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Case report: Pancytopenia as a rare presentation of Sheehan's syndrome

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Abstract

Sheehan's syndrome is a postpartum hypopituitarism state caused by necrosis of the pituitary gland. It is usually the result of severe hypotension or shock caused by massive hemorrhage during or after delivery. Sheehan's syndrome symptoms are often subtle and hence it is diagnosed late. Herein, we report a case of a 41-year-old woman who developed severe postpartum hemorrhage after childbirth that required a total abdominal hysterectomy to control bleeding at the age of 36 years. Since then, she has progressively developed symptoms of headache, general fatigue, and malaise, and finally presented with pancytopenia for investigations. Anemia is a well-known hematological association with Sheehan's syndrome while pancytopenia is rarely reported. However, complete recovery of pancytopenia was observed after the treatment. Pancytopenia (due to bone marrow failure to produce cells) is a serious finding in clinical practice that causes significant stress as it may point to a diagnosis of malignancy (mainly leukemia) and other serious disorders. Despite being a rare cause, a high index of suspicion is required from the physicians in women with pancytopenia, in order to look for a possible treatable cause of pancytopenia (like Sheehan's syndrome), if the common causes were excluded.

Keywords

Hypopituitarism, pancytopenia, Sheehan's syndrome

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Introduction

Sheehan's syndrome is best described as postpartum necrosis of the pituitary gland, most likely secondary to postpartum hemorrhage during or after delivery, and it was first described in 1937.[1] The pituitary gland is enlarged in size during pregnancy physiologically and is therefore sensitive to the reduced blood flow caused by massive hemorrhage and hypotension. Patients with Sheehan's syndrome have varying degrees of hypopituitarism, ranging from pan-hypopituitarism to selective deficiencies.[2]

Interestingly, Sheehan syndrome can cause a wide range of hematological manifestations through unknown complex hormonal effects, the most frequent one is anemia.[3,4] Pancytopenia is rarely present in Sheehan's syndrome and is demonstrated in only a few case reports worldwide.[4] Multiple anterior pituitary hormone deficiencies in Sheehan's syndrome are thought to be the culprit of pancytopenia. The association between the hypopituitarism and hematological abnormalities is further supported by a complete reversal in hematological parameters with hormone replacement (thyroid and cortisol hormones).[4–7]

The spectrum of clinical presentation of Sheehan's syndrome is broad, starting at first with failure to lactate the baby and to restore normal menstrual cycle, but this aspect of the condition can oftentimes be overlooked because emergent hysterectomies are performed to treat unstable postpartum hemorrhage.[8] Then, symptoms may continue with nonspecific complaints, such as weakness, fatigue, headache, and pallor, and may end up with severe pituitary insufficiency, resulting in coma and death.[9] The anterior pituitary gland is more susceptible to damage than the posterior part.[8]

In some cases, the diagnosis is not made until years later, when features of hypopituitarism, such as secondary hypothyroidism or secondary adrenal insufficiency, become evident.[10] A woman with undiagnosed Sheehan's syndrome

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Table 1. Hormonal testing for the patient, using the chemiluminescent enzyme immunometric assay, before and after treatment.

Test name (unit)	Result before treatment	Results after treatment	Reference range
Prolactin (μIU/mL)	38.7	122	102-496
FSH (mIU/mL)	4.25	64	23-116
LH (mIU/mL)	1.1	45	15-62
TSH (μIU/mL)	1.19	0.8	0.27-4.2
T3 (pmol/L)	0.7	3.5	3.1-6.8
T4 (pmol/L)	1.4	16	12-22
ACTH (pmol/L)	15.5	12.5	7.2-63
Cortisol AM (nmol/L)	107	224	133-537
Estradiol E2 (pg/mL)	5	7.5	3-10
IGF-1 (ng/mL)	46	73	65-200

ACTH: adrenocorticotropic hormone; FSH: follicle-stimulating hormone; LH: luteinizing hormone; TSH: thyroid-stimulating hormone; T4: thyroxine, T3: triiodothyronine, IGF-1: insulin-like growth factor-1.

might be relatively asymptomatic initially until she is exposed to a stressful situation that challenges her thyroid and adrenals.[11]

Herein, we report a case of Sheehan's syndrome that presented with hypoglycemia, hyponatremia, and pancytopenia due to bone marrow hypoplasia that showed complete recovery once hormone replacement was initiated.

Case presentation

We present a 40-year-old woman with no known chronic medical conditions of note, with complaints of general fatigue, malaise, and recurrent headache for the last few months. During her illness, basic lab testing including a complete blood count was done that showed pancytopenia, because of which she was referred to our hematology clinic. At presentation, vital signs showed a blood pressure of 100/60 mmHg, a pulse of 75 bpm with no orthostasis, and a temperature of 36.9°C. Physical examination revealed a fatigued woman with pallor, but no lymphadenopathy or hepatosplenomegaly. Otherwise, the examination was unremarkable. An initial laboratory testing showed hyponatremia at 132 mmol/L, but with normal potassium and glucose levels, and normal kidney and liver function tests. Also, her hemogram showed a leukocyte count of 2.45×10^9/L, a neutrophil count of 0.82×10^9/L. Her hemoglobin level was 8.7 g/dL with a mean corpuscular volume at 92.7 fL. Her platelet count was 133×10^9/L. She had negative Coombs testing, normal iron studies, reticulocyte count, vitamin B12, and folate levels. A blood film was nonconclusive, and bone marrow biopsy and aspirate revealed hypocellular marrow with trilineage hypoplasia.

