ORIGINAL RESEARCH PAPER

Hematology

TRANSFUSION DEPENDENT ANEMIA IN A PATIENT OF SHEEHAN SYNDROME WITH COMPLETE RECOVERY AFTER HORMONE REPLACEMENT THERAPY

KEY WORDS: Sheehan's Syndrome; Anemia; Blood Transfusion; Hypopituitarism; Hormones

Dr Vishnu Sharma* MBBS, MD, DM, Department of General Medicine, SMS Medical College, Jaipur. *Corresponding Author

Vansh Bagrodia Final MBBS Student, SMS Medical College, Jaipur.

Dr Sidharth Mahajan MBBS, Government Medical College, Amritsar.

ABSTRACT

Sheehan's syndrome is a state of postpartum hypopituitarism due to necrosis of the pituitary gland resulting from massive hemorrhage during or after delivery. Delayed diagnosis of Sheehan's syndrome is commonly seen. Here, we report a case of a female in her late forties, who was brought in by her daughter with complaints of severe weakness, fatigue and inability to carry out her own activities since last 10 years, which had started a few months after her delivery. She had been getting blood transfusions for a long time but no ascertainable cause for her anemia could be found despite many investigations spanning a variety of diagnoses. Transfusion-dependent anemia is a condition usually seen with conditions linked with hematological disorders and sheehan syndrome is an usually unseen cause, but one which should be considered in women with a history of excessive hemorrhage associated with delivery.

INTRODUCTION

Sheehan syndrome, also called post-partum pituitary necrosis, refers to the necrosis of cells of the anterior pituitary gland following significant post-partum bleeding, hypovolemia, and shock. Sheehan syndrome is a cause of central hypopituitarism and etiology is attributed to infarction either due to reduced blood flow, thrombosis or vascular compression.[1] It can present as either acute or in chronic form depending upon the magnitude of necrosis and dysfunction that has set in. Clinical signs and symptoms correlate with the hormonal deficiencies developed with the most common being prolactin which presents as post-partum lactation failure.[2] MRI is commonly done but may have nonspecific findings in acute phase and describes empty sella in late stages.[3]

Anemia is a unique manifestation in Sheehan Syndrome attributed to various reasons such as reduced erythropoietic effects of pituitary hormones and can range from microcytic hypochromic to normocytic normochromic anemia.[4]

Transfusion-dependent anemia is a type of anemia characterized by the need for continuous blood transfusions. It can result from a variety of diseases and has been shown to have reduced survival rates. Regular transfusion serves the purpose of reducing the symptoms of anemia seen in patient by improving hemoglobin levels. Transfusion dependence is seen when on an average, more than 2 units of blood transfusion is required every 28 days over a period of at least 3 months.

A serious complication of transfusion dependence is iron overloading, which can lead to injury of the heart, liver and endocrine glands. The treatment of iron overload consists of Iron chelation therapy and the commonly used iron chelators are deferasirox, deferiprone and desferoxamine.

Case

We report the case of a female in her late forties, who was brought in by her daughter with complaints of severe weakness, fatigue and inability to carry out her own activities for last 10 years. Patient had consistently had severe anemia which was treated by blood transfusions for the past 10 years, notably, which started a few months after the female gave birth to her 3rd child. Patient's peripheral blood film had always showed features suggestive of normocytic normochromic anemia and low hemoglobin levels with the patient getting blood transfusion of 2-3 units once every month, despite of which patient's quality of life was very poor (Karnofsky performance status score 40). Patient's daughter produced a variety of investigations done on her mother over the years to find out the cause for her anemia and disability, including tests for hemolytic anemia (High Performance Liquid Chromatography, glucose-6-phosphate-dehydrogenase deficiency, osmotic fragility test and Direct Coombs Test & Indirect Coombs Test), chronic infections such as Tuberculosis, hematological malignancies, upper gastrointestinal endoscopy and colonoscopy for chronic GI bleeds but no specific cause was found. On further detailed history, the patient's daughter revealed that patient had experienced severe post-partum hemorrhage following her 3rd delivery, few months after which only the patient had started experiencing the symptoms aforementioned. It was also found that the patient was unable to breastfeed her offspring then and has had amenorrhea ever since. We suspected a diagnosis of Sheehan Syndrome and ordered a hormonal panel for the same, the findings of which are mentioned in table 1.

