Atypical presentations of idiopathic intracranial hypertension

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Abstract:

Idiopathic intracranial hypertension (IIH) is a disorder of unknown etiology that results in isolated raised intracranial pressure. Classic symptoms and signs of IIH include headache, papilledema, diplopia from sixth nerve palsy and divergence insufficiency, and pulsatile tinnitus. Atypical presentations include: (1) highly asymmetric or even unilateral papilledema, and IIH without papilledema; (2) ocular motor disturbances from third nerve palsy, fourth nerve palsy, internuclear ophthalmoplegia, diffuse ophthalmoplegia, and skew deviation; (3) olfactory dysfunction; (4) trigeminal nerve dysfunction; (5) facial nerve dysfunction; (6) hearing loss and vestibular dysfunction; (7) lower cranial nerve dysfunction including deviated uvula, torticollis, and tongue weakness; (8) spontaneous skull base cerebrospinal fluid leak; and (9) seizures. Although atypical findings should raise a red flag and prompt further investigation for an alternative etiology, clinicians should be familiar with these unusual presentations.

Keywords:

Idiopathic intracranial hypertension, magnetic resonance imaging, pseudotumor cerebri

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Introduction

Idiopathic intracranial hypertension (IIH) is a disorder of unknown etiology that results in isolated raised intracranial pressure (ICP) and its associated symptoms and signs. The diagnostic criteria for IIH have evolved since the original Dandy requirements in 1937 to separate IIH from other causes of raised ICP, most notably brain tumors (hence, the commonly used term "pseudotumor cerebri").[1] Before the development of advanced neuroimaging techniques, some patients with IIH mimics such as cerebral venous sinus thrombosis, dural arteriovenous fistula, or a meningeal process were classified as having "pseudotumor cerebri." In the last 20 years, however, the diagnostic criteria for IIH have become very strict,[2-4] incorporating neuroimaging criteria, a higher cutoff for normal cerebrospinal fluid (CSF) opening pressure, and mandating a normal CSF examination [Table 1].

Patients with IIH are typically young obese women. Classic symptoms and signs of IIH are directly related to raised ICP and include headache, papilledema, transient visual obscurations, diplopia from sixth nerve palsy and divergence insufficiency, and pulsatile tinnitus. Atypical clinical presentations, including other cranial nerve dysfunction, have also been described and attributed to IIH if they improved or resolved with the normalization of ICP. However, due to the historically less stringent diagnostic criteria and the confusion underlying what constitutes "pseudotumor cerebri," many of the atypical clinical presentations described were in patients with IIH mimics and not true IIH. Although atypical findings should raise a red flag and prompt further investigation for an alternative etiology, clinicians should be familiar with these unusual presentations that can occasionally occur in diagnostically confirmed cases of true IIH.

Atypical clinical presentations of IIH include: (1) highly asymmetric or even unilateral papilledema, and IIH without papilledema (IIHWOP); (2) ocular motor

Table 1: Diagnostic criteria for idiopathic intracranial hypertension[3]

Required for the diagnosis of IIH

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 (obese women), and MRI, with and without contrast, and MRV for others; if MRI is unavailable or contraindicated, contrast-enhanced CT may be used

D. Normal CSF composition

E. Elevated lumbar puncture CSF opening pressure (≥25 cm CSF in adults and ≥28 cm CSF in children [25 cm CSF if the child is not sedated and not obese]) in a properly performed lumbar puncture

Diagnosis of IIH 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

CSF=Cerebrospinal fluid, CT=Computed tomography, MRI=Magnetic resonance imaging, MRV=Magnetic resonance venography

disturbances from third nerve palsy, fourth nerve palsy, internuclear ophthalmoplegia (INO), diffuse ophthalmoplegia, and skew deviation; (3) olfactory dysfunction; (4) trigeminal nerve dysfunction; (5) facial weakness; (6) hearing loss and vestibular dysfunction; (7) lower cranial nerve dysfunction including deviated uvula, torticollis, and tongue weakness; (8) spontaneous skull base CSF leak; and (9) seizures.

The aim of this review is to provide an overview of each of these atypical manifestations of IIH and to discuss their presumed pathophysiologic mechanisms.

Classic Symptoms and Signs of Idiopathic Intracranial Hypertension

Increased ICP and the effect it has on intracranial structures is responsible for the classic symptoms and signs of IIH including headache, papilledema, sixth nerve palsy, divergence insufficiency, and pulsatile tinnitus.

Headache is a common symptom of IIH reported in over 80% of patients[5] and is thought to arise from the activation of intracranial pain-sensitive structures (the dura and its feeding vessels) or central nociceptive pathways. Headache can have features of migraine or tension-type headaches, and over a third of patients have medication overuse.[5] Headaches typically dramatically improve after the diagnostic lumbar puncture. However, the relationship between headache and ICP is complex as headache severity and headache-related disability are not fully explained by ICP alone. Over 50% of IIH patients have long-term sustained headaches, despite normalization of ICP and resolution of papilledema.[6,7]

Papilledema, or bilateral optic nerve swelling due to raised ICP, is necessary for the diagnosis of IIH and is, by definition, always present in the acute presentation of IIH, unless the patient has already developed optic atrophy.[3] Papilledema is due to a mechanical phenomenon wherein increased CSF pressure in the optic nerve sheath causes axoplasmic flow stasis at the optic nerve head, leading to intraneuronal ischemia and secondary vascular changes within the optic nerves.[8] Papilledema is almost always bilateral and usually relatively symmetric. Papilledema results in episodes of transient visual obscurations, described as sudden, very brief episodes of blackout or graying out of vision in one or both eyes, often precipitated by changes in position, such as bending over and then resuming an upright posture.

Sixth nerve palsy is frequently associated with raised ICP and occurs in 14% of IIH patients.[9] Due to its long course between the brainstem and the lateral rectus muscle, the sixth nerve is vulnerable to injury. Sixth nerve palsy is a classic example of a false localizing sign of raised ICP, and traditionally attributed to traction of the intracranial segment of the nerve due to brainstem shift, or compression of the nerve against the petrous ligament or ridge of the petrous temporal bone.[10,11] However, ICP is diffusely elevated in IIH and in the absence of a space-occupying mass there is no pressure gradient, which makes the traction hypothesis less tenable.[12]

Divergence insufficiency, or comitant esodeviation that is greater at distance than at near, is also described in the setting of IIH, other causes of raised ICP, and Chiari I malformation.[13] The cause is controversial and has been attributed to bilateral sixth nerve palsies when reduced velocity of abducting saccades is present.[14] Among those patients in whom abducting saccades are normal, divergence insufficiency has also been argued to be a disorder of supranuclear origin as a result of increased pressure in the posterior fossa.[15]

Pulsatile tinnitus is the most common otological symptom reported by 52%–61% of IIH patients.[16] Pulsatile tinnitus has been hypothesized to be due to transmission of systolic vascular pulsations of the CSF to the transverse and sigmoid venous sinuses, resulting in periodic compression and turbulent blood flow in these structures which are adjacent to the ears.[17,18] Applying light digital pressure to the internal jugular vein may diminish or completely resolve tinnitus in patients with IIH, presumably by disrupting the mechanisms that lead to periodic compression of the venous sinuses.[19] Pulsatile tinnitus in IIH patients is most often bilateral and relatively symmetric. Unilateral, pronounced pulsatile tinnitus should raise concern for a dural arteriovenous fistula.[20]

Atypical Presentations

Asymmetric or unilateral papilledema

Asymmetric papilledema, defined as an interocular difference of two or more Frisén grades, occurs in about 3.6%–10% of IIH patients.[21-23] IIH with strictly unilateral papilledema is rare. A study of 559 IIH patients at one tertiary neuro-ophthalmology service found only eight (1.4%) patients with unilateral papilledema.[21] Another study of patients seen at two tertiary neuro-ophthalmology referral services over a cumulative period of 24 years identified only ten cases of IIH with unilateral papilledema;[24] however, the total number of IIH patients seen during the same period was not stated.

Several hypotheses have been proposed for unilateral or asymmetric papilledema, including compartmentation of the periopptic subarachnoid space, optic canal asymmetry, and asymmetry of intraocular pressure (IOP).[21,25-29]

Compartmentation of the subarachnoid space of the optic nerve sheath is hypothesized to interfere with the transmission of elevated ICP between the intracranial subarachnoid space and the lamina cribrosa, resulting in asymmetry of papilledema.[25] A study using computed tomography (CT) cisternography with a contrast agent reported three IIH patients with asymmetric papilledema and a lack of contrast-loaded CSF in the subarachnoid spaces around both optic nerves, despite it being present in the intracranial subarachnoid spaces.[25] In two patients, contrast-loaded CSF was blocked within the canalicular portion of the optic nerve. In the third patient, contrast-loaded CSF reached the orbital optic nerve, with the CSF advancing further in the optic nerve with the higher grade of papilledema. This finding was not replicated in an animal study.[8]

The size of the optic canal has been hypothesized to affect the transmission of elevated ICP to the lamina cribrosa. One study of eight IIH patients with asymmetric papilledema found that the eye with the lower grade of papilledema had a smaller optic canal as determined by magnetic resonance imaging (MRI) in seven patients and CT in one.[21] Another MRI study found that a larger optic canal was associated with worse visual function and severity of papilledema in patients with symmetric and asymmetric papilledema.[26] However, studies using CT to delineate bony optic canal anatomy did not find a correlation between optic canal measurements and papilledema grade.[27,28] In addition, there was no difference in the optic canal measurements between the eyes of patients with asymmetric papilledema, and no significant difference in the canal measurements between IIH patients and controls.

