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OLGU SUNUMU

Slow Developing Sheehan Syndrome with Spontaneous Pregnancies: A Case Report and Literature Review

Yavaş Gelişen Sheehan Sendromu ve Spontan Gebelikler: Bir Olgu Işığında Literatürün Gözden Geçirilmesi

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Abstract: Sheehan's syndrome is known as pituitary insufficiency that develops after bleeding and hypovolemia at birth or after birth. The pathological and clinical findings of Sheehan's syndrome were first described by Harold L. Sheehan. Due to improvements in obstetric care, the frequency of the disease has declined worldwide. Sheehan syndrome is a rare cause of hypopituitarism in developed countries. However, it is more common in underdeveloped and developing countries. Small sella size enlargement of the pituitary gland, autoimmunity also play a role in the pathogenesis of the disease. Depending on the pituitary damage, symptoms may appear immediately or years later.

It may be presented as isolated hormone deficiency or panhypopituitarism. For diagnosis, it is important to have a history of excessive hemorrhage at birth, amenorrhea, and the inability to breastfeed. Lymphocytic hypophysitis should be remembered in the differential diagnosis. In this review, a patient with severe post-partum hemorrhage, followed by a history of 3 pregnancies, was presented with a slow-developing and pan hypopituitarism-causing Sheehan's syndrome and current physiopathological data in Sheehan's syndrome were presented.

Keywords: Sheehan Syndrome, Pregnancy, Autoimmunity

Öz: Sheehan sendromu, doğumda veya doğumdan sonra kanama ve hipovolemiye bağlı gelişen hipofiz yetmezliği olarak bilinir. Sheehan sendromunu patolojik ve klinik bulguları ilk olarak Harold L. Sheehan tarafından tanımlanmıştır. Obstetrik takipteki gelişmeler nedeniyle, hastalığın sıklığı dünya çapında azalmıştır. Sheehan sendromu, gelişmiş ülkelerde hipopituitarizmin nadir bir nedenidir. Ancak, az gelişmiş ve gelişmekte olan ülkelerde daha yaygındır. Hipofiz bezinin küçük sella içerisinde büyümesi, otoimmünite de hastalığın patogenezinde rol oynar. Hipofiz hasarına bağlı olarak semptomlar hemen veya yıllar sonra ortaya çıkabilir.

Sheehan sendromu izole hormon eksikliği veya panhipopituitarizm olarak karşımıza çıkabilir. Teşhis için doğumda aşırı kanama, amenore ve emzirememe öyküsü olması önemlidir. Ayırıcı tanıda lenfositik hipofizit akla gelmelidir. Bu derlemede doğum sonrası şiddetli kanamalı ve ardından 3 gebelik öyküsü olan bir hasta, yavaş gelişen ve panhipopitüitarizme neden olan Sheehan sendromu olarak sunulmuş ve Sheehan sendromundaki güncel fizyopatolojik veriler ortaya konulmuştur.

Anahtar Kelimeler: Sheehan Sendromu, Gebelik, Otoimmünite

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1. INTRODUCTION

Sheehan's syndrome (SS) is pituitary insufficiency due to postpartum hemorrhage and hypovolemia (1). In developing countries, it is still one of the major causes of hypopituitarism. Excessive postpartum hemorrhage and prolonged hypotension may cause spasm or thrombosis of hypophyseal arteries leading to hypophysis necrosis and, ultimately, hypopituitarism (2). However, pathogenesis is not clear in SS. Because such endocrine disorders are not seen in most obstetric cases with excessive bleeding. Due to excessive bleeding, reduced blood volume may lead to anterior pituitary necrosis, and this necrosis may not affect all of the pituitary hormones (2). It may be isolated as gonadotropin reserves are protected, and pregnancy may occur in the future, but menstruation rarely happens (3).

Patients may present with various signs and symptoms ranging from nonspecific symptoms to coma. Due to the slow development of SS, diagnosis may not be possible. The slow development of SS is mainly attributed to autoimmunity. Another clinical situation is that the pregnancy that occurred in patients with SS causes pituitary function improvement by making pituitary hyperplasia (4).

In this review, a patient with postpartum hemorrhage and agalactia, followed by three pregnancies, and a slow-developing and late-diagnosed SS is presented. We aimed to evaluate autoimmunity from current physio pathologic data about SS and to predict that pregnancies in SS patients may have improved pituitary function.

Ethical Declaration

Informed consent was obtained from the participant and Helsinki Declaration rules were followed to conduct this study.

