Ophthalmology Clinics & Research
OCR, 2(3): 96-102
www.scitcentral.com

ISSN: 2638-115X

Review Article: Open Access

Idiopathic Intracranial Hypertension

Konica Singla[1], Sapinder Pal Singh[2], Anand Aggarwal[1*], Rajan Gupta[1], Prempal Kaur[1], Karamjit Singh[1] and Jaspreet Singh Bedi[1]

*[*1]Neuroophthalmology, Department of Ophthalmology, Government Medical College Amritsar, Punjab, India.*

[2]Neurology division, Department of Internal Medicine, Government Medical College Amritsar, Punjab, India.

Received June 15, 2019; Accepted June 20, 2019; Published December 07, 2019

ABSTRACT

Idiopathic intracranial hypertension, earlier also known as pseudotumor cerebri (PTC), is a rare idiopathic disease classically manifesting with headache in obese women. It is characterized by raised intracranial pressure (ICP) with normal CSF composition and absence of hydrocephalus or intracranial space occupying lesions. The hallmark of IIH is papilledema, which may be bilateral, asymmetrical or even unilateral; however, IIH can occur in the absence of papilledema. The diagnosis of IIH is, therefore, not always simply achieved.

Keywords: Idiopathic, Hypertension, Pseudotumor cerebri, Intracranial pressure, Papilledema

INTRODUCTION

IIH is a headache syndrome characterized by raised CSF pressure in the absence of any intracranial lesion or other underlying systemic cause. 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]. 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 postulated that inadequate CSF resorption was responsible for the syndrome, a theory that is still entertained by some researchers [2].

Most of the cases (90%) are idiopathic in origin, but in some there exists a secondary cause. Therefore, many authors prefer the term Pseudotumor cerebri over IIH, which includes both: purely IIH and that due to secondary causes of intracranial hypertension such as venous stenosis [3].

ETIOLOGY

As the name suggests, etiology is largely unknown and is mainly idiopathic. There are few associations which are reported as causing raised intracranial hypertension. These are listed in table below:

Associations that have been reported as causing raised intracranial pressure [4,5]

Hematological	Anemia, Polycythemia vera
Obstruction to venous drainage	Cerebral venous sinus thrombosis
	Jugular vein thrombosis
	Superior vena cava syndrome
	Jugular vein ligation following bilateral radical neck dissection
	Increased right heart pressure
	Arteriovenous fistulas
	Previous infection or subarachnoid hemorrhage causing decreased CSF absorption

Corresponding author: Anand Aggarwal, Department of ophthalmology, Regional Institute of Ophthalmology, Government Medical College, Amritsar, Punjab, India (143001) E-mail id: dr.anandaggarwal@gmail.com

Citation: Singla K, Singh SP, Aggarwal A, Gupta R, Kaur P, et al., (2019) Idiopathic Intracranial Hypertension. Ophthalmol Clin Res, 2(3): 96-102.

Medications	Lithium
	Vitamin A derivatives (including isotretinoin and all-transretinoic acid)
	Nalidixic acid
	Danazol
	Tetracycline class antibiotics
	Corticosteroid withdrawal
	Levothyroxine
	Tamoxifen
	Ciclosporin
	Levonorgestrel implant
	Fluoroquinolones
	Growth hormone
	Indomethacin
	Cimetidine
Systemic disorders	Chronic kidney disease/renal failure
	Obstructive sleep apnoea syndrome
	Chronic obstructive pulmonary disease
	Systemic lupus erythematosus
	Psittacosis
Endocrine	Addison's disease
	Cushing's syndrome
	Hypoparathyroidism
	Hypothyroidism
	Hyperthyroidism
Syndromic	Down syndrome
	Craniosynostosis
	Turner syndrome

PRESENTATION

There incidence of IIH peaks in third decade of life. It most frequently occurs in obese females of childbearing age but can occur in all age groups, both genders and both obese and non-obese individuals. The condition is infrequent in children (in whom obesity is less a factor), men and lean adults [5].

PTC classically presents with headache and, frequently, vision changes in women with obesity of childbearing age. Headaches occur in nearly all (90%-94%) patients with PTC—they are characteristically pressure like, throbbing, and usually unremitting and occur with retro-ocular pain and may be accompanied by nausea or vomiting.

