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Idiopathic intracranial hypertension and eye complications

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Abstract

• Idiopathic intracranial hypertension (IIH) is the syndrome of raised intracranial pressure (ICP) without clinical, laboratory or radiological evidence of intracranial pathology. IIH is a relatively rare disease but rapidly increasing incidence is reported due to a global increasing incidence of obesity. Disease course is generally said to be self-limiting within a few months. However, some patients experience a disabling condition of chronic severe headache and visual disturbances for years that limit their capacity to work. Permanent visual defects are serious and not infrequent complications. The pathophysiology of IIH is not fully understood yet. Advances in neuroimaging techniques have facilitated the exclusion of associated conditions that may mimic IIH. No causal treatment is yet known for IIH, and existing treatment is symptomatic and rarely sufficient. The aim of this review is to provide an updated overview of this potentially disabling disease. Theories of pathogenesis, diagnostic criteria and treatment strategies are discussed.

• KEYWORDS: idiopathic intracranial hypertension; pathogenesis; diagnosis; treatment

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INTRODUCTION

Idiopathic intracranial hypertension (IIH) is defined as a syndrome of signs and symptoms of increased intracranial pressure (ICP) without causative lesions on magnetic resonance imaging (MRI) or computed tomography [1]. The terms pseudotumour cerebri and pseudotumour syndrome are also used, but the term benign intracranial hypertension is now obsolete, reflecting current awareness of the major risks to vision from papilledema [2,3]. Although the pathogenesis of this condition remains unknown, diagnostic and therapeutic developments during the past two decades have substantially advanced patient management.

PATHOGENESIS

The pathogenesis of IIH remains to be clarified. Cerebral venous hypertension caused by venous sinus thrombosis, neoplastic obstruction or a dural arteriovenous malformation cause a very similar clinical picture. A rise in venous pressure will induce a reduction in cerebrospinal fluid (CSF) absorption, and it is possible that even with careful non-invasive imaging with brain MRI and magnetic resonance venography, some cases of venous sinus thrombosis are missed, leading to the incorrect diagnosis of IIH. Abnormal pressure gradients within the dural venous sinuses can be shown on manometry even in the presence of apparently normal venous phase catheter angiograms, leading to the suggestion that venous hypertension may play a role in IIH, even when there is no obstruction. However, it is not entirely clear whether such pressure gradients are the cause or the effect of the raised ICP. In practice, the diagnosis of IIH is made when venous obstruction and other causes of raised ICP have been ruled out on conventional imaging [4]. An association between IIH and obesity has long been recognized, especially in individuals with a history of recent weight gain, including children [5-7]. There is evidence that weight reduction may lead to resolution of IIH. A direct cause and effect mechanism has been proposed, with increased intra-abdominal and intrathoracic pressures causing raised central venous pressures, but this does not explain the fact that although obesity is common, IIH is rare. However, it is known that high-pressure headache may arise without papilledema, and it is possible that obesity is the cause of the headache in these patients by this mechanism [8-12]. Secondary IIH may arise in association with a number of medical conditions including obstructive sleep apnea, systemic lupus erythematosis, Behcet's disease and renal impairment and also against a background of a variety of

prescription medications. These include tetracylines, vitamin A analogues and oral contraceptives. In these patients, the association with obesity, female sex and reproductive age is not found, but the symptoms and signs of intracranial hypertension (and the visual consequences) are the same. The mechanism of these associations in the absence of venous sinus thrombosis is not clear [13,14].

DIAGNOSIS

The diagnostic clues are to be found in the history [15]. Patients, particularly obese young women, usually present with symptoms of increased ICP, i.e. a pressing headache that is unrelieved by standard therapy, pulsatile tinnitus or transitory visual obscurations (TVOs). It is also important to emphasize that a patient may experience more than one type of headache. The presence of pre-existing primary headache, i.e. migraine or tension-type headache may obscure the picture. However, IIH is not always associated with either headache or visual and auditory disturbances. The risk of extended delay in diagnosis is not negligible.

Any patients with symptoms of increased ICP or chronic daily headache that are unrelieved by standard management should be further evaluated by neuroimaging and lumbar puncture. A normal MRI is required for diagnosis and must also include magnetic resonance venography (MRV) until further evidence is available. Measurements of opening lumbar pressure must be prior to CSF tapping. A repeat lumbar puncture is indicated if opening pressure is absolutely normal irrespective of clinical features of increased ICP. Monitoring ICP with an epidural, intraventricular or an intradural lumbar transducer for at least 6-24 hours demonstrating periods of increased ICP and pathological pressure wave activity is occasionally needed in order to confirm the diagnosis. Demonstrating increased CSF outflow resistance (>9.1mmHg/min/mL) at lumbar infusion test also helps to uphold the suspicion that intracranial hypertension exists despite normal CSF opening pressures, although it is not included in the present IHS criteria.

