Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children

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Intracranial hypertension can be primary (idiopathic intracranial hypertension; "IIH") or secondary. IIH is an appropriate name for primary intracranial hypertension of an unclear etiology, though intracranial hypertension precipitated by an identifiable secondary cause should be labeled differently and more specifically. Overall, the authors suggest that the terminology of IIH would benefit from a transition to the umbrella term "pseudotumor cerebri syndrome (PTCS)," then secondarily classified as primary (IIH) vs. secondary PTCS based on etiology. Further, the authors proposed a need for a revised discussion of the diagnostic criteria for intracranial hypertension, to establish more reliable diagnoses (i.e. elevated ICP with or without papilledema) in order to guide appropriate management. Here, the authors discussed the current and proposed updated diagnostic considerations for PTCS.

Overview of Diagnostic Criteria and Etiologies for Intracranial Hypertension (Tables 1 & 2):

1) Categories of primary vs. secondary intracranial hypertension:

Primary intracranial hypertension – typically obese female or female with sudden weight gain; PCOS
Elevated ICP without papilledema – without papilledema, often with slightly lower ICP than patients with papilledema, suffers from chronic HA; typically would not develop papilledema and would not require close ophthalmologic follow-up
Secondary intracranial hypertension – requires treatment of the etiology of the elevated ICP as well as the treatment for elevated ICP

2) Secondary causes of intracranial hypertension:

Cerebral venous abnormalities - CVST, bilateral jugular vein thrombosis or surgical ligation, AV fistula, decreased CSF absorption from previous intracranial infection or subarachnoid hemorrhage, hypercoagulable state, middle ear or mastoid infection, increased RHP, SVC syndrome
Medications and Exposures – antibiotics (tetracycline, minocycline, doxycycline, nalidixic acid, sulfa drugs), vitamin A and retinoids (isotretinoin, all-trans retinoic acid for promyelocytic leukemia, excessive liver ingestion), hormones (hGH, thyroxine, levonorgestrel, anabolic steroids, w/d from chronic steroids); lithium, chlordecone
Medical Conditions – endocrine disorders (Addison disease, hypoparathyroidism), hypercapnia, sleep apnea, Pickwickian Syndrome, anemia, renal failure, congenital conditions (Turner, Down)

3) Diagnostic Criteria for Proposed Terminology of Definite and Probable PTCS:

A) Papilledema: disc elevation, blurring of the disc margin, periparillary halo, peripapillary hemorrhages, exudates, cotton-wool spots
B) Normal neurologic examination except for cranial nerve abnormalities
C) Neuroimaging findings: Normal brain parenchyma w/o hydrocephalus, mass, or structural lesion, no abnormal meningeal enhancement on MRI for typical patients (female and obese), and normal MRI and MRV for others. If MRI is unavailable or contraindicated, contrast-enhanced CT may be used
D) Normal CSF composition
E) Elevated lumbar puncture opening pressure (25mmHg in adults and 28mmHg for children). NOTE, this may be misleading as a low OP with typical features of PTCS does not negate the diagnosis, and a high OP w/o other PTCS features is not diagnostic (one can have an elevated OP w/o a clear reason).

Definite or Probable PTCS: Definite if criteria A-E are fulfilled; probable if criteria A-D are met with bilateral papilledema, but measured CSF pressure is lower than specified

PTCS without papilledema: If only criteria B-E are satisfied, but there is additionally a CN VI palsy OR three of the following:

1. Empty sella
2. Flattening of posterior aspects of the globe
3. Distension of perioptic subarachnoid space with or without tortuous optic nerve
4. Transverse venous sinus stenosis

Major Conclusions: The added specificity of the above criteria (specifically, PTCS or PTCS w/o papilledema) provide a more accurate framework for a diagnosis of PTCS, which may help guide appropriate management. Notably, this diagnostic criteria could, however, miss some features that may (uncommonly) accompany PTCS, such as CN7 palsies, hemifacial spasms, radicular pain, or CSF rhinorrhea or otorrhea. The authors also emphasize that headaches, transient visual obscurations, pulse-synchronous tinnitus, binocular diplopia, neck/shoulder/back pain are all nonspecific and should not lead to a diagnosis of PTCS, but can certainly accompany PTCS. In the cases at the end of the study, case 1 described a typical case of PTCS (obese female with vision loss, headaches, papilledema) but w/o an elevated OP, leading to a diagnosis of probable PTCS. Case 2 described another partially typical case of PTCS (obese female, chronic headaches) though without papilledema or organic vision loss. Her OP was elevated, but the absence of other supporting clinical features argued against a diagnosis of PTCS, despite this elevated OP.

Additional discussion points:

Sites of CSF Excretion: Choroid plexus (80-90%) and fluid transport across blood brain barrier (10-20%). Exchange occurs between interstitial fluid and CSF, contributing to the distribution of compounds across different regions of the brain or from systemic circulation

Driver of CSF secretion: hydrostatic pressure gradient between blood, choroid plexus, epithelial cells, ventricles

CSF Drainage: arachnoid villi, extracranial lymphatic system, glymphatics

Treatment options for PTCS:

1) Lumbar Puncture: the response to LPs is not diagnostic, but there may be some temporary improvement of headaches following an LP
1) Weight loss: 5-10% losses can lead to remission
2) Carbonic anhydrase inhibitors: reduce CSF production by up to 50%, also function as diuretics
3) Topiramate: weak carbonic anhydrase inhibitor, but also promotes weight loss
4) Steroids: can rapidly lower ICP if elevated, but caution with use due to risk for weight gain and rebound ICP elevation when tapered off
5) Surgery: if refractory to medical treatment, optic nerve sheath defenestration/decompression and CSF diversion techniques (VP or LP shunts) are considered. Optic nerve sheath procedures are reserved for cases of severe vision loss and CSF diversion techniques are most effective in reducing headaches associated with elevated ICP, though are less effective for vision loss

Additional reading, if interested:

Bothwell, S.W., et al. "Cerebrospinal fluid dynamics and intracranial pressure elevation in neurological diseases." Fluids and Barriers of the CNS (2019). 16 (1): 1-18.

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