Headache attributed to IIH, as described by the International Classification of Headache Disorders, 3rd edition (beta version) (ICHD-3 beta) [6].

a) IIH diagnosed by lumbar puncture opening pressure of >25 cm H_2O.

b) Evidence of causation demonstrated by two of following:

   i. Headache developed in temporal relation to IIH.

   ii. Headache relieved by reducing ICP.

   iii. Headache exacerbated in temporal relationship to increased ICP.

c) Headache not accounted for by another ICHD-3 diagnosis.

Other symptoms, in order of frequency, reported by Markey et al. [7] include:

- Visual obscuration (darkening of vision) (68-72%)
- Pulsatile tinnitus (52-61%)
- Back pain (53%)
- Dizziness (52%)
- Neck pain (42%)
- Blurred vision (32%)
- Cognitive disorder (20%)
- Radicular pain (19%)
- Diplopia, typically horizontal (18%)

Vision loss is the most feared sequel of PTC, thought to be related to ischemia of optic nerve due to increased CSF pressure. Other reason for loss of vision is raised IOP which directly correlates with ICP [8] due to direct anatomic connection between cranial fossa and orbit. Mostly vision loss in this syndrome is transient in nature, less frequently, it takes the form of impairments in the visual field, directly correlated with the extent of disc edema, with the typical impairment presenting as tunnel vision. Diplopia is usually horizontal in nature due to involvement of sixth nerve by raised ICP. Other common symptoms include photopsia and eye pain.

Ophthalmologic signs of PTC consist of diminished visual acuity, visual field losses in nearly all patients, and, most strikingly, papilledema on fundus examination in 40% of patients. Absence of papilledema has been reported in many populations of patients with IIH, but its absence may be more suggestive of an alternative etiology for headache and

vision loss [5]. Other funduscopic findings that may be seen in PTC are choroidal folds, parallel striae of alternating yellow crests and darker troughs; choroidal folds compromise vision and can be seen with elevated ICP, even when papilledema has resolved [9,10].

Cranial nerve palsies, usually of the abducens nerve (CN VI) Rarely, facial nerve (CN VII) palsies may be associated with IIH [11].

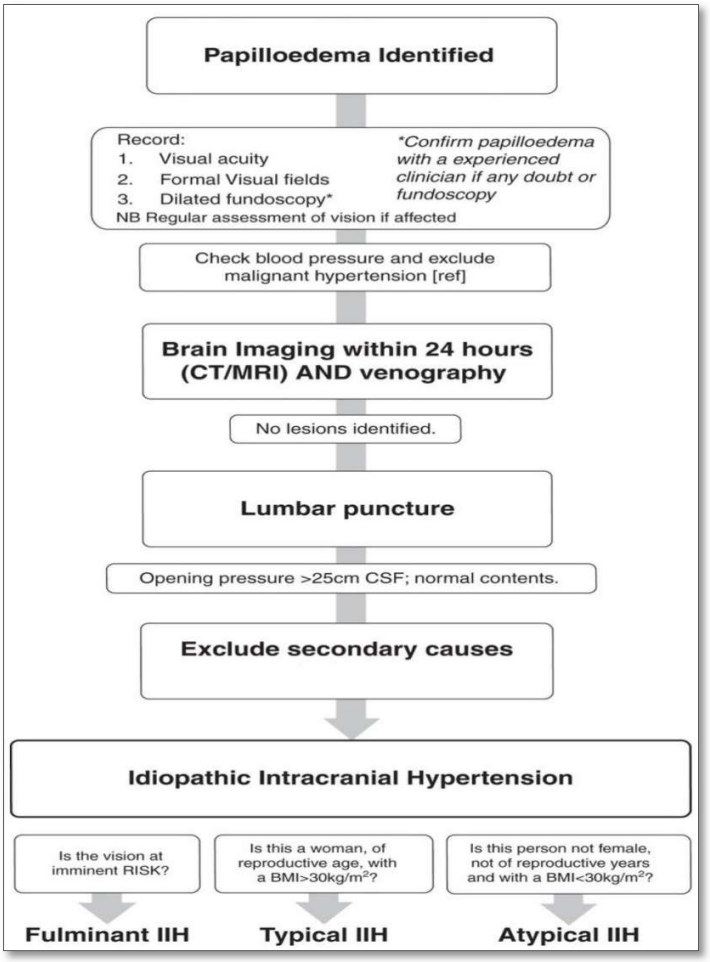
Tinnitus, pulse-synchronous is another commonly reported symptom of PTC and is often described as a unilateral "whooshing" sound by patients and may be exacerbated by positional changes and relieved by jugular compression [5,11,12].

