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CHRONIC DAILY HEADACHE (S-J WANG AND S-P CHEN, SECTION EDITORS)

Overlap and Differences in Migraine and Idiopathic Intracranial Hypertension

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Abstract

Purpose of Review Migraine and idiopathic intracranial hypertension (IIH) are increasingly encountered but remain enigmatic. This review compares the similarities and differences of the diagnostic criteria, pathophysiology, and risk factors for chronic migraine and IIH.

Recent Findings While migraine and IIH are distinct diseases, both conditions are frequently found concurrently and may share a link. Increased intracranial pressure (ICP) in those with or without pre-existing migraine may present with migraine-like headaches and contribute to migraine chronification. Increased intracranial pressure may be a coincidental occurrence in patients with migraine and normalization of pressure does not always translate to headache improvement. Limited information is available regarding the standard of treatment for patients with chronic migraine and IIH without papilledema.

Summary There continues to be controversy over the normal range of cerebral spinal fluid (CSF) values. Recognizing the concurrence of both conditions advances our understanding of headache pathology and demonstrates a striking need for more research.

Keywords Migraine · "Idiopathic intracranial hypertension" · "Chronic migraine" · "Idiopathic intracranial hypertension without papilledema"

Introduction

Understanding and treating chronic headache is a challenge. Chronic daily headache (CDH) includes headache syndromes that occur 15 or more days per month for at least three consecutive months. Chronic migraine (CM) is a subset of CDH and requires a minimum of eight headache attacks that are considered migraines. CM affects 1–2% of the global population. It causes immediate distress and considerably impacts mental health, relationships, and economic well-being [1].

Patients with chronic headache, including chronic migraine, should be evaluated for idiopathic intracranial hypertension (IIH). IIH is a condition of elevated intracranial pressure of unknown etiology. It commonly presents with severe, disabling headaches with peril of vision loss in 25% of patients due to progressive papilledema. Current prevalence is approximately 68/100,000 females, affecting mainly women of working age, with rising prevalence in males, corresponding with the rise in obesity [2••]. Men require surgery for vision loss more often than women, with Black Americans having a greater risk for vision loss [3]. Symptoms of IIH include headache in up to 90% of individuals, transient visual obscurations, diplopia, pulsatile tinnitus, vertigo, back pain, and mild cognitive impairment [4, 5].

The characteristics of headaches from IIH are variable and at times indistinguishable from chronic migraine, especially in cases of IIH without papilledema. Worsening of pre-existing migraine, new-onset migraine, and persistent headache post-elevated pressure resolution have been reported in patients with IIH. If increased intracranial pressure has a role in migraine chronification, one could suppose a subsection of CM patients may respond to treatment with a cerebral spinal fluid (CSF) pressure lowering agents, offering another potential therapeutic avenue. In this review, we will dissect the differences and overlap between chronic migraine and idiopathic intracranial hypertension.

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Terminology

Chronic Migraine

The most recent iteration of the International Classification of Headache Disorders (ICHD-3) defines chronic migraine as having 15 or more headache days per month, of which 8 days meet the criteria for migraine (Table 1) [6]. This does not account for high-frequency episodic migraine (HFEM) sufferers who have 8 migraine attacks per month but less than 15 monthly headache days and are just as disabled as the chronic migraine patient. Chalmer et al. propose broadening the current definition of CM by eliminating the requirement of 15 headache days per month and instead including individuals who have eight or more migraine days per month. HFEM patients do not differ from those with CM based on annual or lifetime migraine attack frequency and comorbid disease [7]. More investigation into stratifying the subtypes of migraine based on disability is needed.

