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COMPLETE ANTERIOR PITUITARY FAILURE AND POSTPARTUM CARDIOMYOPATHY

Amish Parikh, MD, FRCPC, and Shereen Ezzat, MD, FRCPC

ABSTRACT

Objective: To present a case of presumed autoimmune hypophysitis that occurred concurrently with severe postpartum cardiomyopathy and pneumonitis.

Methods: We describe the clinical, laboratory, and imaging findings in a young postpartum woman who presented with decompensated heart failure.

Results: Two weeks after childbirth, a 37-year-old previously healthy woman required urgent pericardiocentesis and inotropic support because of new-onset left ventricular systolic dysfunction, pericardial effusions, and hypotension. Analysis of pericardial fluid was negative for malignant cells and culture, and no cardiac tamponade or thrombus was evident. Results of a rheumatologic serology survey were negative, as was an assessment for antithyroid antibodies. Chest radiography revealed bilateral pleural effusions. Magnetic resonance imaging of the pituitary showed a homogeneously enlarged gland, consistent with the postpartum state, but no discrete pituitary lesions. Laboratory results included low levels of thyrotropin, free triiodothyronine, free thyroxine, and cortisol and a high erythrocyte sedimentation rate. The patient’s symptoms responded to prednisone therapy (60 mg/day) as well as an angiotensin-converting enzyme inhibitor and a β-adrenergic blocking agent. Follow-up magnetic resonance images showed an atrophic pituitary with an empty sella turcica.

Conclusion: To our knowledge, this is the first reported case of concomitant presumed autoimmune hypophysitis, complete anterior pituitary failure, postpartum cardiomyopathy, and pneumonitis. (Endocr Pract. 2006;12:284-287)

Abbreviations:
ACTH = adrenocortotropic hormone (corticotropin); GH = growth hormone; MRI = magnetic resonance imaging

INTRODUCTION

Lymphocytic hypophysitis is a rare inflammatory process of the pituitary gland in which the gland is infiltrated by lymphocytes, plasma cells, and macrophages. Anterior pituitary function can often be affected, with corticotropin (adrenocorticotropic hormone or ACTH) deficit usually being the first hormonal derangement. Female subjects are affected much more frequently than are male subjects; studies have shown a female-to-male ratio ranging from 5:1 to 8:1 (1,2). Furthermore, a strong association with pregnancy has been noted. Lymphocytic hypophysitis frequently affects women during the last 6 months of pregnancy and the first 6 months after childbirth (3). Recent investigations have shown that many patients with lymphocytic hypophysitis have antibodies against several pituitary-specific proteins. O’Dwyer et al (4) identified a role for alpha-1-antitrypsin in lymphocytic hypophysitis. We describe a young postpartum woman who had presumed autoimmune hypophysitis in conjunction with severe postpartum cardiomyopathy and pneumonitis.

CASE REPORT

A 37-year-old previously healthy woman (gravida 1, para 1) had an uneventful vaginal delivery in May 2002 after a normal pregnancy. The patient was originally from Jordan but had been in Toronto, Canada, since 1998. She denied smoking, use of alcohol, or use of illicit drugs. She was not taking any medications at that time. The family history was noncontributory.

Within a week after an uncomplicated vaginal delivery, the patient had severe bilateral peripheral edema associated with hypotension, new-onset left ventricular dysfunction, and substantial pericardial effusion. She was
also unable to breast-feed her baby. Because of her severe decompensated heart failure, 2 weeks after childbirth the patient was admitted to the coronary care unit and treated with urgent pericardiocentesis and inotropic support. Pericardial fluid analysis was negative for malignant cells and culture. An echocardiogram showed severe global left ventricular systolic dysfunction (ejection fraction, <20%) and a hypokinetic right ventricle. No cardiac tamponade or thrombus was seen. Chest radiography revealed bilateral pleural effusions with atelectasis and airspace consolidation in both mid and lower lung fields. Blood and urine cultures were negative. Results of a rheumatologic serology survey, including anti-DNA, antinuclear antibodies, anti-Jo 1, anti-Scl 70, anti-Sm, anti-RNP, anti-Ro, anti-La, antiphospholipid antibodies, were all negative.