DIAGNOSIS

Clinical criteria for diagnosis of IIH (Adapted from Friedman and Jacobson) [13]:

- Symptoms and signs attributed to increased ICP.
- Documented elevated ICP during lumbar puncture with manometry, typically >25 cm H_2O in adults and >28 cm H_2O in children, measured in the lateral decubitus position with legs and head in a straight and relaxed position
- Normal cerebrospinal fluid composition (normal cell count, normal glucose, normal protein)
- No evidence of ventriculomegaly, mass, structural or vascular lesion on magnetic resonance imaging or contrast enhanced computer tomography and normal magnetic resonance venography imaging.
- Normal neurological examination, with exception that patient may have a sixth nerve palsy.

Direct transmission of the elevated CSF pressure results in distension of the perioptic subarachnoid space and ballooning of the optic papilla, causing it to protrude physically into the posterior aspect of the globe [14-17]. The long-standing effect of pulsatile CSF under high pressure also leads to downward herniation of an arachnocele through a defect in the diaphragm sella **(Flowchart 1)** [18].



Flowchart 1. Clinical criteria for diagnosis of IIH.

MR imaging of the optic nerves and pituitary gland may provide important clues for the diagnosis of IIH, with a return to normal appearance after normalization of CSF pressure. The use of high-resolution, thin-slice MR imaging improves the visualization of the optic nerves and pituitary gland. Characteristic MRI findings include [19].

- Flattening of globes
- Partially empty sella
- Narrowing of the distal transverse venous sinus
- Distension of the perioptic subarachnoid space
- Enhancement of the prelaminar optic nerve
- Vertical tortuosity of the orbital optic nerve
- Intraocular protrusion of the prelaminar optic nerve

Patient with suspected elevated intracranial hypertension must also undergo MR venography in addition to traditional MR orbital imaging to evaluate venous thrombosis or stenosis as the etiology of PTC symptoms.

Protrusion of the right optic nerve head and vertical tortuosity of the optic nerve are seen in this 21 year old woman on axial T2-weighted MR imaging **(Figure 1)**. Clinically, the patient presented with headaches, vision changes and papilledema noted on examination [19].

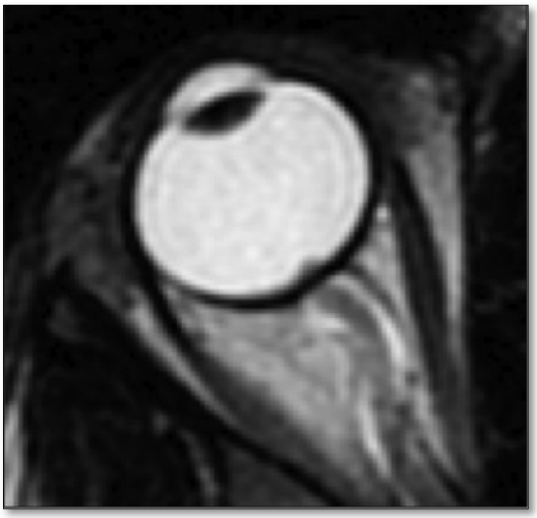


Figure 1. Protrusion and vertical tortuosity of the right optic nerve head.

The Optic Nerve Sheath (ONS) is widened with expanded CSF hyper intensity surrounding the optic nerve, seen on axial T2-weighted MR imaging in conjunction with posterior flattening of the globes. ONS widening is thought to coincide with papilledema, which is seen in this 27 year old woman who presented with headaches **(Figure 2A)**. Coronal T2-weighted MR imaging in a 55 year old woman with headache demonstrates increased peri-ONS space marked by hyper intense signal intensity surrounding the optic nerve [19] **(Figure 2B)**.

