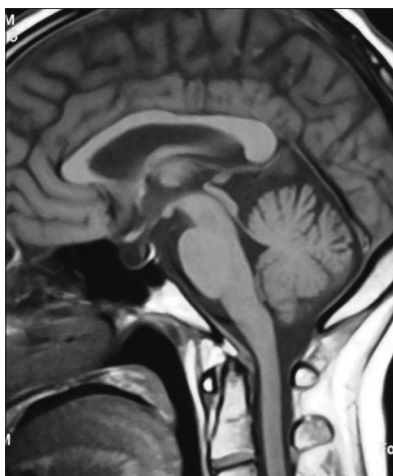
Parameter	Day 1	Day 3	Day 6	Day 7	Day 10	Normal value
Urea (mg/dl)	71	48	48	27	30	20–40
Creatinine (mg/dl)	4.5	2.5	2.2	1.39	1.35	0.5–1.5
pH	7.31	7.41	7.38	7.39	7.39	7.35–7.45
Bicarbonate (meq/l)	13	26.8	26.6	24.3	26.6	22–29
Sodium (meq/l)	130	141	137	141	138	135–145
Potassium (meq/l)	3.6	2.3	2.8	3.4	4.4	3.5–5.5
Calcium (corrected) (mg/dl)	8.25	-	-	-	-	8.8–10.8
Phosphorus (mg/dl)	1.75	-	-	-	-	3.5–5.5
Uric acid (mg/dl)	5.87	-	-	-	-	1.5–6
T4 (µg/dl)	<1	-	-	-	-	4–13
TSH (µIU/ml)	3.53	-	-	-	-	0.5–6.5
LH (U/l)	<0.5	-	-	-	-	3–12
FSH (U/l)	3.53	-	-	-	-	2–6.6
PRL (ng/ml)	<1	-	-	-	-	>2
GH (ng/ml)	0.25	-	-	-	-	>3
Cortisol (µg/dl)	<1	-	-	-	-	>20

T4: thyroxine, TSH: Thyroid stimulating hormone, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, GH: Growth hormone, PRL: Prolactin

hydrocortisone 50 mg intravenously 6 hourly, and levothyroxine given orally at a starting dose of 50 mcg/day. The patient was also given intravenous antibiotics and antiemetics. Urine output began to improve on the 2<sup>nd</sup> day of admission. Her appetite also improved and there was complete cessation of vomiting. On repeating renal function tests and other biochemical tests, there was dramatic improvement in serial renal function parameters. With improvement in the general condition of the patient, intravenous antibiotics were stopped in view of absence of fever and negative septic screen. She was shifted to oral prednisolone 5 mg twice daily, while levothyroxine was continued at a dose of 50 mcg/day. The serial biochemical parameters of the patient are given in Table 1. She was discharged on the same medication on 10th day of admission and was advised to taper prednisolone to 5 mg/day after 2 weeks. Four weeks after discharge, the patient had general sense of well-being with better appetite and renal function had normalized with creatinine 0.64 mg/dl and serum urea 23 mg/dl. The patient was subjected to magnetic resonance imaging (MRI) brain with sellar and parasellar focus which revealed empty sella with normal rest of the brain parenchyma [Figure 1].

## DISCUSSION

The present report describes a 56-year-old woman with SS who presented with acute renal insufficiency owing to depletion of intravascular volume secondary to gastroenteritis. The chronic hypocortisol state has increased the predisposition to renal injury which was precipitated by



**Figure 1:** MRI pituitary sagittal view showing pituitary fossa filled with cerebrospinal fluid and stalk touching the base of pituitary floor; features suggestive of empty sella

mild acute gastroenteritis. SS, first described by HL Sheehan in 1937, classically refers to postpartum hypopituitarism due to pituitary necrosis occurring during severe hypotension or shock secondary to massive bleeding at or just after delivery. The frequency of SS has gradually decreased especially in developed countries, as a result of improved obstetric care including treatment of hemodynamic complications with rapid blood transfusion and/or intravenous fluid replacement. It, however, continues to be the most common cause of hypopituitarism in underdeveloped and developing countries.<sup>[1,2,5]</sup> Enlarged pituitary volume, small sellar size, prothrombotic nature of pregnancy, and autoimmunity have been suggested to play a role in the pathogenesis of SS in women who suffer from severe postpartum hemorrhage. On the other hand, SS may develop rarely without any obvious postpartum hemorrhage.<sup>[1,14]</sup> This was seen in our case also. The spectrum of clinical presentation of SS is quite variable and ranges from non-specific symptoms such as weakness, fatigue, and anemia to severe pituitary insufficiency resulting in coma and death. Clinical manifestations of SS may change from one patient to another, as hormonal deficiency varies from loss of one trophic hormone to classical panhypopituitarism.<sup>[1,5-7]</sup> Failure of postpartum lactation is the most consistent feature of patients with SS and failure of regaining menstrual flow postpartum is the most common symptom of SS.<sup>[1]</sup> Despite the failure to menstruate, gonadotrophin reserve may still be preserved in some patients and these patients can even conceive spontaneously.<sup>[15]</sup>

