CASE REPORT

Sheehan's Syndrome Presenting with Early Postpartum Congestive Heart Failure

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We report the case of a young woman with Sheehan's syndrome who presented with ventricular arrhythmia and congestive heart failure. The patient was admitted because of postpartum hemorrhage and hypovolemic shock; a massive blood transfusion was required to restore blood volume. After initial stabilization, the patient developed acute respiratory distress and congestive heart failure accompanied by hemodynamic instability 2 weeks after delivery. Episodes of ventricular tachycardia of the torsade de pointes type and a prolonged QT interval were noted on baseline electrocardiogram. A low cortisol level was found incidentally, which led to the suspicion of hypopituitarism. The diagnosis was later supported by laboratory findings of multiple pituitary hormone deficiencies. After administration of corticosteroids and thyroxine, the patient's clinical condition improved dramatically. A pituitary magnetic resonance imaging scan 32 days after delivery revealed a diminished and flattened pituitary gland with prominent intrasellar cerebrospinal fluid loculation, which was compatible with the clinical diagnosis of empty sella with panhypopituitarism. The syndrome of acute anterior pituitary necrosis secondary to postpartum hemorrhage and shock was first described by Sheehan in 1939. Although the occurrence of Sheehan's syndrome is now rare, it should still be considered in any woman with a history of peripartum hemorrhage who develops manifestations of pituitary hormone deficiency. Appropriate hormone replacement therapy is essential and always results in dramatic clinical improvement. [*J Chin Med Assoc* 2005;68(8):386–391]

Key Words: congestive heart failure, Sheehan's syndrome, ventricular arrhythmia

Introduction

Sheehan's syndrome is a rarely encountered disease. It was first reported in 1937 by Sheehan et al,[1] who described a case of postpartum pituitary necrosis and insufficiency. Most cases remain undiagnosed until years after parturition. Sheehan's syndrome that presents acutely is comparatively rare. Here, we report such a case of acute Sheehan's syndrome complicated with heart failure, followed by a discussion of the manifestations of acute Sheehan's syndrome and its diagnosis.

Case Report

This case describes a 33-year-old woman without significant past illness who had previously given birth to 3 children via Cesarean section. All 3 deliveries were uneventful, and the patient had normal postpartum lactation. For this fourth pregnancy, placenta previa was identified; therefore, at 39 weeks' gestation, the patient again underwent Cesarean section at the local obstetrics clinic. However, the operation was complicated by massive postpartum hemorrhage, resulting in hypotension and, eventually, circulatory

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shock. After an emergency hysterectomy, the patient was transferred to our hospital.

On arrival, the patient had a body temperature of 35°C, blood pressure of 80/40 mmHg, heart rate of 108 beats/min, and respiratory rate of 28 breaths/min. She appeared somnolent, and her conjunctivae were pale, but she had no scleral icterus. Her jugular veins were collapsed. No palpable goiter or lymph nodes were noted from neck examination. The patient's breathing pattern appeared normal, and her abdomen was notable for a surgical scar. She had no lower extremity edema, and her skin was cold and moist. Initial laboratory findings were remarkable for the following: white blood cell count, 17,800/μL; hemoglobin, 6.6 g/dL; platelet count, 132,000/μL; prothrombin time, 14.3 seconds; activated partial thromboplastin time, 34.9 seconds; fibrinogen, 99.8 mg/dL; D-dimer, 2,878 ng/mL; plasma glucose, 197 mg/dL; blood urea nitrogen, 9.9 mg/dL; serum creatinine, 0.8 mg/dL; sodium, 141 mmol/L; potassium, 4.5 mmol/L. On the day of admission, because of sustained hemorrhage and resulting circulatory shock and respiratory failure, the patient required endotracheal intubation and mechanical ventilation. After resuscitation with liberal amounts of intravenous fluids and blood transfusions, the patient's condition stabilized. On day 10 of hospitalization, she was transferred out of the intensive care unit (ICU) after successful extubation.

