Original Research Paper

Volume-8 | Issue-12 | December-2018 | PRINT ISSN No 2249-555X

Neurology

A REVIEW OF INTRACRANIAL HYPERTENSION

Dr. Dinesh Chaudhari	Clinical Associate, Institute of Neurosciences. Indraprastha Apollo Hospitals – 110076
Pushpendra N Renjen*	Sr. Consultant Neurologist & Academic Coordinator, Institute of Neurosciences, Indraprastha Apollo Hospitals *Corresponding Author
Dr Shivangi Garg	DNB Internal Medicine, Institute of Neurosciences. Indraprastha Apollo Hospitals – 110076

ABSTRACT Intracranial Hypertension is a disorder of unknown cause that results in raised intracranial pressure (ICP) occurring in women of childbearing years. 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. Classically, PTC is more commonly observed in overweight women of reproductive age. A definite diagnosis requires the presence of papilledema, normal level of consciousness, normal MRI (including ventricular size) except for signs referable to intracranial hypertension, and a lumbar puncture with an opening pressure measurement and normal CSF composition confirming the diagnosis. The incidence of IIH is in rapid progression in the wake of the global endemic obesity problem and expertise is absolutely required for scientific progress and a better outcome.

KEYWORDS : IIH, Psedotumor cerebri, ICP, Acetazolamide.

INTRODUCTION –

Intracranial hypertension is a clinical entity with a myriad of known and putative etiologies. In the history of this condition, the name given to the clinical syndrome referred to as PTC (PseudoTumor Cerebri), IIH (Idiopathic Intracranial Hypertension) or BIH (Benign Intracranial Hypertension) has varied widely and been the subject of much contention [1]. It is a disorder of unknown cause that results in raised intracranial pressure (ICP) occurring in women of childbearing years. Heinrich Quincke, an early pioneer in the use of lumbar puncture, reported the first recorded cases of intracranial hypertension of unknown cause in what he described as "meningitis serosa" in 1893; at that time, he posited that inadequate CSF resorption was responsible for the syndrome, a theory that is still entertained by some researchers [2]. It is characterized by increased ICP, with its attendant signs and symptoms, in an alert and oriented patient but without localizing neurologic findings. The term "PTC" was coined in 1904 by Nonne to describe a condition characterized by symptoms associated with intracranial tumors with an unusual course of remission and subsequently termed "benign intracranial hypertension" by Foley in 1955 [1].

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 [3]. With the current obesity epidemic, these figures likely underestimate incidence [4]. Classically, PTC is more commonly observed in overweight women of reproductive age [5]. The incidence of PTC in women who are between 20 and 44 years of age and 20% above ideal body weight increases to 19.3 cases per 100,000 population; the odds ratio of PTC increases from 6.5 for a BMI of 25–29 to 26.0 for a BMI of >35. Obesity has long been associated with the development of PTC [6]. One mechanistic theory proposes that obesity predisposes patients to having elevated intrabdominal pressure, elevated intrathoracic pressure, and thus elevated central venous pressure as the final common pathway leading to IIH [7]. A recent study counters this theory of increased central venous pressure by discovering lower body (gynecoid) obesity as a risk factor for IIH, which may suggest that increased estrogenicity, rather than elevated intrabdominal pressure, is the inciting element by which obesity propagates IIH [8].

PATHOGENESIS –

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 [9].

Changes in cerebral hemodynamics (i.e., 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 [10]. This latter mechanism of an alternative route of drainage through extracranial lymphatics, proposed by Koh et al. [11], may be an important factor in the mechanism of IIH because this route may account for a substantial percentage of CSF absorption.

CLINICAL FEATURES –

A definite diagnosis requires the presence of papilledema, normal level of consciousness, normal MRI (including ventricular size) except for signs referable to intracranial hypertension, and a lumbar puncture with an opening pressure measurement and normal CSF composition confirming the diagnosis. In the absence of papilledema or an abducens palsy, the diagnosis can only be suggested if neuroimaging criteria are met [12]. In most patients IIH manifests with severe headache, visual disturbances and bilateral papilledema.

