Diagnosis Delayed but not Denied - Sheehan's syndrome

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ABSTRACT

Sheehan's syndrome is a rare complication of postpartum hemorrhage. With advancement in obstetric care, Sheehan's syndrome has become uncommon except in developing countries. Here, we report a patient with Sheehan's syndrome who escaped diagnosis for 22 years and presented with life threatening complications. This patient also had certain unusual features of Sheehan's syndrome like pancytopenia and renal failure. A high index of suspicion is necessary in diagnosing such patients.

Keywords: *pancytopenia; renal failure; Sheehan syndrome.*

INTRODUCTION

In 1937, Harold Leeming Sheehan described the occurrence of pituitary infarction and panhypopituitarism following obstetric hemorrhage and vascular collapse. The clinical features of this disease known as Sheehan's syndrome are often subtle and years may pass before pituitary insufficiency is recognised following an ischemic insult.[1]

The symptoms of Sheehan's syndrome range from vague feelings of ill health to symptoms of full blast panhypopituitarism. The gland has a great secretory reserve and more than 75% must be destroyed before clinical manifestations are evident.[2]

CASE REPORT

A 40 year old lady from a rural area, presented to us with easy fatigability, headache, nausea and loss of appetite since two months. There was no history of any comorbid conditions. However, she had been amenorrhoeic for 22 years since the last childbirth. Her first pregnancy had resulted in a stillbirth. The antepartum period of her second pregnancy was uneventful. However during delivery, there was history of increased blood loss. She did not receive any blood transfusion. She also had failure of lactation.

With the above history, we probed further regarding her overall wellbeing following delivery, which revealed history of tiredness, nausea, myalgia, apathy, and poor interaction with family members since the past 20 years. She had consulted a few local doctors for this but had never felt better with any medications.

At the time of presentation the patient was hypotensive (blood pressure of 80/40mm Hg). She was febrile, tachypnoeic and had hypoxia with a saturation of 75% on room air. Clinical examination revealed pallor, facial puffiness, madarosis, pitting pedal edema and cold peripheries. There was loss of secondary sexual characteristics. She was apathetic with slow response to oral commands. There was hypotonia in all four limbs and delayed relaxation of all deep tendon reflexes. Other

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systemic examination was normal.

An intercurrent infection, probably respiratory was suspected and she was started on cephalosporins and azithromycin. Since it was the flu season, oseltamivir was also added. Based on the past clinical history, a provisional diagnosis of postpartum hypopituitarism, (Sheehan's syndrome) was made. Random serum samples for cortisol and thyroid function tests were collected and she was started on hydrocortisone and levothyroxine.

Blood investigations revealed pancytopenia with hemoglobin of 9gm/dl, total count of 2800 and platelet count of 1.05 lakh. The hemoglobin reduced to 7.7g/dl on day three of admission, with no features of bleeding. The random blood sugar was 59mg/dl. Blood urea was 59mg/dl, and creatinine was 2.4mg/dl. Serum ferritin levels were 482.3 ng/ml and vitamin B 12 was 318 pg/ml. Random cortisol was 0.19 mc/dl, TSH -2.13 ru/ml, T4 was 0.21 mcg/dl, LH - 0.62miu and FSH-2.17miu. The chest x ray showed cardiomegaly. There was minimal pericardial effusion on echocardiography.

Intravenous fluids were given according to central venous pressure. Over the next two days, the patient's condition was not satisfactory and antibiotics were changed to piperacillin and tazobactum and she improved by the fourth day. Subsequently, she developed steroid induced psychosis, which improved following dose reduction and risperidone. She was transfused one pint of packed cells during her stay.

MRI brain was done after the patient was stabilized, which revealed an empty sella thus confirming the diagnosis. Oral prednisolone was tapered to physiological doses. At discharge she was on prednisolone 7.5mg/day and levothyroxine at 100mcg. Her blood pressure was 100/60mm Hg, she was alert and cheerful. She is asymptomatic with the above treatment on regular follow up.

DISCUSSION

The pituitary gland becomes physiologically enlarged in pregnancy and is therefore very sensitive to the decreased blood flow caused by massive hemorrhage and hypovolemic shock. Women affected may develop hypopituitarism ranging from panhypopituitarism to selective deficiencies. The anterior pituitary is more sensitive to damage than the posterior lobe.[3]

Failure to lactate is usually the first feature of Sheehan's syndrome, followed by features of hypocortisolism and hypothyroidism. Loss of hormones in decreasing order is prolactin, gonadotrophins and growth hormone, ACTH and TSH.