On postpartum day 19, the patient again developed respiratory distress and became unconscious. Chest radiography revealed acute pulmonary edema (Figure 1). The patient was transferred back to the ICU after endotracheal intubation. A pulmonary perfusion scan obtained later indicated a low probability of pulmonary embolism. Echocardiography revealed normal heart size but diffuse hypokinesis (left ventricular ejection fraction was 40%). Angiotensin converting enzyme inhibitor and diuretic therapy was administered for heart failure. Brief episodes of polymorphic ventricular tachyarrhythmia were detected during this period (Figure 2A), for which amiodarone was administered. A 12-lead electrocardiogram (ECG) showed QT-interval prolongation, with a calculated QTc of 0.56 seconds (Figure 2B). Pertinent laboratory findings were as follows: creatine phosphokinase (CPK), 71 U/L; CPK-MB, < 5 U/L; troponin-I, 0.4 ng/mL; myoglobin, 39.5 U/L; sodium, 141 mmol/L; potassium, 3.2 mmol/L; magnesium, 1.8 mmol/L; ionized calcium, 1.02 mmol/L. On the third day of her ICU stay, she had a seizure. A brain magnetic resonance imaging (MRI) scan obtained afterwards revealed no notable abnormality.

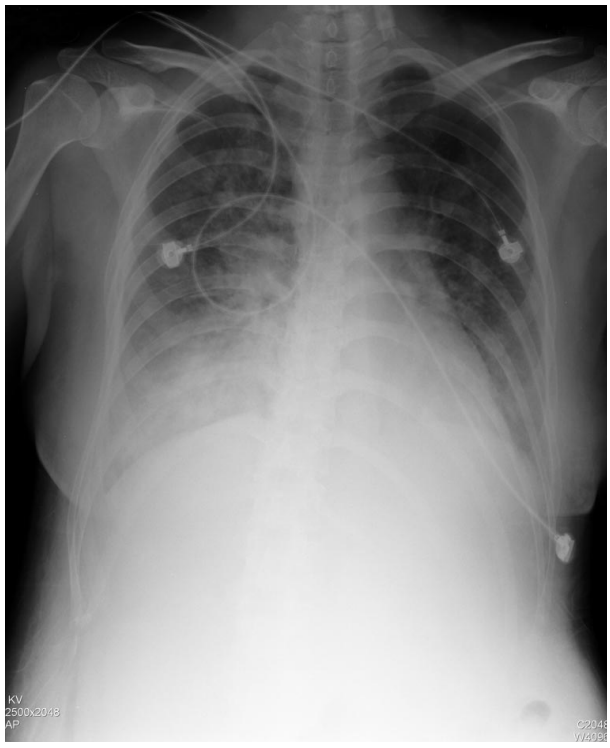

Figure 1. Acute pulmonary edema at postpartum day 19.

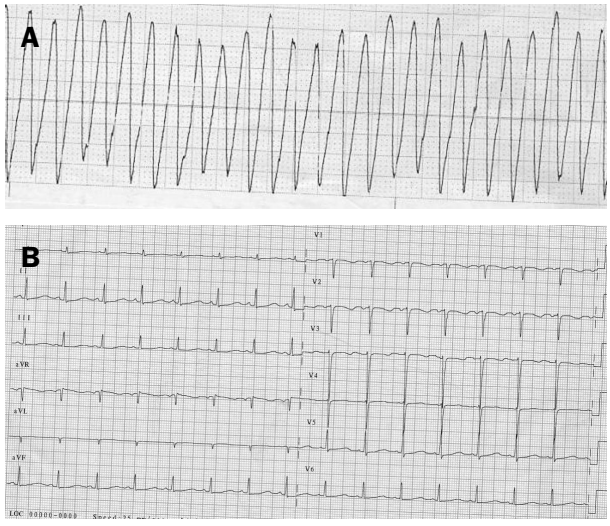

Figure 2. (A) Polymorphic ventricular tachycardia of the torsade de pointes type; (B) complete 12-lead electrocardiogram during normal rhythm.

To determine the cause of the patient's hemodynamic instability, besides her seizure onset, thyroid and adrenal function were assessed. Initial hormone levels suggested hypofunction in both axes, with a thyroid stimulating hormone level of 0.802 IU/L, free thyroxine of 0.4 ng/dL, and morning cortisol level of 2.9 μg/dL. Linking these findings with the patient's history of postpartum hemorrhage,