There is increasing recognition that the pressure gradient across the lamina cribrosa ("translaminar cribrosa pressure difference") likely plays a role in the development of papilledema.[29] Several cases of unilateral papilledema from IIH following surgical reduction of IOP for glaucoma have been described.[30-33] An experimental model in primates induced optic disc edema by lowering IOP, which resolved when IOP returned to normal.[34] Disc edema due to ocular hypotony in the primate model was histologically indistinguishable from disc edema due to raised ICP. However, larger studies of IIH patients with asymmetric papilledema have not found a significant difference in IOP measurements between eyes.[21,24]

Idiopathic intracranial hypertension without papilledema

IIHWOP patients comprise a subset of patients with symptoms of intracranial hypertension, neuroimaging findings suggestive of raised ICP and demonstration of elevated CSF opening pressure by lumbar puncture, but normal funduscopy without papilledema or optic atrophy. Proposed reasons for this include anatomic variations in the optic nerve sheath or its trabeculations limiting transmission of raised ICP to the optic nerve[35] or fluctuating elevations in ICP below the threshold required to develop papilledema.[36] As a group, IIHWOP patients report photopsias and manifest non-physiological visual field constriction more often than IIH patients with papilledema and have a lower elevated opening pressure.[37]

In the absence of papilledema or sixth nerve palsy, the diagnosis of IIHWOP can be suggested by the combination of CSF opening pressure ≥25 cm CSF and the presence of at least three neuroimaging findings, including empty sella, flattening of the posterior aspect of the globes, distension of the periopptic subarachnoid space with or without optic nerve tortuosity, and transverse venous sinus stenosis.[3] However, the diagnosis of IIHWOP is very difficult and must only be made in the presence of very specific criteria[3] as this very rare syndrome is often diagnosed in excess.[38]

Using various criteria, the prevalence of IIHWOP in migraine patients has been estimated to be between 5% and 14%.[37] Using the current diagnostic criteria for IIHWOP outlined above, the prevalence of IIHWOP was 2.5% in patients with chronic headaches refractory to medical therapy.[39] Without disc edema, these patients are not at risk of vision loss and ophthalmologic follow-up is unnecessary.[16,40] Treatment of the headache by an experienced clinician with interest in headache should be the focus of the management of these patients.[16]

Third and fourth nerve palsies

Third and fourth nerve palsies are both rare presentations of IIH.

Third nerve palsy has been reported in mostly case reports of IIH [Table 2].[41-47] However, the diagnostic criteria for IIH were clearly defined in only five cases, including one that was associated with the use of isotretinoin.[43-47] The five patients fulfilled previous diagnostic criteria for IIH.[2,54] There was variability in the clinical manifestations of the third nerve palsy, which invariably resolved within days of lumbar puncture and the initiation of ICP lowering treatment. Work-up ruled out other causes of third nerve palsy.

Similarly, a few case reports and a small series describe patients with fourth nerve palsies in the setting of IIH [Table 2].[48-53] At least four patients appear to meet the most recent diagnostic criteria for IIH based on the descriptions provided in one case report and in one series of three patients.[51,52] One patient had bilateral fourth and sixth nerve palsies,[52] and the remainder had unilateral hypertropia (2–5 PD, when measured) that increased in adduction and with ipsilateral head tilt. These ocular motility findings uniformly improved within hours to a week following lumbar puncture and

initiation of treatment. Other reports of the fourth nerve palsy were in patients with IIH associated with the use of minocycline,[50] nalidixic acid,[49] or topical Vitamin A.[53]

The mechanism of third and fourth nerve palsies in IIH is unknown. Many of the cases describe the finding of a third or fourth nerve palsy as a false localizing sign of raised ICP, presumably due to compression or traction of the cranial nerve. Cases of the third nerve palsy demonstrate variability in the laterality and pupil involvement, which may imply multiple points where the nerve could be stretched or compressed. Bilateral involvement may implicate involvement of the third nerve nuclei located in the midbrain. The slender fourth nerve has a long intracranial course and is therefore especially prone to injury. Another hypothesis relates to alteration in the CSF flow dynamics in the posterior fossa, akin to what is observed in patients with Chiari I malformation, resulting in reduced CSF compliance and decreased damping of the normal effects of respiratory, cardiac, and postural changes on ICP.[44]

All published cases of the third and fourth nerve palsies that met diagnostic criteria for IIH occurred in patients aged 19 years or younger. It has been suggested that sixth nerve palsies also occur more frequently in children with

Table 2: Cases of third and fourth nerve palsy associated with so-called "pseudotumor cerebri syndrome" (presumed idiopathic intracranial hypertension in some publications)

Author (year)	Age/sex	Manifestation	CSF-OP (cm CSF)	Comments
Third nerve palsy				
McCammon et al. (1981)[41]	24/female	Unilateral complete third nerve palsy, stupor, fainting spells, urinary incontinence	55	Normal skull x-ray, CT and angiogram.
Chansoria et al. (2005)[43]	7/male	Unilateral partial third nerve palsy; pupil sparing	26	IIH; normal CT and MRI
Bruce et al. (2006)[44]	19/female	Unilateral partial third; bilateral sixth nerve palsies; pupil sparing	63	IIH; normal MRI and MRV
Thapa and Mukherjee (2008)[45]	5.5/female	Bilateral partial third nerve palsies; pupil sparing	28	IIH; normal MRI
Tan (2010)[46]	14/female	Bilateral partial third nerve palsies; pupil sparing	35	IIH; normal MRI and MRV
Rezazadeh and Rohani (2010)[47]	21/female	Unilateral complete third nerve palsy	40	Isotretinoin; normal CT, CTA, MRI, MRV
Fourth nerve palsy				
Halpern and Gordon (1981)[48]	12/male	Unilateral fourth nerve palsy	"Elevated"	Bilateral chronic mastoiditis on X-ray; normal CT
Gedroyc and Shorvon (1982)[49]	16/female	Unilateral fourth and sixth nerve palsies; pyramidal weakness left leg	25, 19.5	Nalidixic acid; normal CT with and without contrast. Second CSF abnormal
Lee (1995)[50]	13/female	Unilateral fourth nerve palsy	28	Minocycline; normal MRI
Speer et al. (1999)[51]	11/male	Unilateral fourth nerve palsy	55	Normal MRI with contrast
	15/female	Unilateral fourth and contralateral sixth nerve palsies	40	Normal CT with contrast
	8/female	Unilateral fourth nerve palsy	37	Normal CT with contrast
Patton et al. (2000)[52]	15/male	Bilateral fourth and sixth nerve palsies	28	Normal CT and MRI
Totuk et al. (2019)[53]	25/female	Bilateral fourth and sixth nerve palsies	31	Topical vitamin A; asymmetric cavernous sinus on MRI. CSF exam not reported.

Age in years. CSF-OP=Cerebrospinal fluid opening pressure, CT=Computed tomography, CTA=Computed tomography angiography, IIH=Idiopathic intracranial hypertension, MRI=Magnetic resonance imaging, MRV=Magnetic resonance venography

IIH.[55,56] The mechanisms underpinning the increased frequency of ocular motor nerve palsies in children are not fully understood but may relate to anatomical and physiological differences between children and adult brains and how they respond to changes in ICP.

Internuclear ophthalmoplegia, diffuse ophthalmoplegia, and skew deviation

INO is an ocular movement disorder resulting from a lesion in the medial longitudinal fasciculus (MLF) in the pons or midbrain, characterized by an ipsilesional adduction deficit or slow adducting saccades and a contralateral horizontal abducting nystagmus. INO is almost never due to IIH. Seven patients with INO in the setting of so-called pseudotumor cerebri (1985 modified Dandy criteria[4]) have been reported, with a secondary cause for raised ICP identified in at least five patients, including cerebral venous sinus thrombosis, severe anemia, and otitis media [Table 3].[57,58] These patients with venous sinus thrombosis all had bilateral INO, bilateral abduction paresis, limitation of vertical eye movements, and very elevated CSF opening pressure (>55 cm CSF).[58] One other case of bilateral INO was described in a young woman fulfilling the current IIH diagnostic criteria.[59] MRI was normal, but she had CSF-restricted oligoclonal bands. It remains uncertain if her bilateral INO was due to IIH or to concurrent demyelinating disease. Neuroimaging, specifically MRI with attention to the posterior fossa and the MLF, is essential in these patients. However, an MLF lesion may not be apparent if the slice thickness is large or if there is a significant interslice gap.

