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Case Report

Sheehan's syndrome with recurrent hyponatremia and anemia: A case report

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Abstract. Sheehan's syndrome (SS) occurs due to ischemic pituitary necrosis after severe postpartum hemorrhage. The clinical spectrum of SS is wide and changes from non-specific complaints such as weakness, fatigue, and anemia to severe pituitary insufficiency including secondary adrenal failure and hypothyroidism resulting in coma and death. We present a case of Sheehan's syndrome who had recurrent hyponatremia episodes due to the late diagnosis of the disorder.

Key words: Sheehan's syndrome, postpartum hemorhage, recurrent hyponatremia

1. Introduction

Sheehan's syndrome (SS) occurs due to ischemic pituitary necrosis after severe Postpartum hemorrhage (PPH), and it is described for the first time in 1937. SS is one of the important etiology of hypopituitarism in underdeveloped or developing countries (1,2). The definitive pathogenesis of SS has not been clearly understood, yet. However, the main mechanism is the infarction secondary to insufficient blood flow to the pituitary gland, and it may be due to thrombosis or vascular compression (1-3).

The diagnostic criteria recommended for SS are as follows: typical history of severe postpartum blood loss, severe hypotension or shock which result in blood transfusion or fluid replacement, postpartum lactation failure, discontinuation of the menses after the delivery, partial or complete anterior pituitary insufficiency, and empty sella on CT or MRI (1-4).

Hyponatremia and hypoglycemia in SS may occur acutely during immediate postpartum period or chronically in following times (5,6). Many cases with severe hyponatremia developing 16 years after postpartum bleeding that serum sodium levels are below 125 mmol/L have been reported (7). Adrenal insufficiency is one of the most likely causes of hyponatremia in Sheehan's syndrome. SIADH may also be responsible for hyponatremia in patients with Sheehan's syndrome.

Hyponatremia (HN) has a delayed onset and can be due to varying causes including hypocortisolemia, hypothyroidism, hypovolemia, or a syndrome characterized by inappropriate secretion of ADH (SIADH). In contrast, the disease is unusually seen in the early postpartum period due to SS (8). Laboratory parameters will commonly show HN occurring from 33% to 69% of cases and represent the most common electrolytic disorder in SS (7).

Here we present a patient with SS who had recurrent HN episodes due to the late diagnosis of the disorder. According to our knowledge, this is the first case of SS with recurrent HN attacks due to delayed diagnosis reported in the literature.

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2. Case report

A 62-year-old female patient who had been previously diagnosed as Sheehan syndrome was referred to the Emergency Department because of recurrent HN. Blood pressure was 90/60 mm/Hg, pulse: 63/min, fever: 36.5°C and she was mildly dehidrated, JVP was 2 mmHg. Nervous system examination was normal. The patient had four attacks of HN in the last five years. She also had weakness, fatigue, and other nonspecific complaints. Thyroid tests were measured as fT4: 0.6 ng/dL ve TSH:0,8 mLU/mL at the time of diagnosis. Than thyroxine treatment was administered. At the time of HN attacks, saline infusion had been given and thyroxine replacement therapy had been started in a state hospital because of the diagnosis of hypothyroidism. After a detailed obstetrical history, it was noticed that the patient delivered her last baby at home approximately 30 years ago when she was gravidy 7, parity 6. According to the history, since severe PPH occurred following the placental detachment she was hospitalised. Uterine curettage was performed and three units of blood were transfused. She stated lack of lactation and amenorrhea after the delivery. Facial appearance of the patient was consistent with SS regarding hypopituitarism (Figure 1). Gynecological examination revealed absence of the pubic and axillary hair and also, atrophic ovaries and external genital organs.

The laboratory tests revealed a normocytic normochromic anemia with low hemoglobin concentration (10.5g/dL) and low sodium levels (12mEq/L). Basal hormone levels were showed on table 1. The biochemical parameters revealing recurrent hyponatremia are showed in table 2. Low blood osmolality and elevated urine osmolality suggested SIADH. Dynamic tests regarding panhypopituitarism including TRH stimulation test, LHRH stimulation test, and insulin tolerance test (ITT) were done (Table 3). The pituitary MRI of the patient was empty sella consistent with SS (Figure 2a, 2b).

