Sheehan's Syndrome; A Rare Complication of Postpartum Hemorrhage - Case Report and Review of the Literature

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Abstract
Sheehan Syndrome is a Condition that may occur in a woman who bleeds severely during child birth. Severe bleeding during child birth can cause tissue death in the pituitary gland, which may cause the gland to lose its ability to function properly. We reported a case of a 21 year old lady gravida 1 para 1^{+0} (alive) who developed Sheehan's syndrome six months after extreme post partum hemorrhage. High level of suspicious was employed based on clinical history and couple with the laboratory blood tests and magnetic resonance Imaging (MRI) findings in arriving at diagnosis of this rare complication of life-threatening blood loss during or after child birth. We also highlighted the importance of proper medical care in preventing extreme bleeding during child birth, otherwise, Sheehan's syndrome is not preventable.
Keywords: Sheehan's Syndrome, Post Partum Hemorrhage

Introduction
Severe blood loss deprives body tissue and organs of oxygen, causing areas of tissue death. In Sheehan's Syndrome, this damage affects the pituitary gland- a small, bean-shaped gland at the base of the brain. The result, which may not be apparent for months or even years, is permanent underproduction of pituitary hormones[1].

Life threatening postpartum hemorrhage is uncommon as a result of the advances in obstetric care. Thanks to improve prenatal care and medically supervised child birth. Sheehan's syndrome has become rare in parts of the world where access to medical care is available[1]. As this case illustrates, however, the consequences of postpartum hemorrhage can be severe.

Case Report
A 22 year old lady from Soba, a rural Community in Kaduna State, Nigeria who was gravida1 para1^{+0} (alive) presented at accident and Emergency Department with a 5 day history of nausea, vomiting, dizziness, fatigue, loss of appetite, diarrhea and difficulty with lactation. 6 months ago she was rushed to the same Emergency department in coma on account of excessive blood loss after child birth. She was unbooked despite the availability of a health center that runs antenatal clinic in that community. She went into labour at home and delivered a viable male infant weighing 3.9kg under the supervision of traditional birth attendance. The labour was said to last for 18 hours. Immediately after delivery she started bleeding profusely for 3 days non-stopped while she was been managed at home. She went into coma before she was rushed to the Emergency Department.

On presentation she was in hypovolemic shock, hypotensive with pcv of 8%. The patient's uterus was found to be boggy and flabby, there was also a deep cervical laceration extending to the lower uterine segment. After she was resuscitated, she was taken to the theatre where the laceration was repaired. She had considerable bleeding after the procedure and she received misoprostol and dinoprostone. During this period she received numerous units of blood,

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platelets and fresh frozen plasma because she was hypotensive and coagulopathic. The bleeding stopped few hours after the repaired. She remained in the intensive care unit for 3 days and spent a total of 2 weeks in the hospital. A sodium level measured on the 10th day of her hospitalization was normal. She lactated well on her discharge home.

In her current presentation at Emergency Department, the patient was normovolemic. Her blood pressure, pulse, respiratory rate and temperature were essentially normal, and there was no orthostatic hypotension. Her sodium was 100Eq/L. her hemoglobin was 10.5ml/dL, hematocrit 32%, white blood cell count 6,000/uL, potassium 4.8m Eq/L, chloride 90 mEq/L, carbondioxide content 18m Eq/L, blood urea 5.0mg/L and creatinine 0.7mmol/L. She was alert and well oriented and had normal findings on neurologic examination. She was admitted to the hospital for severe hyponatremia.

Initially her hyponatremia rapidly corrected to 120 mEq/L by active hydration with normal saline solution and then frusemide diuresis. The patient subsequently had fluids restricted; however, her sodium level was slow to correct. At admission, her serum osmolality was 210mosm/L, and her urine osmolality was 110mosm/L. Her cortisol level and thyroid-stimulating hormone (TSH) level were also measured at admission and were low at 1.7ug/dL and o.38ng/dL respectively. These laboratory values suggested pituitary failure. To ascertain whether this patient did infact have pituitary failure, an insulin tolerance test was conducted on day 7 of her hospitalization. Her cortisol level never went higher than 3ug/dL. The magnetic resonance Imaging of the brain (MRI) confirmed empty sella (fig1) and this also ruled out the possibility of primary pituitary tumour.