Adrenal insufficiency in Sheehan syndrome can be catastrophic and can range from non-specific complaints to hypotension, and severe adrenal crisis, particularly under stressful conditions such as infections.[4] Our patient presented similarly.

There were few unusual features in our case, one being pancytopenia. There are only a few sporadic case reports in medical literature regarding pancytopenia in Sheehan syndrome.[5] Anaemia as a hematological manifestation is more common.[6] The mechanism by which pancytopenia occurs is not clear. It may be due to pituitary hormone deficiency which affects metabolic reaction to hematopoiesis.[5] Of interest is the fact that pancytopenia occurring with Sheehan syndrome is completely reversible with hormone replacement therapy. Full hematological recovery occurred in all published cases so far. In our patient the blood counts returned to almost normal levels within 8 days.

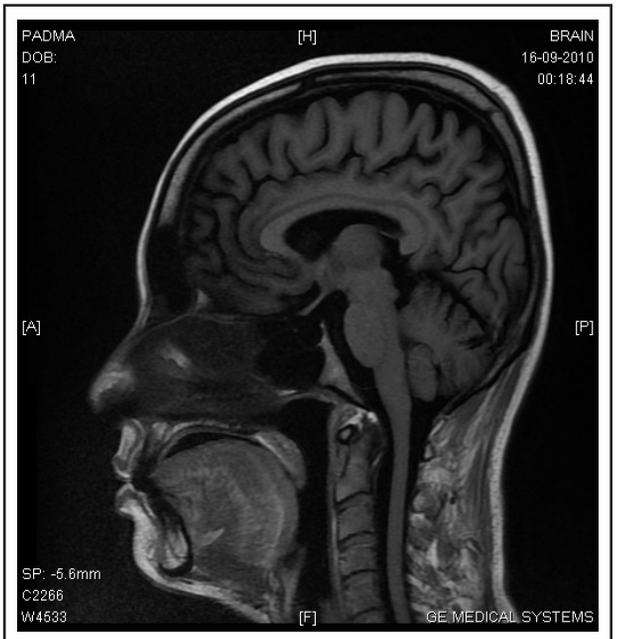

Figure 1. MRI Brain showing empty sella (red arrow) in our patient.

The other unusual feature in the presentation was renal failure. Renal abnormalities in Sheehan syndrome can occur rarely. Acute kidney injury has been reported, hypothyroid myopathy being the most common etiological factor. The latter is characterized by delayed relaxation of tendon reflexes, muscle stiffness, proximal muscle weakness, myalgia, muscle cramps and occasionally elevated muscle enzymes. Rhabdomyolysis may also occur, precipitated by hypoxemia, hypotension, sepsis or exercise. The exact cause for this is not known, however impaired

glycogenolysis and oxidative mitochondrial metabolism may be the reason.[4] The first report on renal failure in Addison's disease was that of Smith in 1897. It was later observed that renal blood flow and glomerular filtration rate (GFR) were reduced even in those patients not in adrenal crisis. GFR improved with steroid replacement.[7] In addition, reduction in GFR seemed unrelated to the blood pressure. The serum creatinine improved within one week in our patient.

Another highlight of our case was the delay in diagnosis. Sheehan syndrome can present in the postpartum period with lactation failure or after many months to years following the inciting delivery.[8]Even in developed countries there is often a delay in diagnosing Sheehan syndrome. In a cohort study conducted by Ramiandrasoa C et al in Southeast France from 1980 to 2011, the mean delay in diagnosis was 9 years. They suggest that all women failing to lactate after postpartum hemorrhage should be evaluated for prolactin levels and also be followed up indefinitely if they continue to have other symptoms even remotely suggestive of hypopituitarism.[9]

Most women with Sheehan syndrome are asymptomatic until a stressful event occurs and precipitates adrenal insufficiency, hypothyroidism or coma, which is another reason for explaining the diagnostic delay. This is probably because patients with ACTH deficiency still produce aldosterone in contrast to patients suffering from peripheral adrenal insufficiency (for whom clinical signs are usually more severe).[9]

Other hypotheses for delayed diagnosis are: symptoms are non-specific, lack of awareness in the medical fraternity regarding the condition and the little importance that is paid to the menstrual history in a woman presenting with such symptoms.

The mortality in patients with hypopituitarism is higher than the general population.[10] Early diagnosis and prompt treatment may thus improve the quality of life and reduce morbidity and mortality.

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