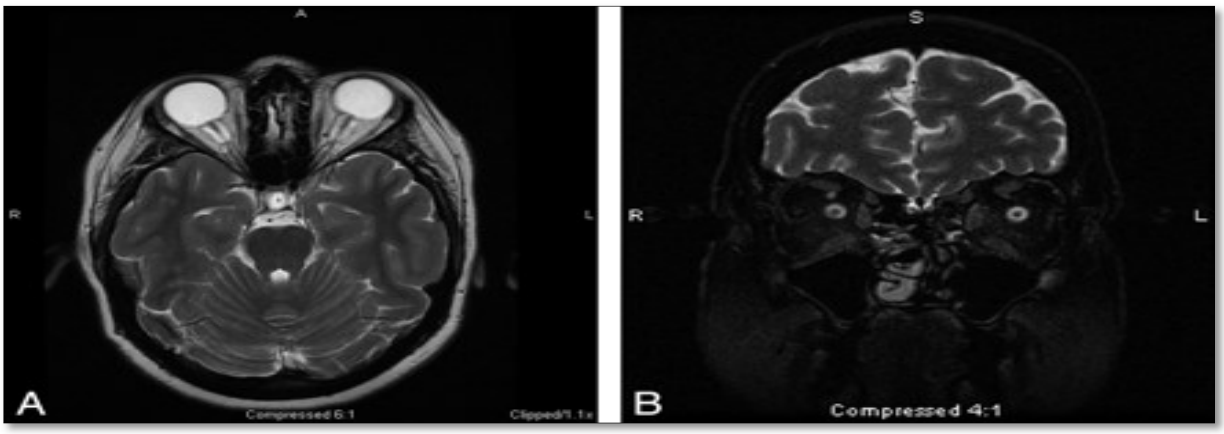


Figure 2. ONS space marked by hyper intense CSF signal intensity around optic nerve.

FOLLOW UP

The ophthalmologist plays a crucial role in the management of IIH. Careful long-term follow up of vision and papilloedema is necessary. Regular examination should include testing of visual acuity, color vision, quantitative perimetery and photograph of optic nerve head. Repeat OCT can also be used but not in isolation to follow papilledema because secondary optic atrophy from untreated papilledema will also result in apparent improvement of the RNFL thickness on OCT. However, it may be differentiated by the ganglion complex at the macula. The frequency of visual field testing depends on the severity of papilledema, the level of optic nerve dysfunction and the patient response to treatment.

Zagardo et al. [20] found that the previously compressed pituitary gland had re expanded to fill the sella turcica after normalization of CSF pressure. This suggests that acute or sub-acute elevation of CSF pressure may be sufficient to compress the pituitary gland. Repeat MR imaging of the present patient also showed reversibility of a partially empty sella and normalization of the volume of the optic nerve sheaths, which had not been previously reported. The return to a normal appearance of the pituitary gland and optic nerves on MR images may indicate a positive response to therapy and possibly denote a corresponding decrease in CSF pressure.

TREATMENT

The main goals of treatment are alleviation of symptoms and preservation of vision. The approach used in a particular patient depends on the severity and time course of their symptoms and visual loss, as determined by perimetry. Obese patients should be encouraged to lose a modest amount of weight. Potential contributing factors (e.g. obstructive sleep apnea) should be treated.

DIET AND LIFESTYLE

In patients with minimal symptoms, signs and visual loss, weight management program with a low-salt diet and lifestyle changes, including an exercise program, is a reasonable initial treatment strategy. A recent prospective study of obese IIH patients found that weight loss leads to reduced symptoms, signs and ICP [21].

MEDICATION

Pharmacologic treatments can be considered for patients with mild to moderate disease.

Acetazolamide

The IIH Treatment Trial reported the use of acetazolamide with a low-sodium weight-reduction diet compared with diet alone resulted in modest improvement in visual field function in patients with mild visual loss [22]. It acts by decreasing CSF production and thereby decreasing ICP.

Dosage: No standardized dose is available. A reasonable starting dosage is 500 mg twice daily. It can be increased up to 4 g daily divided in two dosages.

Contraindications: Known hypersensitivity, including sulfa allergy, liver failure.

It is also relatively contraindicated in patients with a history of renal stones.

Side effects: Paresthesias which may be minimised using potassium supplements, altered taste sensation, lethargy, drowsiness, anorexia and metabolic acidosis.

Topiramate and furosemide can be considered when acetazolamide is poorly tolerated or insufficient.

Topiramate has carbonic anhydrase activity and can suppress appetite. It has been favorably compared with acetazolamide in an uncontrolled open label study for IIH [23].

- There may be a role for topiramate in IIH with weekly dose escalation from 25 mg to 50 mg bd.
- Where topiramate is prescribed, women must be informed that it can reduce the efficacy of the contraceptive pill/oral contraceptives and other hormonal contraceptives.
- When topiramate is prescribed, women must be counselled regarding side effects (including depression and cognitive slowing) and potential teratogenetic risks.

Since angle-closure glaucoma can sometimes develop with topiramate treatment, patients who develop eye pain, eye redness and changes in vision should seek an immediate ophthalmic evaluation.