Diffuse ophthalmoplegia refers to complete or near-complete paralysis of all the extraocular muscles. At least eight patients with diffuse ophthalmoplegia or ophthalmoparesis have been reported [Table 3].[58,60-62,64,65] The majority of these patients would not fulfill the current diagnostic for IIH due to the presence of underlying cerebral venous sinus thrombosis, abnormal CSF examination, or insufficient neuroimaging to exclude secondary causes of raised ICP. At least five cases were associated with reduced or absent deep tendon reflexes on examination.[58,62-65] Three of these cases were preceded by viral illnesses and were areflexic on examination,[58,62,63] suggesting that they may have had Miller Fisher syndrome (MFS), a presumed autoimmune disorder with a triad of ophthalmoplegia, areflexia, and ataxia.[67] Co-occurrence of raised ICP and papilledema has been described in patients with MFS, and patients may present with a clinical picture similar to IIH, particularly as neuroimaging is usually normal.[63,68,69] The presence of an abnormally elevated CSF protein, and the identification of an anti-ganglioside antibody against GQ1b, found on the neuronal cells with higher percentages in the third, fourth, and sixth cranial nerves, is helpful in making a

diagnosis of MFS and distinguishing it from IIH even in the setting of elevated ICP.[70] The timing of CSF examination is important as an early lumbar puncture may miss abnormal elevation of CSF protein.[67]

Skew deviation is a vertical ocular misalignment that is caused by damage to the prenuclear vestibular input to ocular motor nuclei. Skew deviation can be associated with other neurological signs and may be part of the ocular tilt reaction. Five cases of skew deviation have been described in the setting of IIH [Table 3].[44,57,66] Only one of these patients fulfills the current IIH diagnostic criteria.[44] This patient presented with headache, severe papilledema, and bilaterally constricted visual fields and had alternating skew deviation on the lateral gaze and upbeat nystagmus on the upgaze, with no posterior fossa lesions on MRI to account for the eye movement disorder. Lesions that give rise to the skew deviation occur in the posterior fossa, but skew deviation can also occur in the setting of raised ICP without a demonstrable posterior fossa lesion on high-resolution neuroimaging.[71,72] Lesions of the peripheral vestibular structures that are involved in the utriculo-ocular pathway can also give rise to a skew deviation and a pathologic ocular tilt reaction.[73] It has been postulated that raised ICP may affect the inner ear and cause imbalance in stimulation of the utriculo-ocular pathways, resulting in skew deviation.

Olfactory dysfunction

Altered sense of smell in IIH patients, presumably secondary to dysfunction of the olfactory nerves, is of unknown prevalence, especially clinically. One study found that eight of ten patients with acute clinical manifestations of IIH displayed hyposmia, defined as scoring in the bottom tenth percentile or less compared to normosmic subjects on the Sniffin' Sticks' test, a psychophysical test of nasal chemosensory performance based on pen-like odor dispensing devices.[74] Olfactory dysfunction is hypothesized to occur due to compression of the olfactory nerves around the cribriform plate.[75]

Several studies have demonstrated evidence of olfactory dysfunction on the Sniffin' Sticks' test and the University of Pennsylvania Smell Identification Test among IIH patients.[74,76-79] Compared to age- and sex-matched controls, IIH patients have significantly impaired olfactory detection thresholds and reduced ability to identify and discriminate among odors.[74] Although they have reduced scores compared to healthy controls, most IIH patients are not aware of their olfactory dysfunction.[78] There is conflicting evidence regarding the relationship between olfactory dysfunction and IIH disease activity, disease duration, CSF opening pressure, and visual function.[77,79] A recent study found that compared to controls, olfactory function in IIH patients measured with

Table 3: Cases of internuclear ophthalmoplegia, diffuse ophthalmoplegia, and skew deviation associated with so-called "pseudotumor cerebri syndrome" (presumed idiopathic intracranial hypertension in some publications)

Author (year)	Age/sex	Manifestation	CSF-OP (cm CSF)	Comments
Internuclear ophthalmoplegia				

Author (year)	Age/sex	Manifestation	CSF-OP (cm CSF)	Comments
Internuclear ophthalmoplegia				
Baker and Buncic (1985)[57]	5/female	Bilateral INO, bilateral sixth nerve palsy, left hypertropia	43	Otitis media 1 month prior; normal CT and vertebral angiogram
Friedman et al. (1998)[58]	9/male	Right INO	35	IIH; normal MRI and MRV
	34/female	Bilateral INO, bilateral sixth nerve palsy	42	Severe anemia; normal MRI and MRV
	20/female	Bilateral INO, bilateral sixth nerve palsy, unilateral seventh, ataxia	>55	IIH; normal MRI and MRV
	20/female	Bilateral INO, bilateral sixth nerve palsy, downgaze palsy, mild bilateral ptosis	>55	CVST
	14/female	Bilateral INO, bilateral sixth nerve palsy, vertical ophthalmoparesis	>55	CVST
	30/female	Bilateral INO, bilateral sixth nerve palsy, limited upgaze, unilateral seventh, paresthesia	36, >55	CVST
Keereman et al. (2018)[59]	25/female	(Wall-eyed) bilateral INO	38	Positive OCB on CSF; normal MRI and MRV
Ophthalmoparesis and ophthalmoplegia				
Snyder and Frenkel (1979)[60]	25/female	Complete external ophthalmoparesis, bilateral mydriasis, right ptosis, prominent left globe, unilateral facial nerve palsy	30	Small ventricles on CT; normal angiogram
Landan et al. (1987)[61]	28/female	Complete external ophthalmoplegia	>56	Slit-like ventricles on CT; normal angiogram
Kidron and Pomeranz (1989)[62]	18/female	Complete ophthalmoplegia (right), global ophthalmoparesis (left), bilateral nonreactive pupils; diminished corneal reflexes, areflexic in the lower limbs	>60	Upper respiratory tract infection 10 days prior; normal CT, MRI and angiogram, except slowed vascular passage time
	26/female	Complete global bilateral ophthalmoparesis, hyporeflexia of lower limbs; transient unilateral facial paresis	>60	Normal CT and slowed vascular passage time on angiogram. Xanthochromic CSF with crenated erythrocytes
Friedman et al. (1998)[58]	20/female	Global ophthalmoparesis	>55	Normal CT
	16/female	Ophthalmoplegia; mild arm and right iliopsoas weakness; areflexic	>55	Preceding viral illness; normal CT
	33/female	Global supranuclear ophthalmoparesis	>55	CVST
Yeak et al. (2019)[63]	28/female	"Acute ophthalmoparesis" characterized by bilateral sixth nerve palsies and hypometric saccades; hyporeflexic in all limbs	50	MFS; anti-GQ1b and anti-GQ1a positive; normal MRI
Ragab et al. (2017)[64]	17/female	Unilateral disc edema, contralateral optic atrophy, bilateral sixth nerve palsy, limited contralateral adduction, bilateral mid-dilated nonreactive pupils, flaccid quadriparesis and areflexia	50	Slit-like ventricles on MRI; bilateral transverse venous sinus stenosis on MRV; normal MRI cervical spine; diffuse radiculopathy on NCS
Nathan et al. (2020)[65]	27/female	Diffuse ophthalmoparesis, prominent decreased bilateral adduction deficits, unilateral peripheral facial weakness, bilateral upper limb weakness and reduced left biceps reflex	56	IIH; normal MRI and MRV brain; normal MRI spine; bilateral C5-6 radiculopathy on NCS/EMG
Skew deviation				
Merikangas (1978)[66]	35/female	Intermittent right hypertropia	55	Small ventricle on CT; normal angiogram
Baker and Buncic (1985)[57]	5/female	Bilateral INO, bilateral sixth nerve palsy, left hypertropia	43	Otitis media 1 month prior; normal CT and vertebral angiogram
	15/female	Bilateral sixth nerve palsy, alternating skew deviation versus bilateral fourth, incomitant vertical deviation, no head tilt	35	Normal skull X-ray and CT
	7/male	Bilateral sixth nerve palsy, right hypertropia	Not stated	Investigations not stated
Bruce et al. (2006)[44]	38/female	Alternating skew deviation on lateral gaze; upbeat nystagmus on upgaze	41	IIH; normal MRI and MRV

Age in years. CSF-OP=Cerebrospinal fluid opening pressure, CT=Computed tomography, CVST=Cerebral venous sinus thrombosis, EMG=Electromyography, IIH=Idiopathic intracranial hypertension, INO=Internuclear ophthalmoplegia, MFS=Miller fisher syndrome, MRI=Magnetic resonance imaging, MRV=Magnetic resonance venography, NCS=Nerve conduction study, OCB=Oligoclonal band

the Sniffin' Stick's test improved when CSF pressure was lowered into the normal range by lumbar puncture.[78] However, the study had several limitations, including no lumbar punctures for any of the controls and inclusion of smokers. In addition, the post-lumbar puncture smell test in the IIH patients was completed after a mean of 17.5 h after the procedure, by which time several cycles of CSF regeneration would have occurred.

An MRI study did not find any significant difference in the volume of the olfactory bulb or depth of the olfactory sulcus in 23 IIH patients compared to matched controls.[80] Subanalysis of eight patients with disease duration of <1 year revealed a significantly smaller olfactory bulb volume compared to controls, which was associated with decreased olfactory function.

Trigeminal nerve dysfunction

There are rare reports of IIH manifesting with unilateral paresthesia (abnormal sensation) and hypoesthesia (decreased sensation) in the distribution of the trigeminal nerve [Table 4].[81-83] Three patients were found to have a reduction in light touch, pain, and/or temperature sensation involving all divisions of the trigeminal nerve, accompanied by diminished or absent corneal reflexes.[81-83] Trigeminal dysfunction was confirmed using electrophysiological techniques in one patient,[83] with absent orbicularis oculi muscle response following supraorbital nerve stimulation on blink reflex testing and no response within the masseter muscle on jaw reflex testing. Two further reports described patients with unilateral neuralgia in the V2 division of the trigeminal nerve and in the lower half of the face.[84,85] Resolution of pain occurred following reduction of CSF pressure by lumbar puncture in both cases. However, neither report provides details regarding the presence of adjacent vascular structures that could cause trigeminal nerve compression.