Table 1: Patient's Hormonal Panel

Parameter	Patient Levels	Reference Range
Prolactin (in nanogram/ milliliter)	1.56	2.8-29.2
Triodothyronine (in nanogram/milliliter)	0.21	0.6-1.78
Thyroxine (in microgram/deciliter)	0.45	4.50-12.23
TSH ultrasenstive (in micro international unit/milliliter)	0.48	0.55-4.78
FSH (in milli-international unit /milliliter) (pre-menopausal levels)	3.25	4.7 to 21.5
LH (in international unit/milliliter) (pre-menopausal levels)	2.7	5 to 25
Sodium Level (in millimoles per litre)	129	136-145
Potassium Level (in milliequivalents per Liter)	2.8	3.5-5.2

With the investigations being in favor of a diagnosis of Sheehan Syndrome, the patient was initially put on a treatment of levothyroxine 100 mcg once daily + prednisolone 10 mg twice daily for 2 weeks followed by hydrocortisone (10 mg morning + 5 mg afternoon + 5 mg evening) + calcium supplementation for a period of 1 month. After 1 month of therapy, patient had a dramatic improvement in her quality of life and blood profile and was put on lifelong treatment of levothyroxine + hydrocortisone. She was regularly followed up for the next 12 months and is now transfusion-free and is living a normal life.

DISCUSSION

Sheehan syndrome is known to occur after hemorrhagic shock in pregnancy, and diagnosis could be delayed as symptoms might not arise until exposure to stressful situations like trauma, infection, or surgery.[5] Symptoms of Sheehan syndrome are associated with hormone deficiencies, with prolactin deficiency being the most common, which manifests as failure to lactate. Other hormone deficiencies that can occur include gonadotropin deficiency (leading to amenorrhea), corticotropin deficiency (causing fatigue, weakness, hypoglycemia, and orthostatic hypotension), growth hormone deficiency (causing fatigue, decreased quality of life, and weight loss), and central hypothyroidism (resulting in fatigue, constipation, and bradycardia).[6]

Diagnosis is made based on clinical presentation, which can be acute (failure to lactate and amenorrhea after pregnancy), chronic (symptoms of weight loss, dizziness, nausea, vomiting, and abdominal pain due to secondary adrenal insufficiency), or a stage between progression from acute to chronic (progression from lactational failure and amenorrhea to secondary adrenal insufficiency).[7,8]

Our patient also experienced failure of lactation and amenorrhea a few months after her delivery but didn't report for the same then and hence wasn't tested for or diagnosed with Sheehan Syndrome at the onset of symptoms. Patient reported to us with severe weakness, fatigue and inability to carry out her own activities since last 10 years.

In a study by Ramiandrosoa et al., the mean delay in the diagnosis of Sheehan Syndrome was 9 ± 9.7 years. In our patient, a delay in diagnosis of about 10 years was seen.[9]

Laboratory tests include a wide range of findings, including reduced levels of Prolactin, FSH, LH, Growth Hormone, TSH, hyponatremia and hypokalemia.[10] In our patient, reduced Prolactin, Triodothyronine, Thyroxine, TSH, FSH, LH levels and hyponatremia and hypokalemia were found. Hematological abnormalities seen can be anemia, coagulation abnormalities and pancytopenia. Our patient's transfusion dependent anemia was caused by her undiagnosed Sheehan Syndrome and none of the usual causes of transfusion dependent anemia, most notably myelodysplastic syndromes (MDS) and thalassemia.

Various other investigations to find out the cause of patient's transfusion dependent anemia like hemolytic anemias (hemoglobinopathies, thalassemias, glucose-6-phosphate-dehydrogenase deficiency disease, hereditary spherocytosis, autoimmune hemolytic anemias), infections like tuberculosis, hematological malignancies, chronic GI bleeds were done but were all found to be normal.

Treatment for Sheehan syndrome focuses on hormone replacement therapy, starting with hydrocortisone to prevent adrenal crisis from early thyroxine administration. Hydrocortisone is administered in the dose of 20mg/daily following the circadian rhythm with doses distributed as- 10 mg in morning + 5 mg in afternoon + 5 mg in evening. Dose administered can be monitored with nonspecific signs like blood pressure, weight gain and serum glucose/lipid levels.

Our patient was given the same standard treatment and had a positive outcome with a significant improvement in quality of life.

CONCLUSION

Lack in properly eliciting history and absence of any particular pathognomic clinical features can lead to prolonged delay in diagnosis of diseases like Sheehan Syndrome, which can be chronically disabling if not treated but has a good patient outcome once patient is placed on treatment. Female patients with transfusion dependent anemia negative for its usual hematological etiologies should be interviewed and investigated thoroughly for a possible diagnosis of sheehan syndrome.

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