

Case in Point

Idiopathic Intracranial Hypertension in Pregnancy

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Treatment for a patient who presented with severe headaches and decreased vision caused by idiopathic intracranial hypertension was complicated by nonadherence and pregnancy, but the patient's symptoms resolved after a successful delivery.

A 27-year-old white woman presented to the clinic with headaches and decreased vision through her reading glasses while performing near tasks. Her medical history was significant for herpes simplex, hyperlipidemia, and migraine headaches with aura. Her migraines began following an earlier motor vehicle accident, and her most recent magnetic resonance imaging (MRI) showed no abnormalities. Her current medications included prophylactic acyclovir for herpes and acetaminophen and caffeine tablets as needed for headache. She reported no other trauma or surgery and no known allergies. The patient's best-corrected Snellen visual acuities in both eyes were 20/20 (distance) and 20/30 (near).

Preliminary testing, including pupils, extraocular motilities, confrontation fields, and color vision, were all within normal limits. Her slit-lamp examination was unremarkable. A dilated fundus examination revealed

crowded, elevated discs without vessel obscuration, hemorrhage, hyperemia, or drusen (Figure 1). The fundus examination was otherwise unremarkable. Optical coherence tomography of the optic nerves showed increased nerve fiber layer thickness in both eyes (Figure 2). Her blood pressure (BP) at this visit was 106/77 mm/Hg.

The diagnosis based on these findings was bilateral optic nerve elevation with long-standing migraine headaches. The plan was for the patient to return to the clinic for repeat visual field testing and B-scan ultrasonography to rule out buried optic nerve head drusen.

Two months later, the patient presented to the clinic 19 weeks pregnant and reported that her headaches had increased in frequency, but she had no diplopia. All preliminary testing, including visual acuities, pupil reaction, color vision, and slit-lamp examination remained normal. Fundus examination showed the patient's nerves were unchanged in appearance from the initial presentation. Visual fields revealed an enlarged blind spot in the right eye and paracentral defects in the left eye. The B-scan testing was negative for optic

nerve drusen. Due to the increased frequency of headaches, pregnancy, and suspicious optic nerves, an urgent consult was placed to neurology.

At the neurology appointment 1 month later, the patient was diagnosed with migraine headache syndrome and idiopathic intracranial hypertension (IIH). The neurologist believed her headaches might have been resulting from analgesic rebound. He suggested that the patient discontinue or decrease use of oral butalbital, acetaminophen and caffeine tablets, and other forms of caffeine. It was decided that divalproex sodium and verapamil were not feasible due to pregnancy. The neurologist started her on oral acetazolamide 500 mg twice daily.

The patient returned to her obstetrician 1 month later for a routine follow-up; the headaches had worsened and were now accompanied by nausea and vomiting twice daily on average. Her medications still included acetaminophen and caffeine tablets, although it had been recommended she discontinue them, prochlorperazine, and acetazolamide. Due to the worsening of her symptoms and visual fields (eFigure 1, available at www.fedprac.com), the

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obstetrician recommended that the patient deliver by cesarean section at 38 to 39 weeks.

Following an uncomplicated cesarean delivery at 38 weeks, the patient returned to the clinic for visual field testing. Humphrey visual fields were full in the right eye and showed some scattered central depressions in the left. Both eyes were significantly improved from previous fields (eFigure 2, available at www.fedprac.com). The patient had discontinued acetazolamide and reported minor tension headaches she believed were due to lack of sleep but stated that she was no longer having migraines. There was no papilledema noted on fundus examination, and Snellen distance visual acuity measured 20/20 in both eyes. An MRI had been performed after delivery and was negative for intracranial hemorrhage, mass, or hydrocephalus).

Three months later, the patient returned for her yearly comprehensive examination. At that visit, she reported a decrease in frequency of the migraine headaches. Optical coherence tomography was performed and showed a significant decrease in optic nerve head swelling.