Of the five total cases of trigeminal dysfunction described, only two patients fulfill the current diagnostic criteria for IIH,[83,85] with the three remaining patients having undergone insufficient imaging to exclude cerebral venous sinus thrombosis or an alternative cause of raised ICP.

The trigeminal root fibers form a sharp angle as they cross the apex of the petrous portion of the temporal bone and enter the trigeminal cistern. The pathophysiologic mechanisms for trigeminal dysfunction or neuralgia in the setting of raised ICP may involve stretching of the trigeminal root fibers over the petrous apex by a slightly displaced brainstem, direct compression of the trigeminal root at the petrous apex by the petrosal sinus, or compression within Meckel's cave by raised ICP superiorly.[84,86] In some patients, trigeminal neuralgia may be secondary to herniation of the trigeminal nerve into a skull base meningocele, sometimes in the setting of CSF leak (see below).

Facial nerve dysfunction

Peripheral facial weakness is an uncommon finding among IIH patients. A series of 30 children with IIH (defined as an CSF pressure of >20 cm CSF, normal CSF contents, and no mass or hydrocephalus on neuroimaging), seen between 1960 and 1990, identified only one child with unilateral facial nerve palsy.[87] Another series of 140 adults and children with IIH (1985 modified Dandy Criteria[4]), seen between 1989 and 1994, identified only two patients (aged 12 and 36 years) with unilateral facial nerve palsy.[88] Despite the infrequent occurrence in larger series, various presentations of facial nerve palsy have been described in case reports [Table 5], with the most common presentation being unilateral peripheral facial weakness.[81,88-95] More than half of these cases are accompanied by other cranial nerve involvement, most often the sixth nerve.[88,92-94,90]

Facial diplegia, or bilateral peripheral facial weakness, is less frequent.[96-98] One case of facial diplegia was associated with bilateral sixth nerve palsy and features suggestive of Guillain–Barré syndrome (GBS)

Table 4: Cases of trigeminal nerve dysfunction associated with so-called "pseudotumor cerebri syndrome" (presumed idiopathic intracranial hypertension in some publications)

Author (year)	Age/sex	Manifestation	CSF-OP (cm CSF)	Comments
Hart and Carter (1982)[84]	34/female	Previous history of unilateral facial numbness; recurrent ipsilateral V2 facial pain and paresthesia without headache	45, 23	Normal skull x-ray, small ventricles on CT
Zachariah *et al.* (1990)[81]	29/female	Unilateral sensory loss and numbness (all divisions), ipsilateral peripheral facial weakness, hemisensory loss, and hyperreflexia	45	Normal CT with contrast and MRI
Davenport *et al.* (1994)[82]	20/female	Unilateral sensory loss and numbness (all divisions)	39	Normal CT with contrast
Arsava *et al.* (2002)[83]	37/female	Unilateral sensory loss and numbness (all divisions)	32	IIH; normal CT and MRV
Algahtani *et al.* (2007)[85]	36/female	"Classic trigeminal neuralgia" involving unilateral lower face	40	IIH; normal MRV and MRA

Age in years. CSF-OP=Cerebrospinal fluid opening pressure, CT=Computed tomography, CTV=Computed tomography venography, IIH=Idiopathic intracranial hypertension, MRA=Magnetic resonance angiography, MRI=Magnetic resonance imaging, MRV=Magnetic resonance venography

Table 5: Cases of facial nerve dysfunction associated with so-called "pseudotumor cerebri syndrome" (presumed idiopathic intracranial hypertension in some publications)

Author (year)	Age/sex	Manifestation	CSF-OP (cm CSF)	Comments
Unilateral peripheral facial weakness				
Chutorian et al. (1977)[89]	12/male	Unilateral peripheral facial weakness	34	Normal skull X-ray
	14/male	Unilateral peripheral facial weakness	32	Normal skull X-ray, CT with contrast, and angiogram
	11/male	Unilateral peripheral facial weakness	20, 31	Normal skull X-ray, angiogram, and pneumocephalogram
Zachariah et al. (1990)[81]	29/female	Unilateral sensory loss and numbness (all divisions), ipsilateral peripheral facial weakness, hemisensory loss, and hyperreflexia	45	Normal CT with contrast and MRI
Davie et al. (1992)[90]	25/female	Unilateral peripheral facial weakness; bilateral sixth nerve palsy	30	Normal CT with contrast
Capobianco et al. (1997)[88]	12/female	Unilateral peripheral facial weakness	20.5, 49	Normal CT, MRI, and MRA
	36/female	Unilateral peripheral facial weakness; ipsilateral sixth nerve palsy	45	Normal MRI and MRA with contrast
Brackmann and Doherty (2007)[91]	8/male	Unilateral peripheral facial weakness and asymmetric hearing loss two months after diagnosed with IIH	Not stated	CT and MRI showed enlarged facial canal
Kearsey et al.[92] (2010)	19/female	Unilateral peripheral facial weakness; bilateral sixth nerve palsy	35	Topical vitamin A; normal CT and CTV
Tzoufi et al. (2010)[93]	11/female	Unilateral peripheral facial weakness five days after diagnosed with IIH and sixth nerve palsy	26	Normal CT, MRI, MRV, and MRA
Soroken et al. (2016)[94]	13/female	Unilateral peripheral facial weakness; ipsilateral sixth nerve palsy; unilateral disc edema	50	Normal MRI and MRA without contrast
Samara et al. (2019)[95]	40/female	Unilateral peripheral facial weakness	28	Normal MRI, transverse venous sinus stenosis on MRV
Facial diplegia				
Kiwak and Levine (1984)[96]	28/female	Facial diplegia, bilateral hyperacusis, reduced taste tip of tongue	60	Tetracycline and oral contraception; slit-like ventricles on CT; normal angiogram
Bakshi et al. (1992)[97]	23/female	Facial diplegia, unilateral sixth nerve palsy	67	Normal CT and MRI
Obeid et al. (2000)[98]	24/female	Facial diplegia, bilateral sixth nerve palsy, progressive quadriparesis and areflexia, radiculopathy	36, 42	Normal MRI brain and cervical spine; radiculopathy on NCS/EMG; negative serum anti-GM1 antibodies
Hemifacial spasm				
Selky and Purvin (1994)[99]	46/female	Unilateral hemifacial spasm	35	Normal MRI
Benegas et al. (1996)[100]	54/female	Unilateral hemifacial spasm	48	Normal CT and MRI
Grassi et al. (2001)[101]	50/female	Unilateral hemifacial spasm	34, 30	Normal CT with contrast and MRI; spontaneous activity and chronic denervation on EMG; abnormal blink reflex recording
Poff et al. (2020)[102]	43/female	Unilateral hemifacial spasm	26	Normal CT; bilateral AICA vascular loops and bilateral transverse sinus narrowing on MRI
Garcia et al. (2020)[103]	32/female	Unilateral hemifacial spasm	41	Normal MRI and MRA; transverse venous sinus stenosis on MRV

Age in years. AICA=Anterior inferior cerebellar artery, CSF-OP=Cerebrospinal fluid opening pressure, CT=Computed tomography, CTV=Computed tomography venography, EMG=Electromyography, MRA=Magnetic resonance angiography, MRI=Magnetic resonance imaging, MRV=Magnetic resonance venography, NCS=Nerve conduction study

including progressive quadriparesis and areflexia.[98] GBS is a common cause of facial diplegia, and almost half of these patients have facial nerve involvement during their illness. Clinicians should be aware of a subtype of GBS that can manifest with progressive facial weakness in the absence of other cranial neuropathies, ataxia, or limb weakness.[104] Papilledema

is a recognized but infrequently reported finding of GBS.[105]

The relationship between facial nerve dysfunction and raised ICP is questionable in several of the cases described. In most cases, facial weakness recovered within two days,[81,90,92] or one week[95,96] of initiating

treatment to lower ICP. Several cases recovered after three weeks or longer.[88,89,94,93] In one case of unilateral facial weakness associated with bilateral sixth nerve palsies, papilledema resolved after 1.5 months, while facial weakness resolved after four months.[93] Many of the patients did not undergo MRI, contrast-enhanced imaging, or venous imaging with CT venography or magnetic resonance venography (MRV) and would not fulfill the current diagnostic criteria for IIH. We could only identify two IIH cases who met the current diagnostic criteria, one of which was associated with the use of topical Vitamin A cream.[92,95] In both cases, the facial nerve palsy resolved within one week. However, one patient was also treated with oral prednisone (60 mg) daily for five days, an established treatment for idiopathic facial palsy (Bell's palsy).[106] Indeed, the coincidence of IIH and Bell's palsy, the most common cause of unilateral facial paralysis, is certainly possible. The annual incidence of Bell's palsy is 15–40 per 100,000,[106] while the incidence of IIH in the general population in one study was 4.7 per 100,000.[107] Patients with Bell's palsy who are not treated with prednisone have poor rates of recovery, with only two-thirds achieving complete recovery by three months.[106]

The precise location along the course of the facial nerve which makes it vulnerable to the effects of raised ICP remains speculative. The intracranial segment of the facial nerve, beginning from the facial nucleus in the pons to the point where it passes through the internal auditory meatus to enter the facial canal, is less susceptible to traction forces due to its anatomy.[95] None of the cases of unilateral peripheral facial weakness have been associated with an ipsilateral gaze palsy suggesting involvement of the facial colliculus in the pons.