Panhypopituitarism was suspected, and the diagnosis of SS was confirmed by basal hormonal levels, stimulation tests, and imaging methods. All the anterior pituitary hormones were deficient including severe adrenocortical insufficiency and hypothyroidism.

Based on the clinical and laboratory findings, the patient had saline infusion. The complaints were resolved completely after glucocorticoid (prednisolone) and thyroid (thyroxine) replacement therapies. Estrogen replacement was never made in follow. During one-year follow up, she had no complaints regarding hormone deficiencies or HN.

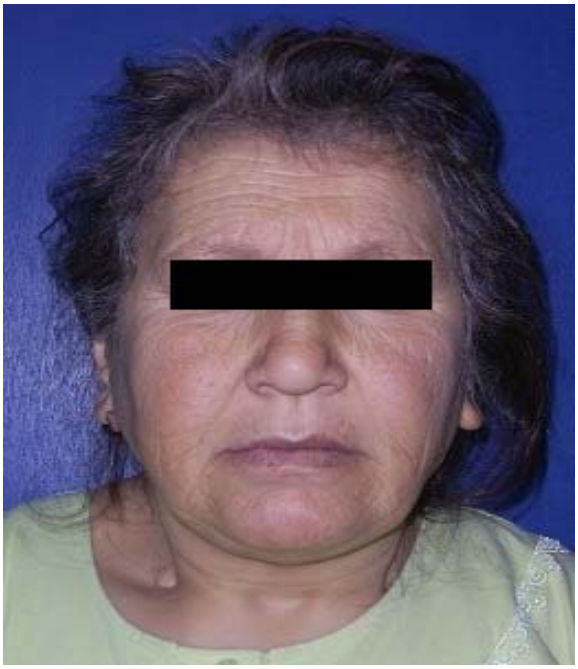

Fig. 1. The facial appearance of the patient is consistent with SS regarding GH deficiency and hypogonadism.

Table 1. Basal hormone levels

	Blood	Normal Range	
FSH	<0.1	Postmenopausal 26.72-133.41	mIU/mL
LH	<0.1	Postmenopausal 10.39-64.57	mIU/mL
E2	<10	10-28-	pg/mL
FT3	1.16	1.8-4.8	pg/mL
FT4	0.64	0.8-1.9	ng/dL
TSH	2.28	0.35-4.94	mIU/mL
PRL	1.8	5.18-26.53	ng/mL
GH	0.03	0.1-10	ng/mL
IGF-1	31	123-463	ng/mL
ACTH	<3.0	0-46	pg/mL
Cortisol	<2.1	3.7-19.4	µg/dL

Table 2. Biochemical results

	Blood	Urine
Osmolality (mosm/kg)	263	624
Sodium (mmol/l)	126	152
Chloride (mmol/l)	105	82
Potassium (mmol/l)	4.1	48
Glucose mg/dl	71	0
Protein g/l	55	0
Creatinine mg/dl	0.6	–

Table 3. Dynamic tests and peak results

		Basal level	Peak response
Insulin hypoglycemia test	Cortisol (µg/dL)	<2.1	5.6
	GH (pg/ml)	0.03	0.2
TRH test	TSH (mIU/ml)	2.28	2.36
	FT3 (pmol/Lt)	1.16	
	FT4 (pmol/Lt)	0.64	
LHRH test	FSH (IU/Lt)	<0.1	<0.1
	LH (IU/Lt)	<0.1	<0.1
	Estradiol (pg/ml)	<10	

