A Late-onset of Sheehan’s Syndrome Presenting with Life-threatening Hypoglycemia

Abera H*, Berhe T, Mezgebu T and Woldeyes E
Department of Internal Medicine, St. Paul’s Hospital, Millennium Medical College, Addis Ababa, Ethiopia

*Corresponding author: Hailu Abera, Department of Internal Medicine, St. Paul’s Hospital, Millennium Medical College, Addis Ababa, Ethiopia, Tel: + 251 112 76 35 36; E-mail: dhailu2001@gmail.com

Received date: January 28, 2017; Accepted date: February 10, 2017; Published date: February 15, 2017

Abstract
We described a case of 40-year-old lady who presented with a 16 year history of generalized fatigue and recurrent episodes of hypoglycemia. She had a complete clinical evaluation, endocrine studies, and a pituitary magnetic resonance scans that revealed pan-hypopituitarism secondary to Sheehan’s syndrome. She was given hormone replacement therapy, which led to a significant improvement in lethargy, anorexia, muscle weakness, and episodes of hypoglycemia. This case shows the impact of delay in the diagnosis of an easily treatable medical condition and its consequences, especially for the population of a developing country like Ethiopia.

Introduction
Sheehan’s syndrome has an insidious course with variable presentations. The majority of cases remain undiagnosed for many years after delivery. Here, we present a case of Sheehan’s syndrome presenting with recurrent hypoglycemia where a delay in its diagnosis resulted in significant morbidity to the patient.

Case Presentation
A 40-year-old lady presented to our hospital on August 1st 2016 with generalized fatigue of 16 years and change in mentation of one week duration. The history dates back to 16 years when she had her second child with cesarean section for twin pregnancy with breech presentation after which she had in hospital profuse vaginal bleeding for which she was transfused with 6 units of blood. After the delivery, she had failed to lactate and remained amenorrheic since then and had never had any gynecologic evaluation. She was complaining of progressive generalized fatigue and decreased exercise capacity since the time of delivery. She had also a history of repeated low blood glucose measurements for the past eight years for which she was being managed with intravenous dextrose infusion and advised to take caloric diet at the nearest health center.

Since the last one year she had excessive daytime sleepiness, spending most of the day in bed. She also noticed a progressive loss of axillary hairs and only sparse pubic hairs. Examination of other systems was unremarkable.

One week prior to her current presentation, she developed bizarre behavior followed by loss of consciousness within two days. She was then taken to a clinic where her blood glucose level was 39 mg/dl, given dextrose infusion and referred to our hospital.

She has no history of long standing, headache, blurring of vision or diplopia. She has no history of head trauma, surgery or irradiation.

On examination, she was confused with a Glasgow Coma Scale of 14/15, hypotensive with blood pressure 85/50 mmHg, pulse rate 62 beats per minute and afebrile. She had facial puffiness. There was a loss of axillary hairs and only sparse pubic hairs. Examination of other systems was unremarkable.

Laboratory findings showed a white cell count 4,000/µl, hematocrit 27.6%, MCV 95 fl, normal liver and renal functions, urine specific gravity 1.000, Na+ 110 mEq/L, K+ 4.35 mEq/L, random blood sugar 54 mg/dl, total cholesterol 130 mg/dl and triglyceride 62 mg/dl. Brain MRI with Gadolinium revealed empty sella turcica as shown in (Figure 1).

Figure 1: Sagittal gadolinium-enhanced T1-weighted MRI shows an empty sella (red circle).

As the clinical manifestations related to the patient’s previous obstetric history suggested Sheehan’s syndrome, relevant and available hormonal studies were done (Table 1). After all these tests were performed, the diagnosis of Sheehan’s syndrome was made.

The patient was started on intravenous hydrocortisone on an emergency basis as inpatient and subsequently Prednisolone and levothyroxine. She became conscious, started ambulating; hypoglycemic episodes disappeared and discharged with significant improvement. She was strictly educated about her illness and need to take both Prednisolone and levothyroxine therapy for the rest of her life.
Laboratory findings at presentation

<table>
<thead>
<tr>
<th>Plasma Hormone</th>
<th>Patient’s measurements</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luteinizing hormone (mIU/ml)</td>
<td>0.10</td>
<td>7.7-58.5 (post menopause)</td>
</tr>
<tr>
<td>Follicle-stimulating hormone (mIU/ml)</td>
<td>0.16</td>
<td>25.8-134.8 (post menopause)</td>
</tr>
<tr>
<td>Adreno-cortico trophic hormone (ng/ml)</td>
<td>&lt;1.0</td>
<td>1.6 - 13.9</td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td>&lt;0.05</td>
<td>4.79-23.3</td>
</tr>
<tr>
<td>Thyroid stimulating hormone (µIU/ml)</td>
<td>0.16</td>
<td>2.5-5</td>
</tr>
<tr>
<td>Plasma cortisol at 8 Am (µg /dl)</td>
<td>2.57</td>
<td>6.2-19.9</td>
</tr>
<tr>
<td>Total triiodothyronine (µg/dl)</td>
<td>0.44</td>
<td>0.92-2.33</td>
</tr>
<tr>
<td>Total thyroxine (µg/dl)</td>
<td>0.63</td>
<td>4.0-6.0</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>&lt;5.0</td>
<td>5.0-54.7 (post menopause)</td>
</tr>
<tr>
<td>Progesterone (ng/ml)</td>
<td>&lt;0.03</td>
<td>0.1-0.8 (post menopause)</td>
</tr>
</tbody>
</table>

Table 1: Endocrine studies at presentation.

