Acute Loss of Vision During Pregnancy Due to a Suprasellar Mass

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(In keeping with the purpose of a clinical pathological conference, the abstract and key words appear at the end of the article.)

Case Report: A 28-year-old woman presented during the third trimester of pregnancy in July of 1994 with intermittent headaches, bilateral transient obscurations of vision, and gradually progressive bilateral visual loss. She was taking no medications. Past medical history was significant for removal of a benign breast mass at the age of 13, and three previous pregnancies which were uncomplicated. She had a five pack year smoking history and rarely drank alcohol. Family history was unremarkable.

She complained of moderately severe, frontal and temporal headaches for nine weeks prior to presentation. These headaches lasted several hours, were not exacerbated by Valsalva maneuver or posture, and were not associated with nausea or vomiting. In addition, she had intermittent episodes of bilateral transient visual obscurations, which she described as “like a sheet of water” before both her eyes. Six weeks prior to presentation, she noted gradually progressive visual loss in the right eye greater than the left eye. Neuro-ophthalmologic examination revealed visual acuity of counting fingers at two feet OD and 20/20 OS.

Pupil examination revealed 5 mm pupils in each eye, a diminished light reaction in the right eye, and a right relative afferent pupillary defect. She correctly named 0 out of 10 Ishihara color plates OD and 8 out of 10 plates OS. Goldmann perimetry revealed a dense central scotoma with a superotemporal hemianopic defect to the V4e and I3e stimuli OD and a superotemporal hemianopic defect to the V4e and I4e stimuli OS (Fig. 1). Slit-lamp examination and intraocular pressure measurements were normal in both eyes. Ophthalmoscopy revealed mild temporal optic disk pallor in both eyes. Cranial nerves five and seven were intact.

Based upon the above history and neuro-ophthalmologic examination, what is the differential diagnosis? What further studies should be performed?

Comments

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The patient's history of headache and gradual progressive visual loss, along with the finding of a "junctional" scotoma, are consistent with a parasellar lesion compressing the right optic nerve at its junction with the optic chiasm. The leading differential diagnostic considerations in a young pregnant woman include a prolactin-secreting pituitary adenoma, other pituitary tumors (both secreting and nonsecreting), and lymphocytic hypophysitis. In addition, one must consider the usual gamut of parasellar lesions that are seen in this age group but are unrelated to pregnancy. These include sphenoid wing meningioma, craniopharyngioma, and more rarely, carotid aneurysm, demyelinating disease, and chiasmal glioma. In the post-partum period, pituitary apoplexy would also be an important consideration. At this point, the appropriate study would be a gadolinium enhanced MRI scan to further define the chiasmal and parasellar pathology. A complete endocrinologic evaluation is also indicated, both as an adjunct to diagnosis and as a necessary part of the patient's management.

**Case Report (Continued)**

A magnetic resonance (MR) scan of the head was performed and revealed a 25 mm by 25 mm, homogenous, isointense, intrasellar mass with suprasellar extension and compression of the optic chiasm on the T1-weighted image (Fig. 2). There was homogenous enhancement of the lesion after the administration of gadolinium-DTPA (Fig. 3). The patient was started on bromocriptine 2.5 mg t.i.d. Endocrinologic studies revealed a prolactin of 68 ng/ml (range 0-8 ng/ml), a normal cortisol, and gestational appropriate follicle stimulating hormone and luteinizing hormone levels. She had mild polydipsia but did not have diabetes insipidus. Urinalysis and routine chemistries were normal. The bromocriptine was subsequently discontinued.

What is the differential diagnosis now? What should be the treatment plan and how quickly should treatment be initiated in this pregnant female?

**Comments (Continued)**

The differential diagnosis and management of pituitary enlargement and chiasmal compression...
during pregnancy and the immediate post-partum period is a difficult problem requiring a multidisciplinary approach. From a practical point of view, the major diagnostic considerations are limited and include prolactinoma, lymphocytic hypophysitis, and nonsecreting pituitary tumors. Although prolactinoma is the most common cause of pituitary enlargement and chiasmal compression in this setting, the differential diagnosis is complicated by the fact that pituitary enlargement and lactotroph stimulation, with elevated serum prolactin levels, are normal occurrences during pregnancy. Moreover, these changes are progressive, making it difficult to differentiate physiologic enlargement of the pituitary gland from expansion due to tumor or inflammation. Recent MRI studies have shown that the pituitary gland enlarges between 50% and 400% during the course of a normal pregnancy. In addition, serum prolactin levels undergo an approximately six-fold rise during pregnancy, making the diagnosis of prolactinoma quite difficult. To make matters even more complex, prolactinomas may occasionally cause a paradoxical decrease in prolactin secretion during pregnancy. Finally, MR scanning is often not sufficiently specific to differentiate between tumor and lymphocytic hypophysitis. These complexities mean that most patients will require a tissue diagnosis in order to plan appropriate therapy.