Since certain medications have been associated with IIH, any medical treatment should be reviewed and stopped if possible and the clinical effect assessed. In chronic cases the patient's current approach to headache treatment is also important since many headache sufferers overuse analgesics. Excessive use of these agents can produce withdrawal or rebound headaches and thus camouflage the effectiveness of later treatment.

Clinical examination, including a general medical examination as well as a thorough neurological and ophthalmological examination, is mandatory and serves to exclude most other neurological disorders. Papilledema will usually be found. All patients should be evaluated with fundus photography and perimetry in order to exclude pseudopapilledema and determine visual status. Normal optic discs are insufficient to exclude the presence of intracranial hypertension.

Visual Fields Although visual acuity (VA) and color perception are generally preserved in papilledema unless it enters a chronic and atrophic stage [16-19]. Visual fields and contrast sensitivity may be abnormally earlier. Visual field testing is far more sensitive for detecting optic nerve damage producing visual loss, particularly in the early stages of the disorder. Quantitative perimetry with static or kinetic methods is the current standard for assessing visual fields in IIH. The sensitivity to the detection of visual field defects is similar using either technique, assuming an experienced perimetrist performs the kinetic test [18,20]. Newer perimetric techniques, such as frequencydoubling technology perimetry, short-wavelength automated perimetry, tendency-oriented perimetry, and highpass resolution (ring) perimetry, have been examined in patients with glaucoma, but with the exception of high-pass resolution perimetry [21], not well-studied in other optic neuropathies or in IIH. Motion perimetry, in which computer graphics generate small circular regions of coherent motion perception targets throughout the central visual field, identified the visual field defects in patients with IIH detected with conventional automated perimetry, as well as some defects that were not identified using automated perimetry [22]. These results, with those elicited with other newer perimetric techniques, must be confirmed and validated before the current visual field testing methods are replaced by newer tools.

Monitoring the Optic Nerve Head Whereas the results of visual field testing provide functional information concerning the degree of optic nerve damage, assessment of the degree of papilledema change over time often provides a useful structural measure of the clinical course and effect of treatment. In some patients, however, papilledema never resolves completely despite resolution of symptoms and stabilization of visual function. It is important to document the appearance of the optic disc with photographs, ideally at the first evaluation and whenever there is a change. Confocal scanning tomography is a new tool that can quantify the degree of papilledema and measure changes over time [23]. Tomographic parameters of the optic nerve

head seem to correlate with visual field sensitivity loss [24]. For routine patient care, however, confocal scanning tomography is not a practical tool and may not provide more useful information than carefully performed and interpreted visual fields. Future studies are needed before deciding if this technique will find a place in routine patient management.

Visual Acuity Loss of VA generally does not occur in acute papilledema unless there is macular edema. As untreated papilledema becomes more chronic, however, progressive impairment of visual acuity can be expected from a variety of causes, such as chorioretinal folds, macular edema or exudates, infarction of the optic disc, subretinal peripapillary hemorrhage extending through the fovea, subretinal peripapillary neovascular membrane.

Contrast Sensitivity Loss of contrast sensitivity is frequently identified in patients with IIH, regardless of the technique used [17-19]. For that reason, some investigators recommend contrast sensitivity testing as an adjunctive measure to assess optic nerve function. Whereas this tool may detect a global abnormality of optic nerve function when other standard measures are normal [18], its specificity for optic nerve dysfunction is low.

Visual Evoked Potentials Assessment of visual evoked potentials (VEP) is often performed to screen for injury to the optic nerve. However, this technique probes only the central 10 degrees of visual field, a region that is insensitive to visual loss in papilledema [18]. Thus, there is no role for VEP in evaluating patients with IIH. The future role of multifocal VEP, which is capable of assessing nonfoveal neurotransmission, remains to be determined.

Diagnostic Criteria Modified Dandy criteria for diagnosis of IIH include the following [2]: ① high-pressure headache and papilledema; ② CSF opening pressure of >25cm water; ③ awake and alert patient; ④ no localizing signs other than lateral rectus paresis; ⑤ normal CSF constituents; ⑥ normal brain imaging with no evidence of venous obstruction; ⑦ benign clinical course apart from visual deterioration; ⑧ no other cause of raised ICP.

TREATMENT

Treatment recommendations for IIH are largely based on retrospective studies, case series, and collective experience [25]. Both medical and surgical treatments are used, depending on the patient's symptoms and visual function. The main goal of treatment is to preserve vision, and treatment decisions are primarily based on the patient's visual function. All patients with IIH should be comanaged by neurologist and an ophthalmologist to monitor their visual status, perimetry, and papilledema grade.