Headache is the most common symptom, present in approximately 80% to 90% of patients at diagnosis, and is frequently the initial symptom. No distinguishing characteristics of the headache occur, although it often represents a new or different headache and may be quite severe. In the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT) that prospectively studied 165 patients newly diagnosed with papilledema and mild visual field loss from IIH (perimetric mean deviation from −2 dB to −7 dB on Humphrey automated perimetry), headache was present in 84% at the baseline visit [12]. Characteristic for the condition is the presence of a pulsatile tinnitus that is believed to arise from intensified vascular pulsation occurring with high ICP. Although very common, it is often not reported by the patients unless specifically queried about it. Most enrollees in the IIHTT with headache also had other symptoms suggesting a secondary cause, such as constant visual loss (34%), transient visual obscurations (68%), diplopia (22%), and dizziness (53%). However, 14% of those with headache had none of those symptoms despite having papilledema. Of all enrollees, intermittent or daily pulse-synchronous tinnitus occurred in 52% of patients and was most frequently bilateral (66%) [13].

DIAGNOSIS –

The diagnostic criteria of pseudotumor cerebri syndrome are listed in Table 1 [14]. {{Table -1}}. The importance of visual assessment in pseudotumor cerebri syndrome cannot be overemphasized. Any patient with headache and visual symptoms needs, at a minimum, a measurement of visual acuity in each eye, assessment of visual fields,

pupil examination to look for an afferent pupillary defect or poor pupillary reaction, and a fundus examination.

MRI of the brain with contrast is the imaging test of choice. Orbital images are helpful, although most intra-orbital findings can be seen on a high-quality brain image. The T1-weighted midline sagittal images may demonstrate an expanded/empty sella or tonsillar descent. T2-weighted axial images best show flattening of the posterior sclerae, which is assessed at the level where the optic nerves exit the globe. Other findings include distention of the optic nerve sheath complex with enlargement of the perioptic subarachnoid space, tortuosity of the optic nerves, protrusion of the optic nerve head into the vitreous cavity (papilledema), and widening of the foramen ovale. Skull base CSF leaks with meningoceles and meningoencephaloceles may occur [15].

Table I - Diagnosis of Pseudotumor Cerebri Syndrome [14].

Diagnostic Criteria for the Pseudotumor Cerebri Syndrome [14]	
1 Required for Diagnosis of Pseudotumor Cerebri Syndrome	
A	Papilledema
B	Normal neurologic examination except for cranial nerve abnormalities
C	Neuroimaging: normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion and no abnormal meningeal enhancement on MRI, with and without gadolinium, for typical patients (female and obese), and MRI, with and without gadolinium, and magnetic resonance venography for others; if MRI is unavailable or contraindicated, contrast-enhanced CT may be used
D	Normal CSF composition
E	Elevated lumbar puncture opening pressure (≥250 mm CSF in adults and ≥280 mm CSF in children [≥250mm CSF if the child is not sedated and not obese]) in a properly performed lumbar puncture.
2	Diagnosis of Pseudotumor Cerebri Syndrome Without Papilledema
A	In the absence of papilledema, a diagnosis of pseudotumor cerebri syndrome can be made if B–E from above are satisfied and, in addition, the patient has a unilateral or bilateral abducens nerve palsy
B	In the absence of papilledema or sixth nerve palsy, a diagnosis of pseudotumor cerebri syndrome can be suggested but not made if B–E from above are satisfied and, in addition, at least three of the following neuroimaging criteria are satisfied:
I	Empty sella
ii	Flattening of the posterior aspect of the globe
iii	Distention of the perioptic subarachnoid space with or without a tortuous optic nerve
iv	Transverse venous sinus stenosis
CSF = cerebrospinal fluid; CT = computed tomography; MRI = magnetic resonance imaging. A diagnosis of pseudotumor cerebri syndrome is definite if the patient fulfills criteria A–E. The diagnosis is considered probable if criteria A–D are met but the measured CSF pressure is lower than specified for a definite diagnosis.	

A lumbar puncture is required for the diagnosis. CSF pressure–lowering agents should be discontinued for 24 to 36 hours prior to the lumbar puncture. For the most accurate reading, the opening pressure should be measured with the patient in the lateral decubitus position with the legs at least partially extended; studies in both children and adults suggest that the leg position does not appreciably alter the opening pressure in most cases, but the difference of approximately 10 mm CSF may be meaningful in some patients who have pressures at the upper end of normal [16].CSF pressures of 250mm or greater in adults or 280 mm or greater in children are considered abnormal [17].

