Indian Journal of Medical Case Reports ISSN: 2319–3832(Online)
An Open Access, Online International Journal Available at http://www.cibtech.org/jcr.htm
2017 Vol.6 (2) April-June, pp. 3-6/Yadavalli et al.

Case Report

HYPONATREMIC ENCEPHALOPATHY WITH PANHYPOPITUITARISM AS A MANIFESTATION OF LATE ONSET SHEEHAN'S SYNDROME

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ABSTRACT
Sheehan's syndrome is postpartum pituitary necrosis which manifests itself with varying degrees of hypopituitarism. These manifestations can either be immediate as in postpartum lactation failure or late with subtle signs of hypopituitarism. The rare forms of presentation include circulatory collapse, hyponatremia, diabetes insipidus, hypoglycemia, congestive cardiac failure or psychosis. Herein we report a case who presented with features of hyponatremia and panhypopituitarism nearly twenty three years after her last pregnancy.

Keywords: *Encephalopathy, Hyponatremia, Panhypopituitarism, Postpartum, Sheehan's Syndrome*

INTRODUCTION
Sheehan's syndrome is a potentially life threatening condition resulting in hypopituitarism following postpartum hemorrhage and hypotensive shock during childbirth. The excessive acute blood loss deprives the body of oxygen and leads to ischemic necrosis of the pituitary. In literature it has been described that the presentation of Sheehan's syndrome can either be an acute form recognized within hours to-days after delivery or chronic form recognized in weeks-to-years after delivery (Molitch, 1998). Although, rare is still one of the commonest causes of hypopituitarism in developing countries due to lack of facilities to treat or prevent postpartum hemorrhage (Montgomery *et al*., 2014). Women present with a varying degree of symptoms ranging from panhypopituitarism to only selective deficiencies, failure to lactate and amenorrhea are common initial symptoms; however, many times women may be asymptomatic until triggered by a stressing factor. Hyponatremia is a rare acute presentation of Sheehan's syndrome which was seen in our case. The treatment of Sheehan's syndrome involves lifelong hormone replacement therapy.

CASES
A 52 year old female who is a known case of hypothyroidism presented with the complaints of vomiting, five episodes since morning, irrelevant talk for the two to three days and generalized weakness for one week. All her symptoms started one week after a ten day excursion. Patient denied any history of loose stools, pain abdomen, fever, dizziness or headache. She was on regular treatment for hypothyroidism (Tablet Thyronorm 25mcg OD). On admission, her vitals were stable, Pulse: 60bpm, blood pressure: 106/68 mmHg, Respiratory rate: 20/min, SpO2 saturation: 98% and was afebrile. Local examination showed dry tongue with signs of mild dehydration. Her systemic examination showed no detectable abnormality. Initial work up done showed hyponatremia (Na^+: 115.6) and a low TSH: (0.38) and low cortisol levels (Table 1)
The patient was admitted to ICU in view of hyponatremia and dehydration and correction for the same was started with 3% sodium chloride. Routine investigations done such as complete blood count, urine routine, renal function test and liver function tests were within normal limits. The initial saline fluid resuscitation reversed the signs of dehydration. The sodium levels was corrected slowly and normalized after 72 hours. Further investigations done showed increased urine and serum osmolality. USG abdomen

showed mild fatty changes in liver and cholelithiasis. Further imaging revealed a normal CT Brain and 2D echocardiography. MRI of brain revealed empty sella with atrophic anterior pituitary (Figure 1).