Based on these results, pituitary failure caused by Sheehan's syndrome was diagnosed. The patient was started on cortisone acetate while still in-patient and on levothyroxine and estrogen 1 week after her discharge. She is to be placed under surveillance for adrenal insufficiency. The patient will need to remain on both estrogen and levothyroxine therapy for the rest of her life. She will also need adreno-cortical steroid replacement whenever she has surgery or is severely ill. But she was lost to follow-up.

Discussion
Sheehan's Syndrome, also known as post partum hypopituitarism or postpartum pituitary necrosis, is a condition in which hypopituitarism develops after severe bleeding (postpartum hemorrhage) during or immediately after child birth[2].

Pituitary necrosis is a complication of post partum hemorrhage initially described by Harold Sheehan in 1937[3]. This case illustrates an example of Sheehan's syndrome at 6 months postpartum with severe hyponatremia. The pituitary gland is physiologically enlarged in pregnancy without a corresponding increase in blood supply and is therefore very sensitive to the decreased blood flow caused by massive hemorrhage and hypovolemic shock. Women with Sheehan's syndrome have varying degrees of hypopituitarism, varying from pan hypopiptuitarism to only selective pituitary deficiencies[4-6]. The anterior pituitary is more susceptible to damage than the posterior pituitary because it is supplied by a low pressure portal venous system[7]. The posterior pituitary is usually not affected due to its direct arterial supply. The incidence of Sheehan's syndrome world wide has decreased with better health care during child birth and delivery but is still about 0.5% of all cases of hypopituitanrism in women[2]. In Nigeria, the exact incidence of Sheehan's syndrome is unknown, but the maternal mortality from child birth is high 800/100,000 live birth ranging from 165/100,000 live births in the southwest part of Nigeria to as high as 1549/100,000 live births in the far North eastern part of Nigeria with postpartum hemorrhage and infection as leading cause of death[8, 9]. However, the incidence of Sheehan's syndrome is rare because most patients with severe postpartum hemorrhage died before they develop the disease due to non- availability of good health faculties and blood banking systems most especially in the rural areas. Blood loss generally has to be more than 800ml for Sheehan's syndrome to develop[2]. But in certain

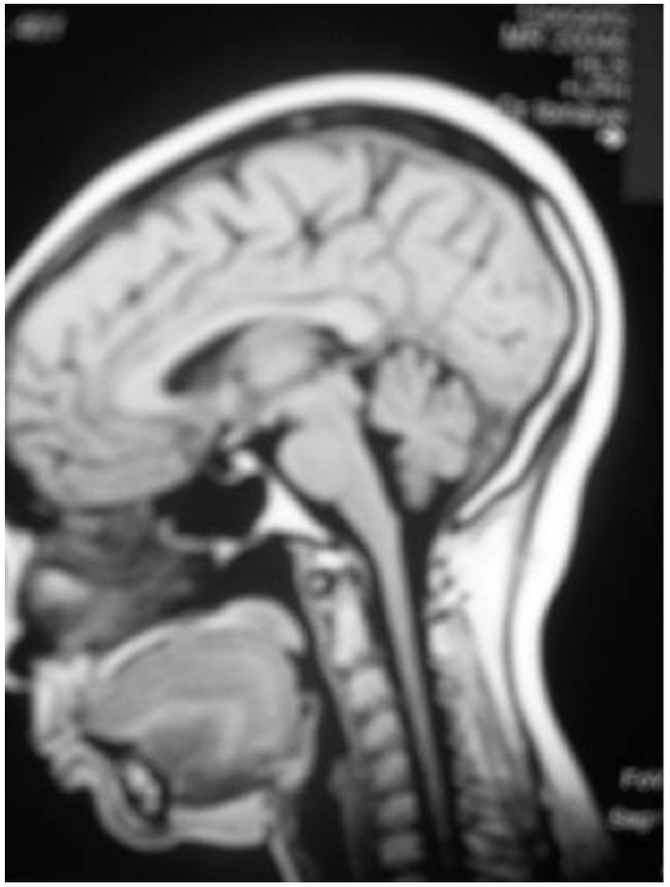

Figure 1: Brain MRI Shows Empty Sella

women, even minimal bleeding seems to cause this condition[2]. In this case, the exact amount of blood loss could not be ascertained but the patient was said to have bled profusely at home for 3 days until she became unconscious before she was rushed to the hospital.