After confirmation of a pituitary-based suprasellar mass by MRI, endocrinologic studies in this patient demonstrated normal pituitary function, with the exception of hypoprolactinemia. The presence of low prolactin makes lymphocytic hypophysitis more likely than prolactinoma, though a nonsecreting pituitary tumor is still possible. It is important to note, however, that prolactin may actually be depressed in some pregnant patients with prolactinomas, as mentioned above. In view of the subnormal prolactin, the excellent response of most patients with lymphocytic hypophysitis to corticosteroids, and the risk of premature labor following a neurosurgical procedure, it is reasonable to initiate a diagnostic trial of steroids. Given the patient’s very poor vision in the right eye, a fairly rapid decompression is needed. If a ten-day course of steroids produces no visual improvement, an immediate diagnostic biopsy should be undertaken.

**Case Report (Continued)**

A preliminary diagnosis of a nonsecreting pituitary adenoma was made. It was elected to induce the pregnancy and proceed with transphenoidal surgery after delivery. At the time of surgery, an enlarged, firm, pituitary gland with dense surrounding inflammatory tissue was noted. Frozen section biopsy of the lesion revealed a diffuse lymphocytic infiltration and fibrosis of the anterior pituitary gland consistent with the diagnosis of lymphocytic hypophysitis. The neurosurgeon elected not to complete the resection and closed without complication. Permanent pathologic section confirmed the diagnosis of lymphocytic hypophysitis (Fig. 4). Postoperatively, the patient was treated
Fig. 4. Permanent section pathology of the pituitary mass demonstrates infiltration of the pituitary tissue with lymphocytes. (H & E, 40 x)

with dexamethasone 4 mg every six hours. Three days later, visual acuity was 20/20 in each eye, and the correctly named 10 out of 10 Ishihara color plates in each eye. Visual field testing revealed marked resolution of her visual field defects in both eyes (Fig. 5). The dexamethasone was tapered slowly over the next several weeks and she had complete resolution of her symptoms without recurrence. At follow-up by telephone, several weeks after discharge, she remained visually asymptomatic.

Comments (Continued)

The frozen section was very helpful in this patient and saved her the risk of permanent hypopituitarism that would have attended a more radical debulking procedure. In many patients (and perhaps in this one), there may not be sufficient clinical information to differentiate inflammation from tumor. The presence of other autoimmune phenomena, as noted below, may be highly suggestive. If other autoimmune phenomena are present, if other clinical data are consistent with the diagnosis of lymphocytic hypophysitis, and if visual loss has not been too precipitous, a therapeutic trial of corticosteroids would seem reasonable.

Most patients with lymphocytic hypophysitis present with headache, visual loss, and symptoms of pituitary insufficiency during the third trimester of pregnancy or shortly after parturition. This patient is clinically fairly typical of others reported in the literature. Other simultaneous autoimmune

Fig. 5. Kinetic visual fields after surgery reveal marked resolution of previous defects.
disturbances have been frequently reported in the literature, but are not mentioned in this patient. The most common association is thyroiditis," but adrenalitis,4,5,6 gastritis (with pernicious anemia),6,8 and various other autoimmune disturbances may be present. In addition, antipituitary antibodies have been reported in some patients,20,45,57 but are not disease-specific and may be seen in patients without pituitary dysfunction.56,7 The presence of antibodies to pituitary is not mentioned in this report. Finally, the syndrome seems to be quite responsive to corticosteroid treatment. This has led some authors to suggest that tissue diagnosis may not be necessary in selected patients with typical clinical features who respond to corticosteroids.5,53 In atypical patients, these authors suggest that the diagnosis should be determined by diagnostic biopsy. If lymphocytic hypophysitis is confirmed by frozen section, extensive surgical debulking may not be necessary.

The etiology of this fascinating autoimmune disorder remains unknown. An experimental model has been developed in hamsters by Yoon et al.6 The authors have succeeded in producing an organ-specific autoimmune lymphocytic hypophysitis by intradural injection of rubella nucleoprotein. These findings suggest that viral exposure may trigger autoimmune hypophysitis in susceptible individuals. The role of pregnancy in this disorder remains unexplained, however.