Serum thyrotropin (thyroid-stimulating hormone) was 0.38 µIU/mL (normal, 0.50 to 5.00), free triodothyronine was 136 pg/dL (normal, 140 to 440), free thyroxine was 0.31 ng/dL (normal, 0.8 to 2.7), 11 AM plasma cortisol was 3.08 µg/dL (normal, 5 to 25), and the erythrocyte sedimentation rate was elevated at 132 mm in 1 hour (normal, <20). Serum ACTH was <9 pg/mL (normal, 6 to 76), follicle-stimulating hormone was 1.2 mIU/mL, luteinizing hormone was <1.0 mIU/mL, and prolactin was 11.5 ng/mL (normal, 3 to 27). Antithyroglobulin and antimicrosomal antithyroid antibodies were negative. Initial assessment of serum electrolytes showed the following: sodium 128 mEq/L, potassium 6.2 mEq/L, chloride 105 mEq/L, and creatinine 1.05 mg/dL.

Magnetic resonance imaging (MRI) of the pituitary revealed a symmetrically and homogeneously enlarged gland, consistent with the postpartum state (Fig. 1). Treatment with prednisone (60 mg/day orally) was initiated, and the addition of levothyroxine 1 week later yielded appreciable symptomatic improvement. Computed tomographic scanning of the abdomen showed no evidence of adrenal hemorrhage or lymphadenopathy. The patient was dismissed from the hospital in stable condition.

Three months later, while the patient was receiving a weaning dose of prednisone, she presented again to the emergency department with shortness of breath and pleuritic chest pain. Computed tomography of the thorax and echocardiography did not reveal pulmonary embolism or pericardial effusion, respectively. Echocardiography, performed in September 2002, showed mild left ventricular dysfunction (ejection fraction, 40% to 59%) but normal right ventricular function. Blood and pleural fluid cultures were negative. Stress-dose glucocorticoids and antibiotics were administered intravenously. Cultures from bronchosopic washings were unremarkable. The daily dose of glucocorticoids (prednisone, 60 mg orally) could not be tapered because of recurrent pleuritic chest pain and pleural effusions. Upper and lower gastrointestinal endoscopic investigations, prompted by the detection of anemia, showed normal findings. A repeated rheumatologic assessment including serology was again negative. A repeated MRI of the brain showed a considerably reduced pituitary gland size and no focal abnormalities. A bone marrow biopsy specimen was normal. Bone densitometry

Fig. 1. Magnetic resonance image (coronal view) of pituitary fossa of study patient 1 week after childbirth, revealing a diffusely enlarged gland, consistent with the postpartum state.
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marrow biopsy specimen was normal. Bone densitometry
showed a T-score of -2.6 at L1 through L4 and a T-score of -1.1 at the femoral neck. At the time of her dismissal from the hospital, the patient was receiving prednisone, 60 mg daily, for management of her corticosteroid-responsive pneumonitis.

During the subsequent 2 years, the patient remained free of clinical heart failure and responded well to treatment with an angiotensin-converting enzyme inhibitor and a β-adrenergic blocking agent. She continues to receive thyroid replacement therapy and glucocorticoid hormone replacement, currently at a maintenance dose (prednisone, 5 mg in the morning and 2.5 mg in the evening). Menstrual function did not resume spontaneously, and the patient continues to use an oral contraceptive agent. A recent bone mineral density study showed persistent osteopenia with a T-score of -2.1 at L1 through L4 and a T-score of -1.1 at the femoral neck. A bisphosphonate was added to her therapeutic regimen, along with calcium and vitamin D supplements. Her most recent echocardiogram showed minimal global systolic left ventricular dysfunction (ejection fraction, 50% to 59%). A recent hormonal assessment revealed a persistently low serum insulin-like growth factor-I level at 93 ng/mL (normal, 190 to 284) and a low serum prolactin level of <1 ng/mL (normal, 3 to 27), consistent with disruption of the somatotroph and lactotroph axes.

Serial MRI studies of the pituitary fossa during the 2-year follow-up have shown an atrophic pituitary gland with an empty sella turcica (Fig. 2). No discrete pituitary lesions have been identified.