Medical Treatment Weight loss is encouraged for obese patients. The envidence supporting weight loss as an effective treatment is largely retrospective and suggests that losing approximately 6% of body weight is associated with an improvement in papilledema grade [26]. In general, weight loss is considered a long-term therapy for IIH and is not useful in the setting of acute visual loss. The role of bariatric surgery is health of morbidly obese patients but does guarantee relief of IIH symptoms. Proponents of bariatric surgery postulate that its effectiveness is related to decreasing intra-abdominal pressure [27], but this proposed mechanism has no physiologic basis [28].

Diuretics are routinely used in the treatment of IIH, although there are no randomized trials showing their effectiveness. Acetazolamide, a carbonic anhydrase inhibitor, is used as a first-line therapy to decrease CSF secretion from the choroid plexus. Dosages of 1 to 2g daily are usually used in adults [29]. Higher dosage, up to 4g daily, may be as tolerated. Common side effects of acetazolamide include paresthesias, drowsiness, and altered taste sensation(especially for carbonated beverages). Severe adverse reactions include allergy, Steven-Johnson syndrome, aplastic anemia, and renal stones. Methazolamide, also a carbonic anhydrase inhibitor, is an alternative to acetazolamide. If carbonic anhydrase inhibitors are not successful, Triamterene or spironolacrtone may be used for patients who are allergic to carbonic anhydrase inhibitors and furosemid.

Medications for headache prevention are useful, such as topirimate, tricyclic antidepressants, verapamil, and valproate. Symptomatic treatment with migraine-specific medications may be useful, but the use of daily analgesics should be avoided to prevent medication overuse headache. In general, corticosteroid use should be avoided in IIH patients because the ICP may increase as dose is tapered, and because of weight gain [30].

Surgical Treatment Surgery is used when patients have significant visual loss at presentation (based on visual acuity or visual field) and when they continue to worsen despite maximum medical treatment. Surgery is not advocated for the treatment of headache alone. The most commonly used treatments are optic nerve sheath fenestration and shunting. Neither procedure has been prospectively studied, and there are no studies directly comparing the two procedures. Some

patients may require both procedures if one surgical modality fails [31].

Optic nerve sheath fenestration is performed by an experienced orbital surgeon. Papilledema must be present to consider this therapeutic option. Unilateral (on the most affected eye) or bilateral procedures may be performed using either a medial or lateral orbital approach. The surgeon places several fenestrations, or excises a window, along the optic nerve sheath. Papilledema usually improves after optic nerve sheath fenestration. Approximately 75% of eyes have improvement in the visual field, 65% of patients have improvement in their headaches, and 50% experience improved vision in the unoperated eye [32,33]. The procedure is similarly effective in children [34]. The complications are generally minor and transient, including diplopia, ocular discomfort, and tonic pupil. The major advantages of the procedure are the lack of hardware, short duration of the procedure, and amenability to outpatient surgery.

Various types of shunts are used to treat IIH. Proponents of shunting over optic nerve sheath decompression surgery emphasize ICP. According to a national hospital admission database, the number of shunt procedures for IIH increased by 350% from 1998 to 2002, with new shunt placements increasing by 320% [35]. Shunting almost always works initially, but shunts frequently fail. Visual loss may be the first evidence of shunt failure [36]. Lumboperitoneal shunts are most commonly used for IIH. Their disadvantages include overdrainage with an acquired Chiari malformation or low-pressure headaches, radiculopathy, and a high incidence of shunt failure. The most common reasons for shunt revision were shunt failure and low CSF pressure [37]. Review of a 30-year experience with shunting for IIH at Johns Hopkins School of Medicine studied 115 shunt procedures in 42 patients [38]. Although 95% had a significant improvement in headaches 1 month after the procedure, headaches recurred in 48% of patients by 36 months. Lumboperitoneal shunts were more likely require revision (86%) than were ventricular shunts (44%). Overdrainage and tonsillar herniation only occurred with lumboperitoneal shunts, which were twice as likely as ventricular shunts placed with frameless stereotactic guidance were all successfully placed, but 75% failed by 24 months post-insertion. In this series, lack of papilledema and symptoms lasting longer than 2 years were risk factors for treatment failure. Ventriculoperitoneal shunts have the advantage of incorporating programmable valves, although their utility in IIH has not been confirmed.

In conclusion, the incidence of IIH is increasing, requiring a high level of suspicion by medical practitioners. The evaluation of patients with a new onset of headaches, particularly if they are obese women or using medications known to be associated with intracranial hypertension, should include an ophthalmologic examination. Once diagnosed, treatment is initiated and continued based on the patient's visual function and headache diability. Monitoring of vision, headaches, and medical status requires a team approach that is generally coordinated by a neurologist. Although the visual prognosis is generally good, permanent loss of vision may occur.

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