During a follow-up visit to the clinic 1 week later to get the results of the bone marrow biopsy, her labs showed persistence of her pancytopenia, but surprisingly her sodium level was 116 mmol/L, and her fasting blood sugar was 50 m/dL. She reported worsening fatigue. She was admitted to the hospital to continue management there. By further interviewing, she reported a history of excessive postpartum bleeding after her last normal vaginal delivery at the age of 36 years, which had required a total abdominal hysterectomy to control the bleeding, and so she has developed amenorrhea since then. Furthermore, she reported failure of lactation after this event. Detailed examination showed depigmentation of areolas, with loss of pupils and axillary hair. While investigating her hyponatremia, her lab testing was consistent with hyponatremia of adrenal insufficiency (low serum sodium, low serum osmolality, and high urine osmolality).

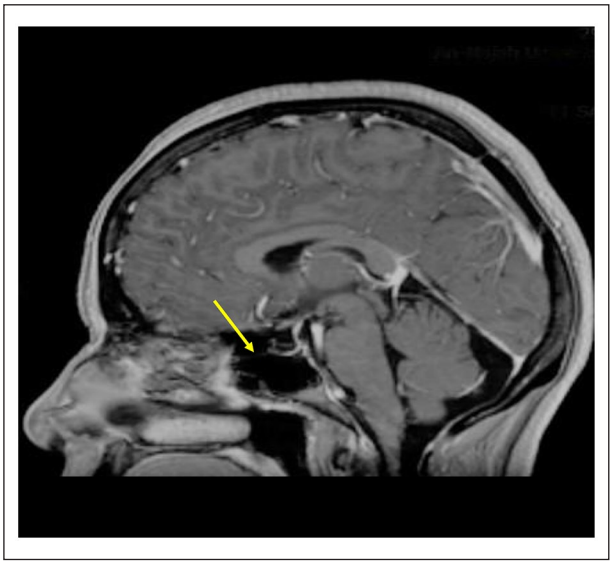

Figure 1. Sagittal gadolinium-enhanced T1-weighted magnetic resonance imaging demonstrates a partially empty sella (arrow).

Sheehan's syndrome was suspected, and related hormonal studies were made. The hormone profile was consistent with primary pituitary insufficiency (Table 1). Magnetic resonance imaging of the head showed partially empty sella turcica (Figure 1), which further supported our diagnosis. The diagnosis of Sheehan's syndrome was confirmed with a combination of clinical and laboratory findings, supported

Table 2. Basic laboratory tests, before and after treatment.

Test name (unit)	Before treatment	After treatment	Reference range
White blood cell count (cells/L)	2.45×10^9	4.7×10^9	$4.5\text{-}10.5 \times 10^9$
Neutrophil count (cells/L)	0.82×10^9	4×10^9	$2.5\text{-}6 \times 10^9$
Hemoglobin level (g/dL)	8.7	9.5	12-15
Platelet count (cells/L)	133	193×10^9	$150\text{-}450 \times 10^9$
Sodium level (mmol/L)	116	136	135-145
Glucose level (mg/dL)	50	120	70-139

by the magnetic resonance imaging findings.[8] The patient was started on hormone replacement therapy of hydrocortisone 20 mg per day, followed by L-Thyroxine 50 μcg per day with an increment dose.

The patient was followed for several weeks after being discharged, and we noticed a complete hematological recovery within 2 weeks, with a euglycemic, eunatremic, eucortisolemic, and euthyroid state (Table 2).

Discussion

Sheehan's syndrome is diagnosed only when high clinical suspicion is present; this is because the early symptoms of Sheehan (such as failure to lactate the baby) may be subtle and usually neglected by the patient, and so the diagnosis may not be possible until years (and even decades) after the peripartum events. However, some patients may present acutely with a life-threatening condition like acute adrenal insufficiency and hypothyroidism.[1] Diagnosis is first made by a thorough clinical history and physical examination, supported by the appropriate laboratory tests including anterior pituitary hormones levels.[3,8] The abnormalities are not only limited to the hormone levels but also include hyponatremia, which occurs mainly due to adrenal insufficiency.[10] Although rare, this also includes hematologic abnormalities, including anemia and even pancytopenia, which can occur in up to 65% of patients with Sheehan syndrome.[5,12]

Although anemia in those patients could be explained in some ways, including pituitary hormone deficiencies,[5] and lower oxygen demand in those patients, and hence lower erythropoietin production,[7] pancytopenia could not be fully explained, mainly due to the rarity of the presentation and hence it is still not well studied.

Herein, we present this young female with pancytopenia and hyponatremia who attended the hematology clinic for diagnosis. And after excluding serious hematologic diseases including malignancies, Sheehan syndrome was diagnosed based on the history, physical examination, and confirmatory laboratory testing. This presentation of Sheehan syndrome was mentioned in the literature, although rarely. The mean age of these patients—as mentioned in the literature—was 41 years, which is very similar to our patient. Also, the finding of a years-lag between the syndrome occurrences and the diagnosis is a common feature.[4]

According to the assumed culprit pathology, all the published cases were treated with steroid and L-thyroxin replacement therapy, and all attained full hematologic recovery within days to weeks from starting treatment.[4,5,7] We also managed our patient with glucocorticoid and thyroid hormone replacement with strict endocrinology and hematology follow-up. She accomplished full hematologic and endocrinologic recovery after only 2 weeks of therapy.

Conclusion

Pancytopenia is a very rare presentation of Sheehan syndrome, although the mechanism is not well known. It requires a high level of suspicion because of its rarity and late presentation. A constellation of clinical and laboratory testing is needed to confirm the diagnosis after exclusion of other hematologic diseases. The full hematologic recovery after replacement of the pituitary hormones (glucocorticoid and thyroxin) supports this association and directs us to a treatable cause of pancytopenia that we should be aware of it.

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Ethical approval

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