A potential site for the facial nerve to be compressed or stretched is the intratemporal segment of the nerve as it traverses the facial canal, a bony canal within the temporal bone extending from the internal acoustic meatus to the stylomastoid foramen. Accompanying the nerve through the facial canal is an extensive venous complex. Venous congestion within the plexus could increase the pressure within the canal and compromise the microscopic vasculature within the nerve itself, resulting in nerve injury. There is one case report of an 8-year-old boy with an established diagnosis of IIH, who was evaluated for peripheral facial palsy and found to have CSF-filled enlargement of the geniculate fossa in the facial canal on imaging.[91] It was not determined if enlargement of the bony fossa was a consequence of chronically elevated ICP or if a congenitally enlarged fossa enabled transmission of CSF pressure along the nerve causing damage. The patient denied hearing loss but had evidence of a progressive asymmetric sensorineural hearing loss on audiometry.

Five patients with hemifacial spasm in the setting of IIH have been described.[99-103] The cause in several patients was speculated to be compression or traction of the nerve due to raised ICP.[100,101,103] However, it is unclear why this mechanism would result in facial nerve hyperexcitability in these patients and facial weakness in other patients. A more plausible hypothesis proposes that elevated ICP shifts the facial nerve to an intimate position against brainstem vascular structures, triggering a hyperexcitable response.[99]

Hearing loss and vestibular dysfunction

Hearing loss of variable degree is a symptom reported by 30%–85% of patients with IIH.[17,108] Earlier studies of patients with presumed pseudotumor cerebri, including those with IIH mimics such as cerebral venous sinus thrombosis, characterized the hearing loss as sensorineural affecting the lower frequencies (250 and 500 Hz).[17] A recent study of IIH patients (2002 modified Dandy criteria[2]) found asymmetry of the frequencies affected in each ear.[108] Lowering CSF pressure into the normal range led to improved hearing, particularly in the lower frequencies.[17,109]

Hearing loss as a prominent presenting feature of IIH has been reported in five patients [Table 6].[110-114] Four patients presented with bilateral sensorineural hearing loss, and one had unilateral conductive hearing loss.[113] The diagnosis of IIH was questionable in four patients, due to the absence of papilledema or insufficient imaging to exclude venous sinus thrombosis.[110,111,113,114] Hearing improved between one day and six months after normalization of CSF pressure in all five patients.

Vestibular dysfunction in IIH patients is difficult to study. Dizziness and vertigo are reported in 23%–50% of patients.[17,108,109] Objective evidence of central and peripheral dysfunction of the vestibular pathways has been described, with one study of 20 patients finding evidence of central pathology on electronystagmography, including saccadic latency prolongation, optokinetic asymmetry, and tracking test abnormalities, in ten patients.

Caloric reflex tests were performed in three studies, with the proportion of abnormal tests in IIH patients ranging from 10% to 56%.[17,108,115] However, compared to healthy controls, there is no difference in the frequency of abnormal caloric reflex responses.[108] Improvement in self-reported symptoms of vestibular dysfunction and on objective tests of vestibular function following treatment to lower CSF pressure has been reported.[17,108,109,115] However, none of these studies established a direct correlation between subjective symptoms of vestibular dysfunction and abnormal vestibular testing. Dysfunction of the saccule or the inferior vestibular nerve has been

Table 6: Cases of hearing loss as a prominent feature of so-called "pseudotumor cerebri syndrome" (presumed idiopathic intracranial hypertension in some publications)

Author (year)	Age/sex	Manifestation	CSF-OP (cm CSF)	Comments
Dorman *et al.* (1995)[113]	24/female	Unilateral mild conductive hearing loss several months after diagnosed with IIH	29	Normal CT, MRI and MRA
Malomo *et al.* (2006)[110]	14/female	Bilateral asymmetric sensorineural hearing loss; bilateral sixth nerve palsies	40.7	Normal CT with contrast
Reitsma *et al.* (2015)[114]	9/male	History of bilateral otitis media with effusions requiring grommets, and left mastoiditis 1 year prior. Progressive mixed hearing loss with significant sensorineural component. No papilledema	49	Normal CT; small ventricles on MRI
Bahr Hosseini *et al.* (2016)[112]	49/male	Remote history of motor vehicle accident. History of headache, blurred vision, and diffuse weakness and treated empirically for polyradiculoneuropathy. Severe bilateral asymmetric sensorineural hearing loss at presentation	45	Petrous apex cephaloceles, meningoceles into bilateral IACs, bilateral optic vein engorgement, and bilateral perioptic CSF distension on MRI; normal MRV
Tobia *et al.* (2019)[111]	13/male	Bilateral severe mixed hearing loss with significant sensorineural component	60	Normal MRI

Age in years. CSF-OP=Cerebrospinal fluid opening pressure, CT=Computed tomography, IACs=Internal auditory canals, MRA=Magnetic resonance angiography, MRI=Magnetic resonance imaging, MRV=Magnetic resonance venography

found in around 40% of IIH patients, as evidenced by abnormal vestibular evoked myogenic potentials elicited from the sternocleidomastoid muscle.[108] In addition, raised ICP has been found to cause a reduction in vestibular evoked myogenic potentials elicited from the orbicularis oculi muscle (oVEMP), a test of utricular and superior vestibular nerve function. Lowering ICP into the normal range in IIH patients leads to increased amplitude of air conduction sound oVEMP, but not bone conduction vibration oVEMP.[116]

Different mechanisms have been proposed to explain otological symptoms in IIH. Transmitted pressure into the inner ear from the subarachnoid space via the vestibular aqueduct or from increased perilymphatic pressure via the cochlear aqueduct has both been proposed.[114,116,117] Alterations in perilymphatic and endolymphatic pressures by raised ICP, akin to endolymphatic hydrops, has also been speculated.[109]

Dysfunction of the audiovestibular pathways at the level of the brainstem and vestibulocochlear nerve giving rise to an auditory neuropathy spectrum disorder (ANSD) has also been considered.[111] A diagnosis of ANSD is suggested if tests of the outer hair cell function are normal (otoacoustic emissions), but the auditory brainstem response (ABR) is absent or abnormal. Raised ICP is postulated to compress or stretch the vestibulocochlear nerve, or damage the nucleus or its ascending pathways by distorting the brainstem. Around one-third of IIH patients have abnormal ABR, with prolonged interpeak latencies and prolonged absolute wave V latencies.[118] Inversion of ABR waveforms in response to a change in stimulus polarity and absence of ABR recordings has also been reported in case reports.[111,112] These findings improved or normalized as ICP returned to normal.

In some patients, pulsatile high hydrostatic CSF pressure erodes the facial canal, leading to the formation of a CSF fistula with or without CSF otorrhea, which can be responsible for unilateral hearing loss.[119]

Lower cranial nerve dysfunction

Dysfunction of the lower cranial nerves in IIH is very rare, probably on account of the anatomic location of their nuclei in the brainstem and where they emerge from the lower brainstem. Only one case with involvement of the vagus nerve has been described, manifesting with right-sided uvula deviation.[120] The patient also had left sixth nerve palsy and left facial nerve palsy with very high CSF opening pressure (57.5 cm CSF). His cranial nerve palsies resolved within one month of the lumbar puncture and starting acetazolamide.

There are several case reports of IIH patients presenting with stiff neck. Involvement of the accessory nerve can be inferred in six patients presenting with torticollis.[121-124] Accessory nerve dysfunction is questionable in two cases. One patient developed involuntary head turning and neck pain, which resolved during sleep.[121] Her symptoms persisted despite placement of a CSF shunt. The other patient was suspected of pre-existing "early life torticollis" with evidence of asymmetry of the second cervical ribs and tilting of the body of the odontoid process on the cervical spine X-ray and an enlarged cisterna magna on CT.[122] The four remaining patients were all children aged between 7 and 9 years.[123,124] They all had a history of head tilt and a painful stiff neck, with reduced voluntary and passive neck movements due to tight neck muscles. These symptoms improved following lumbar puncture, with recovery occurring between 30 min and two days after the procedure.