Treatment –

The target of IIH management is to reduce ICP with the main goals of preservation of vision and relief of headache. Over the years the management strategy for IIH has been based on clinical experience, but in recent times, well designed clinical trials assessing acetazolamide and weight loss have been published [18,19]. The IIHTT demonstrated that acetazolamide was superior to placebo in improving the visual field, papilledema grade, visual quality of life, and general quality of life in adults with IIH and mild visual field loss. The medical regimen was combined with a weight loss program with a goal of losing at least 6% of a patient's bodyweight [20]. Thus, acetazolamide initiated at 500 mg twice daily and gradually increasing the dosage to 2000 mg twice daily as needed/tolerated is recommended for treatment of such patients. Other diuretics (not studied in the IIHTT) may be employed in patients who cannot tolerate acetazolamide, including methazolamide, furosemide, bumetanide, or thiazide diuretics. Spironolactone, ethacrynic acid, or triamterene may be used in patients who are allergic to carbonic anhydrase inhibitors, loop diuretics, and thiazide diuretics. Small case series support the use of IM octreotide to induce remission of IIH [21]. Although pregnant women were excluded from participation in the IIHTT, clinical experience supports the use of acetazolamide during pregnancy [22].
Some enrolees in the IIHTT were treated with a low dose of amitriptyline (up to 50 mg/d) for headache prevention, which did not impede their overall weight loss during the trial; the small number of participants precluded analysis of effectiveness [23]. Acetazolamide, a carbonic anhydrase inhibitor, is perhaps the most commonly used drug of first choice. In adult patients, an oral dose of 1 g/day has been shown to resolve papilledema and 4 g/day to decrease CSF pressure. Side effects are dose related, which may limit its use if high doses are required. These include gastrointestinal upset, perioral and digital tingling, loss of appetite, acidosis and electrolyte imbalance, and rarely nephrocalcinosis. Continuous medication may result in "low" pressure headaches, which are initiated or exacerbated by moving from the lying position to sitting or standing. In the absence of papilloedema, a trial of medication may help to clarify the situation [24].

Evidence of the effectiveness of steroids in treating BIH relies on retrospective clinical analysis of patients with this condition. Clinical experience has shown that decrease of symptoms and resolution of papilloedema can be expected in the first two weeks of treatment. Surgical management is indicated in those with deteriorating visual function and/or severe incapacitating headaches interfering with daily activities despite vigorous medical management. Currently, lumboperitoneal shunting (LPS) and optic nerve sheath fenestration (ONSF) are the two surgical procedures employed [24]. After the initial diagnosis is made, patients need close visual monitoring to incorporate testing mentioned in the diagnosis section of this article. Office visits gradually become less frequent as the patient improves or stabilizes. Most patients have a good visual outcome, but severe visual loss may occur in up to 10% of patients [25].

CONCLUSION –

IIH is a challenging and serious disease with a significant burden on the individual and the society. The IIHTT provided evidence supporting the use of high-dose acetazolamide, up to 4 g/d, in patients with mild visual field loss. However, data from the IIHTT also indicate that controlling the intracranial pressure alone may not improve headache disability, so neurologists have an important role to play in the management of this symptom that so greatly impacts quality of life [12]. The incidence of IIH is in rapid progression in the wake of the global endemic obesity problem and expertise is absolutely required for scientific progress and a better outcome.