CLINICAL PICTURE

Idiopathic intracranial hypertension presents clinically with signs and symptoms of increased intracranial pressure (ICP). Headache is the most common symptom, usually presenting as daily and pulsatile.¹ Nausea may be associated with the headache, although vomiting is rare, and the headache may awaken the patient. The headache may remain after resolution of elevated ICP (Table).²

Papilledema is the most common sign of IIH.^{1,2} Visual loss associated with papilledema is generally mild at first but progressive. Transient blur lasts usually 30 seconds and may be

Table. Signs and Symptoms of Papilledema^{1,2}

Symptoms	Signs
Headache, worse in the morning	Normal or decreased visual acuity
Nausea, emesis	Decreased color vision
Transient visual obscurations	Blurred disc margins
Whooshing sounds	Optic nerve hyperemia
Tinnitus	Disc hemorrhage, cotton wool spots
Diplopia	Paton's lines
Blind spot enlargement	Atrophy, pallor

monocular or binocular.¹ The cause is thought to be related to transient ischemia of the optic nerve.¹ Vision loss is typically reversible with resolution of optic nerve swelling, but 25% of patients may develop optic atrophy, which results in permanent vision loss.² Common patterns of visual abnormalities include enlargement of the physiologic blind spot, inferonasal and arcuate defects, and eventually severe peripheral constriction.^{1,2} It is imperative that all patients with IIH have visual field testing performed.

About one-third of patients with IIH experience diplopia. This binocular, horizontal diplopia is caused by a sixth nerve palsy in 10% to 20% of patients.¹ Cranial nerves II, VI, and VII make a 90-degree bend and seem to be prone to damage at the site of the bend.¹

Pulse-synchronous tinnitus is common in IIH as well.^{2,3} This generally occurs unilaterally and may be eliminated by jugular compression or the head turning to the ipsilateral side.^{1,3} The sound is caused by the transmission of an increase in the vascular pulse due to high pressure on the cerebrospinal fluid (CSF).^{1,3}

Idiopathic intracranial hypertension most typically presents in obese women of childbearing age.^{1,3} An increasing degree of obesity is gener-

ally associated with an increased risk of vision loss.^{1,2} Men seem to have worse acuity and visual fields at presentation than do women.² Men are less likely to report headaches than are women and, therefore, have double the likelihood of severe vision loss.² Hence, closer monitoring and more aggressive intervention is recommended for men due to their lesser tendency for headaches.² Black patients also demonstrate more aggressive disease and, therefore, require closer monitoring and early aggressive intervention.^{1,2}

Papilledema is the most common sign of IIH and may be caused by several processes. In this case, most were ruled out given the patient's normal visual acuities, pupillary reaction, color vision testing, BP measurement, and B-scan imaging. The patient's systemic history was negative for thyroid-related disease, diabetes, hypertension, autoimmune disease, or infection. She had no family history of vision loss or hereditary ocular conditions. The most recent MRI was negative for any long-standing space-occupying lesion or hydrocephalus.

Pathophysiology

Several mechanisms leading to increased ICP have been proposed. These include increased brain water

Figure 1. Fundus Photos at Initial Presentation



content, excess CSF production, reduced CSF absorption, and increased cerebral venous pressure.^{2,3} There is also a suspicion of the role of sex hormones in IIH due to its high predilection for females.²

The role of vitamin A metabolism has also been studied in IIH.¹ Retinol levels are elevated in the CSF of patients with IIH. Patients may ingest an abnormally large amount of vitamin A, metabolize it abnormally, or be sensitive to its effects.^{2,4} The function of adipose tissue as an actively secreting endocrine tissue may play a role in IIH due to its release of adipose tissue-derived retinol binding protein.² Other adipose-produced cytokines include leptin, which has been implicated in IIH due to its elevated levels found in the CSF of patients with IIH.²

Stenosis of the cerebral sinuses is another proposed mechanism of IIH.¹⁻³ Cerebrospinal fluid exits the cranium into the venous sinuses via the arachnoid villi.² An obstruction in these sinuses may impair CSF outflow and result in intracranial hypertension. Microthrombosis caused by hypercoagulable disorders may result in increased cerebral venous pressure and impaired CSF absorption as well.^{2,4}

Some medications have been

found in association with IIH. These include tetracycline, cyclosporine, lithium, nalidixic acid, nitrofurantoin, oral contraceptives, levonorgestrel, danaxol, and tamoxifen.¹⁻⁴ Tetracycline seems to have the strongest association with IIH and should be discontinued in those patients where the association is very likely to be the causative factor.² The link to oral contraceptives may occur simply due to their association with young women most at risk for IIH.¹⁻³

Management

The goals of treatment with IIH are to preserve vision and relieve symptoms, particularly headache. The general recommendation is that pregnant women with IIH should be managed and treated the same as any other patient with IIH. However, imaging and some drug contraindications exist between these 2 groups.