DISCUSSION

To our knowledge, this is the first reported case of a patient who presented with the concurrent conditions of presumed hypophysitis, complete anterior pituitary failure, postpartum cardiomyopathy, and pneumonitis.

In the classic form, primary hypophysitis can be classified into 3 main types, which are similar in clinical and radiographic features and can typically be distinguished from one another only by histologic examination. These subtypes include (1) lymphocytic hypophysitis, (2) granulomatous hypophysitis, and (3) xanthomatous hypophysitis (2). Symptoms and signs of lymphocytic hypophysitis can be categorized into those related to pituitary enlargement and those related to abnormal and altered pituitary hormone secretion. In the first category, headache, visual field impairment, and, more rarely, diplopia are present. Abnormal pituitary hormone secretion can take the form of hyperprolactinemia, hypopituitarism, isolated ACTH deficiency, hypogonadotrophic hypogonadism, and, rarely, isolated growth hormone (GH) deficiency.

Thodou et al (1) examined the clinicopathologic features of 16 patients (14 female and 2 male) with lymphocytic hypophysitis. In 10 (71%) of the female patients, the presentation was associated with pregnancy. In the overall study cohort, 10 patients (63%) presented with anterior pituitary hypofunction, 9 (56%) with symptoms of an expanding sellar mass, 6 (38%) with hyperprolactinemia, and 3 (19%) with diabetes insipidus. In that report, 25% of the patients had associated autoimmune thyroiditis.

Fig. 2. Magnetic resonance image (coronal view) of pituitary fossa of study patient 2 years after initial presentation, showing a largely empty sella with no focal abnormalities.
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Several authors have reported the coexistence and association of hypophysitis with other autoimmune conditions. Goyal et al (5) reported a case of granulomatous hypophysitis due to Wegener's granulomatosis in a patient who presented with diabetes insipidus, headache, and progressive loss of vision. Toth et al (6) reported a case of granulomatous hypophysitis associated with Takayasu's disease.

We have not been able to find a documented association between hypophysitis and postpartum cardiomyopathy. Nevertheless, Sundstrom et al (7) suggested that postpartum cardiomyopathy may have an autoimmune basis, in that a distinct set of cardiac-specific intracellular protein autoantigens is associated with this condition. Patients with postpartum cardiomyopathy demonstrate high serum titers of antibodies for 27-, 33-, and 37-kd molecular weight autoantigens expressed in normal human cardiac tissue. Therefore, it may be hypothesized that our patient had multiple tissue-specific autoantigens and thus a severe autoimmune condition developed affecting multiple organs concomitantly.

The relationship between hypopituitarism and cardiac function has been studied in detail, especially in patients with GH deficiency. The association between GH deficiency and increased cardiovascular mortality has been well established. Cardiovascular abnormalities include, but are not limited to, increased formation of atherosclerotic plaques in conjunction with endothelial dysfunction (8). In reference to cardiac function specifically, Oz bey et al (9) studied this factor in 19 patients with GH deficiency who had at least 3 additional pituitary hormone deficits and compared their findings with those in control subjects matched for age, sex, and body mass index. Patients with untreated GH deficiency demonstrated impaired variables of left ventricular diastolic function (deceleration time and isovolumic relaxation time) more often than did the control subjects, even though systolic function at rest did not differ between the 2 groups. An investigation by Shahi et al (10) also found evidence of left ventricular diastolic dysfunction in patients with hypopituitarism and GH deficiency. Therefore, pituitary hormones, especially GH, are likely permissive for optimal cardiac health.

Although our patient had GH deficiency, she also exhibited cardiac deficits that cannot be explained on the basis of hormonal deficiency alone. Indeed, the presence of pericardial effusions and fluctuations in cardiac function in the absence of GH treatment suggest an independent intrinsic cardiac defect as a component of her multisystem disease.

CONCLUSION

To the best of our knowledge, this is the first published report of presumed autoimmune hypophysitis in conjunction with complete anterior pituitary failure, severe postpartum cardiomyopathy, and pneumonitis. Physicians should be aware of this potential coexistence of disorders.

REFERENCES