Idiopathic Intracranial Hypertension

Since pseudotumor cerebri (PTC) was first termed in 1916, our understanding of the disease has progressed, and the nomenclature has been revised numerous times. Benign intracranial hypertension was used in 1955 but fell out of favor as this condition is not "benign" and carries the risk of permanent vision loss. Eventually, idiopathic intracranial hypertension was adopted in 1966 [8]. IIH has been classified into primary and secondary type. Rightly, Friedman et al. point out that secondary idiopathic intracranial hypertension defies the meaning of "idiopathic" and prefer using the term pseudotumor cerebri syndrome (PTCS), which can be allocated into primary and secondary PTCS. This can be further subdivided into PTC with and without papilledema (Table 1).

Increased intracranial pressure presents with a wide clinical presentation. Unlike IIH with papilledema (IIHWP), patients with IIH without papilledema (IIHWOP) usually do not develop papilledema or vision loss. These patients have a lower CSF opening pressure (OP) than those with IIHWP [9, 10]. This raises the question of whether elevated intracranial pressure, in the absence of papilledema, can cause chronic headache. Or is elevated intracranial pressure and chronic headache a chance occurrence that is observed in patients with IIHWOP? It should be pointed out that there is a subgroup of patients who have IIHWP or IIHWOP and do not have headache [11].

In those with headache, the ICHD-3 defines headache attributed to IIH as a new or significant worsening of a pre-existing headache that develops or worsens in temporal relation to IIH or leads to its discovery [6]. The ICHD-3 does not define IIHWOP in those without pulsatile tinnitus and does not account for the subset of IIH patients who do not have headache (Table 1). Of note, pulsatile tinnitus is a strong predictor of IIHWOP in those with chronic daily headaches [12]. Accordingly, the ICHD-3 specifies that IIH can be diagnosed without papilledema if pulsatile tinnitus is present. The European Headache Federation guidelines and Friedman's criteria assert that a diagnosis of IIHWOP may be made in those who have a normal neurologic examination (exemption for unilateral or bilateral CN VI palsy), normal brain imaging, normal CSF components, and an opening pressure > 25 cm. In the absence of an abducens nerve palsy, IIHWOP may be diagnosed using three out of four radiographic signs (Table 1). Thus, supplementing with imaging criteria may aid to differentiate IIHWOP from chronic migraine with coincidentally elevated opening pressure. However, more explicit details regarding imaging, like degree of empty sella (i.e., partial versus complete) and severity of sinus venous stenosis, are not provided.

Change in Accepted Threshold of Normal Spinal Fluid Pressure

The cutoff for normal CSF pressure is controversial. The range of normal opening pressure values has increased over the years. In the past, opening pressure > 20 cm H_2O was considered elevated. However, the 2013 revised diagnostic criteria by Friedman redefined opening pressure of > 25 cm H_2O as elevated [13••, 14]. A cross-sectional study of 242 normal patients who underwent lumbar puncture (LP) found the 95% reference interval of normal pressure ranged from 10 to 25 cm H_2O [15]. Importantly, headache improvement following an LP is not diagnostic of elevated pressure. Patients with non-IIH headache types may experience temporary improvement after an LP. Likewise, patients with elevated ICP may not see headache improvement following CSF removal. Furthermore, CSF pressures have diurnal fluctuations and are transiently elevated by anxiety, certain anesthetics, and positions that increase intrathoracic pressure. There is an ongoing argument that the elevated CSF pressure threshold should be lowered to 20 cm H_2O and that the value of 25 cm H_2O is overly strict [13••, 16•]. When reviewing studies about CM and IIH coexistence, this definition change is of considerable significance and affects the incidence and prevalence of IIH.