The mechanism that leads to neck stiffness and torticollis is unknown. One hypothesis proposes cerebellar tonsillar herniation causing irritation of the upper cervical nerves, similar to patients with Chiari I malformation.[124] Tonsillar herniation is a recognized radiological finding in IIH patients, with a pooled prevalence of 16%,[125] but not specifically mentioned in any of the torticollis cases.[121-124] Another hypothesis is that increased ICP may trigger production of cytokines and serotonins that irritate pain receptors, inducing pain and spasm of the neck extensor muscles, akin to meningitis.[123] However, headache was not a significant symptom in the torticollis cases, and it is unclear why the sternocleidomastoid muscles would be preferentially affected. This hypothesis may also account for back pain, which has been described in 53% of IIH patients,[16] and may co-exist with the hypothesis that back pain is the result of expansion of the spinal dural sac and root pouches by congested CSF.[126]

Individual cases with hypoglossal dysfunction have been included in larger series of IIH patients, but with a paucity of clinical details.[115,127]

Spontaneous cerebrospinal fluid skull base leak

There is increasing recognition of the relationship between spontaneous CSF leak and IIH. A striking overlap exists between the demographic, clinical, and radiological characteristics of patients with IIH and those with spontaneous CSF leak. Both occur in mainly obese women.[128] The CSF leak may act as an auto-diversion for CSF, eliminating the characteristic signs and symptoms of IIH.[129] Headache and pulsatile tinnitus feature prominently as the initial symptoms of both conditions,[128] and papilledema is more likely to occur following CSF leak repair in patients with bilateral transverse venous sinus stenosis. Both groups show similar radiological features, including empty sella, but IIH patients have more orbital findings and CSF leak patients have more prominent signs of bony erosion such as cephaloceles.[129] Meningoceles have been reported in around 11% of IIH patients and occur in Meckel's cave and the petrous apex of the temporal bone,[130] potentially causing trigeminal dysfunction[86] and CSF leak, respectively. Erosion into the facial canal can result in unilateral peripheral facial weakness and hearing loss as described earlier.[91,119]

Seizures

Seizures due to meningoencephaloceles of the temporal lobe may be a rare presentation of IIH. Temporal meningoencephaloceles are an increasingly recognized cause of drug-resistant temporal lobe epilepsy and are commonly associated with radiographic findings, suggestive of IIH.[131] One study of 22 patients with temporal lobe-onset seizures due to anteroinferior temporal meningoencephaloceles found that roughly a third of patients were obese and had MRI signs of IIH, including empty sella, transverse sinus stenosis, posterior globe flattening, and perioptic CSF distension.[132]

Conclusion

IIH is a disorder of raised ICP of unknown etiology that can only be diagnosed after secondary causes of raised ICP have been excluded. Many of the cases described in the literature of patients presenting with atypical signs or symptoms would not fulfill the current diagnostic criteria for IIH, which incorporates neuroimaging findings, a higher cutoff for normal CSF pressure, and mandates normal CSF contents. Many signs and symptoms of IIH improve after lumbar puncture. However, an improvement in signs or symptoms after lowering ICP into the normal range should not be used as evidence of an association with IIH, as this finding is not specific. Certainly, the lack of improvement following lumbar puncture increases suspicion for an alternative etiology. Even in patients who meet diagnostic criteria for IIH, atypical presentations should prompt investigation for other diagnostic possibilities. Some signs, such as diffuse ophthalmoplegia, are almost never due to IIH, while others such as spontaneous CSF leak may occur as a consequence of chronically elevated ICP of any cause. Contrast-enhanced brain MRI to exclude a meningeal process, MRV to exclude cerebral venous sinus thrombosis and dural arteriovenous fistula, and CSF analysis are necessary in all patients suspected of having IIH, especially in those presenting with atypical signs or symptoms. Neuroimaging with CT and MRI can also be helpful in identifying radiological changes of chronically elevated ICP, such as bony erosion of the skull base and herniation of intracranial contents that may account for some of the atypical signs or symptoms of IIH.

Conflicts of interest
The authors declare that there are no conflicts of interests of this paper.

References

1. Dandy WE. Intracranial pressure without brain tumor: Diagnosis and treatment. Ann Surg 1937;106:492-513.
2. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. Neurology 2002;59:1492-5.
3. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology 2013;81:1159-65.
4. Smith JL. Whence pseudotumor cerebri? J Clin Neuroophthalmol 1985;5:55-6.

5. Friedman DI, Quiros PA, Subramanian PS, Mejico LJ, Gao S, McDermott M, *et al.* Headache in idiopathic intracranial hypertension: Findings from the idiopathic intracranial hypertension treatment trial. Headache 2017;57:1195-205.

6. Friedman DI, Rausch EA. Headache diagnoses in patients with treated idiopathic intracranial hypertension. Neurology 2002;58:1551-3.

7. Yri HM, Rönnbäck C, Wegener M, Hamann S, Jensen RH. The course of headache in idiopathic intracranial hypertension: A 12-month prospective follow-up study. Eur J Neurol 2014;21:1458-64.

8. Hayreh SS. Pathogenesis of optic disc edema in raised intracranial pressure. Prog Retin Eye Res 2016;50:108-44.

9. Round R, Keane JR. The minor symptoms of increased intracranial pressure: 101 patients with benign intracranial hypertension. Neurology 1988;38:1461-4.

10. Larner AJ. False localising signs. J Neurol Neurosurg Psychiatry 2003;74:415-8.

11. Collier J. The false localising signs of intracranial tumour. Brain 1904;27:490-508.

12. Lepore FE. False and non-localizing signs in neuro-ophthalmology. Curr Opin Ophthalmol 2002;13:371-4.

13. Jacobson DM. Divergence insufficiency revisited: Natural history of idiopathic cases and neurologic associations. Arch Ophthalmol 2000;118:1237-41.

14. Kirkham TH, Bird AC, Sanders MD. Divergence paralysis with raised intracranial pressure. An electro-oculographic study. Br J Ophthalmol 1972;56:776-82.

15. Lewis AR, Kline LB, Sharpe JA. Acquired esotropia due to Arnold-Chiari I malformation. J Neuroophthalmol 1996;16:49-54.

16. Mollan SP, Davies B, Silver NC, Shaw S, Mallucci CL, Wakerley BR, *et al*. Idiopathic intracranial hypertension: Consensus guidelines on management. J Neurol Neurosurg Psychiatry 2018;89:1088-100.

17. Sismanis A. Otologic manifestations of benign intracranial hypertension syndrome: Diagnosis and management. Laryngoscope 1987;97:1-7.

18. Sismanis A. Pulsatile tinnitus. A 15-year experience. Am J Otol 1998;19:472-7.

19. Sismanis A, Butts FM, Hughes GB. Objective tinnitus in benign intracranial hypertension: An update. Laryngoscope 1990;100:33-6.

20. Cognard C, Casasco A, Toevi M, Houdart E, Chiras J, Merland JJ. Dural arteriovenous fistulas as a cause of intracranial hypertension due to impairment of cranial venous outflow. J Neurol Neurosurg Psychiatry 1998;65:308-16.

21. Bidot S, Bruce BB, Saindane AM, Newman NJ, Biousse V. Asymmetric papilledema in idiopathic intracranial hypertension. J Neuroophthalmol 2015;35:31-36.

22. Wall M, White WN 2nd. Asymmetric papilledema in idiopathic intracranial hypertension: Prospective interocular comparison of sensory visual function. Invest Ophthalmol Vis Sci 1998;39:134-42.

23. Wall M, Kupersmith MJ, Kieburtz KD, Corbett JJ, Feldon SE, Friedman DI, *et al*. The idiopathic intracranial hypertension treatment trial: Clinical profile at baseline. JAMA Neurol 2014;71:693-701.

24. Huna-Baron R, Landau K, Rosenberg M, Warren FA, Kupersmith MJ. Unilateral swollen disc due to increased intracranial pressure. Neurology 2001;56:1588-90.

25. Killer HE, Jaggi GP, Flammer J, Miller NR, Huber AR, Mironov A. Cerebrospinal fluid dynamics between the intracranial and the subarachnoid space of the optic nerve. Is it always bidirectional? Brain 2007;130:514-20.

26. Bidot S, Clough L, Saindane AM, Newman NJ, Biousse V, Bruce BB. The optic canal size is associated with the severity of papilledema and poor visual function in idiopathic intracranial hypertension. J Neuroophthalmol 2016;36:120-5.

27. Skipper NT, Igra MS, Littlewood R, Armitage P, Laud PJ, Mollan SP, *et al*. Do optic canal dimensions measured on CT influence the degree of papilloedema and visual dysfunction in idiopathic intracranial hypertension? Neuroophthalmology. 2019;43:3-9.

28. Farrokhi Y, Sharif Kashani S, Aghsaei Fard M, Pakdel F, Yadegari S. Optic canal size in idiopathic intracranial hypertension and asymmetric papilledema. Clin Neurol Neurosurg 2019;184:105376.

29. Liu KC, Fleischman D, Lee AG, Killer HE, Chen JJ, Bhatti MT. Current concepts of cerebrospinal fluid dynamics and the translaminar cribrosa pressure gradient: A paradigm of optic disk disease. Surv Ophthalmol 2020;65:48-66.

30. Abegg M, Fleischhauer J, Landau K. Unilateral papilledema after trabeculectomy in a patient with intracranial hypertension. Klin Monbl Augenheilkd 2008;225:441-2.

31. Greenfield DS, Wanichwecharungruang B, Liebmann JM, Ritch R. Pseudotumor cerebri appearing with unilateral papilledema after trabeculectomy. Arch Ophthalmol 1997;115:423-6.

32. Kawasaki A, Purvin V. Unilateral optic disc edema following trabeculectomy. J Neuroophthalmol 1998;18:121-3.

33. Lawlor M, Zhang MG, Virgo J, Plant GT. Asymmetrical intraocular pressures and asymmetrical papilloedema in pseudotumor cerebri syndrome. Neuroophthalmology 2016;40:292-6.