Table 1: Investigations

	INV	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7
1	Hemoglobin (gm/dl)	11.5						
2	PCV	32.6						
3	TLC (cells/mm^3)	4700						
4	Platelet count(cells/mm^3	2.5						
5	ESR (mg/dl)	13						
6	Serum creatinine(mg/dl)	0.7						
7	BUN (mg/dl)	7.2						
8	Uric Acid (mg/dl)	1.5						
9	Sodium(mEq/l)	115.6	112.4	120.0	125.0	132.0		
10	Potassium (mEq/l)	4	4.8	4.8	5.1	4.3		
11	Chloride (mEq/l)	82.9	83.8	90.0	93	96		
12	Urine Albumin		nil					
13	Urine Sugar		nil					
14	Urine WBC		3-4					
15	Urine RBC		1-2					
16	Urine Sodium mmol/L		135.9					
17	Ser Calcium(mg/dl)	7.9						
18	Ser Phosphorus (mg/dl)	3.5						
19	Ser TSH (microIU/ml)	0.38						
20	Free T4 (ng/dl)			0.62				
21	Cortisol, random (3.09-22.4microg/dl)	0.2						
22	Cortisol, AM (5-23micrg/dl)			0.2				
23	Cortisol, PM			42.2				
24	Urine Osmolality		345					
25	Ser Osmolality		255					
26	ALP (U/L)	60						
27	AST (U/L)	31						
28	ALT (U/L)	21						
29	GGT (IU/L)	18						
30	Total Bil (mg/dl)	0.77						
31	Direct Bil (mg/dl)	0.18						
32	Total Protein (g/dl)	6.6						
33	Albumin (g/dl)	3.9						
34	Ser Globulin (g/dl)	2.7						
35	A/G Ratio	1.4						
36	CPK (U/L)			1640		501		
37	FSH (mIU/ml)			3.77				
38	LH (mIU/ml)			1.06				

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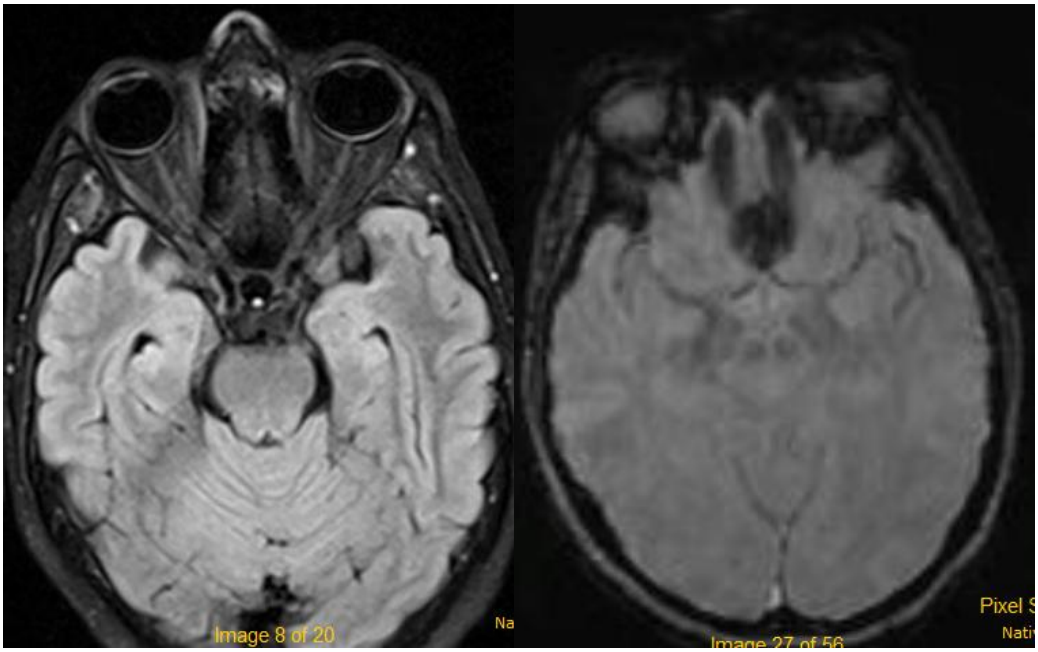

Figure 1: Empty Sella Turcica with Atrophic Anterior Pituitary

On further probing regarding menstrual history, patient revealed history of amenorrhea since twenty three years. She had a history of postpartum hemorrhage during the delivery of her second child, one year later she developed amenorrhea. Investigations were sent for LH (luteinizing hormone) and FSH (Follicle-stimulating hormone) levels which were low. Her CPK levels were elevated (1640U/L). In view of panhypopituitarism and history PPH, Sheehan's syndrome was suspected and the patient was started on Tab. Hydrocortisone (10mg-5mg-5mg). Vitamin D supplementation was also given. The sodium levels soon returned to within normal limits. She improved symptomatically and was discharged home.

