ORIGINAL RESEARCH PAPER

Internal Medicine

A RARE CAUSE OF HYPOPITUITARISM - SHEEHAN SYNDROME

KEY WORDS:

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ABSTRACT

Sheehan syndrome is a rare complication of post-partum hemorrhage causing post-partum ischemic necrosis of the pituitary gland. It is a disease with declining incidence, more prevalent in developing countries. The incidence of Sheehan syndrome is 1 in 100,000 births. It was first described by a British pathologist Harold Leeming Sheehan in 1937.We present the case of a 42 year old female who presented with bilateral knee pain for 4 years, on over-the-counter steroids. She gave a history of lactational failure and secondary amenorrhea following childbirth. Her investigations revealed central hypothyroidism and she was diagnosed as Sheehan syndrome.

Introduction

Sheehan syndrome occurs due to ischemic necrosis of the pituitary gland following massive post-partum hemorrhage. It has a delayed presentation ranging from several months to years following childbirth. Clinical manifestations vary based on the degree of hypopituitarism, ranging from complete panhypopituitarism to selective hypopituitarism .1 Most common clinical manifestation that heralds the disease is agalactia and/or amenorrhea but it may present with life-threatening emergency with circulatory collapse, hypoglycemia, adrenal crisis .[2,3]

Case report

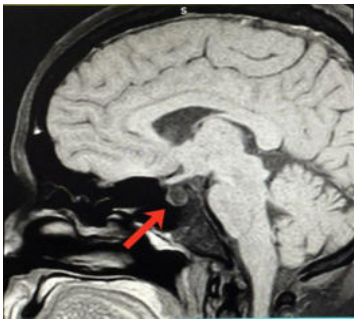
A 46 year old female presented with bilateral knee joint associated with occasional swelling for 4 years, which increased in intensity over 3 days prior to presentation to the hospital. There was no history of early morning stiffness, involvement of other joints or joint deformities. There was history of intermittent over-the-counter steroids abuse for 3 years for her complaints, following which she developed dyspepsia lasting for 2 years. Her obstretic score was P1L1 and she was post-menopausal.

Her physical examination including examination of knee joints was unremarkable but for dryness of skin and mild pallor. Baseline investigation revealed mild anaemia with hemoglobin of 10.5 g/dL of the normocytic normochromic type. Autoimmune work up including Rheumatoid factor, Anti-CCP and ANA were negative as were her ESR and CRP levels.

Her thyroid function test results were consistent with central hypothyroidism with FT3 of 1.72 pg/ml, FT4 of 0.44 NT/dl and TSH of 2.69 mIU/ml. With the clinical picture of early menopause and associated central hypothyroidism, a thorough menstrual and obstretic history was obtained which revealed childbirth at the age of 24years, following which she developed massive postpartum hemorrhage requiring multiple blood transfusions and hysterectomy. Following parturition, she had lactation failure within a few days and persistent amenorrhea thereafter.

Based on her history and clinical picture, Sheehan syndrome was suspected and the patient was investigated further and her hormone assays revealed Prolactin levels below the lower limit of normal for males (2.0 ng/ml). FSH and LH levels were below the normal limit for post-menopausal age group (2.27 mIU/ml and 1.71 mIU/ml respectively). Ultrasound abdomen showed Atrophic ovaries and PAP smear was Atrophic. MRI brain with pituitary cuts showed completely empty sella.

Investigation	Patient's value	Reference range
FT3	1.72	2.77-5.27
FT4	0.44	0.78-2.19
TSH	2.69	0.46-4.68
Prolactin	2.0	Non-pregnant female: 3.0-19.0 Pregnancy: 9.7-208.5 Post-menopausal: 1.-18.5 Male: 3.7-17.9
FSH	2.27	Follicular phase: 1.08-11.8 Mid-cycle peak: 5.14-29.4 Luteal phase: 1.38-9.59 Post-menopausal: 21.5-151 Male: 1.55-8.74
LH	1.71	Follicular phase: 2.58-12.1 Mid cycle peak: 27.0- 96.9 Luteal phase: 0.83-15.5 Post-menopausal: 10.1-86.5 Male: 1.5-9.3



Patient was continued on oral steroids at tapering doses and started on thyroxine supplementation at a dose of 75 mcg. Serum cortisol assay was planned on review and she was planned for Hormone Replacement Therapy.

Discussion

Sheehan syndrome is post-partum permanent hypopituitarism resulting from ischemic necrosis of the pituitary gland in the immediate post-partum period, secondary to massive post-partum hemorrhage. During pregnancy, under the influence of placental estrogen, the pituitary gland undergoes markers hypertrophy and hyperplasia causing compression of blood vessels. In the setting of severe post-partum hemorrhage causing hypotension and shock, the enlarged pituitary undergoes ischemic necrosis as a result of compromised blood flow. Risk factors include hypercoagulability, Disseminated Intravascular Coagulation, smaller than normal sized sella, infections and surgeries.[3]

Clinical manifestations depend on the extent of pituitary damage and present as individual hormone deficiencies. Usually the patient presents several decades after post-

partum hemorrhage but can present as early as within 6 weeks when it is labelled as acute Sheehan syndrome. [4] The mean duration between post-partum hemorrhage and clinical manifestions varies between 1 to 33 years. [3,5] Commonest presentation is lactational failure and secondary amenorrhea but life-threatening emergencies like hypotension, hypoglycemia, myxedema coma, hyponatremia can lead to coma and death. [6]

Growth hormone secreting cells are in the periphery of the gland and are most vulnerable to ischemia but adult women seldom present with growth hormone deficiency. The order of damage is somatotropes, lactotropes, gonadotropes, corticotropes and thyrotropes. [6] Patients can either present with panhypopituitarism or more commonly, selective hormone deficiencies.

Posterior pituitary involvement is seen in only 5% cases of Sheehan syndrome as posterior pituitary hormones are neurohormones transported from the hypothalamus. [6]

Diagnosis of Sheehan syndrome requires a strong clinical suspicion and thorough history taking. History of post-partum hemorrhage, failure to lactate and cessation of menses are important clues to the diagnosis. In this patient, despite low levels of FT3 and FT4, the TSH levels were inappropriately normal as opposed to elevated which gave the clue to diagnosis. Further probing into the history led to the diagnosis of this condition.

The mainstay of treatment is lifelong replacement of the deficient hormones and prevention of lethal complications. [3,2]

Conclusion

Sheehan syndrome has a slow indolent course and is often diagnosed very late. Early diagnosis and treatment can prevent life threatening complications of the disease. It is important to note that a normal TSH is not synonymous with a normal Thyroid Function Test. [4] Replacement of thyroxine must follow replacement of steroids in patients with Sheehan syndrome as thyroxine supplementation can increase the metabolic demands and lead to full-blown adrenal crisis, if not preceded by steroids.

Declarations

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