2. CASE REPORT

A 55-year-old female patient with no known systemic disease history was admitted to the emergency with complaints of diarrhea, nonspecific nausea and vomiting, fatigue, and fever lasting for two days. She had three live births, and she used medication for hypothyroidism for a while, and then stopped. In her physical examination; she was conscious, her blood pressure was: 100/60 mm/Hg, pulse was: 90/bpm., fever was: 37°C. Her skin and conjunctivae were faint, oropharynx had dehydrated appearance, and other system findings were within normal limits.

Her laboratory findings were; C-reactive protein (CRP): 18mg/L, erythrocyte sedimentation rate: 30mm/h, in biochemistry; creatinine: 2.75mg/dL, urea: 52mg/dL, thyroid-stimulating hormone (TSH): 1.5uIU/mL, feces examination: 10-12 erythrocytes, 8-10 leukocyte amoebic cysts in every area, white blood cell: 8.7 x10^3/µ, hemoglobin: 12.7g/dL, hematocrit: %38.6, MCV: 96.3 fL, platelet: 217 10^3/µl /µL. Other parameters and urinalysis were normal. The patient was hospitalized for prerenal acute renal failure due to diarrhea. The patient received the appropriate fluid replacement, metronidazole 2x500 mg IV, and symptomatic treatment. Creatinine and CRP values were reduced in the patients' follow-ups. On the eighth and last day of her admission, Na was: 128 mmol/L, and the patient was discharged on her request. Low Na values were attributed to iatrogenic causes. One week later, the patient was brought back to the emergency due to excessive fatigue, loss of appetite, and an altered state of consciousness. All other biochemical values except for Na: 114 mmol / L and hemogram were normal. The patient was hospitalized due to acute symptomatic hyponatremia. Na deficit was calculated, and Na replacement was performed. The patient's Na values were increased initially but then decreased again. Her electrocardiogram (ECG) was normal except for low voltage in all derivations. Ejection fraction was 60% in echocardiography, pericardial effusion without tamponade was detected. Abdominal ultrasonography of the patient revealed bilateral pleural effusion, minimal perihepatic, and perisplenic free fluid. The patient's anamnesis deepened, and she told that she first gave birth 35 years ago, with excessive postpartum bleeding, and needed to have a blood transfusion in the hospital. She also couldn't lactate after birth and had no menstruation. The patient said that she was referred to different doctors for periods of nonspecific complaints that include fatigue and weakness after birth. The patient wanted to conceive again but could not get pregnant, but she could become pregnant seven years after her first pregnancy. She also wanted to conceive after the second gestation, but she could only conceive after five years. The patient who had no headache after her pregnancy went to the neurology doctor with a complaint of headache one year ago, and brain magnetic resonance (MR) was examined, and no pathology was detected. There weren't any traits in her family history.

Considering all this information, hormone examinations were requested considering the pituitary insufficiency in the patient; TSH: 1.4 uIU/mL (0.34-5.6), free T4: 0.1 ng/ dL (0.93-1.7), free T3 1.3 pg/mL (2-4.4), FSH 2.8 mIU/mL (menopause: 25.8-134.8), LH: 0.75 mIU/ mL (menopause: 7.7-58.5), prolactin: 1.34 ng/mL (4.7-23.3), cortisol: 2 µg/dL (6.2-19.4) was found.

Partial empty sella in the pituitary gland was detected in the pituitary MR (Figures 1 and 2). As the patient was unable to breastfeed her three children, in terms of

exclusion of possible breast pathologies, a breast MR was examined, and no pathology was detected.

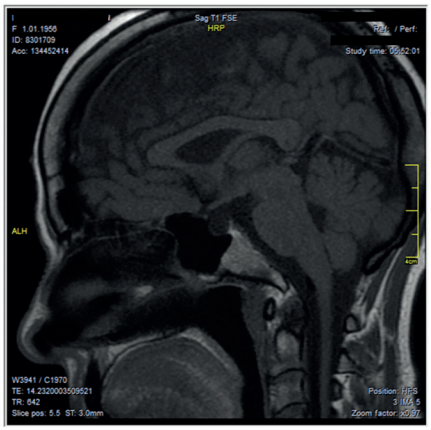

Figure 1: The sagittal T1 weighted magnetic resonance imaging of the brain shows an empty sella turcica