DISCUSSION

Sheehan's Syndrome (SS) is defined as a result of ischemic pituitary necrosis due to severe postpartum hemorrhage and/or decreased blood pressure. Sheehan described pituitary infarction and panhypopituitarism after a postpartum hemorrhage in 1938, but the mechanism of ischemia is still not clear. Postpartum hemorrhage (PPH) is the leading cause of maternal death in developing countries and accounts to nearly one quarter of all maternal deaths (Montgomery *et al.*, 2014). It has been noted there is variable degree of hypopituitarism in nearly one-third of patients with severe postpartum hemorrhage. The clinically symptomatic SS are relatively uncommon but many have impaired neurohypophyseal function tests (Atmaca *et al.*, 2007). The underlying pathogenesis of SS is vasospasm, thrombosis and vascular compression of the hypophyseal arteries have been described as possible causes of the syndrome. The reason why it occurs in pregnant ladies has been attributed to enlargement of pituitary gland, small sellar size, disseminated intravascular coagulation and autoimmunity which have been suggested to play a role in the pathogenesis of SS. It is of note that majority of the deliveries were conducted at home. A epidemiological study from the Kashmir valley in the India estimated the prevalence to be about 3% for women above 20 years of age, almost two thirds of whom had delivered babies at home (Atmaca *et al.*, 2007; Zargar *et al.*, 2005).

The time of clinical symptoms of SS can either be in immediate postpartum period with lactation failure or after many months to years after the causative labor. The extent of anterior pituitary dysfunction varies in different series. The deficiency of growth hormone (GH) and prolactin (90–100%) was the most common, while deficiencies in cortisol secretion, gonadotropin and thyroid stimulating hormone (TSH) ranged from 50 to 100% (Sert *et al.*, 2003). At least 75% of pituitary must be destroyed before clinical

manifestations become evident. GH deficiency is very common in SS because somatotrophs are located in the lower and lateral regions of the pituitary gland and are most likely to be damaged by ischemic necrosis of the pituitary (Huang *et al.*, 2000). In a study of 60 patients, the average time between the previous obstetric event and diagnosis of SS was 13 years (Gei-Guardia *et al.*, 2011). Characteristic clinical manifestations of SS are failure to lactate or to resume menses, genital and axillary hair loss, asthenia and weakness, fine wrinkles around the eyes and lips, signs of premature aging, dry skin, hypo-pigmentation and other evidence of hypopituitarism. The absence of amenorrhea in the postpartum period or presence of postpartum lactation, however, does not rule out the diagnosis. Uncommonly, it can present acutely with circulatory collapse, severe hyponatremia, diabetes insipidus, hypoglycemia, congestive cardiac failure or psychosis (Weston *et al.*, 2005). The most common electrolyte disturbance was hyponatremia, occurring in 33–69% of all cases. The mechanisms responsible for hyponatremia, were hypothyroidism and glucocorticoid deficiency which by decreasing free water clearance independent of vasopressin cause hyponatremia. SIADH and volume depletion also contribute to some extent (Berretta *et al.*, 2008).

Our patient presented with irrelevant talk and vomiting, with a serum sodium level of 112 meq/liter, suggestive of a hyponatremic encephalopathy. The elevated CPK was attributed to her hyponatremia induced myopathy and partly to her recent travel. Her serum levels of cortisol, FSH and LH were all low suggesting panhypopituitarism.

Conclusion

In conclusion, diagnosis of SS is difficult and challenging. A high index of suspicion and systematic approach to hyponatremia will help in early diagnosis. A empty sella on MRI is neither diagnostic or essential. Sheehan's syndrome should be a part of differential diagnosis in all postpartum women who present with confusion and neuropsychiatric manifestations due to hyponatremia.

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