REFERENCES –

1. Pearce JM. From pseudotumour cerebri to idiopathic intracranial hypertension. Pract Neurol 2009;9:353–56
2. Johnston I. The historical development of the pseudotumor concept. Neurosurg Focus 2001;11:1–9
3. Durcan FJ, Corbett JJ, Wall M: The incidence of pseudotumor cerebri. Population studies in Iowa and Louisiana. Arch Neurol 1988, 45:875–877.
4. Garrett J, Corbett JJ, Braswell RA, Santiago M: The increasing incidence of IIH. The effect of obesity on frequency of occurrence in Mississippi. Ann Neurol 2004, 56(Suppl 8):S69.
5. Sajjadi SA, Harirchian MH, Sheikhbahaei N, et al. The relation between intracranial and intraocular pressures: study of 50 patients. Ann Neurol 2006;59:867–70.
6. Degnan AJ, Levy LM. Pseudotumor cerebri: brief review of clinical syndrome and imaging findings. AJNR Am J Neuroradiol 2011;32:1986–93
7. Sugerman HJ, DeMaria EJ, Felton WL, et al. Increased intra-abdominal pressure and cardiac filling pressures in obesity-associated pseudotumor cerebri. Neurology 1997;49:507–11
8. Kesler A, Kliper E, Shenkerman G, et al. Idiopathic intracranial hypertension is associated with lower body adiposity. Ophthalmology 2010;117:169–74
9. Wall, M. Idiopathic intracranial hypertension (pseudotumor cerebri). Curr Neurol Neurosci Rep. 2008;8:87–93.
10. Boulton M, Armstrong D, Flessner M, et al.: Raised intracranial pressure increases CSF drainage through arachnoid villi and extracranial lymphatics. Am J Physiol 1998, 275 (3 Pt2):889–896.
11. Koh L, Nagra G, Johnston M: Properties of the lymphatic cerebrospinal fluid transport system in the rat: impact of elevated intracranial pressure. J Vasc Res 2007, 44:423–432.
12. Friedman DI. Headaches Due to Low and High Intracranial Pressure. Continuum (minneap minn) 2018;24(4, headache):1066–1091.
13. Wall M, Kupersmith MJ, Kieburtz KD, et al. The Idiopathic Intracranial Hypertension Treatment Trial: clinical profile at baseline. JAMA Neurol 2014; 71(6):693–701. doi:10.1001/jamaneurol.2014.133.
14. Friedman, D., Liu, G. and Digre, K. (2013) Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology 81: 1159–1165.
15. Bidot S, Saindane AM, Peragallo JH, et al. Brain imaging in idiopathic intracranial hypertension. J Neuroophthalmol 2015;35(4):400–411. doi:10.1097/WNO.

0000000000000303.
16. Rajagopal V, Lumsden DE. Best BETs from the Manchester Royal Infirmary. BET 4: does leg position alter cerebrospinal fluid opening pressure during lumbar puncture? Emerg Med J 2013;30(9): 771–773. doi:10.1136/emermed-2013-202981.4.
17. Avery RA. Interpretation of lumbar puncture opening pressure measurements in children. J Neuroophthalmol 2014;34(3):284–287. doi:10.1097/WNO.0000000000000154.
18. Ball, A., Howman, A., Wheatley, K., Burdon, M., Matthews, T., Jacks, A. et al. (2011) A randomised controlled trial of treatment for idiopathic intracranial hypertension. J Neurol 258: 874–881.
19. Wall, M., McDermott, M., Kieburtz, K.., Corbett, J., Feldon, S., Friedman, D. et al. (2014b) Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: the idiopathic intracranial hypertension treatment trial. JAMA 311: 1641–1651.
20. NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee; Wall M, McDermottMP, et al. Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: the idiopathic intracranial hypertension treatment trial. JAMA 2014;311(16): 1641–1651. doi:10.1001/jama.2014.3312.
21. House PM, Stodieck SR. Octreotide: the IIH therapy beyond weight loss, carbonic anhydrase inhibitors, lumbar punctures and surgical/ interventional treatments. Clin Neurol Neurosurg 2016;150:181–184. doi:10.1016/j.clineuro.2016.09.016.
22. Falardeau J, Lobb BM, Golden S, et al. The use of acetazolamide during pregnancy in intracranial hypertension patients. J Neuroophthalmol 2013; 33(1):9–12. doi:10.1097/WNO.0b013e3182594001.
23. Friedman DI, Quiros PA, Subramanian, et al. Headache in idiopathic intracranial hypertension: findings from the idiopathic intracranial hypertension treatment trial. Headache 2017; 57(8):1195–1205. doi:10.1111/head.13153.
24. Soler D, Cox T, Bullock P, Calver DM, Robinson RO. Diagnosis and management of benign intracranial hypertension. Arch Dis Child 1998;78:89–94
25. Baheti NN, Nair M, Thomas Sv. Long-term visual outcome in idiopathic intracranial hypertension. Ann Indian Acad Neurol 2011;14(1):19–22. doi:10.4103/0972-2327.78044.