

## CASE REPORT

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## SHEEHAN'S SYNDROME

**CASE:** A 61 year old female was referred to University Hospital for evaluation due to altered mental status. The patient's symptoms, which had increased over the preceding 12 hours, were characterized as lethargy and decreasing responsiveness. There was no report of fever, chills, recent URI, UTI symptoms, recent nausea or vomiting, diarrhea or headache. Neither were there any reports or evidence of tick or insect bites. Some melena had been noted at the referring facility but this was not corroborated with an FOBT.

Her PMH was remarkable for a history of urinary incontinence and an episode of post-partum hemorrhage; she had since undergone a hysterectomy. The patient was a nonsmoker and did not use alcohol or illicit drugs. Of note, approximately 1 year ago, she was treated for a similar episode of altered mental status, associated with a headache; though hyponatremia was noted, the remainder of her workup, including an LP, had been unremarkable. Current medications were limited to oxybutynin and estrogen supplementation. Her family history was significant for breast cancer.

On initial exam, she was noted to be very lethargic and was unable to provide any reliable history (the above data was provided by her husband). Her T was 35 C, P 65, R 14, BP 128/71, O<sub>2</sub> sat 98% on 4L of oxygen. She was in no apparent distress. Her head and neck exam was normal; no thyromegaly or adenopathy was found. Chest was clear and cardiovascular exam was WNL. Abdomen was soft and nontender with no organomegaly. Her neurologic exam did not reveal any focal neurologic deficits; diminished DTRs were noted.

An ABG revealed a pH of 7.4, pCO<sub>2</sub> 46, PO<sub>2</sub> 67, HCO<sub>3</sub> 28 and O<sub>2</sub> sat of 94.5% on 4L of oxygen. Other initial labs included WBC 5.3, Hgb 10.9, MCV 94.6, Platelet Count 159, Na 123, K 3.2, Gluc 71, BUN 22, Creat 0.97, Alb 3.8, AST 71, ALT 49, TB 0.1, INR 0.9, PTT 61.6, CK 4135, CKMB 57.8, Trop 0.08, TSH 1.1, spot cortisol 18.4

An EKG revealed sinus bradycardia with first degree AVB and low voltage QRS. A CT of her head was reported to be normal from the outside facility but an MRI revealed partial empty sella. An echocardiogram demonstrated a small pericardial effusion. An LP returned a CSF protein of 102, glucose 59, negative gram stain, WBC 30 (92N, 4M, 4L) RBC 4. A sample was sent for ehrlichia via PCR.

The patient was admitted to the ICU, pancultured and placed on IV fluids. Infectious Disease and Endocrinology were consulted. Her free T<sub>4</sub> was nondetectable and there was no response to an ACTH stimulation test. A diagnosis of myxedema coma with panhypopituitarism was made, presumably secondary to Sheehan's syndrome, especially in light of her history and her partially empty sella. Noting that myxedema coma carries a mortality rate of 40%, Endocrinology recommended the administration of 150 mcg of levothyroxine IV; this was followed by 200 micrograms IV on day 2 and thereafter changed to 125 mcg PO daily. She was also treated with hydrocortisone 100 mg IV q8h, tapered to 50 mg q8h and then switched to oral hydrocortisone 20 mg q AM and 10 mg q PM. Since myxedema can blunt a patient's ability to respond to infection with leukocytosis, empiric antibiotic coverage was considered but, based on the lack of other clinical findings, was not initiated. Her hyponatremia responded to conservative measures and to the above therapeutic regimen and the patient's overall clinical condition gradually improved. She was discharged to home within a week of her admission and will be followed by her PCP and the Endocrinology Clinic.

(continued)

**DISCUSSION:**

Hypopituitarism is caused by pituitary adenomas or their therapy (radiation, surgery) in about 75% of cases. Another 13% are caused by extrapituitary tumors and almost 10% of cases are idiopathic. Rare causes include tuberculosis, Wegener's granulomatosis, hemochromatosis and sarcoidosis. Sheehan's Syndrome (postpartum pituitary necrosis) is responsible for about 0.5% of cases in developed countries (though significantly higher in developing countries with limited resources for post-partum care). However, as discussed below, the incidence of this syndrome may be more common than realized since symptoms may be mild and the diagnosis is often delayed for many years.

Enlargement of the anterior pituitary is a normal physiologic development during pregnancy, compressing the superior hypophyseal artery and placing the organ at risk for infarction should hypotension or vasospasm develop in the face of postpartum hemorrhage. Rapid response with fluid resuscitation and transfusion mitigates this complication though focal ischemia and infarction may occur even with aggressive therapy. In rare cases, acute decompensation may result, but, in the majority of cases, the endocrinologic effects are mild and, though failure of lactation and postpartum amenorrhea are common, the patient may otherwise remain asymptomatic for years or even decades. Indeed, in a study by Ozkan and Colak [2], 20 cases of Sheehan's syndrome were reviewed; the age at diagnosis ranged from 40 to 65 years, with a mean age of 51 years. All 20 patients were found to have GH, Prolactin, FSH, TSH and ACTH insufficiency; 11 had empty sella and the other 9 had partial empty sella.

Empty sella on CT or MRI may be primary or secondary. Primary empty sella is due to a defect in the diaphragm sella, allowing CSF pressure to enlarge the sella space; these patients usually have normal pituitary function. Secondary empty sella is due to destructive lesions (or surgical resection) of the pituitary; the sella itself is normal in size but the pituitary mass is small and hormonal deficiencies develop. Patients with Sheehan's syndrome may have one or more pituitary hormone deficiencies, related to the degree of infarction and atrophy that occurs. Though some have postulated that an abnormally small sella may predispose a woman to Sheehan's syndrome, the great majority of cases have been associated with a normal sized sella on imaging.

The role of autoimmunity in the development of Sheehan's syndrome remains controversial. This condition has not been clearly associated with any other autoimmune diseases and, while some studies have demonstrated an increase in anti-pituitary antibody in these patients, this may be secondary to antigen shedding following the initial tissue infarction. Lymphocytic hypophysitis, which occurs in both men and women, may mimic Sheehan's syndrome, especially since its development is postpartum in almost 60% of the female patients; however, this condition has no association with postpartum hemorrhage.

**REFERENCES:**

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