Table 1. Serum hormonal levels via radioimmunoassay at postpartum day 21

Hormones	Basal value	Normal value
Cortisol (morning; μg/dL)	2.9	4.3–22.4
Adrenocorticotropic hormone (pg/mL)	8.1	9–46
Free thyroxine (ng/dL)	0.4	0.89–1.76
Thyroid stimulating hormone (μIU/mL)	0.802	0.35–5.5
Prolactin (ng/mL)	12.1	> 20 (in postpartum)
Luteinizing hormone (mIU/mL)	0.9	3–9
Follicle stimulating hormone (mIU/mL)	0.5	4–9
Estradiol (pg/mL)	13.2	33–100
Growth hormone (ng/mL)	0.1	< 8.6

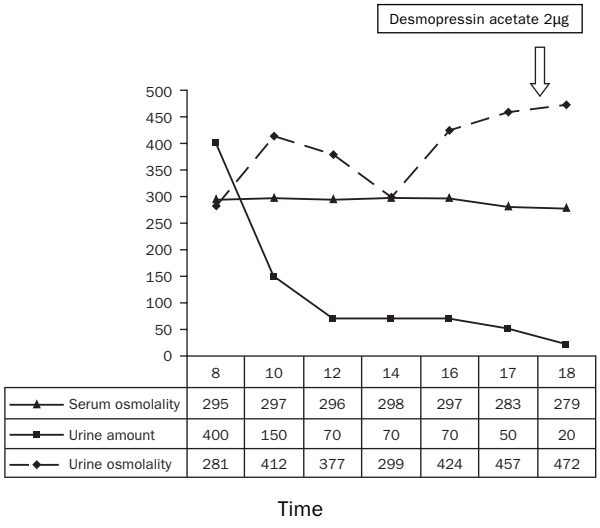

Figure 3. Water deprivation test.

and based on a high likelihood of Sheehan's syndrome, we decided to further evaluate pituitary function. As subnormal levels were noted across the panel of pituitary hormones, the diagnosis of panhypopituitarism was established (Table 1). The patient was then promptly given intravenous injections of hydrocortisone 100 mg 8-hourly, followed by oral thyroxine 0.05 mg/day. Such therapeutic measures resulted in dramatic clinical improvement. Arrhythmia did not recur during the patient's subsequent course. After 3 days, mechanical ventilation was stopped and the patient was transferred out of the ICU. The patient's post-ICU course was notable for excessive urine output (> 3 L/day). However, a water deprivation test did not confirm diabetes insipidus (Figure 3). On postpartum day 32, a pituitary MRI scan was obtained (Figure 4). It revealed a flattened pituitary gland and loculation of cerebrospinal fluid within the sella turcica. These findings were compatible with the clinical diagnosis of empty sella with hypopituitarism. On postpartum day 37, the patient was discharged home uneventfully.