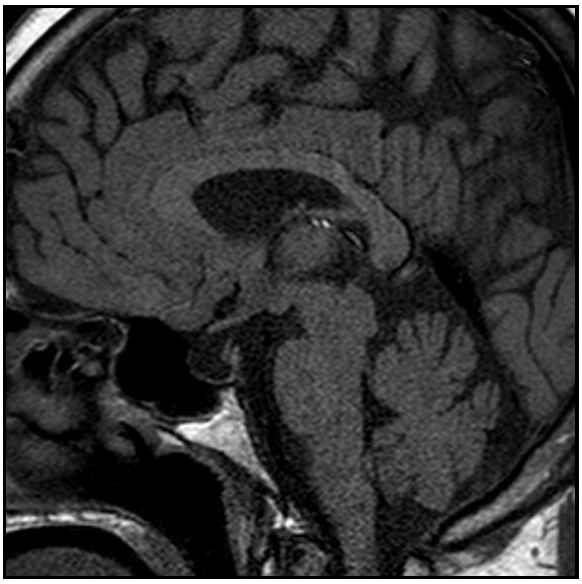

Fig. 2a. Sagittal MRI section displaying empty sella.

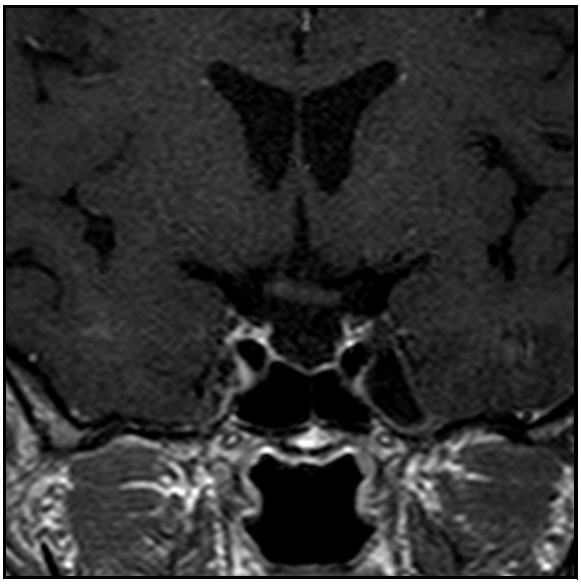

Fig. 2b. Sagittal MRI section displaying empty sella.

3. Discussion

The definitive etiopathology of SS has not been clearly understood. But the basic mechanism is thought to be infarction secondary to ischaemia of the anterior pituitary gland, and it may be due to vasospasm, thrombosis or vascular compression (1,7,9). The clinical spectrum of SS is very large and changes from non-specific complaints such as weakness, fatigue, anemia, and HN to severe pituitary insufficiency including secondary adrenal failure and hypothyroidism resulting in coma and death. Although a small percentage of patients with SS may cause rapid onset pituitary failure immediately after the birth, most cases have mild disease and go undiagnosed for a long time and they are managed inappropriately. Cases with SS commonly present months to years after the last birth complicated by severe vaginal bleeding with a history oflactation failure to resume menses and the findings of anterior hypopituitarism as in our case (1,9,10).

SS, also known as postpartum pituitary necrosis, may be diagnosed through clinical and laboratory tests. Deep periorbital and perioral wrinkles are characteristic of estrogen and growth hormone deficiency.In accordance with literature the facial appearance of the patient is consistent with SS regarding GH deficiency and hypogonadism (1). Panhypopituitarism is often accompanied by normocytic normochromic anemia as in the current case, which is usually mild and seldom below 9 g/dL values. The anemia in SS is due to cortisol deficiency, hypothyroidism and hypogonadism. The exact cause of pancytopenia in these patients is not clear, however adrenal, thyroid and androgen hormone deficiencies are likely the major contributors to the anemia etiology and glucocorticoids have a predominant role in reversing the pancytopenia associated with Sheehan's syndrome (10-12).