Concurrence of IIHWP and CM

In the IIH treatment trial (IIHTT), the first randomized control trial to study acetazolamide and weight loss impact on vision, headache was present in 139 of 165 untreated IIH patients. Of the 139 subjects, 52% had migraine-type headache, 22%

Table 1 IIH and migraine criteria

ICHD-3: headache attributed to IIH	**IIHWP diagnostic criteria** (Friedman PTC with papilledema)	**IIHWOP diagnostic criteria** (Friedman PTC without papilledema)
New headache or a significant worsening (twofold or greater) of pre-existing headache and not better accounted for by other ICHD-3 diagnosis Fulfills both of the following: - 1. Idiopathic intracranial hypertension (IIH) has been diagnosed 2. Cerebrospinal fluid (CSF) pressure exceeds 25 cm CSF (or 28 cm CSF in obese children) Fulfills either or both of the following: 1. Headache has developed or significantly worsened in temporal relation to the IIH, or led to its discovery 2. Headache is accompanied by either or both of the following: a) pulsatile tinnitus b) papilledema	A. Papilledema B. Normal neurologic examination (except for cranial nerve VI palsy) C. Neuroimaging: normal brain parenchyma (no hydrocephalus, mass, structural lesion, meningeal enhancement, and sinus venous thrombosis) D. Normal CSF composition E. Elevated lumbar puncture opening pressure (≥ 25 cm CSF in adults and ≥ 28 cm CSF in children)	Fulfills criteria B–E and cranial nerve VI palsy is present **Suggestion of IIHWOP:** Fulfills criteria B–E and at least three neuroimaging criteria are present: - Empty sella - Flattening of the posterior aspect of the globe - Distention of the perioptic subarachnoid space with or without a tortuous optic nerve - Transverse venous sinus stenosis
Chronic migraine 3. Headache (migraine like or tension type like) on ≥ 15 days/month for > 3 months, and fulfilling criteria B and C 4. Occurring in a patient who has had at least five attacks fulfilling ICHD-3 migraine with aura and/or without aura criteria 5. On ≥ 8 days/month for > 3 months, fulfilling any of the following: 6. Migraine without aura 7. Migraine with aura 8. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative 9. Not better accounted for by another ICHD-3 diagnosis [6, 73]		

tension-type headache, 16% probable migraine, and 4% probable tension-type headache [17••]. A recent large population-based, age-matched, and BMI-matched cohort showed women with IIH had a three times increased occurrence of new-onset headache and twofold higher occurrence of new-onset migraine compared to women without IIH or migraine [18••]. Migraine-type headaches are the most common headache type in IIHWP patients.

It is unknown whether a personal or family history of migraine increases the risk of developing headache in IIH [19, 20]. The IIHTT and 1 cross-sectional study respectively found 41% and 63.4% of patients with IIH had a prior history of migraine [19, 21]. This adds to the enigma of whether migraine history is a precursor to developing headache in IIH or whether IIH is a risk factor for worsening migraine. Patients with migraine who have a change or worsening of headaches should be evaluated for IIH.

In addition, while headache associated with IIH is often accompanied by rising intracranial pressure, patients frequently have persistent headache following the normalization of CSF pressure. Up to 63% of patients with IIH headache report continued headaches at 12 months after the initial diagnosis is made [22]. In a 2017 cross-sectional study, 45 of 68 patients (63.2%) with IIH and resolved papilledema met the diagnostic criteria of migraine headaches [21]. Therefore, pressure reduction does not necessarily equate to headache relief.

In a single-center cohort study, 10 out of 158 (6%) consecutive migraine patients were found to have papilledema. Of this population, 9.3% and 5.6% of CM and episodic migraine (EM), respectively, demonstrated papilledema. While a small sample, more patients with CM had papilledema than those with EM [23].

Concurrence of IIHWOP and CM

The proportion of patients with IIHWOP in refractory chronic headache is estimated to be 2.5 to 86.4% [13••, 24]. This broad range is due to the selection of varying normal opening pressure values, the inclusion of IIHWOP imaging criteria, and the definition of refractory chronic headache used by investigators.