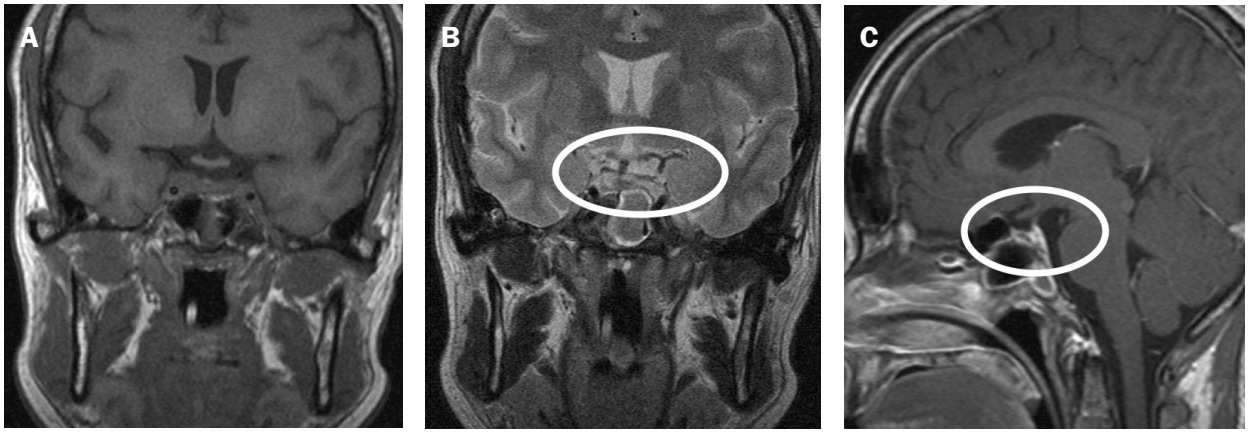

Figure 4. Pituitary magnetic resonance imaging (MRI) scan at postpartum day 32: (A) T1-weighted coronal image; (B) T2-weighted coronal image; (C) post Gd-DTPA enhancement of sagittal image. The pituitary gland appears more flattened than normal, with cerebrospinal fluid loculation within the sella turcica. High signal intensity is noted in the T2-weighted image. The pituitary stalk appears deviated to the right. No abnormal signaling is noted after contrast enhancement and no tumors are noted. Enhancement with Gd-DTPA shows no intrasellar mass or adenoma with delayed enhancement. MRI findings are thus compatible with a clinical diagnosis of Sheehan's syndrome.

Discussion

During pregnancy, the pituitary gland enlarges to twice its normal size. Because of the consequent increase in the demand for blood supply, the gland becomes liable to ischemic injury if blood flow is compromised by hemorrhage, shock, or compression of the portal vessels by the enlarged gland. The adenohypophysis is more vulnerable than the neurohypophysis because of its relatively smaller blood supply. Thus, isolated anterior pituitary insufficiency occurs far more commonly than posterior insufficiency as a complication of postpartum hemorrhage, with diabetes insipidus occurring only 5% of the time.[2] Our patient also had isolated anterior pituitary disease. In line with advances in modern obstetrics, the occurrence of Sheehan's syndrome has declined appreciably. Predisposing factors include multiple gestation and malpositioning of the placenta, and our patient was at risk of postpartum hemorrhage because of placenta previa.

The diagnosis of Sheehan's syndrome remains difficult. A history of postpartum hemorrhage and the subsequent appearance of hypopituitarism constitute the main basis for clinical suspicion. Hypopituitarism may range from mild to life-threatening, and may involve single or multiple hormone deficiencies. Acutely, patients may present with breast atrophy, lack of lactation, fatigue, hypotension, and hypoglycemia, with each hormone deficiency giving rise to a characteristic picture. Corticotropin deficiency, for example, results in weakness, fatigue, hypoglycemia, and dizziness, whereas gonadotropin deficiency manifests as amenorrhea, oligomenorrhea, hot flashes, and decreased libido.

In our patient, the diagnosis of Sheehan's syndrome was corroborated by her history, lack of postpartum lactation, and abnormal hormonal radioimmunoassays and MRI findings. Hormone stimulation tests, in particular the insulin hypoglycemic test, were not conducted during hospitalization because of the patient's predisposition to seizure and arrhythmia and because they would have provided limited clinical information for acute management. Regrettably, for personal reasons, the patient discontinued treatment at our hospital soon after discharge, and we were unable to perform follow-up stimulation tests.

According to published literature, stimulatory testing for patients with Sheehan's syndrome most commonly reveals a lack of growth hormone (GH) and prolactin responses to insulin-induced hypoglycemia, or lack of a prolactin response to stimulation with thyrotropin-releasing hormone (TRH). A possible explanation might be the sequestration of somatotrophs and lactotrophs in the inferolateral aspects of the pituitary gland, which are most susceptible to ischemic insult.[3] Stimulation via insulin-induced hypoglycemia is potentially hazardous for elderly patients and those with impaired heart function. Therefore, stimulation of prolactin release with TRH, which is safer, faster, and more practical than stimulation by insulin-induced hypoglycemia, might be the favored approach for Sheehan's syndrome screening.[4]

The differential diagnoses of Sheehan's syndrome include lymphocytic hypophysitis and pituitary hemorrhage or infarction secondary to overgrowth of an adenoma. Clinical manifestations of these conditions are similar, but imaging modalities such as MRI should permit accurate differentiation. A pre-existing adenoma may give rise to the appearance of a deviated pituitary stalk, enlargement of the sella turcica, or erosion of the floor of the sella. Lymphocytic hypophysitis appears on MRI as a symmetrically enlarged pituitary gland which is contrast-enhanced by gadolinium diethylenetriamine penta-acetic acid (Gd-DTPA). The pituitary gland in Sheehan's syndrome characteristically appears as a high-intensity lesion on T2-weighted imaging, but without contrast enhancement after Gd-DTPA. This has been attributed to acute ischemia of the gland.[5] Nonetheless, a history of postpartum hemorrhage remains the cornerstone for the diagnosis of Sheehan's syndrome, with imaging studies playing only a secondary diagnostic role.