In the present report, the case had anemia, which improved after adequate cortisone, thyroid hormone. While glucocorticoids stimulate

erythropoiesis, thyroid hormones stimulate both erythropoietin production and the proliferation of erythroid progenitor cells. The other noteworthy clinical finding in the case was HN that is a common electrolytic abnormality, occurring in 33% to 69% of all cases with SS (8). The etiologic factors of HN in the present case were volume depletion, cortisol deficiency and hypothyroidism. In SS patients, HN responds to combined saline (NaCl), hydrocortisone and thyroxine treatment. As a hormone replacement therapy, initially glucocorticoids should be started, than thyroxine should be given in terms of the management of HN and anterior pituitary failure. Also, saline infusion is necessary in addition to hormone therapy. The normalization of serum sodium levels may be abrupt instead of gradual in the treatment of HN in patients with SS. It should be kept in mind that normalizing serum sodium levels without causing any cerebral alterations including central pontinemyelinolysis is very important, when HN is rapidly controlled (8). The case had asymptomatic hyponatremia, that is not an ordinary lab finding. However, in spite of the recurrent replacement therapy in terms of saline infusion, the underlying etiology did not diagnosed by admitted clinics. Also there is only replacement therapy for secondary hypothyroidism and when giving the thyroxin therapy, especially for secondary hypothyroidism, we have to rule out adrenal insufficiency. Also, before starting for the differential diagnosis in case of hyponatremia, we have to rule out that the patient is eucortisolemic or euthyroidic.That is why, this may be an educative case report in aspect of these topics. Also, there is a misdiagnosis and malpractice, especially in terms of thyroxin replacement therapy in a patient with secondary adrenal insufficiency. According to us, it may cause adrenal crisis. Therefore, this is more important than hyponatremia treatment. By this case, we want to point out that hyponatremia may be recurrent and may be due to Sheehan syndrome. Also, the differential diagnosis of the patient can be sometimes much more important than the supportive therapy. Hyponatremia in these patients may be due to decreased free water clearance by hypothyroidism or glucocorticoid deficiency independent of vasopressin. Moreover, hypopituitiarism can stimulate the vasopressin secretion and cause hyponatremia by severe inappropriate ADH secretion. Hyponatremia in Sheehan syndrome can not be corrected by only sodium replacement (13). Although obstetrical care and medical facilities have been improved remarkably in our country, SS may still occur.

HN as the presenting manifestation of SS in the early post-partum period has been reported twice (12,14,15). However, according to our knowledge, recurrent HN episodes in patients with SS are not reported in the literature. Many hypotheses are suggested to explain HN in the existence of hypopituitarism. It is reported that hypersecretion of arginine vasopressin may have an important role in aspect of the abnormal water metabolism due to ACTH deficiency, and glucocorticoids induce normal water diuresis by inhibiting the secretion of it from the neurohypophysis. Hypothyroidism can also result in HN. It is revealed that hypothyroid cases have a decreased ability to excrete free water, fail to achieve maximum urine dilution, and show delayed excretion of a water load (9,14). Also, it is investigated that the correlation between serum arginine vasopressin levels and the capacity in excretion of water load is weak in patients with hypothyroidism (14,16).

However, the case had misdiagnosis and mistreated in aspect of the etiology of HN and hypothyroidism. She had initially thyroxine therapy that is contraindicated when the patient had also adrenal insufficiency. Therefore, this life threatening malpractice should not be forgotten, and the underlying disorder should be investigated if the patient has HN and central hypothyroidism. This delay may be sometimes due to the lack of symptoms or its misrecognition. In just case, the patient should be consultated with the related expert.

In conclusion, the current case report investigates a rather rare form of SS, which was presented with anemia and HN that significantly improved after adequate treatment including saline infusion, thyroxine andcortisone therapy. It should be kept in mind that if the patient has hypothyroidism, it may be associated with adrenal insufficiency. Therefore, firstly glucocorticoid replacement therapy should be given, and then thyroxine should be added to the treatment. Otherwise, adrenal crisis may become or deepened whether there is. On the other hand, SS is still an important problem in developing countries and one of the major cause in aspect of pituitary failure (11,12,14). According to our knowledge, this is the first case of SS in with recurrent HN episodes due to delayed diagnosis reported in the English literature.

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