Discussion

Lymphocytic hypophysitis (LH) is an uncommon, nonneoplastic, autoimmune, inflammatory disorder affecting the pituitary gland. The clinical features of LH include variable endocrinological abnormalities such as partial or complete hypopituitarism, hyperprolactinemia, or diabetes insipidus; headaches with or without nausea or vomiting; visual loss in cases with compression of the anterior visual pathway; and an intrasellar or suprasellar mass on neuroimaging studies.1-6,52,53 LH may be indistinguishable both clinically and radiographically from pituitary adenoma and may present with an elevated prolactin level, secondary galactorrhea, and amenorrhea.50,9,24,34,35,50,52

LH usually occurs in pregnant or postpartum females, and the majority of pregnant patients present in the third trimester.13 However, LH has been reported in males,12,19,31,45,49,50 and in nulliparous females.46,47,53 The histopathological features include a diffuse or focal lymphoplasmacytic infiltration of the anterior pituitary gland; occasional lymphoid follicles with germinal centers; and edema, fibrosis, atrophy or destruction of the anterior pituitary gland.1-6 Although the etiology of LH is unknown, the evidence for an autoimmune basis includes an association of the disorder with other autoimmune diseases such as thyroiditis, adenitis, oophoritis, orchitis, and gastritis;6,10,18,14,52,8,19,29,45,47,49 the variable presence of antibodies to pituitary gland and other organs;3,6,34,35,46 and a few studies that have demonstrated interdigititation of activated lymphocytes and pituitary cells on electron microscopy.7 A number of immunologic abnormalities have been reported in patients with LH, including positive antinuclear antibody,8 an increased peripheral blood CD4 to CD8 lymphocyte ratio, a predominance of CD4 subpopulation in the lymphocytic infiltrate, and an increase in the CD8 lymphocyte subpopulation.21,24,30,41,47,48,49 In addition, histologic features similar to those of LH have been produced experimentally in rats injected with whole pituitary gland, and the severity of the disorder was noted to be worse in postpartum animals.50

The clinical presentation of LH may mimic pituitary adenoma, and the diagnosis should be suspected in any pregnant or postpartum patient with an intrasellar or suprasellar mass.50,55,58 Computed tomographic scans typically demonstrate a contrast-enhancing, homogenous, intrasellar or suprasellar mass. MR scan of the head may demonstrate homogenous, isointense to brain signal intensity on T1-weighted images; isointense or hyperintense to white matter signal intensity on T2-weighted images; and homogenous or peripheral enhancement after the administration of gadolinium-DTPA. These radiographic features, however, are not specific for LH and may, in fact, be indistinguishable from pituitary adenoma.

Rapidly progressive hypopituitarism,17 hypopituitarism out of proportion to the size of the intrasellar mass,10 or peripheral gadolinium enhancement on MR scan are suggestive of the diagnosis of LH10,23 but there are no pathognomonic preoperative clinical, radiographic or laboratory features of LH. Biopsy of the lesion is required for the definitive diagnosis.

Patients suspected of having LH should undergo frozen section biopsy at the time of surgery. If the diagnosis is confirmed pathologically, then a trial of steroid therapy could be instituted.52,54,56 Patients who fail conservative treatment may require decompression of the anterior visual pathway. All patients should have aggressive and prompt evaluation and treatment of preoperative and postoperative hypopituitarism. Our patient was treated postoperatively with steroids after subtotal resection and decompression and had a complete recovery of visual function.
References


Abstract. A pregnant woman presented with headaches, bilateral decreased visual acuity, and a central scotoma with a supertemporal hemianopic defect in the right eye and a supertemporal hemianopic defect in the left eye, and bilateral temporal optic disk pallor. Neuroimaging revealed an intrasellar mass with suprasellar extension. Biopsy of the lesion revealed lymphocytic hypophysitis (LH). Treatment with steroids produced marked improvement in visual function. The clinical presentation of lymphocytic hypophysitis may mimic pituitary adenoma and the diagnosis should be suspected in any pregnant or postpartum patient with an intrasellar or suprasellar mass. (Surv Ophthalmol 41:402-408, 1997. © 1997 by Elsevier Science Inc. All rights reserved.)

Key words. lymphocytic hypophysitis  •  pituitary adenoma  •  pregnancy