INTERVENTIONAL TREATMENT

Lumbar puncture

IIH symptoms (e.g. headache) often improve following the diagnostic lumbar puncture. In most cases, the improvement is transient, but occasional patients can have a lasting remission following a lumbar puncture [24]. Repeated lumbar punctures have been used for treatment for IIH, but should no longer be considered standard treatment as they are often technically difficult and poorly tolerated.

SURGICAL TREATMENT

Optic nerve sheath fenestration (ONSF) surgery

ONSF is a surgical technique to reduce the hydrostatic pressure on the ONH by following mechanisms:

a) Opening within the optic nerve sheath allow for a sudden and sustained drop in the sub arachnoid Space (SAS) pressure and relief of the compartment syndrome on the ONH.

b) It creates a CSF filter from the SAS of the optic nerve into the surrounding orbital tissue, thereby reducing the CSF volume and pressure surrounding the ONH.

c) ONSF is thought to increase the velocity of CSF in the optic nerve sheath and thereby decrease the CSF pressure transmitted to ONH [25].

d) ONSF promotes fibrous tissue proliferation at the incisional site, thereby preventing the transmission of elevated CSF pressure to the ONH [26,27].

In a recent study, 62 IIH patients with bilateral papilledema who underwent unilateral ONSF were found to have a decrease in the median grade of papilledema in both the operated and the non-operated eye. The median grade of papilledema in the operated eye decreased from grade 3 preoperatively to grade 0.5 by 12 months. The median grade of papilledema in the non-operated eye decreased from grade 2 before surgery to a grade 1, 12 months postoperatively [28].

CONTRAINDICATIONS

Contraindications to ONSF include infection at the surgical site and anticoagulation use.

COMPLICATIONS

Complications are usually minor if the surgeon is experienced. A tonic pupil can occur if the ciliary nerves are damaged. Transient or permanent visual loss can occur if there is trauma to the optic nerve or its vascular supply.

Cerebrospinal fluid shunting

It causes rapid reduction in ICP and thereby leads to rapid improvement in symptoms and signs. The two procedures most commonly performed are lumbo-peritoneal (LP) and ventriculo-peritoneal (VP) shunting. VP shunting is more difficult and usually requires a stereotactic approach, as IIH patients do not have enlarged ventricles, however, it is preferred due to its lower complication rate [29,30] Contraindications of CSF shunting include:

- When there is active infection
- In patients taking anticoagulants, due to increased risk of bleeding.

Complications of CSF shunting include:

- Shunt infections
- Shunt obstruction
- Migration of the shunt tubing
- Shunt failure
- Over-shunting and intracranial hypotension can occasionally occur, but are less common since the introduction of programmable shunt valves.

SUMMARY AND CONCLUSION

IIH is not an uncommon entity in routine ophthalmic practice. The diagnosis requires a considerable degree of suspicion on part of the ophthalmologist. Collaboration between ophthalmologists and neurologists is vital in the optimal management of this potentially sight threatening condition. Timely detection and early treatment including life style modification and adjuvant drug therapy should improve prognosis in majority of the patients and also avoid the need for surgical procedure in majority of such patients.

REFERENCES

1. Pearce JM (2009) From pseudotumor cerebri to idiopathic intracranial hypertension. Pract Neurol 9: 353-356.
2. Johnston I (2001) The historical development of the pseudotumor concept. Neurosurg Focus 11: 1-9.
3. Sylaja PN, Ahsan Moosa NV, Radhakrishnan K, Sankara Sarma P, Pradeep Kumar S (2003) Differential diagnosis of patients with intracranial sinus venous thrombosis-related isolated intracranial hypertension from those with idiopathic intracranial hypertension. J Neurol Sci 215: 9-12.
4. Friedman DI (1998) Novel.utah.edu Walshand Hoyt Text, Chapter 5. In: Mille N, Newman NJ, Walsh and Hoyt's Clinical Neuro-Ophthalmology. 5th Edn. Baltimore, MD: Williams & Wilkins Ed, pp: 237-291.
5. Aggarwal A, Kaur P, Chhabra K, Singh K, Goyal P (2017) Idiopathic IHT in pediatric patient. Nepal J Ophthalmol 9: 74-78.
6. Headache Classification Committee of the International Headache Society (IHS) (2013) The international classification of headache disorders. 3rd Edn (beta version). Cephalalgia 33: 629-808.
7. Markey KA, Mollan SP, Jensen RH, Sinclair AJ (2016) Understanding idiopathic intracranial hypertension: mechanisms, management and future directions. Lancet Neurol 15: 78-91.
8. Mills RP, Heijl A, Wall M (1991) The morphology of visual field damage in idiopathic intracranial hypertension: An anatomic region analysis. In: Mills RP, Heijl A, eds. Perimetry Update 1990/1991. Amsterdam, the Netherlands: Kugler Publishers, pp: 20-27.
9. Griebel SR, Kosmorsky GS (2000) Choroidal folds associated with increased intracranial pressure. Am J Ophthalmol 129: 513-516.
10. Randhawa S, Van Stavern GP (2008) Idiopathic intracranial hypertension (pseudotumor cerebri). Curr Opin Ophthalmol 19: 445-453.