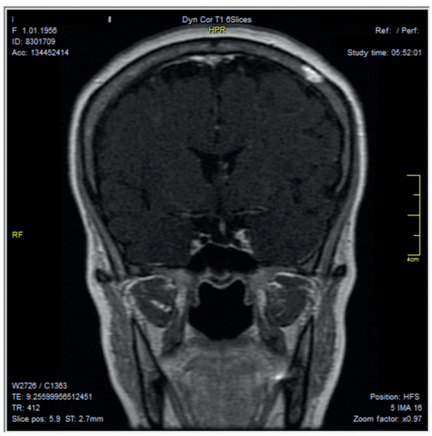

Figure 2: The Coronal T1 weighted magnetic resonance imaging of the brain shows an empty sella turcica

The patient was diagnosed with a slowly developing SS. The patient was initiated 2x1 5 mg oral prednisolone therapy. After three days, 25 mg levothyroxine sodium was added to the treatment. After hormone replacement therapy, the general condition of the patient improved quickly, blood pressure and sodium levels rose. After hormone replacement Na: 138 mmol / L was detected. The patient was discharged with outpatient clinic control recommendations.

3. DISCUSSION

The pituitary gland enlarges physiologically during pregnancy. This condition is considered to be due to the hyperplasia of prolactin-secreting cells under the influence of increasing estrogen. After birth, the pituitary gland gradually involutes. Physiologically, these involutions occur frequently in women. In some diseases, pathological involution may occur in the pituitary gland. These include postpartum pituitary necrosis, diabetes, vascular diseases, increased intracranial pressure, meningitis, cavernous sinus thrombosis, and head trauma.

The main event in SS is the anterior pituitary necrosis due to excessive bleeding resulting in reduced blood volume (2-4). The pathogenesis of SS is not fully known. Expansion of the pituitary gland, small sella size, disseminated intravascular coagulation, and autoimmunity are implicated in the pathogenesis of the disease. Normal functions continue even if the pituitary gland is damaged by 50% (2). Partial (isolated hormone deficiency) or total loss of function may occur if the gland is damaged by 70-90% (5). It has been reported that only 32% of pregnant women with excessive postpartum hemorrhage have developed hypopituitarism (6). It has been reported with cases in the literature that SS patients may be spontaneously conceived (4, 7). Pregnancy occurring in SS patients can improve the pituitary function by enlarging the pituitary gland (8).

Many patients with SS are diagnosed many years later. In a study performed with 60 patients, the time between the obstetric event and the diagnosis of SS was found to be 13 years (9). In the study conducted by Dökmetaş et al. (10) in our country, the mean time between the postpartum hemorrhage and the clinical findings of hypopituitarism was 26.8 ± 2.5 years (2 to 40 years), and in a study conducted by Sert et al. (11) 28 cases of SS were evaluated and the mean time between the postpartum hemorrhage and the clinical findings of hypopituitarism was found to be 13.9 ± 6.1 years (6 to 30 years). There are two cases of SS diagnosed in senescence in the literature, and both cases have been reported from our country (12).

TSH levels in hypothyroidism due to SS may be unexpectedly normal or high. The pulsatility of TSH secretion deteriorates and begins to be secreted in a tonic form. Its biological activity is reduced. TSH response to TRH stimulation decreases (13).

The first finding in SS is the decrease or cessation in breast milk production, due to decreased prolactin secretion. This is followed by complaints of a decrease in pubic hair and menstrual irregularities such as amenorrhea and oligomenorrhea due to lack of gonadotropins. Symptoms of hypothyroidism and adrenal insufficiency may occur later (14). Some of the patients develop complete or incomplete empty sella syndrome years later.

Patients with SS can have hyponatremia. As the cause of hyponatremia, hypothyroidism may reduce free water clearance, glucocorticoid insufficiency may reduce free

water clearance independent of vasopressin, and hypopituitarism itself may cause inappropriate antidiuretic hormone (ADH) secretion by stimulating vasopressin secretion.

Hormone replacement therapy is used in patients with SS. Hydrocortisone treatment should be started initially. Because initiating a thyroxine therapy to the patient may affect glucocorticoid levels and may cause adrenal crisis (15).

4. CONCLUSION

In our case, we had a history of slow-developing SS, spontaneous conception, high probability of pituitary healing due to conception, subclinical course, high probability of increased TSH in a certain period, triggering by a stress factor such as infection, a deep hyponatremic period after curing dehydration, and hyponatremia that did not respond to sodium replacement but had the ability to respond to hormone replacement. As a result, SS patients can conceive spontaneously, pregnancy can improve pituitary functions, and thus panhypopituitarism may occur later. The cause of slow-developing SS may be autoimmunity. Patients with excess postpartum hemorrhage should be carefully monitored for slow-developing SS.

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