Idiopathic Intracranial Hypertension (Pseudotumor Cerebri)

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Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebri, is a disorder of elevated intracranial pressure of unknown cause. Patients present with daily headache, pulse-synchronous tinnitus, transient visual obscurations, papilledema with its associated visual loss, and diplopia from sixth nerve paresis. Many disease associations have been alleged, but few besides obesity, hypervitaminosis A and related compounds, steroid withdrawal, and female gender have been proven. Although absorption of cerebrospinal fluid (CSF) occurs through arachnoid granulations and extracranial lymphatics, outflow resistance is increased in IIH; therefore, intracranial pressure must increase for CSF to be absorbed. The mainstays of medical treatment are a reduced-sodium weight-reduction program and acetazolamide. If patients fail medical therapy, surgical procedures, most commonly optic nerve sheath fenestration and CSF shunting, are employed. The main morbidity of IIH is visual loss. This is present in most patients and can usually be reversed if recognized early in the course of the disease and treated.

Epidemiology
The annual incidence of IIH is 0.9 per 100,000 in all persons but 3.5 per 100,000 in women aged 15 to 44 years [1]. In obese women aged 20 to 44 years who are 20% or more over ideal weight, the annual incidence is 19 per 100,000 persons [1]. With the current obesity epidemic, these figures likely underestimate incidence [2]. Weight gain in the year prior to diagnosis is associated with disease onset in both obese and non-obese patients [3].

More than 90% of IIH patients are obese, and over 90% are women of childbearing age. This preponderance in women and association with obesity only holds for postpubertal patients [4]. The mean age at the time of diagnosis is 30 years [1].

Etiology and Pathogenesis
Studies of conditions associated with IIH are mostly uncontrolled and retrospective. This has led to erroneous conclusions because investigators have reported chance and spurious associations with common medical conditions and medications. Also, there are many case reports of associations with intracranial hypertension (ICH) where the cases do not meet the modified Dandy criteria of IIH. For example, pregnancy, irregular menses, and oral contraceptive use are reported associations that have been shown to be due to chance alone [5–7]. In case-control studies, no significant association is found between IIH and use of multivitamins, oral contraceptives, or antibiotics [6,7]. A case-control study has found strong associations between IIH and obesity and weight gain during the 12 months before diagnosis [7].
Any hypothesis of pathogenesis of IIH should explain the following observations of patients with the disorder: 1) high rate of occurrence in women of childbearing age, 2) association with obesity, 3) decreased conductance to CSF outflow, and 4) normal ventricular size and no hydrocephalus.

Changes in cerebral hemodynamics (ie, increased cerebral blood volume and decreased cerebral blood flow) have been reported. However, other studies have found no significant changes in these factors. The most popular hypothesis is that IIH is a syndrome of reduced CSF absorption. Decreased conductance to CSF outflow may be due to dysfunction of the absorptive mechanism of arachnoid granulations or extracranial lymphatics [8]. This latter mechanism of an alternative route of drainage through extracranial lymphatics, proposed by Koh et al. [9], may be an important factor in the mechanism of IIH because this route may account for a substantial percentage of CSF absorption.

Therefore, regardless of the outflow mechanism, if outflow resistance is increased, then ICP must increase for CSF to be absorbed. Although interstitial and intracellular edema have been reported in brain biopsy specimens [10], current methods of analysis have concluded that the histologic features of the brain parenchyma are normal and the findings from previous reports are artifactual [11].

Clinical Features
The symptoms of IIH patients are headache (94%), transient visual obscurations (68%), pulse-synchronous tinnitus (58%), photopsia (54%), and retrobulbar pain (44%). Diplopia (38%) and visual loss (30%) are less common accompaniments of IIH, but some of these symptoms are also common in controls.

The presence of headache is nearly ubiquitous in patients with IIH and is the usual presenting symptom. The headache profile of the IIH patient is that of severe daily headaches described as pulsatile [12]. They are different from previous headaches, may awaken the patient, and usually last for hours. Nausea is common and vomiting less so. The headache is usually reported as the worst head pain ever experienced by the patient. In addition, other headache syndromes frequently co-exist, such as rebound headache from analgesic overuse [13].

Transient visual obscurations
Visual obscurations are episodes of transient blurred vision that usually last less than 30 seconds and are followed by visual recovery to baseline. Visual obscurations occur in about 75% of IIH patients [7]. The symptom may be monocular or binocular. The cause of these episodes is thought to be transient ischemia of the optic nerve head caused by increased tissue pressure. Visual obscurations do not appear to be associated with poor visual outcome.

Pulse-synchronous tinnitus
Pulsatile intracranial noises or pulse-synchronous tinnitus is common in IIH (found in about 60% of patients) [7]. The sound is often unilateral, with neither side predominating. In patients with ICH, jugular compression ipsilateral to the sound abolishes it [14]. The sound is thought to be due to transmission of intensified vascular pulsations by means of CSF under high pressure and turbulence through smooth-walled venous stenoses, related to transverse sinus compression by high CSF pressure [15].

Papilledema
Papilledema is the cardinal sign of IIH. Optic disc edema either directly or indirectly is the cause of visual loss of IIH. The higher the grade of the papilledema, the worse the visual loss [16]; however, in the individual patient, the severity of visual loss cannot accurately be predicted from the severity of the papilledema. A partial explanation for this is that when papilledema causes axonal death, the amount of papilledema decreases.

Ocular motility disturbances
Horizontal diplopia occurs in about 33% of IIH patients, and sixth nerve palsies are found in 10% to 20% [17]. Motility disturbances other than sixth nerve palsies have been reported. Some of these reflect erroneous conclusions from the small vertical ocular motor imbalance that is known to accompany sixth nerve palsies. The diagnosis of IIH should be viewed with suspicion in patients with ocular motility disturbances other than sixth nerve palsies.

Sensory visual function
Visual acuity usually is normal in patients with papilledema except when the condition is long standing and severe or when optic disc edema causes a serous retinal detachment. Snellen acuity testing is insensitive to the amount of visual loss found by perimetry and to worsening of papilledema grade [17].

Visual field loss
Visual field loss is ubiquitous in IIH. In a prospective study of patients with IIH, visual loss in at least one eye (other than enlargement of the physiologic blind spot) was found in 96% of patients with Goldmann perimetry using a disease-specific strategy and in 92% with automated perimetry. About 25% of this visual loss is mild and unlikely to be noticed by the patient but serves as a marker with which to gauge therapy [17].

The visual field defects found in IIH are the same as those reported to occur in papilledema due to other causes. The most common defects are enlargement of the physiologic blind spot and loss of inferonasal portions of the visual field, along with constriction of isopters. Central defects are distinctly uncommon and warrant a search for another diagnosis unless there is a large serous retinal detachment from high-grade optic disc edema spreading