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Coexistence of migraine and idiopathic intracranial hypertension without papilledema

Ninan T. Mathew, MD; K. Ravishankar, MD; and Luis C. Sanin, MD

Article abstract—Eighty-five patients with refractory transformed migraine type of chronic daily headache (CDH) had spinal tap as a part of diagnostic work-up. Twelve had increased intracranial pressure without papilledema, transient visual obscurations, or visual field defects. The headache profile of these 12 patients was not different from that of transformed migraine type of CDH. Acute headache exacerbations responded to specific antimigraine agents such as ergotamine, dihydroergotamine (DHE), and sumatriptan, whereas prophylactic antimigraine medications were only partially helpful. Addition of agents such as acetazolamide and furosemide, after the diagnosis of increased intracranial pressure, resulted in better control of symptoms. These observations suggest a link between migraine and idiopathic intracranial hypertension that needs further research. In refractory CDH with migrainous features, a spinal tap to exclude coexistent idiopathic intracranial hypertension without papilledema may be indicated.

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Headache, papilledema, and elevated CSF pressure above 200 mm of water in a patient with normal neurologic examination and neuro-imaging meet the International Headache Society (IHS) diagnostic criteria for idiopathic intracranial hypertension (IIH).¹ Transient visual obscurations (TVOs), diplopia, visual loss, and noises in the head can occur in many of these patients.²⁻⁶ Papilledema is the most consistent neurologic sign of IIH but, rarely, IIH can occur without papilledema.⁷⁻¹⁰

Headache is the most common symptom of IIH, occurring in 90% of patients,²⁻⁵ and on a daily basis in 75%.¹¹ Although there has been considerable attention given to the visual symptomatology of IIH, only one study has detailed the headache profile. Pulsatile, predominantly focal (retro-ocular), sometimes generalized headache, waking the patient up in the morning, with nausea and vomiting, occurred in the majority.¹¹ This headache profile is not strikingly different from that of migraine.¹² Corbett³ and Sorenson and Corbett¹³ noted that preexisting migraine may worsen with IIH, and prophylactic migraine drugs, especially beta blockers and naproxen sodium, are useful in the treatment of headache from intracranial hypertension. In a related condition, namely slit ventricle syndrome, antimigraine agents were highly effective in controlling headache.¹⁴ Ramadan¹⁵ reported transformation of episodic migraine into chronic daily headache (CDH) in a patient who developed IIH without papilledema. Marcellis and Silberstein¹⁰ described 10 patients with IIH without papilledema who presented with CDH. Many of their patients had a headache profile similar to that of migraine and were treated with antimigraine agents. Silberstein and Corbett¹⁶ emphasized

the importance of performing lumbar puncture in patients with intractable CDH to rule out IIH without papilledema.

Patients. The Houston Headache Clinic is a referral center. We use uniform standardized forms to obtain headache, general medical, neurologic, and family histories. Information regarding comorbid and trigger factors is also recorded in the intake form. The interviews and physical and neurologic examinations were conducted by neurologists, both initially and on follow-up visits.

Among the patients with the transformed migraine type of CDH^{17,18} treated at the Houston Headache Clinic between 1986 and 1993, 85 who were considered refractory form the cases for the present study. All these patients gave a history of migraine in the past but developed daily headache subsequently. All patients had daily headache at the time of study. The response to abortive antimigraine agents such as ergotamine, sumatriptan, and dihydroergotamine (DHE) during acute phases were satisfactory in most of these patients but, over time, their daily headaches persisted. They developed repeated prolonged periods of very frequent severe migraine-like and nondescript headaches resulting in over-medication. This resulted in frequent clinic and emergency room visits and sometimes hospitalization. This group of 85 chronic refractory patients was subjected to lumbar puncture as part of a further work-up to rule out chronic meningitis or increased intracranial pressure. All patients had normal CT or MRI.

After obtaining informed consent, lumbar puncture was performed with patients positioned in the lateral decubitus position on a level surface. A standard 20-gauge spinal needle was used with the manometer positioned at a 90-degree angle to the spinal cord. The opening pressure was measured with the patient's knee and hips in the extended position and neck straightened.

Patients with elevated CSF pressure were treated with

From the Houston Headache Clinic, Houston, TX.

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Address correspondence and reprint requests to Dr. Ninan T. Mathew, Houston Headache Clinic, 1213 Herman Drive, Suite 350, Houston, TX 77004.

