A decade without diagnosis: Sheehan’s syndrome

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ABSTRACT

Sheehan’s Syndrome (SS) occurs as a result of ischemic pituitary necrosis due to severe postpartum hemorrhage. We report a 41-year-old woman with a history of severe postpartum hemorrhage 18 years prior to presentation. During this period of time, she experienced severe fatigue. Three months prior to being admitted to our hospital, the patient started to notice alopecia, generalized edema and cognitive impairment. After proper investigation, laboratory tests and clinical findings indicated panhypopituitarism. In addition to neuroimaging and past medical history, SS was diagnosed and treatment started. We emphasize the importance of thorough investigation, further diagnosis and management of this condition (especially in third world countries), since SS is a neurological and endocrinological emergency and potentially life threatening.

Keywords: Sheehan’s Syndrome; Pituitary Insufficiency; Empty Sella

1. INTRODUCTION

Sheehan’s Syndrome (SS) is a result of ischemic pituitary necrosis due to severe postpartum hemorrhage. SS is characterized by varying degrees of anterior pituitary dysfunction. Some degrees of hypopituitarism occurs in nearly one third of patients with severe obstetric hemorrhage. Its epidemiology is discrepant depending on the location. The main reason for the different incidence relates to the quality of medical care a patient receives in her local hospital.

Although this condition has been first described seventy-five years ago [1], it still is not promptly diagnosed by physicians. In fact, it is under-diagnosed in third world countries, given that in these nations the proportion of home baby deliveries is high [2]. On the other hand, the incidence of Sheehan’s Syndrome in first world countries shows to have declined significantly.

Regarding the etiology, the most frequent causes of postpartum hemorrhage are uterine atony, trauma, retained placenta and coagulopathy [2,3].

The aim of this presented transcript is to report a case of a patient with a history of obstetric hemorrhage until the diagnosis of panhypopituitarism. This was due to ischemic necrosis. We will review the main topics of how the diagnosis was made, the main complementary tests and reviewing the disease in general. We intend to alert clinicians on how important it is to remember that SS can occur in any patient with a history of postpartum bleeding, and may be preceded with a clinical presentation of panhypopituitarism.

2. CASE PRESENTATION

A 41-year-old caucasian female was admitted to our hospital on October 1st, 2012. Her main complaint was weakness and edema (Figure 1). She presented with hair loss, bleeding gums and cognitive impairment. After further inquiry we found that she had been on amenorrhea for 6 years and that she had been on iron supplementation for anemia, which did not resolve despite the treatment.

Regarding her past medical history, she suffered from severe postpartum hemorrhage when she delivered her only child, 18 years ago. At this occasion, she needed to be admitted to the ICU and received blood transfusions. Furthermore, she was unable to breastfeed her child. There was no similar case in her family history. Physical examination showed generalized non-pitting edema, psychomotor lentification, altered level of consciousness and myxedema facies. Her blood pressure was 100 × 75 mmHg, heart rate of 80 beats per minute, respiratory rate of 16 respirations per minute, dry and coarse hair, alopecia and thinning of the outer third of her eyebrows.
Laboratory findings indicated normochromic normocytic anemia, free T4 level of 0.4 ng/mL and TSH level of 1.23 mUI/mL. We suspected central hypothyroidism. Therefore, the patient was started on 1.5 mcg/kg/day of levothyroxine and prednisone in doses of 5 mg/day.

As the clinical manifestations associated to the patient’s past medical history suggested Sheehan’s syndrome, related endocrinological tests were ordered (Table 1) as well as an MRI of the skull (Figure 2). After all these tests were performed the diagnosis of SS was made.

3. DISCUSSION

In 1937 Sheehan reported 11 cases of women who died in the puerperium, all of whom had necrosis of the anterior pituitary gland-adenohypophysis. Nine of the 11 cases had severe hemorrhage at delivery. The other two cases had no hemorrhage but were gravely ill prior to delivery [4]. Postpartum hypopituitarism has been known as Sheehan’s Syndrome ever since [5].

Regarding its pathogenesis, the basic process is infarctation secondary to the arrest of blood flow to the anterior lobe of the pituitary gland (usually there is blood loss of at least 1 to 2 liters and consequently hypovolemic shock). Whether this process results from vaso-spasm, thrombosis, or vascular compression is unclear. The fact that the posterior lobe of the pituitary is less commonly involved can be explained by how the neurohypophysis’ vascular supply arrangement: it contains an anastomotic ring of blood vessels, which the adenohypophysis lacks [6,7]. The patient described by us had these symptoms, consistent to that described in literature, as well as a history of significant blood loss after delivery, which resulted in a blood transfusion and admission to the intensive care unit.

Only a small number of patients with SS develop acute postpartum hypopituitarism after postpartum hemorrhage. The most frequent scenario is a woman with amenorrhea occurring years later, with the diagnosis of SS being made retrospectively. However, it is important to emphasize that SS is a neurological and endocrinological emergency and is potentially lethal [8]. According to a group of 60 patients with Sheehan’s Syndrome, studied by Gei-Guardia et al. [9], the period of time between the postpartum episode of bleeding and the diagnosis of SS is 13 years. Focusing again on our patient, she was diagnosed after 18 years from the obstetric event of bleeding.