In a study of 62 consecutive patients with refractory headaches, one patient had IIHWP and 6 had IIHWOP when using an opening pressure of $\geq$ 20 cm H_2O as a marker of elevated ICP. If $\geq$ 25 cm H_2O is substituted as the upper limit of normal opening pressure, then only 3 patients meet the criteria for IIHWOP [25]. Thus, by applying Friedman's 2013 criteria, which includes strict imaging requirements and elevated opening pressure $\geq$ 25 cm H_2O, the prevalence of IIHWOP is markedly lower than previously thought. Favoni et al. studied 40 refractory chronic headache patients and found one patient or 2.5% fulfilled the criteria for IIHWOP using the Friedman criteria. Notably, 22.5% of this group of refractory headache patients had an opening pressure of $\geq$ 20 cm H_2O. In contrast, an earlier study by De Simone et al. reported a higher number of patients with IIHWOP. Of 44 subjects with refractory CM and incidental venous sinus stenosis without evidence of papilledema, 86.4% had an opening pressure above 20 cm H_2O and 43.2% had an opening pressure above 25 mm H_2O [24]. In CM patients, sinus venous stenosis, which is also found in asymptomatic, headache-free patients, could be a risk factor for IIHWOP and headache chronification.

Due to stringent requirements for the upper limit of CSF pressure, fewer patients fulfill the current definition of IIHWOP. It is possible that if routine lumbar punctures are recommended for all CM patients with neuroimaging signs of IIH, the detection of IIHWOP may increase. However, performing lumbar punctures on CM patients may not alter treatment and could lead to unnecessary distress to the patient. Further research into the selection criteria and necessity to assay CSF pressure in refractory chronic headache patients without papilledema needs to be explored.

Pathophysiology

Pathophysiology of Migraine

The trigeminovascular system is the widely accepted theory for the pathogenesis of migraine. Nociceptive input from trigeminal afferents and C1 and C2 dorsal nerve roots converge in the trigeminal nucleus caudalis. Second-order neurons project to the thalamus and third-order neurons to the somatosensory cortex and result in pain [26]. This process may be activated by cortical spreading depression, which has been detailed as the basis for migraine aura [27].

Calcitonin gene-related peptide (CGRP) is a vasoactive neuropeptide that is released by trigeminal afferents and is implicated in migraine. In migraine pathophysiology, CGRP causes mast cell degranulation and neurogenic inflammation, and meningeal dilation, and acts on trigeminal ganglion cells to promote the sensitization and propagation of migraine [28].

Pathophysiology of IIH

Several theories advance our understanding of the pathogenesis of IIH. No single theory explains the mechanism of IIH and incorporates the disease's predilection for obese women between the ages of 20–40 years. Thus, it is plausible that more than one process exists [29].

IIH has been attributed to an imbalance in CSF secretion/resorption and increased venous pressure [30]. Approximately two-thirds of CSF is produced by the choroid plexus, and the remaining is produced by extrachoroidal structures. The traditional view of CSF resorption via arachnoid granulations to the dural sinuses and venous system has been challenged with the discovery of the brain lymphatic and glymphatic systems, which also participate in CSF outflow. Resistance in CSF venous or lymphatic outflow systems can disrupt CSF equilibrium [31•]. Glymphatic congestion may imply lymphatic outflow dysfunction [32]. The number and size of arachnoid granulations increase in patients with IIH, conceivably in response to elevated intracranial pressure. However, a sizable growth of an arachnoid granulation can disrupt CSF venous outflow by causing venous stenosis [33].

Venous stenosis has increasingly been proposed as either a cause or consequence of increased intracranial pressure. The area of compression mimics a "Starling resistor" and produces a pressure gradient over the site of stenosis. The reduced venous pressure distal to the stenosis leads to decreased CSF absorption from the pressure sensitive arachnoid granulations and results in a new baseline elevated intracranial pressure [34, 35].

Elevated CSF Pressure and IIH

The correlation between headache and elevated CSF pressure is not well understood. Headache may persist or a different headache may develop following the treatment of elevated pressure in IIH [36]. One study found new-onset migraine is reported in 37.14% of patients following the diagnosis and treatment of IIH, significantly greater than the prevalence in the general population [37, 38]. A small prospective study found significant headache improvement in 43% of individuals, while another 43% continued to have chronic headache even after undergoing the same treatment for the normalization of CSF pressure and resolution of papilledema [39].