Patient	Sex	Age	Headache history (years)	Frequency of headache	Location	Quality	Associated symptoms					Family history of migraine	Menstrual aggravation	Associated neurologic symptoms	Comorbidity
							Nausea	Vomiting	Photophobia	Phonophobia	Aura				
1	F	40	20; worse during the 6 months prior to initial consultation	Daily; superimposed severe episodes 2/week; initial frequency 1/month	Bioccipital-nuchal	Pulsating when severe, dull, continuous	++	+	++	+	0	0	+	Vertigo, noises in the head	Depression, obesity
2	F	34	14	Daily; severe perimenstrual aggravation	L temple, L parietal, occasionally switching sides	Pulsating when severe, pressure-like when less severe	++	+	+	+	Sensory aura, L hand and face	+	+	-	-
3	F	39	24	Daily; severe exacerbation 1/week	L temple	Pulsating with dull ache as background	++	+	0	0	Photopsia	+	+	-	Depression
4	F	13	3	Daily; intermittent to start with	Bifrontal-temporal	Pulsating intermittently	+	0	+	+	0	+	++	-	-
5	F	45	25; worse in the previous 20 days	Daily; severe for 20 days	Bilateral R>L retro-orbital bifrontal	Pulsating, stabbing pain, dull ache	+	+	+	+	Visual, photopsia sensory, L hand	+	Headache diminished during pregnancy	Confusion, lethargy during exacerbations	Anxiety, depression
6	M	48	30; severe for 4 months	Daily; intermittent for many years	Bifrontal and generalized severe headache is confined to one side	Dull continuous headache most of the time	+	+	+	+	0	+	NA	Noises in the head	Hypertension, obesity
7	F	29	3 $\frac{1}{2}$	Daily for 3 months; intermittent initially	Bilateral, retro-orbital, temporal but asymmetric	Dull background, mild headache with pulsating aggravation frequently	+	+	0	0	0	0	Estrogen therapy increased headache	-	Depression, obesity
8	F	54	30; severity and frequency increased in the prior 2 years	Daily	L temporal; L parietal	Pulsating when severe, otherwise dull headache	+	0	+	0	Photopsia (rare)	+	0	-	Depression, diabetes, hypertension, obesity
9	M	23	4; severity increased in the past 2 years	Daily	Bifrontal	Nonthrobbing	+	0	+	+	0	+	NA	Vertigo	Depression, drug dependency, obesity
10	F	20	9	Daily with intermittent severe attacks lasting for 2-3 days	Generalized	Dull ache continuous, temples pulsating when severe	+	0	+	+	Photopsia (occasional)	+	++	-	Anxiety, depression
11	F	30	10; severity increased in the past 6 months	Daily with fluctuations of severity; severe episodes 2/week	R temple; R supraorbital	Pulsating when severe	+	0	+	+	0	Adopted	+	Noises in the head	Anxiety, depression, obesity
12	F	33	6; intermittent exacerbations	Daily; severe attacks 3-4 times/week	L retro-orbital; L temple	Constant ache (moderate) with intermittent pulsating pain	+	0	+	0	0	+	+	Noises in the head	Panic attacks, depression, obesity

Table 2 International Headache Society diagnosis, duration of treatment before spinal tap, and length of follow-up after diagnosis of idiopathic intracranial hypertension

Patient	IHS diagnosis before spinal tap	Duration of treatment before spinal tap	Follow-up after diagnosis of IIH (mo)
1	MO, CTH	8 mo	11
2	MA, MO, CTH	4 mo	12
3	MA, MO, CTH	72 mo	24
4	MO, CTH	7 days	14
5	MA, MO, CTH, CSU	21 days	18
6	CTH, MO	7 days	13
7	MO, CTH	42 mo	6
8	MA, MO, CTH, CSU	73 mo	11
9	MO, CTH, CSU	25 mo	28
10	MA, MO, CTH, CSU	12 mo	44
11	MO, CTH, CSU	48 mo	23
12	MO, CTH, CSU	37 mo	40

MA = migraine with aura; MO = migraine without aura; CTH = chronic tension-type headache; CSU = chronic substance-use headache.

acetazolamide and furosemide in combination with abortive antimigraine agents (ergotamine, DHE, or sumatriptan), and prophylactic agents such as beta blockers, amitriptyline, or methysergide.

Results. Of the 85 patients with refractory chronic headache with migrainous features who underwent spinal tap, 12 had elevated CSF pressure. None had papilledema, TVOs, or diplopia. The visual fields in all these patients were normal. The clinical and headache profiles of these 12 patients are given in table 1.

The IHS classification assigned to these patients, the duration of treatment at our clinic prior to the spinal tap, and duration of follow-up period after the spinal tap are given in table 2. All the patients had more than one IHS diagnosis. Using Metropolitan Life Insurance criteria for the diagnosis of obesity, 5 of 10 females in the series were considered obese. Both males in the series were obese by the same criteria.