34. Minckler DS, Tso MO. Experimental papilledema produced by cyclocryotherapy. Am J Ophthalmol 1976;82:577-89.

35. Wall M. Idiopathic intracranial hypertension. Neurol Clin 2010;28:593-617.

36. Marcelis J, Silberstein SD. Idiopathic intracranial hypertension without papilledema. Arch Neurol 1991;48:392-9.

37. Digre KB, Nakamoto BK, Warner JE, Langeberg WJ, Baggaley SK, Katz BJ. A comparison of idiopathic intracranial hypertension with and without papilledema. Headache 2009;49:185-93.

38. Fisayo A, Bruce BB, Newman NJ, Biousse V. Overdiagnosis of idiopathic intracranial hypertension. Neurology 2016;86:341-50.

39. Favoni V, Pierangeli G, Toni F, Cirillo L, La Morgia C, Abu-Rumeileh S, *et al*. Idiopathic intracranial hypertension without papilledema (IIHWOP) in chronic refractory headache. Front Neurol 2018;9:503.

40. Hoffmann J, Mollan SP, Paemeleire K, Lampl C, Jensen RH, Sinclair AJ. European headache federation guideline on idiopathic intracranial hypertension. J Headache Pain 2018;19:93.

41. McCammon A, Kaufman HH, Sears ES. Transient oculomotor paralysis in pseudotumor cerebri. Neurology 1981;31:182-4.

42. Agarwal MP, Mansharamani GG, Dewan R. Cranial nerve palsies in benign intracranial hypertension. J Assoc Physicians India 1989;37:533-4.

43. Chansoria M, Agrawal A, Ganghoriya P, Raghu Raman B. Pseudotumor cerebri with transient oculomotor palsy. Indian J Pediatr 2005;72:1047-8.

44. Bruce BB, Newman NJ, Biousse V. Ophthalmoparesis in idiopathic intracranial hypertension. Am J Ophthalmol 2006;142:878-80.

45. Thapa R, Mukherjee S. Transient bilateral oculomotor palsy in pseudotumor cerebri. J Child Neurol 2008;23:580-1.

46. Tan H. Bilateral oculomotor palsy secondary to pseudotumor cerebri. Pediatr Neurol 2010;42:141-2.

47. Rezazadeh A, Rohani M. Idiopathic intracranial hypertension with complete oculomotor palsy. Neurol India 2010;58:820-1.

48. Halpern JI, Gordon WH Jr. Trochlear nerve palsy as a false localizing sign. Ann Ophthalmol 1981;13:53-6.

49. Gedroyc W, Shorvon SD. Acute intracranial hypertension and nalidixic acid therapy. Neurology 1982;32:212-5.

50. Lee AG. Fourth nerve palsy in pseudotumor cerebri. Strabismus 1995;3:57-9.

51. Speer C, Pearlman J, Phillips PH, Cooney M, Repka MX. Fourth cranial nerve palsy in pediatric patients with pseudotumor cerebri. Am J Ophthalmol 1999;127:236-7.

52. Patton N, Beatty S, Lloyd IC. Bilateral sixth and fourth cranial nerve palsies in idiopathic intracranial hypertension. J R Soc Med 2000;93:80-1.

53. Totuk OM, Aldroubı N, Aykan U. A case of bilateral fourth nerve palsy associated with pseudotumor cerebri syndrome. Arq Bras Oftalmol 2019;82:332-5.

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

55. Lessell S. Pediatric pseudotumor cerebri (idiopathic intracranial hypertension). Surv Ophthalmol 1992;37:155-66.

56. Phillips PH, Repka MX, Lambert SR. Pseudotumor cerebri in children. J AAPOS 1998;2:33-8.

57. Baker RS, Buncic JR. Vertical ocular motility disturbance in pseudotumor cerebri. J Clin Neuroophthalmol 1985;5:41-4.

58. Friedman DI, Forman S, Levi L, Lavin PJ, Donahue S. Unusual ocular motility disturbances with increased intracranial pressure. Neurology 1998;50:1893-6.

59. Keereman V, Platteau E, Crevits L, Algoed L. Wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) in a patient with idiopathic intracranial hypertension. Neurologist 2018;23:157-9.

60. Snyder DA, Frenkel M. An unusual presentation of pseudotumor cerebri. Ann Ophthalmol 1979;11:1823-7.

61. Landan I, Policherla H, McLaurin J. Complete external ophthalmoplegia in a case of pseudotumor cerebri. Headache 1987;27:573-4.

62. Kidron D, Pomeranz S. Malignant pseudotumor cerebri. Report of two cases. J Neurosurg 1989;71:443-5.

63. Yeak J, Zahari M, Singh S, Mohamad NF. Co-occurrence of acute ophthalmoplegia (without ataxia) and idiopathic intracranial hypertension. Eur J Ophthalmol 2019;29:NP1-4.

64. Ragab O, Ghali A, Al-Malt A, Al-Ahwal S. Radiculopathy as unusual presentation of idiopathic intracranial hypertension: A case report. Clin Neurol Neurosurg 2017;163:81-3.

65. Nathan C, O'Kula S, Bausell R, Hamedani A. Pseudotumor cerebri syndrome complicated by diffuse ophthalmoparesis and polyradiculopathy. Neurohospitalist 2020. doi:10.1177/1941874420945565.

66. Merikangas JR. Skew deviation in pseudotumor cerebri. Ann Neurol 1978;4:583.

67. Al Othman B, Raabe J, Kini A, Lee AG. Update: The Miller Fisher variants of Guillain-Barré syndrome. Curr Opin Ophthalmol 2019;30:462-6.

68. Bruce CT, McClelland CM, Van Stavern GP. Papilledema in an otherwise clinically typical case of Miller Fisher syndrome. Can J Ophthalmol 2015;50:e69-71.

69. Mewasingh LD, Sékhara T, Dachy B, Djeunang MC, Dan B. Benign intracranial hypertension: Atypical presentation of Miller Fisher syndrome? Pediatr Neurol 2002;26:228-30.

70. Chiba A, Kusunoki S, Obata H, Machinami R, Kanazawa I. Ganglioside composition of the human cranial nerves, with special reference to pathophysiology of Miller Fisher syndrome. Brain Res 1997;745:32-6.

71. Frohman LP, Kupersmith MJ. Reversible vertical ocular deviations associated with raised intracranial pressure. J Clin Neuroophthalmol 1985;5:158-63.

72. Keane JR. Alternating skew deviation: 47 patients. Neurology 1985;35:725-8.

73. Wong AM. Understanding skew deviation and a new clinical test to differentiate it from trochlear nerve palsy. J AAPOS 2010;14:61-7.

74. Kunte H, Schmidt F, Kronenberg G, Hoffmann J, Schmidt C, Harms L, et al. Olfactory dysfunction in patients with idiopathic intracranial hypertension. Neurology 2013;81:379-82.

75. Kapoor KG. Do patients with idiopathic intracranial hypertension suffer from hyposmia? Med Hypotheses 2008;71:816-7.

76. Bershad EM, Urfy MZ, Calvillo E, Tang R, Cajavilca C, Lee AG, et al. Marked olfactory impairment in idiopathic intracranial hypertension. J Neurol Neurosurg Psychiatry 2014;85:959-64.

77. Dotan G, Cohen E, Klein A, Kesler A. Reduced suprathreshold odor identification in patients with pseudotumor cerebri: A non-randomized prospective study. Isr Med Assoc J 2018;20:34-7.

78. Becker NJ, Enge S, Kreutz KM, Schmidt F, Harms L, Wiener E, et al. Lumbar puncture rapidly improves olfaction in patients with idiopathic intracranial hypertension: A cohort study. Cephalalgia 2020;40:429-36.

79. Samancı B, Samancı Y, Şen C, Şahin E, Sezgin M, Kocasoy Orhan E, et al. Assessment of the olfactory function in patients with idiopathic intracranial hypertension using the Sniffin' sticks test: A case-control study. Headache 2019;59:848-57.

80. Schmidt C, Wiener E, Hoffmann J, Klingebiel R, Schmidt F, Hofmann T, et al. Structural olfactory nerve changes in patients suffering from idiopathic intracranial hypertension. PLoS One 2012;7:e35221.

81. Zachariah SB, Jimenez L, Zachariah B, Prockop LD. Pseudotumour cerebri with focal neurological deficit. J Neurol Neurosurg Psychiatry 1990;53:360-1.

82. Davenport RJ, Will RG, Galloway PJ. Isolated intracranial hypertension presenting with trigeminal neuropathy. J Neurol Neurosurg Psychiatry 1994;57:381.

83. Arsava EM, Uluc K, Nurlu G, Kansu T. Electrophysiological evidence of trigeminal neuropathy in pseudotumor cerebri. J Neurol 2002;249:1601-2.

84. Hart RG, Carter JE. Pseudotumor cerebri and facial pain. Arch Neurol 1982;39:440-2.

85. Algahtani HA, Baeesa SS, Obeid TH, Abuzinadah AR. Idiopathic intracranial hypertension. Atypical presentation. Saudi Med J 2007;28:762-5.

86. Gaillard F. Idiopathic intracranial hypertension with trigeminal compression; 2016. Available from: https://radiopaedia.org/cases/idiopathic-intracranial-hypertension-with-trigeminal-compression. [Last accessed on 2020 Aug 01].

