Pseudotumor Cerebri and Papilledema

AN OVERVIEW OF THIS PERPLEXING SYNDROME AND ITS HALLMARK PRESENTATION.

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Pseudotumor cerebri, also known as *idiopathic intracranial hypertension* (IIH), describes the perplexing syndrome of increased intracranial pressure (ICP) in the absence of a space-occupying lesion on neuroimaging or other etiology. Although the disease can be observed in patients of any age, IIH classically presents among obese (body mass index >30) women of childbearing age. Due to the increased prevalence of obesity in recent years, a significant increase in cases of IIH has been noted, and, as such, an ability to recognize and understand the disease is important.[1]

PATHOGENESIS

Although IIH is, by definition, idiopathic, increased ICP can be caused by increased cerebrospinal fluid (CSF) production, reduced CSF absorption, increased cerebral venous pressure, venous sinus stenosis, increased brain water content, or a combination of these mechanisms.[2] One theory has postulated elevated intracranial venous pressure as both the primary mechanism and a final common pathway for IIH. This theory is supported by the similar clinical appearance of IIH and secondary intracranial hypertension due to cerebral venous thrombosis and other causes of obstructed venous outflow.

Additionally, several systemic diseases, drugs, and vitamin deficiencies or excesses have been reported to be associated with IIH. Of medications associated with IIH, growth hormones, tetracyclines, and retinoids have been the most often reported.[3-5] Other systemic illnesses associated with pseudotumor cerebri include Addison disease, hypoparathyroidism, sleep apnea, systemic lupus erythematous, and polycystic ovary syndrome.[6-8]

CLINICAL MANIFESTATIONS

Headache is the most common symptom of IIH. Although not specific, headaches associated with IIH are often daily and are retroocular.[9] The headaches may resemble migraine headaches with associated symptoms of nausea, vomiting, and photophobia. In fact, many patients with IIH have coexisting migraine headaches, making the diagnosis difficult.[10]

Transient visual obscurations (TVOs) have been found to occur in about two-thirds of patients with papilledema. TVOs typically last only seconds at a time and may be bilateral or unilateral and postural. TVOs are likely a manifestation of disc edema leading to transient ischemia of the optic nerve head.[11]

Perhaps the most suggestive clinical presentation of IIH is pulsatile tinnitus, with which patients describe

AT A GLANCE

- Papilledema is the hallmark sign of idiopathic intracranial hypertension and occurs due to raised intracranial pressure transmitted to the optic nerve sheath.
- Patients with papilledema should be evaluated for an intracranial cause.

TABLE 1. SYMPTOMS OF IDIOPATHIC INTRACRANIAL HYPERTENSION

Symptoms	Frequency
Headache	84%
Transient visual obscuration	68%
Back pain	53%
Pulsatile tinnitus	52%
Photopsia	48%
Sustained vision loss	32%
Diplopia	18%

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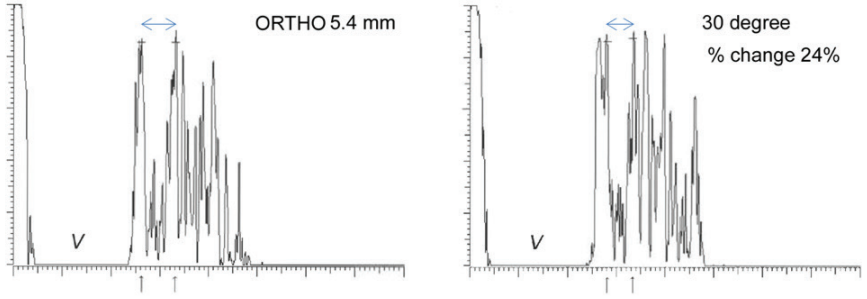

(Courtesy of Thomas Prager, PhD; Houston Eye Associates)

Figure 1. A-scan ultrasonography can be a useful diagnostic tool. Reduction by greater than 20% on eccentric gaze (30° test), as shown above, indicates increased subarachnoid fluid level surrounding the optic nerve.

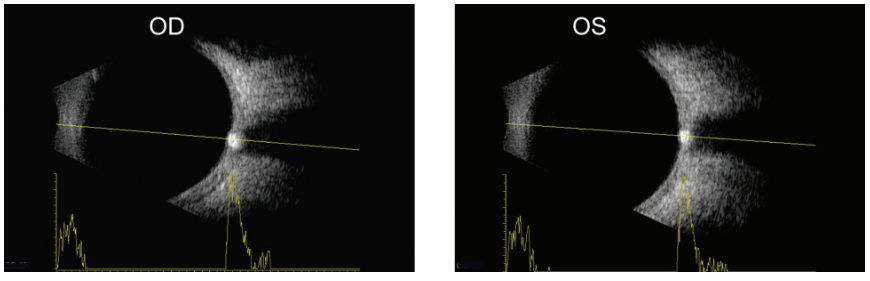

Figure 2. B- and A-scan ultrasonography of optic disc drusen. Note that the optic nerve head is highly reflective. Calcified drusen leading to pseudopapilledema maintain high signal intensity, whereas the signal intensity is decreased in the setting of papilledema.

hearing rushing water or wind. This symptom can be persistent or intermittent, and it is believed to represent vascular pulsations transmitted by the CSF under high pressure to the venous sinus.[12] Other ocular presentations include horizontal diplopia, often in association with sixth nerve palsy; transient episodes of visual loss; and visual field disturbance, with predilection for inferonasal defect and arcuate defect (Table 1).[9,13]

PAPILLEDEMA

Papilledema is the hallmark sign of IIH. It occurs due to raised ICP transmitted to the optic nerve sheath. The elevated pressure, in turn, disrupts the axoplasmic flow within the nerve, resulting in swelling of the axons and leakage of water, protein, and other cellular content into the extracellular space of the optic disc, leading to optic disc edema.[14] Although typically bilateral and symmetric, papilledema in the setting of IIH may be asymmetric or frankly unilateral; in one series of 478 IIH patients, 10% had highly asymmetric papilledema and greater visual loss in the eye with the higher grade of papilledema.[15] In addition, the absence of papilledema does not exclude elevated ICP.