The ages ranged from 13 to 54 years. All patients gave a long history of headache ranging from 3 to 30 years. All had a history of migraine—five with attacks with aura (four with visual aura, one with sensory aura, and one with both sensory and visual aura). The others had migraine without aura. Nine patients gave a positive family history of migraine. History of menstrual aggravation or hormonally influenced headache aggravation was obtained in 9 of the 10 females. Ten patients had associated comorbidity including depression, anxiety, panic attacks, and hypertension. Four patients reported noises in the head (pulse synchronous tinnitus). Empty sella was found in one (patient 8).

Headache profile. Five patients had strictly unilateral headache, sometimes switching sides. Others had predominantly bifrontal or frontotemporal headaches. Pulsating pain was present in 9, nausea of different degrees in all 12, vomiting in 6, photophobia in 10, and phonophobia in 8. Table 3 compares the headache profile of patients with migraine¹² with the headache profile of patients in this

series and a series of IIH with papilledema published by Wall.¹¹ Similarities in the headache profile between migraine and IIH with and without papilledema are very striking.

Findings. Table 4 shows the CSF findings in this series. All patients had elevated CSF. Repeat spinal tap in all 12 patients revealed continuing intracranial hypertension. There was no pleocytosis in the spinal fluid, nor was there any other abnormality except in one (patient 6) whose spinal fluid protein was 59 in the first lumbar puncture and 43 in the second. A brief summary of patient 6 is given below.

Patient 6. This 48-year-old obese white male complained of recurrent headache for many years. Headache had become severe and daily for 4 months prior to referral to our center. There was no history of fever or any systemic symptoms. He was not a diabetic. Neurologic examination, MRI of the brain, and CT of the sinus were normal. CSF pressure was 280 mm of water during the first lumbar puncture and 285 mm of water during the second. CSF protein was 59 during the first lumbar puncture and 43 during the second. There were no cells. CSF cytology, India ink preparation, and bacterial, fungal, and tuberculosis cultures were normal. Because of the elevated protein, a cerebral arteriogram was performed, which revealed no evidence of cerebral vasculitis. During the 13-month follow-up, the patient showed no evidence of any other underlying disease to account for the elevated CSF protein.

The figure shows the pressure values in the present series compared with the normal values in obese and non-obese patients published by Corbett and Mehta.¹⁹

The lumbar punctures resulted in transient improvement of headache in 4 of the 12 patients. Three patients had post-lumbar puncture headache, of which two required epidural blood patch.

Treatment. Before the spinal tap the patients were routinely treated with prophylactic antimigraine agents in different combinations, including beta blockers, tricyclic antidepressants, calcium channel blockers, serotonin an-

Table 3 Comparison of headache profile of patients with IIH (with papilledema), migraine, and present series

Headache characteristics	Migraine* (%)		IIH with papilledema† (%)	Present series (%)
	MA	MO		
Pulsating	74.2	81	83	83.3 (10/12)
Intensity slowly increases			76	
Awakens patient			62	66.6 (8/12)
Nausea	80.6	94.8	57	100 (12/12)
Vomiting	51.6	62.1	38	50 (6/12)
Photophobia	83.9	94.8		83.3 (10/12)
Phonophobia	87.1	98.3		66.6 (8/12)
Location:				
Generalized or bilateral	41.9	39.7	43‡	33.3 (4/12)
Unilateral or focal	58.1	60.3	70§	66.6 (8/12)
Retro-ocular pain			43	50 (6/12)
(Aggravated by eye movement)			24	
Fronto-orbital			31	50 (6/12)
Occipito-nuchal			14	8.5 (1/12)
Hemicranial			16	41.6 (5/12)
Temporal			7	
Vertex			2	
Aggravated by physical activity, coughing, etc.	96.8	94.8		100 (12/12)
Neck muscle stiffness			59	

* Rasmussen and Olesen, 1992.¹²

† Wall, 1990.¹¹

‡ Some focal pain in addition.

§ Some had generalized headache also.

IIH = idiopathic intracranial hypertension; MA = migraine with aura; MO = migraine without aura.

tagonists such as methysergide, and acute antimigraine agents such as sumatriptan, ergotamine, and DHE for exacerbations. Nonsteroidal anti-inflammatory agents were also used. Overall prophylactic antimigraine therapy was less than satisfactory. After the IIH was detected, a combination of acetazolamide and furosemide was also given to these patients during the follow-up period. A combination of antimigraine agents and medication to reduce increased intracranial pressure resulted in a reduction in the number of days of severe headache, reduced consumption of abortive agents, and overall improvement of quality of life. None of the patients developed papilledema or TVOs during the follow-up period (ranging from 6 to 40 months) even though the CSF pressure remained above the normal range.