The IIHTT did not show a connection between headache disability and CSF opening pressure [40]. A later randomized trial of 66 women with IIH identified a direct association between a greater reduction of ICP over 12-month and a greater reduction in headache days, severity, and quality of life [41•]. Based on these findings, the cause of headache cannot simply be explained by elevated ICP.

Elevated CSF Pressure and Migraine

The link between elevated pressure and migraine is obscure. In 1986, van Alphen postulated that migraine is caused by increased CSF pressure based on a series of 40 patients, many of whom had signs of increased intracranial pressure, e.g., increased pain with coughing, cerebellar ectopia. His study does not explicitly state whether these patients had papilledema or a normal neurologic examination [42].

A case-control study of 70 patients with IIH identified comorbid migraine in 64.8% and migraine relief in 17.14% after treatment of IIH [37]. Likewise, Mathew et al. reported greater improvement in 12/85 patients with refractory chronic daily headache after the addition of diuretics to antimigraine prophylactic therapy. These patients had elevated ICP and no evidence of papilledema or vision loss, highlighting the diagnostic conundrum of separating IIH without papilledema from chronic migraine patients [43].

Radiographic findings of bilateral transverse stenosis are common in patients with IIH. De Simone et al. assessed a subset of refractory chronic migraine patients who also had sinus venous stenosis and no evidence of papilledema. After a single lumbar puncture, 77.3% of patients who had an opening pressure $\geq$ 20 cm H_2O reported substantial headache improvement. This improvement was maintained at two months in over half [24].

Mechanism of Headache Due to Elevated CSF Pressure

An emerging theory is that elevated intracranial pressure may present as a clinical spectrum ranging from asymptomatic patients to those who have symptomatic IIHWOP and those who develop IIH with papilledema [44]. The mechanism of increased intracranial pressure producing headaches, specifically with migraine phenotype, is unknown. It is presumed that elevated pressure causes traction on pain-sensitive regions of the brain, and thereby activates the trigeminal pain pathway that has been well detailed in migraine pathophysiology [8].

Venous sinus stenosis may be a nidus for pain [19]. It is debatable whether venous sinus stenosis is a product of elevated pressure or a potentially treatable cause of IIH. In some individuals, removal of CSF following a single lumbar puncture produces immediate and lasting headache improvement due to resolution of the collapsed vein [44].

Bilateral transverse sinus stenosis has been observed in chronic migraine sufferers and the implications it has in producing pain are unknown [19, 24]. Conversely, bilateral transverse sinus stenosis has been reported in asymptomatic individuals with CSF pressure less than 25 cm H_2O [45]. It is possible that normal CSF pressure is preserved in these situations because of compensatory drainage via the brain glymphatic system [33].

Migraine-Like Phenotype in IIH

Headaches induced by elevated intracranial pressure have a heterogeneous phenotype. Two prospective series characterized headaches due to IIH as daily, pulsating pain with associated nausea [46, 47]. The IIHTT found migraine and

probable migraine were seen in 68% of patients with diagnosed IIH [17••].

Due to an overlap in features, discerning headache attributed to IIH vs migraine is challenging. In the IIHTT, the location of headache varied largely with 30% presenting with unilateral, 36% global, 68% frontal, 47% ocular, 39% posterior, and 47% nuchal pain. Additionally, associated symptoms of photophobia were noted in 70%, phonophobia in 52%, nausea in 47%, vomiting in 17%, and worsening with physical activity in 50%. Retrobulbar eye pain that increases with eye movement, due to optic nerve sheath distension, may be more specific to IIH [8, 19, 46–48]. Furthermore, headaches due to IIH tend to increase in the recumbent position and with Valsalva maneuvers due to transient increases in ICP [22, 41•].