Failure to lactate or difficulties with lactation are common initial symptoms of Sheehan's syndrome[10]. However, in this case, the difficulties with lactation and other symptoms started 6 months after the extreme post partum hemorrhage. Many women also report amenorrhea or oligomenorrhea after delivery[1]. In this case, the patient was yet to establish menstruation after delivery before she developed Sheehan's syndrome. In some cases, the diagnosis of Sheehan's syndrome is not made until years later, when features of hypopituitarism, such as secondary hypothyroidism or secondary adrenal insufificiency, become evident in a woman who had a post partum hemorrhage[1]. A woman with undiagnosed hypopipuitarism from Sheehan's syndrome might be relatively asymptomatic until her body is stressed by a severe infection or surgery years after her delivery, and she goes into an adrenal crisis[1].

Hyponatremia is an uncommon acute presentation of sheehan's syndrome [11-13]. There are several possible mechanism by which hypopituitarism can result in hyponatremia. Hypothyroidism can cause decreased free water clearance and subsequent hyponatremia. Glucocorticoid deficiency can also cause decrease free water clearance independent of vasopression. Hypopituitarism itself can

stimulate vasopression secretion and can cause severe inappropriate secretion of anti diuretic hormone, which can also cause hyponatremia. The potassium level in these situations is normal, because adrenal production of aldosterone is not dependent on the pituitary. In this case, the patient serum potassium level was normal throughout on admission. Also in this case, the patient responded slightly to fluid restriction, but her sodium levels did not return to normal until she received hydrocortisone replacement therapy.

Diagnosis of Sheehan's syndrome can be difficult. The diagnosis is based on clinical evidence of hypopituitarism in a woman with a history of a post partum hemorrhage[1] as seen in this case report. Deficiencies of specific anterior pituitary hormones will cause varied symptoms. Corticotropin deficiency can cause weakness, fatigue, hypoglycemia, or dizziness as noted in this case. Gonadotropin deficiency will often cause amenorrhea, oligomenorrhea, hot flashes, or decreased libido. Growth hormone deficiency causes many vague symptoms including fatigue, decreased quality of life and decreased muscle mass.

Secondary hypothyroidism is clinically indistinguishable from primary hypothyroidism, patients with hypothyroidism caused by hypopituitarism have low T3 and T4 levels with normal or even inappropriately low TSH levels[1]. Diagnosis of pan hypopituitarism is straightforward, but partial deficiencies are often difficult to elicit[14]. A woman with panhypopituitarism will have low levels of pituitary hormones (luteinizing, hormone, corticotrophin, and thyrotropin) as well as the target hormones (cortisol and thyroxine). Stimulation tests (insulin-induced hypoglycemia or metyrapone stimulation test) are often necessary for diagnosis in the acute phase or in situation where a partial deficiency is suspected[15].

In this case, the diagnosis of sheehan's syndrome was suspected because of her history, hyponatremia and low baseline cortisol and thyroid hormones levels. Neither cortisol, corticotrophin or growth hormone levels responded to a hypoglycemic state. The insulin tolerance test induces transient hypoglucemia, which in a person with normal pituitary gland stimulates corticotrophin production and cortisol release. Normal stimulated level of cortisol range in the hundreds[1]. This patient's cortisol level never went higher than 2ug/dl. The insulin tolerance test can also test for growth hormone deficiency but is an unpleasant test for the patient and is contraindicated in patients who have coronary artery disease or seizures. This test was not done in this case.

Radiologic imaging with either computed tomography or magnetic resonance imaging is usually helpful further into the disease process [16-18]. Several studies have shown an empty sella. However, MRI may not be helpful in the acute phase and has not been used frequently in acute diagnosis[16-19]. Imaging can be helpful in situations where the diagnosis is not apparent. In this case, the patient had MRI scan of the brain which demonstrated empty sella and it also helped to rule out the presence of pituitary tumour.

Treatment of young women with hypopituitarism usually includes replacement of hydrocortisone first and then replacement of thyroid hormone, and estrogen with or without progesterone depending on whether she has a uterus[1]. Hydrocortisone is replaced first because thyroxine therapy can exacerbate glucocorticoid deficiency and theoretically induce an adrenal crises[13-20]. The standard dose of hydrocortisone is 20mg/d for an adult (15mg every morning and 5mg every evening). Both thyroxine replacement and gonadotropin replacement are common, and doses are titrated to each individual[1]. Replacement of growth hormone is necessary in children with hypopituitarism but is controversial in adult[1]. Some people with severe growth hormone deficiency derive great benefit from replacement but standard recommendations are not available[21].

Conclusion: Although Sheehan's syndrome is uncommon as a result of improved obstetric care, it should be a consideration in any woman who has a history of a postpartum hemorrhage and who reports signs or symptoms of pituitary deficiency.

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