The diagnostic test for IIH is a lumbar puncture, which is also the most effective treatment.^{1-3,5} Lumbar puncture should be performed in the relaxed lateral decubitus position without sedation.¹⁻³ The opening pressure should be measured and is the most clinically significant diagnostic tool for diagnosis of IIH. Opening pressures of > 250 mm H₂O are diagnostic of IIH.^{1,3,5}

Weight loss is an essential part of treatment in obese patients with IIH.¹⁻³ A low-calorie, low-salt diet with mild fluid restriction seems to reverse the symptoms of IIH. A 5% to 10% reduction in body weight may reduce symptoms and signs of IIH.²

Carbonic anhydrase inhibitors (CAIs), such as acetazolamide, have a multifactorial role in IIH.⁴ They are usually prescribed in 1 to 2 grams over several doses and function by decreasing CSF production.¹ Carbonic anhydrase inhibitors also are known to change the taste of foods and may, therefore, aid in weight loss.^{1,2} Patients prescribed CAIs commonly experience a tingling in their fingers, toes, and perioral region, an indication that the medication is working.^{1,2} A rare but serious adverse effect (AE) is aplastic anemia, which generally occurs in the first 6 months of treatment in elderly patients.¹ The use of CAIs in pregnancy is controversial, and although rare complications are reported, it is considered a class C drug.⁵

In patients with rapidly progressive vision loss but with minimal headache, optic nerve sheath fenestration (ONSF) is the surgical treatment of choice.^{2,3,6} In this procedure, a window or series of slits are created behind the globe in the optic nerve sheath.¹ About 50% of patients achieve adequate headache control with ONSF, especially for frontal headaches.^{1,2}

For patients with vision loss, papilledema, and headache that do not respond to medical therapy, a CSF diversion procedure is the preferred treatment. Cerebrospinal fluid diversion with ventriculoperitoneal or lumboperitoneal shunts may prevent progressive loss of vision.^{1,4,6} However, variable response rates and shunt failure requiring subsequent revisions are common and may occur

in as many as half of patients undergoing these procedures.¹

Increased intracranial venous pressure due to stenosis of the venous sinuses has been thought to be a possible cause of IIH. Stenting of the transverse venous sinus stenosis has been shown to reduce cerebral venous pressure, reduce ICP, and improve symptoms in patients with IIH.¹⁻³ It is unclear whether elevations in ICP cause transverse sinus stenosis or whether transverse sinus stenosis causes increased ICP.² Regardless, stents have a high rate of complications, including subdural hemorrhage, venous sinus perforation, in-stent thrombosis, and recurrent stenosis proximal to the stent.²