Risk Factors of IIH and Migraine

Multiple factors are involved in the complexities of developing migraine and IIH. Both diseases have shared risk factors and comorbid conditions.

Gender

The tendency of migraine and IIH to occur predominantly in women implies a possible role of sex hormones. Before puberty, boys and girls are affected non-discriminatorily. After puberty, a gender preference for the female sex emerges and continues until menopause. Women are reported to have longer and more severe migraine attacks than men [49]. Conversely, men with IIH tend to have a more serious course and are at greater risk for vision loss [50].

The role of estrogen has been explored in both conditions, albeit less in IIH. In migraine, fluctuating estrogen levels elucidate why migraine increases after menarche and in perimenopause and improves during pregnancy and menopause. Furthermore, the use of combined oral contraceptive medication may induce new-onset migraine or migraine aura, increase migraine frequency, reduce migraine frequency, or result in no change [51].

Intriguingly, men with migraine also have higher levels of estrogen [52]. Furthermore, karyotypically male patients undergoing male-to-female gender reassignment with antiandrogens and high estrogen therapy have an increase in migraine prevalence that is akin to genetic females [49, 53•]. In women with IIH, limited studies are available and do not show an increase in estradiol levels [30]. Contrary to early case reports, oral contraceptive medications and pregnancy are not associated with an increased risk for developing IIH [54•], and the rate of IIH in pregnancy mirrors that of the general population [55•].

The endocrine profile of women with IIH points to an excess of androgenous hormone that is not explicable by obesity or comorbid polycystic ovarian syndrome that may be present in this population [56]. Truncal adiposity is believed to be the source of increased androgens [57•]. In contrast, men with IIH and migraine present with lower testosterone levels than controls [52, 56, 58]. Because testosterone exerts dimorphic effects on metabolism in males and females, females with androgen excess and males with androgen deficiency present with similar metabolic dysfunction [56, 59].

The effects of sex hormones on migraine and IIH are not fully understood. Estrogen has several effects on the brain including enhancing serotonergic activity and increasing cortical excitability [51]. Testosterone is associated with anti-inflammatory and antinociceptive effects and may exert a neuroprotective benefit in individuals with migraine [58]. In rodent studies, CSF testosterone increases secretion of CSF by the choroid plexus whereas estrogen reduces CSF secretion [30, 56].

Obesity

Obesity is a metabolic disease associated with chronic, low-grade inflammation and has been linked to migraine and IIH. In migraine, obesity is associated with greater severity of migraine attacks, increased number of headache days, and is a risk factor for migraine chronification [60]. A weight gain of 5–15% increases the risk of developing IIH, even in the nonobese individual [61]. The mechanism between obesity and headache is multifaceted and not fully understood.

Elevated adipokine leptin levels are seen in obesity, migraine with aura, and IIH [62•]. Leptin is associated with satiety and is involved in the modulation of pain and inflammation [63•]. In lean rats, infusion of leptin increases cortical spreading depression, which may increase migraine aura [60, 62•]. In IIH, the leptin levels are higher than explained solely by obesity and are theorized to increase CSF secretion by enhancing the activity of the Na+K+-ATPase pump within the choroid plexus [62•, 63•, 64•].

A potential link between CGRP, migraine, and obesity exists. Obese women have been observed to have elevated plasma CGRP levels. Elevated CGRP secretion is also seen in preobese Zucker mice [62•]. Furthermore, mice lacking α-CGRP are protected from diet-induced obesity [65]. A study of 60 patients with chronic migraine and morbid obesity who underwent bariatric surgery showed a reduction in plasma CGRP levels coinciding with weight loss and migraine improvement [66•].