Discussion. One of the criticisms that can be raised in the diagnosis of IIH without papilledema is the limitations of direct ophthalmoscopy in detecting early papilledema. Indirect ophthalmoscopy or stereo fundus photography is the most reliable method of identifying early papilledema. In this series, absence of papilledema was confirmed based only on careful and repeated direct ophthalmoscopy.

The diagnosis of IIH without papilledema, TVOs, or any visual changes⁷⁻¹⁰ is impossible without a spinal tap. The headache profiles of patients suffering

from increased intracranial hypertension with and without papilledema have no specificity or diagnostic characteristics. Our series indicates that the headache profile meeting the IHS criteria for migraine (with and without aura) and chronic tension-type headache can occur in patients with IIH. The similarity between the headache profile in our patients and that of migraine patients from an epidemiologic survey by Rasmussen and Olesen¹² is striking. Thus, in a given case, the headache profile of IIH may be indistinguishable from that of mixed migraine and chronic tension-type headache.

We found that abortive antimigraine medications such as sumatriptan, DHE, and ergotamine are useful in the management of acute exacerbations of headache in patients with coexisting IIH and migraine. This response is comparable with that of the CDH patients without IIH. All the patients were on prophylactic antimigraine agents prior to the diagnosis of IIH with partial results; however, addition of acetazolamide and furosemide resulted in further improvement of the overall headache control. In other words, in these patients, the response to migraine prophylactic agents alone is not as good as in CDH patients with normal pressure.

Previously reported beneficial response to antimi-

Table 4 IIH without papilledema

Patient	Age	Sex	CSF opening pressure*		
			1st LP	2nd LP†	3rd LP
1	40	F	270	270	
2	34	F	300	260	
3	39	F	230	270	
4	13	F	280	250	
5	45	F	325	300	
6	48	M	280	285	
7	29	F	300	275	
8	54	F	270	265	
9	23	M	300	360	
10	20	F	310	210	258‡
11	30	F	440	270	
12	33	F	450	300	320‡

* CSF was normal in all cases except patient 6, whose protein was 59 in the first LP and 43 in the second LP.

† Average interval between first and second LP, 8 months (range 3 to 20 months).

‡ Interval between second and third LP in patient 10, 10 months; patient 12, 18 months.

LP = lumbar puncture.

graine medications in cases with IIH¹³ and slit ventricle syndrome,¹⁴ combined with our experience with the present series, links migraine and IIH. Van Alphen²⁰ argued, based on his experience in 40 patients, that migraine results from some unknown disturbance in the CSF circulation causing increased pressure in the basal cisterns and posterior fossa. He postulated that this resulted in transient acquired cerebellar herniation and spasm of the vertebral arteries accounting for headache and the neurologic manifestation of migraine, but he did not present

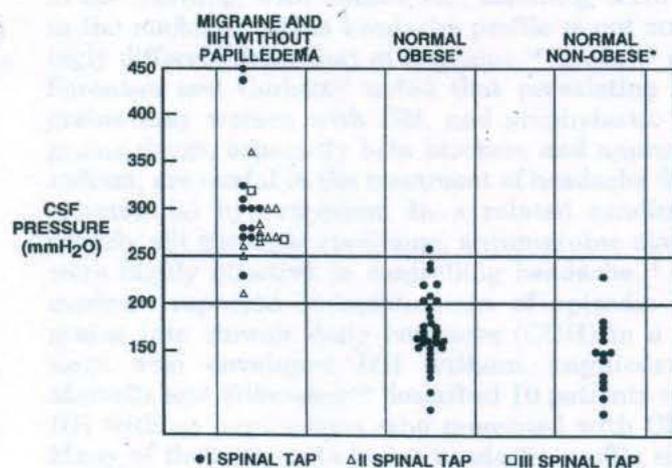


Figure. Compares the CSF pressure values of patients in the current series with CSF pressure in normal nonobese and obese persons (data from Corbett and Mehta,¹⁹ 1983).

adequate convincing data to substantiate his postulations. In many of our patients, the spinal fluid pressure remained above the normal range during the treatment, and the CSF pressure had no correlation with the degree of improvement they exhibited with antimigraine and diuretic therapy.

The practical conclusion from the study of this series is that any patient with CDH with migrainous features who is refractory to conventional therapy with prophylactic antimigraine agents should have a spinal tap to exclude coexisting IIH. This leads to the question of whether there is a shared pathophysiology between IIH and migraine. The clinical observations in our series suggest that further study is required to clarify if IIH is an entity in the migraine spectrum.

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