Another important clinical presentation in SS is related to secondary hypothyroidism and patients may present with weight gain, cold intolerance, tiredness, aches and pains, and muscle disorders ranging from elevation of muscle

enzymes to frank rhabdomyolysis and renal failure.<sup>[11-13]</sup> Our patient also had severe central hypothyroidism as was evident from history, examination, and hormone tests. Adrenal insufficiency in SS can be catastrophic and can range from non-specific complaints to hypotension, sallow skin, and severe adrenal crisis, particularly under stressful conditions such as infection. Renal abnormalities in SS occur rarely. Only few cases have been reported in which AKI was caused by rhabdomyolysis.<sup>[11-13]</sup> AKI has been defined as rapid decline in kidney function, as measured by rising serum creatinine or decline in urine output (oligo/anuria). Introduced by Acute Kidney Injury Network, specific criteria exist for diagnosing AKI.<sup>[16]</sup> Our case presented with rapid deterioration of renal function in the form of oliguria together with rise in serum creatinine, thus meeting the criteria for AKI. Although, as stated earlier, AKI can occur in SS, hypothyroid myopathy is the most common etiological factor.<sup>[11-13]</sup> Hypothyroid myopathy is usually manifested by delayed relaxation of tendon reflexes, muscle stiffness, proximal muscle weakness, myalgia, muscle cramps, and occasional elevated muscle enzymes. However, rhabdomyolysis is rare. Rhabdomyolysis can occur spontaneously or is precipitated by hypoxemia, hypotension, sepsis, or vigorous exercise.<sup>[11]</sup> The exact cause of rhabdomyolysis in hypothyroidism is unclear, but both impaired glycogenolysis and oxidative mitochondrial metabolism have been implicated.<sup>[11-13]</sup>

Although our patient had subtle features of hypothyroid myopathy as revealed by history, examination, and lab evaluation, there was no evidence of rhabdomyolysis. The most probable cause of AKI in our patient was chronic hypocortisolemia as renal function in our patient rapidly improved after initiation of intravenous hydrocortisone; an association between adrenal insufficiency and disturbed renal function has been demonstrated repeatedly. A study was done by Christine Waterhouse and Henry Keutmann in 1947, in which kidney function of 13 patients with adrenal insufficiency was studied. It was concluded that there is reduction in effective vascular bed in the kidney, resulting in decreased renal plasma flow with concomitant decrease in the rate of glomerular filtration.<sup>[17]</sup> Besides, it has been found that cortisol has major effects on hemodynamics and absence of cortisol causes decrease in cardiac index with an inadequate response of systemic vascular resistance to maintain the mean arterial pressure.<sup>[18]</sup>

In summary, a middle-aged woman with SS presented with AKI which reversed completely with conservative management including glucocorticoids. Cause of AKI possibly was secondary adrenal insufficiency.

## REFERENCES

1. Kelestimur F. Sheehan's syndrome. *Pituitary* 2003;6:181-8.
2. Zargar AH, Singh B, Laway BA, Masoodi SR, Wani AI, Bashir MI. Epidemiological aspects of postpartum pituitary hypofunction (Sheehan's syndrome). *Fertil Steril* 2005;84:523-8.
3. Shivaprasad C. Sheehan's syndrome: Newer advances. *Indian J Endocrinol Metab* 2011;Suppl 3:S203-7.
4. Zargar AH, Laway BA. Inadequate obstetric care and Sheehan's syndrome in young women. *Indian J Endocrinol Metab* 2008;12:1-2.
5. Gei-Guardia O, Soto-Herrera E, Gei-Brealey A, Chen-Ku CH. Sheehan syndrome in Costa Rica: Clinical experience with 60 cases. *Endocr Pract* 2011;17:337-44.
6. Zargar AH, Masoodi SR, Laway BA, Shah NA, Salahuddin M, Siddiqi M, *et al.* Clinical spectrum of Sheehan's syndrome. *Ann Saudi Med* 1996;16:338-41.
7. 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;15 Suppl 3:S238-41.
8. Laway BA, Bhat JR, Mir SA, Khan RS, Lone MI, Zargar AH. Sheehan's syndrome with pancytopenia—complete recovery after hormone replacement (case series with review). *Ann Hematol* 2010;89:305-8.
9. 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.
10. Laway BA, Alai MS, Gojwari T, Ganie MA, Zargar AH. Sheehan syndrome with reversible dilated cardiomyopathy. *Ann Saudi Med* 2010;30:321-4.
11. Soltani P, Rezvanfar MR, Pirasteh S. Acute renal failure in a patient with Sheehan syndrome and rhabdomyolysis. *Iran J Kidney Dis* 2008;2:50-2.
12. Mooraki A, Broumand B, Neekdoost F, Amirmokri P, Bastani B. Reversible acute renal failure associated with hypothyroidism: Report of four cases with a brief review of literature. *Nephrology (Carlton)* 2003;8:57-60.
13. Sekine N, Yamamoto M, Michikawa M, Enomoto T, Hayashi M, Ozawa E, *et al.* Rhabdomyolysis and acute renal failure in a patient with hypothyroidism. *Intern Med* 1993;32:269-71.
14. Goswami R, Kochupillai N, Crock PA, Jaleel A, Gupta N. Autoimmunity in patients with Sheehan's syndrome. *J Clin Endocrinol Metab* 2002;87:4137-41.
15. Laway BA, Ganie MA, Wani IR, Butt TP. Multiple spontaneous pregnancies in Sheehan's syndrome with preserved gonadotroph function. *The Endocrinologist* 2009;19:253-4.
16. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, *et al.* Rife criteria for acute kidney injury is associated with hospital mortality in critically ill patients: A cohort analysis. *Crit Care* 2006;10: R73.
17. Waterhouse C, Keutmann EH, Cusson KY. Kidney function in adrenal insufficiency. *J Clin Invest* 1948;27:372-9.
18. Connor A, Care S, Taylor J. Addison's disease presenting with acute kidney injury. *Clin Med* 2010;10:515-6.

**Cite this article as:** Bhat MA, Laway BA, Allaqaband FA, Kotwal SK, Wani IA, Bandy KA. Acute renal failure: A rare presentation of Sheehan's syndrome. *Indian J Endocr Metab* 2012;16:306-9.

**Source of Support:** Nil, **Conflict of Interest:** None declared.