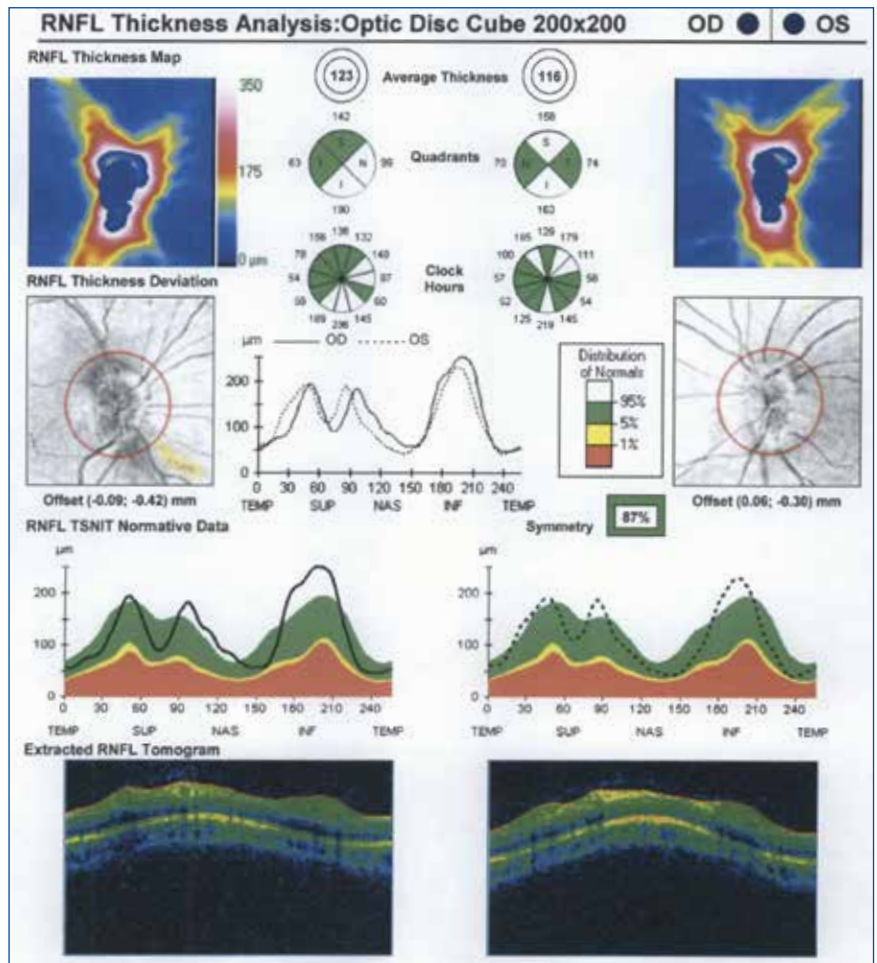
Steroids have been used to treat IIH in the past, although their mechanism of action remains unclear.² There may be recurrence of papilloedema if they are tapered too quickly. Due to their association with long-term AEs, including weight gain, they should be avoided.²

Management in Pregnancy

Several studies agree that vision loss occurs in the same frequency in pregnant and nonpregnant patients with IIH.^{4,7} Idiopathic intracranial hypertension can occur in any trimester in pregnancy. It has been found that patients have the same spontaneous abortion rate and visual outcomes as the general population.⁶⁻⁸ It has also been concluded that treatment should be the same in both patient populations with slight variability in the use of acetazolamide.^{4,6,7}

The use of dilating drops during pregnancy is controversial. Although there have been no teratogenic effects reported with use of topical anesthetics and dilating drops, all drugs should be avoided during the first trimester.⁷⁻¹⁰ Guidelines have been established by the American Congress

Figure 2. Optical Coherence Tomography of the Optic Nerves



Abbreviations: INF, inferior; NAS, nasal; OD, oculus dexter; OS, oculus sinister; RNFL, renal fiber layer; SUP, superior; TEMP, temporal; TSNIT, temporal superior nasal inferior temporal.

of Obstetricians and Gynecologists for X-ray examination and exposure during pregnancy. It has been determined that exposure from a single diagnostic X-ray procedure does not result in harmful fetal effects.¹¹ Magnetic resonance imaging is not associated with any known adverse fetal effects and is a better imaging option during pregnancy, because it is not associated with the use of ionizing radiation.¹¹

The use of CAIs in the first trimester is controversial.^{4,7} Some believe it should be avoided because it is a Pregnancy Category C drug. How-

ever, a single case of sacrococcygeal teratoma has been reported in humans; therefore, some believe this is not a strong basis for withholding the medication in patients with the potential risk for severe vision loss.^{4,7} In this case, a consult to the patient's obstetrician was made, and the use of acetazolamide had no effect on the health of the baby.

In pregnant women with IIH with progressive vision loss, failed treatment, or nonadherence, surgery may be necessary. Optic nerve sheath fenestration is preferred due to lower

morbidity and mortality compared with shunting procedures.^{1,2,4,6} The growing fetus may be affected by the peritoneal end of the shunt.⁴

CONCLUSIONS

Vision loss associated with IIH can be severe and permanent if left untreated. The best treatments and often the most effective involve weight loss and lumbar puncture. Acetazolamide has been a proven effective treatment in some patients, but some debate exists over the safety of its use during pregnancy. This patient did not have any AEs from its use; however, it did not prove valuable in her treatment. Studies often disagree on the use of acetazolamide in pregnancy; however, all agree that proper patient counseling on potential AEs and management by an obstetrician are important. With proper management, pregnant women with IIH have had outcomes similar to those of the general population.

Author disclosures

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