11. Wall M (2010) Idiopathic intracranial hypertension. Neurol Clin 28: 593-617.

12. Giuseffi V, Wall M, Siegel PZ, Rojas PB (1991) Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumor cerebri): A case-control study. Neurology 41: 239-244.

13. Friedman DI, Jacobson DM (2004) Idiopathic intracranial hypertension. J Neuroophthalmol 24: 138-145.

14. Soler D, Cox T, Bullock P, Calver DM, Robinson RO (1998) Diagnosis and management of benign intracranial hypertension. Arch Dis Child 78: 89-94.

15. Brodsky MC, Vaphiades M (1998) Magnetic resonance imaging in pseudotumor cerebri. Ophthalmology 105: 1686-1693.

16. Jinkins JR, Athale S, Xiong L, Yuh WTC, Rothman MI, et al. (1996) MR of optic papilla protrusion in patients with high intracranial pressure. AJNR Am J Neuroradiol 17: 665-668.

17. Gass A, Barker GJ, Riordan-Eva P, MacManus D, Sanders M, et al. (1996) MRI of the optic nerve in benign intracranial hypertension. Neuroradiology 38: 769-773.

18. Geoge AE (1989) Idiopathic intracranial hypertension: Pathogenesis and the role of MR imaging. Radiology 170: 21-22.

19. Degnan AJ, Levy LM (2011) Pseudotumor cerebri: Brief review of clinical syndrome and imaging findings. AJNR AM J Neuroradiol 32: 1986-1993.

20. Zagardo MT, Cali WS, Kelman SE, Rothman MI (1996) Reversible empty sella in idiopathic intracranial hypertension: An indicator of successful therapy? Am J Neuroradiol 17: 1953-1956.

21. Sinclair AJ, Burdon MA, Nightingale PG, Ball AK, Good P, et al. (2010) Low energy diet and intracranial pressure in women with idiopathic intracranial hypertension: Prospective cohort study. BMJ 341: c2701.

22. Wall M, McDermott MP, Kieburtz KD, Corbett JJ, Feldon SE, et al. (2014) 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.

23. Celebisoy N, Gökçay F, Sirin H, Akyürekli O (2007) Treatment of idiopathic intracranial hypertension: Topiramate vs. acetazolamide, an open-label study. Acta Neurol Scand 116: 322-327.

24. De Simone R, Marano E, Fiorillo C, Briganti F, Di Salle F, et al. (2005) Sudden re-opening of collapsed transverse sinuses and longstanding clinical remission after a single lumbar puncture in a case of idiopathic intracranial hypertension: Pathogenetic implications. Neurol Sci 25: 342-344.

25. Seiff SR, Shah L (1990) Model for the mechanism of optic nerve sheath fenestration. Arch Ophthalmol 108: 1326-1329.

26. Tsai JC, Petrovichm S, Sadun AA (1995) Histopathological and ultrastructural examination of optic nerve sheath decompression, Br J Ophthalmol 79: 182-185.

27. Davidson SI (1970) A surgical approach to plerocephalic disc edema. Trans Ophthalmol Soc U K 89: 669-690.

28. Alsuhaibani AH, Carter KD, Nerad JA, Lee AG (2011) Effect of optic nerve sheath fenestration on papilledema of the operated and the contralateral non-operated eyes in idiopathic intracranial hypertension. Ophthalmology 118: 412-414.

29. Bynke G, Zemack G, Bynke H, Romner B (2004) Ventriculoperitoneal shunting for idiopathic intracranial hypertension. Neurology 63: 1314-1316.

30. McGirt MJ, Woodworth G, Thomas G, Miller N, Williams M, et al. (2004) Cerebrospinal fluid shunt placement for pseudotumor cerebri-associated intractable headache: Predictors of treatment response and an analysis of long-term outcomes. J Neurosurg 101: 627-632.