Glucagon-like peptide 1 (GLP-1) receptor agonists are used to treat diabetes and more recently weight loss. In preliminary rodent studies, GLP-1 receptor agonists decrease chronic migraine-associated allodynia/central sensitization

[67•]. GLP-1 receptors have been identified in the choroid plexus. In animal studies, GLP-1 receptor agonists inhibit Na+K+-ATPase in the choroid plexus and result in reduced CSF secretion. Thus, GLP-1 receptor activation may be a future target for treatment of IIH, migraine, and weight loss [57•, 64•].

Visceral fat weight loss is associated with remission from IIH [57•] and weight gain increases the risk of recurrence [68]. Our understanding of the benefit of weight loss in migraine and IIH is unfolding, and further studies are needed.

Obstructive Sleep Apnea

Obstructive sleep apnea is more common in men and is a comorbid disease that is seen in frequently in migraine and IIH. OSA does not appear to be a risk factor for developing migraine or IIH. Conversely, patients with migraine, particularly chronic migraine, and IIH are at increased risk of developing OSA. It is unclear if this is due to increased obesity in these populations versus a shared neurovascular pathology [69–71].

In early case series, OSA was identified as a risk factor for IIH. This has not been substantiated by larger studies when accounting for age, sex, race, and BMI. The number of male subjects assessed is small and larger investigations are lacking [69]. The treatment of OSA in IIH may improve papilledema [72•]. Treatment of OSA is associated with a reduction in migraine frequency, duration, pain severity, and acute medication use [70]. Regardless of the casual relationship, all patients with migraine and IIH should be screened for a sleep-related breathing disorder.

Treatments

Migraine preventative therapy has a role in the treatment of the headache associated with IIH. The chief goal of IIH treatment aims at reducing CSF pressure. Acetazolamide is often considered first line for reduction of CSF pressure and improving visual function [73]. However, even after normalization of CSF pressure, headaches and headache-related disability can persist [17••]. Therefore, migraine preventative therapy is often utilized in conjunction with pressure lowering treatments. While there are no randomized control trials for topiramate in IIH management, topiramate, which is a migraine preventative medication, lowers CSF pressure and improves headaches potentially more than acetazolamide [74, 75]. Other commonly used migraine prevention medications could contribute to potential weight gain (i.e., sodium valproate, tricyclic antidepressants, and beta-blockers) and thereby could lead to the exacerbation of IIH [76]. When medications are unsuccessful, not tolerated, or contraindicated, surgery is offered in cases of progressive papilledema; surgeries offered include optic nerve sheath fenestration, CSF diversion surgery, and cerebral venous stenting [4].

Erenumab, an anti-CGRP receptor monoclonal antibody, that is FDA-approved for the treatment of episodic and chronic migraine was investigated in an open-label study of 55 IIH patients with resolved papilledema and continued headaches. Erenumab reduced monthly moderate-severe headache days by 71% and all headache days by 45% at 12 months. It is worth noting that all 55 patients had a chronic migraine-like phenotype, and the benefit to IIH in patients with a tension-type presentation has not been assessed. Seven patients experienced weight gain and had reemergence of papilledema but not headache. This strengthens evidence that CGRP, widely recognized for its part in migraine pathophysiology, may also play a role in headache generation in patients with elevated intracranial pressure [77•].

Conclusion

IIH may explain chronification of headaches in patients with migraines. Moreover, IIH can contribute to de novo chronic migraine and migraine-type headache that may persist even after the resolution of elevated pressure. The studies discussed in this review highlight the relationship between IIH and migraine. More research is needed to understand the clinical spectrum produced by elevated pressure. The role of routine lumbar puncture in those with CM without papilledema or signs of optic nerve atrophy is an area of uncertainty. While performing a lumbar puncture may aid in the diagnosis IIHWOP, it may not significantly alter management. Thus, there is a need for a standardized evaluation and treatment approach for patients with coexisting CM and IIH.

Compliance with Ethical Standards

Conflict of Interest Sweta Sengupta, M.D. and Jaskiran Vidwan, D.O. declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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