Due to the evolving course of papilledema, the Frisén scale was developed to describe papilledema in clinically meaningful stages.[13] B-scan ultrasonography can assist in diagnosis of IIH by measuring the diameter of the optic nerve sheath.[16] The diameters in primary gaze and in 30° eccentric gaze are compared, and a 20% reduction in diameter in eccentric gaze (30° test) bilaterally is considered a positive test result, indicating increased subarachnoid fluid surrounding the optic nerve (Figure 1). Additionally, B-scan ultrasonography can aid in differentiating pseudopapilledema from papilledema by identifying optic disc drusen (Figure 2).[17]

DIAGNOSIS

When elevation of ICP is suspected, MRI of the brain with gadolinium and magnetic resonance venography should be promptly conducted to exclude secondary causes of ICP. If no structural abnormality is identified, a lumbar puncture should be performed, documenting the opening pressure, and a CSF sample should be forwarded for analysis and culture. IIH is diagnosed according to the Idiopathic Intracranial Hypertension Treatment Trial modified Dandy criteria (Table 2).[18]

MEDICAL MANAGEMENT

The goal of treatment for IIH is alleviation of symptoms and preservation of vision. Weight loss in the range of 6% to 10% has been demonstrated to lead to IIH remission.[19] Although a low-sodium weight reduction program is recommended for all obese patients with IIH, those unable to lose weight may benefit from bariatric surgery. A meta-analysis of bariatric surgery's effects on

TABLE 2. IIHTT MODIFIED DANDY CRITERIA

1. Signs and symptoms of increased intracranial pressure
2. No localizing findings on neurologic examination
3. No deformity, displacement, or obstruction of the ventricular system and otherwise normal neurodiagnostic studies, except for increased cerebrospinal fluid (CSF) pressure >200 mm H_2O (abnormal neuroimaging except for empty sella turcica, optic nerve sheath with filled-out CSF spaces, and smooth-walled, non–flow-related venous sinus stenosis or collapse should lead to another diagnosis)
4. Awake and alert patient
5. No other known cause of increased intracranial pressure; opening CSF pressure of 200 to 250 mm H_2O and at least one of the following: • Pulse synchronous tinnitus • Sixth nerve palsy • Frisén grade 2 papilledema • Echography negative for drusen and no other disc anomalies mimicking disc edema • Magnetic resonance venography with lateral sinus collapse or stenosis, preferably using the auto-triggered elliptic centric ordered technique • Partially empty sella on coronal or sagittal views and optic nerve sheaths with filled-out CSF spaces next to the globe on T2 weighted axial scans

IIH demonstrated 100% papilledema resolution and a 90.2% reduction in headache symptoms.[20]

Acetazolamide (ACZ) is the most effective and the only randomized control trial–proven therapy for IIH; however, treatment with ACZ led to only modest improvement in visual function in the Idiopathic Intracranial Hypertension Treatment Trial.[21] In a long-term follow-up study, ACZ treatment was found to decrease reoccurrence of IIH compared with no ACZ treatment.[22]

ACZ should be initiated at 500 mg twice daily and can be increased to as much as 4 g per day if tolerated by the patient.[23] Topiramate has demonstrated efficacy similar to that of ACZ with regard to visual field improvement and symptom relief, and it has the additional benefit of causing weight loss, making it an excellent alternative.[24]

Patients who do not respond to maximal medical treatment, who are noncompliant, or who are intolerant to medication may benefit from surgical intervention. Optic nerve sheath fenestration (ONSF) has been shown to reverse optic nerve edema and may lead to some recovery of optic nerve function. ONSF has also been shown to be safe and effective in children and could be an option for patients with IIH with predominantly visual symptoms,[25,26] especially those with fulminant IIH with rapid deterioration of visual fields. Central acuity can be preserved until final stages and should not be used alone as a guide to decide on the necessity of surgical management.

CSF shunts (eg, lumboperitoneal shunt, ventriculoperitoneal shunt, or ventriculoatrial shunt) have been reported primarily to alleviate headache with stabilization of visual remission. However, CSF shunts have a higher inpatient mortality risk (0.9% with ventriculoperitoneal shunting and 0.3% with lumboperitoneal shunting) compared with ONSF, which, to the best of our knowledge, has had no reported case of mortality.[26]

Transverse dural venous sinus stenting has been found to be a promising novel management option for IIH, but a randomized, controlled study is needed to establish the safety and efficacy of the procedure in the setting of IIH.[27] A lumbar drain can be placed in the interim while awaiting final definitive surgical procedure and preoperative evaluation in patients with fulminant IIH and rapidly deteriorating vision to prevent further worsening.[28]

SUMMARY

Patients with papilledema should be evaluated for an intracranial cause. Negative neuroimaging (eg, cranial, contrast MRI with magnetic resonance venography); normal CSF content; and an elevated ICP on opening pressure on lumbar puncture establish the diagnosis of IIH. Treatment with weight loss and acetazolamide is the first step in the treatment of IIH. Some patients who do not respond to maximum medical therapy may require surgery, such as ONSF, CSF diversion, or venous sinus stenting. ■

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