Discussion

Sheehan’s syndrome is defined as a pituitary hormone deficiency due to ischemic necrosis of the pituitary gland from massive postpartum uterine bleeding [1]. It is an uncommon sequel of postpartum hemorrhage in developed nations. It was first described by Sheehan [1]. However, in developing countries, postpartum pituitary infarction remains a common cause of hypopituitarism [2]. Although Sheehan’s syndrome can present with acute severe pan-hypopituitarism in some patients, the majority of patients is recognized with a clinical subtle partial pituitary deficiency and therefore their diagnosis and treatments are delayed for many years [3]. The magnitude of Sheehan’s syndrome is not well known, presumably because of the great number of patients are undiagnosed. It is a rarely encountered disorder in developed countries due to a better obstetric care [2,3]. But its prevalence is estimated to be still higher in developing countries where many deliveries take place at home [2].

The magnitude of Sheehan’s syndrome in Africa is unknown, but as observed from different case reports a significant number of the patients are young women. The major risk factors identified are home delivery and lack of obstetric care. Typical clinical presentations are commonly seen, but typical manifestations, including neuropsychiatric or electrolyte abnormalities are also observed. The delay in onset of overt disease can also be too long [4]. There are no nationwide data on the duration of onset of Sheehan’s syndrome, but there are many case reports on literature. In a study of 60 cases, the average time between the postpartum hemorrhage and diagnosis of Sheehan’s syndrome was 13 years [5].

Failure to lactate is often a common initial complaint in patients with Sheehan syndrome (6). Many of them also report amenorrhea after delivery [7]. The diagnosis of Sheehan’s syndrome is not made until several years in certain cases, when the features of hypopituitarism become apparent in a woman who had a postpartum bleeding [8]. A woman with Sheehan’s syndrome with undiagnosed hypopituitarism might be apparently asymptomatic until her body is exposed to stressful situations like surgery or infection for many years after her delivery, when she presents with adrenal crisis [9].

Less commonly, Sheehan’s syndrome can present acutely with hypovolemic shock, hypoglycemia, severe hyponatremia, diabetes insipidus or psychosis [10]. There are multiple mechanisms resulting in hyponatremia in these patients. Hypothyroidism and cortisol deficiency can cause decreased free-water clearance and subsequent hyponatremia. In Sheehan’s syndrome, there will also be severe inappropriate secretion of antidiuretic hormone, which can also cause hyponatremia [11,12]. Potassium level in this syndrome is not affected, because adrenal production of aldosterone is independent of the pituitary gland [13]. The response to fluid restriction is not complete. Therefore, treatment with hydrocortisone is important to bring the sodium levels to normal.

The diagnosis of Sheehan’s syndrome is challenging. It is based on clinical features of hypopituitarism in a woman with a history of massive postpartum bleeding. Various symptoms will occur for specific deficiencies of anterior pituitary hormones. Prolactin deficiency can cause failure of lactation. Gonadotropin deficiency will often cause amenorrhea or genital hair loss. Corticotropin deficiency can result in generalized fatigue, weakness, hypoglycemia, or dizziness. Deficiency of growth hormone causes fatigue, decreased quality of life, and weight loss. Symptoms of central hypothyroidism are clinically similar to primary hypothyroidism, but patients with central hypothyroidism have low T3 and T4 levels with normal or even inappropriately low TSH levels. Diagnosis of panhypopituitarism is straightforward, but partial deficiencies are often difficult to elicit [14].

A patient with panhypopituitarism will have low levels of pituitary hormones (prolactin, luteinizing hormone, corticotropin, and thyrotropin) as well as the target hormones (estrogen, progesterone, cortisol and thyroxin) [15].
In our patient, the possibility of Sheehan's syndrome was suspected because of her obstetric history, recurrent hyponatremia, hypoglycemia, and low baseline hormone levels.

Pituitary imaging with either computed tomography or magnetic resonance imaging is usually not helpful in the acute phase and has not been used frequently in acute diagnosis. In a chronic phase of the disease, neuroimaging typically shows atrophy of the pituitary and empty sella [16,17].

In the treatment of women with hypopituitarism one should replace hydrocortisone first, followed by thyroid hormone and estrogen with or without progesterone depending on whether she has a uterus. Hydrocortisone is replaced first because thyroxine therapy can exacerbate glucocorticoid deficiency and can induce an adrenal crisis [14,18]. The recommended dose of hydrocortisone is 20 mg/d for an adult (15 mg in the morning and 5 mg in the evening). Both thyroxine and gonadotropin replacements are commonly practiced, and doses are titrated depending on the response of each patient. Growth hormone replacement is currently not strongly recommended in adults even though certain patients with severe growth hormone deficiency may benefit from replacement [19].

Although the Sheehan's syndrome is not common as a result of improved obstetric care in many parts of the world; it should be considered in any woman who has a history of significant postpartum hemorrhage and presented with signs or symptoms of pituitary deficiency.

In our patient, there was a significant delay in reaching at the diagnosis even though there are several conditions, including agalactorrea, secondary amenorrhea and recurrent hyponatremia during these several years to suspect Sheehan's syndrome. Some of the possible reasons that had contributed to this delay are; [1] inadequate counseling on discharge after her eventful delivery and postpartum hemorrhage, and [2] lack of awareness to seek help for secondary amenorrhea for many. Once she presented to health professionals, her management remained symptom-driven for a number of years without an attempt to diagnose the underlying cause. The patient had been suffering from poor health for many years and several episodes of life-threatening hyponatremia related to adrenal crises.

Conclusion

Detailed medical history and physical examination supported by laboratory tests are still the cornerstone for the diagnosis, reminding clinicians to think about rarely reported disease like Sheehan's syndrome.

References