In Sheehan’s syndrome, inability to lactate after delivery due to prolactin deficiency and the development of amenorrhea from gonadotrophin deficiency classically occurs. In addition, these patients become infertile, there is failure to regrow shaved pubic hair and signs of hypothyroidism and hypoadrenalism occur [10,11]. Our patient, in agreement to documented literature, informed us that she could not lactate after delivery and that she noted failure to regrow her pubic and axillary hair.

Figure 1. Patient at presentation. Note the facial edema and alopecia.

Figure 2. Sagittal gadolinium-enhanced T1-weighted MR image shows an empty sella (red circle).

Table 1. Laboratory findings at presentation.

<table>
<thead>
<tr>
<th>Laboratory findings at presentation</th>
<th>Patient’s measurements</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth hormone (ng/mL)</td>
<td>0.1</td>
<td>0.06 - 5.00</td>
</tr>
<tr>
<td>Prolactin (ng/mL)</td>
<td>0.83</td>
<td>3.46 - 19.40</td>
</tr>
<tr>
<td>Follicle-stimulating hormone (mUI/mL)</td>
<td>0.36</td>
<td>27.72 - 133.4 (menopause)</td>
</tr>
<tr>
<td>Luteinizing hormone (mUI/mL)</td>
<td>0.09</td>
<td>10.39 - 64.57 (menopause)</td>
</tr>
<tr>
<td>Plasmatic cortisol at 8 am (mcg/mL)</td>
<td>0</td>
<td>3.7 - 18.4</td>
</tr>
<tr>
<td>24-Hour urinary free cortisol (mcg/24h)</td>
<td>0.4</td>
<td>4.3 - 176.0</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>28.7</td>
<td>36.7 - 46.3</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>9.9</td>
<td>12.5 - 15.7</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>86.7</td>
<td>80 - 99</td>
</tr>
<tr>
<td>MCHC (g/dL)</td>
<td>34.5</td>
<td>32.2 - 36.0</td>
</tr>
</tbody>
</table>

a. MCV: mean corpuscular volume; MCHC: mean corpuscular hemoglobin concentration.
Regarding laboratory exams, in order to diagnose and confirm SS, literature recommends dosing the following substances: prolactin, free thyroxine (fT4), thyroid-stimulating hormone (TSH), cortisol, luteinizing hormone (LH), estradiol and insulin-like growth factor 1 (IGF-1) [1,12,13]. Our patient reports showed low levels of all these hormones, except for adrenocorticotropic hormone (ACTH), which was not measured (Table 1).

Similar to what occurred to our patient, there have been reports of individuals that were submitted to long-standing clinical treatment for chronic anemia, which never resolved, before actually being diagnosed with Sheehan’s syndrome [14-17]. Gokalp et al., in 2009, showed that 80% of the studied population with this syndrome suffered from anemia. Leucopenia, iron deficiency and thrombocytopenia were also commonly found on these patients [18]. These hematologic findings, and their refractoriness to standard clinical therapy, showed to be useful for ultimately diagnosing Sheehan’s syndrome.

The neuroimaging characteristics of SS are distinctive. In pregnancy, there is enlargement of the pituitary from diffuse nodular hyperplasia of prolactin secreting cells. The MRI shows the normal pituitary gland is largest in the immediate postpartum period, measuring up to 11.8 mm in height and convex in appearance. The anterior pituitary is usually hyperintense on T1-weighted images in pregnant and postpartum women when compared to controls. After delivery, the size of the pituitary gland rapidly returns to normal beyond the first week postpartum. In a chronic phase of the disease, neuroimaging classically shows atrophy of the pituitary and empty sella [19,20]. Our patient’s imaging evidently showed the last two findings in an MRI performed 18 years after the delivery. Unfortunately, the patient did not undergo a previous MRI. Therefore, the only MRI available is the one showed in the photo (Figure 2).

Sheehan’s syndrome treatment aims is to replace the missing hormones and restore endocrine homeostasis. The hormones ACTH and TSH may be replaced in addition to glucocorticoids and thyroxine respectively. Replacing mineral corticoids, on the other hand, is not necessary in most cases. It is important to replace a patient’s sexual hormones as part of the treatment before menopause and replacing GH is useful for lipid-lower therapy and to enhance the patient’s quality of life [21,22]. In our patient, the treatment showed an excellent result (Figure 3).

In terms of prognosis, it depends on how soon the diagnosis is made and the proper treatment is initiated. If the syndrome is early diagnosed and adequate medical therapy is provided, the prognosis of Sheehan’s syndrome is excellent [23,24]. On the other hand, if there is delay in identifying and managing these patients, they may present to medical services (at some point after the event of postpartum hemorrhage) with severe and multiple clinical abnormalities—such as adrenal crisis, symptomatic hypoglycemia, symptomatic hyponatremia, among many others [25-27].

4. CONCLUSION

Evidently, it is important to emphasize the clinical importance of a careful and meticulous review of a patient’s medical history, physical exam and complementary tests, thus reminding clinicians and yielding awareness that Sheehan’s Syndrome does occur, and it is not as rare as one may think.

REFERENCES


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