There have been previous reports of hypopituitarism associated with ECG abnormalities.[6] Findings include ST-segment depression, T-wave inversion, and QT-interval prolongation, the reasons for which are unknown, although Iga et al[7] proposed a mechanism based on hypoglycemia. Indeed, patients with hypoadrenalism might be susceptible to hypoglycemia-invoked catecholamine release, resulting in arrhythmias or abnormal ventricular contractions. Other researchers have suggested that hypomagnesemia associated with adrenal insufficiency may contribute to an electrical imbalance across the cardiac myocyte membrane and, therefore, produce contractile dysfunction. Our patient, however, did not develop hypomagnesemia (serum magnesium, 1.8 mg/dL). She had an initial random plasma glucose level of 197 mg/dL, which was measured when her condition was critical. During hospitalization, she had only 1 episode of hypoglycemia (59 mg/dL). Another possible cause for her heart failure may have been fluid overload, particularly as free water clearance is impaired in both

hypothyroidism and hypoadrenalism. The increase in our patient's urine output after hormone replacement supports this hypothesis.

Prolongation of the QT interval might trigger the onset of polymorphic ventricular tachycardias (PVTs). QT prolongation has many causes, including drugs, electrolyte imbalance, myocardial disease, cerebrovascular disease, and congenital long QT syndrome. In addition, hypothyroidism may also lengthen the QT interval.[8] Our patient had multiple episodes of PVTs, without associated electrolyte abnormalities or the previous use of arrhythmogenic drugs, although prolongation of the QT interval was identified. After instituting hormone replacement, the arrhythmias did not recur and the QT interval normalized. Therefore, for patients with PVTs and a prolonged QT interval, the possibility of endocrinologic disorders should also be considered. Timely correction of hormonal imbalances may prevent the development of fatal arrhythmias.

The pathogenesis of acute Sheehan's syndrome is not entirely clear, although there is no doubt that the basic process is infarction secondary to arrest of blood flow to the pituitary gland. Nevertheless, pituitary gland pathology in acute Sheehan's syndrome has rarely been reported. In 1 case report, histologic examination revealed extensive acute necrosis of the pituitary gland. In the necrotic area, adenohypophyseal cells could not be recognized. They had been replaced by ghost cells, necrotic debris, coagulated blood, and inflammatory cells.[9] In the later phases of Sheehan's syndrome, marked shrinkage of the pituitary gland has been found, together with massive fibrosis and the loss of adenohypophyseal cells.

Acute presentation of Sheehan's syndrome is rarely described. There have been previous reports of acute Sheehan's syndrome presenting with either hypoglycemic coma or hyponatremia,[10] but none with acute heart failure as in the present case. The endocrine diseases associated with heart failure include acromegaly, hypoparathyroidism, hypothyroidism, hyperthyroidism, and malignant carcinoid syndrome.[11] There has been only 1 report of an adult patient with pituitary hypoadrenalism complicated with cardiomyopathy and heart failure; after appropriate hormone replacement, cardiac contractile function improved and heart failure resolved completely.[12] In our case, besides adrenal insufficiency and hypothyroidism, tachyarrhythmia was also implicated in the development of heart failure. Fortunately, prompt hormone replacement improved and stabilized the patient's clinical course.

The treatment of Sheehan's syndrome consists of correction of hormone deficiencies. Acutely, corticosteroid therapy should be administered, followed by thyroxine and estrogen replacement (the presence of an intact uterus also necessitates progestin replacement). For GH deficiency, adult GH replacement therapy remains controversial.[13] Several reports have demonstrated beneficial effects of GH on body composition (reduction of body fat and augmentation of lean body mass), blood lipid profile, and cardiovascular risk.[14] However, an impact of GH on quality of life has not been shown consistently: Gilchrist et al[15] reported improved life quality among patients treated with GH for up to 9 years, whereas Hoffman et al,[16] in a double-blind, controlled trial, found no benefit for GH on exercise tolerance or quality of life.

In summary, Sheehan's syndrome is rarely encountered. It is even more unusual for it to manifest in the weeks immediately after delivery. Nevertheless, the index of suspicion is raised when a patient presents with a history of massive postpartum hemorrhage complicated with shock, and clearly, clinicians should be mindful of the clinical picture of Sheehan's syndrome.

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