87. Babikian P, Corbett J, Bell W. Idiopathic intracranial hypertension in children: The Iowa experience. J Child Neurol 1994;9:144-9.

88. Capobianco DJ, Brazis PW, Cheshire WP. Idiopathic intracranial hypertension and seventh nerve palsy. Headache 1997;37:286-8.

89. Chutorian AM, Gold AP, Braun CW. Benign intracranial hypertension and Bell's palsy. N Engl J Med 1977;296:1214-5.

90. Davie C, Kennedy P, Katifi HA. Seventh nerve palsy as a false localising sign. J Neurol Neurosurg Psychiatry 1992;55:510-1.

91. Brackmann DE, Doherty JK. Facial palsy and fallopian canal expansion associated with idiopathic intracranial hypertension. Otol Neurotol 2007;28:715-8.

92. Kearsey C, Fernando P, Benamer HT, Buch H. Seventh nerve palsy as a false localizing sign in benign intracranial hypertension. J R Soc Med 2010;103:412-4.

93. Tzoufi M, Makis A, Grammeniatis V, Nakou I, Exarchakos G, Asproudis I, et al. Idiopathic intracranial hypertension and facial palsy: Case report and review of the literature. J Child Neurol 2010;25:1529-34.

94. Soroken C, Lacroix L, Korff CM. Combined VIth and VIIth nerve palsy: Consider idiopathic intracranial hypertension! Eur J Paediatr Neurol 2016;20:336-8.

95. Samara A, Ghazaleh D, Berry B, Ghannam M. Idiopathic intracranial hypertension presenting with isolated unilateral facial nerve palsy: A case report. J Med Case Rep 2019;13:94

96. Kiwak KJ, Levine SE. Benign intracranial hypertension and facial diplegia. Arch Neurol 1984;41:787-8.

97. Bakshi SK, Oak JL, Chawla KP, Kulkarni SD, Apte N. Facial nerve involvement in pseudotumor cerebri. J Postgrad Med 1992;38:144-5.

98. Obeid T, Awada A, Mousali Y, Nusair M, Muhayawi S, Memish S. Extensive radiculopathy: A manifestation of intracranial hypertension. Eur J Neurol 2000;7:549-53.

99. Selky AK, Purvin VA. Hemifacial spasm. An unusual manifestation of idiopathic intracranial hypertension. J Neuroophthalmol 1994;14:196-8.

100. Benegas NM, Volpe NJ, Liu GT, Galetta SL. Hemifacial spasm and idiopathic intracranial hypertension. J Neuroophthalmol 1996;16:70.

101. Grassi MP, Carella F, Perin C, Borella M. Hemifacial spasm in benign intracranial hypertension. Neurol Sci 2001;22:337.

102. Poff CB, Lipschitz N, Kohlberg GD, Breen JT, Samy RN. Hemifacial Spasm as a rare clinical presentation of idiopathic intracranial hypertension: Case report and literature review. Ann Otol Rhinol Laryngol 2020;129:829-32.

103. Garcia MD, Mansukhani SA, Chen JJ, Bhatti MT. Idiopathic intracranial hypertension triggering hemifacial spasm. J Neuroophthalmol 2020. doi: 10.1097/WNO.0000000000001048.

104. Wakerley BR, Yuki N. Isolated facial diplegia in Guillain-Barré syndrome: Bifacial weakness with paresthesias. Muscle Nerve 2015;52:927-32.

105. Drew AL, Magee KR. Papilledema in the Guillain-Barré syndrome. AMA Arch Neurol Psychiatry 1951;66:744-51.

106. Reich SG. Bell's palsy. Continuum (Minneap Minn) 2017;23:447-66.

107. Mollan SP, Aguiar M, Evison F, Frew E, Sinclair AJ. The expanding burden of idiopathic intracranial hypertension. Eye (Lond) 2019;33:478-85.

108. Çoban K, Aydın E, Özlüoğlu LN. Audio-vestibular findings in increased intracranial hypertension syndrome. J Int Adv Otol 2017;13:100-4.

109. Ranieri A, Cavaliere M, Sicignano S, Falco P, Cautiero F, De Simone R. Endolymphatic hydrops in idiopathic intracranial hypertension: Prevalence and clinical outcome after lumbar puncture. Preliminary data. Neurol Sci 2017;38:193-6.

110. Malomo AO, Idowu OE, Shokunbi MT, Nwaorgu OG, Oluleye TS. Non-operative management of benign intracranial hypertension presenting with complete visual loss and deafness. Pediatr Neurosurg 2006;42:62-4.

111. Tobia A, Khayr R, Shpak T, Peleg C, Genizi J, Khnifes R, *et al*. Idiopathic intracranial hypertension presenting as auditory neuropathy hearing disorder in a child. Laryngoscope 2019;129:E407-E411.

112. Bahr Hosseini M, Stone McGuire L, Stosic M, Moss HE, Carrithers MD. Pearls & Oy-sters: A rare presentation of chronic intracranial hypertension with concurrent deafness and blindness. Neurology 2016;87:e26-8.

113. Dorman PJ, Campbell MJ, Maw AR. Hearing loss as a false localising sign in raised intracranial pressure. J Neurol Neurosurg Psychiatry 1995;58:516.

114. Reitsma S, Stokroos R, Weber JW, van Tongeren J. Pediatric idiopathic intracranial hypertension presenting with sensorineural hearing loss. Ann Otol Rhinol Laryngol 2015;124:996-1001.

115. Kaaber EG, Zilstorff K. Vestibular function in benign intracranial hypertension. Clin Otolaryngol Allied Sci 1978;3:183-8.

116. Gürkov R, Wittwer L, Speierer G, Müri R, Mantokoudis G, Kalla R. Idiopathic intracranial hypertension: Ocular vestibular evoked myogenic potentials as a new evaluation tool. Clin Neurophysiol 2017;128:2048-9.

117. Lemmerling MM, Mancuso AA, Antonelli PJ, Kubilis PS. Normal modiolus: CT appearance in patients with a large vestibular aqueduct. Radiology 1997;204:213-9.

118. Sismanis A, Callari RH, Slomka WS, Butts FM. Auditory-evoked responses in benign intracranial hypertension syndrome. Laryngoscope 1990;100:1152-5.

119. Franco-Vidal V, Baretto GP, Vignes JR, Darrouzet V. Spontaneous cerebrospinal fluid fistula through a congenitally patent facial nerve canal: Incrimination of idiopathic intracranial hypertension. Otol Neurotol 2009;30:123-4.

120. Antoun J, Rami HE, Jabbour E, Chelala E. Sixth, seventh and tenth cranial nerve palsies associated with pseudotumor cerebri in a 13-year-old boy. J Fr Ophtalmol 2013;36:e173-6.

121. Bohlega S, Idriss A. Torticollis: A presenting sign in idiopathic intracranial hypertension. Ann Saudi Med 1997;17:260-1.

122. Baquis GD, Rosman NP. Pressure-related torticollis: An unusual manifestation of pseudotumor cerebri. Pediatr Neurol 1989;5:111-3.

123. Straussberg R, Harel L, Amir J. Pseudotumor cerebri manifesting as stiff neck and torticollis. Pediatr Neurol 2002;26:225-7.

124. Saifudheen K. Idiopathic intracranial hypertension presenting as stiff neck and torticollis. Neurol India 2010;58:982.

125. Bidot S, Saindane AM, Peragallo JH, Bruce BB, Newman NJ, Biousse V. Brain imaging in idiopathic intracranial hypertension. J Neuroophthalmol 2015;35:400-11.

126. Bortoluzzi M, Di Lauro L, Marini G. Benign intracranial hypertension with spinal and radicular pain. Case report. J Neurosurg 1982;57:833-6.

127. Baker RS, Baumann RJ, Buncic JR. Idiopathic intracranial hypertension (pseudotumor cerebri) in pediatric patients. Pediatr Neurol 1989;5:5-11.

128. Bidot S, Levy JM, Saindane AM, Oyesiku NM, Newman NJ, Biousse V. Do most patients with a spontaneous cerebrospinal fluid leak have idiopathic intracranial hypertension? J Neuroophthalmol 2019;39:487-95.

129. Bidot S, Levy JM, Saindane AM, Narayana KM, Dattilo M, DelGaudio JM, *et al*. Spontaneous skull base cerebrospinal fluid leaks and their relationship to idiopathic intracranial hypertension. Am J Rhinol Allergy 2020. doi: 10.1177/1945892420932490.

130. Bialer OY, Rueda MP, Bruce BB, Newman NJ, Biousse V, Saindane AM. Meningoceles in idiopathic intracranial hypertension. AJR Am J Roentgenol 2014;202:608-13.

131. Campbell ZM, Hyer JM, Lauzon S, Bonilha L, Spampinato MV, Yazdani M. Detection and characteristics of temporal encephaloceles in patients with refractory epilepsy. AJNR Am J Neuroradiol 2018;39:1468-72.

132. Urbach H, Jamneala G, Mader I, Egger K, Yang S, Altenmüller D. Temporal lobe epilepsy due to meningoencephaloceles into the greater sphenoid wing: A consequence of idiopathic intracranial hypertension? Neuroradiology 2018;60:51-60.