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Original Article

Clinical course of asymptomatic patients with papilledema from idiopathic intracranial hypertension

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Objective: Idiopathic intracranial hypertension (IIH) is defined as elevated intracranial pressure (ICP) with normal cerebrospinal fluid content in the absence of an identifiable cause. Patients often experience symptoms related to elevated ICP (e.g., headache); however, a subgroup of patients with elevated ICP may have optic disc edema without any associated symptoms. There are limited data about this subgroup in the literature. Our aim in this study was to characterize the initial clinical findings and visual outcomes over the follow-up period in this group of asymptomatic patients.

Methods: We performed a retrospective review of all patients who were referred to the neuro-ophthalmology service at Baylor College of Medicine for evaluation of papilledema between January 2012 and June 2020. Medical records of 139 consecutive patients with papilledema were reviewed. Patients were included in the analysis if they met the criteria for the diagnosis of IIH, had bilateral optic disc edema, and did not have any symptoms of elevated ICP.

Results: Of the 139 charts reviewed, 5 patients met the inclusion criteria. All 5 patients were female with a mean age of 25.2 years (range, 13–48 years). The mean body mass index was 36.3 kg/m^2 (range, 31.5–40 kg/m^2), and the mean follow-up period was 3 years (range, 12 months–5 years).

Conclusion: Our results demonstrate that the disease course for patients who present with asymptomatic IIH can be variable, yet still visually significant. Despite the absence of symptoms, patients can progress to symptomatic disease or experience persistent optic disc swelling or pallor even with the use of medication to lower ICP. To our knowledge, this is the first retrospective study characterizing the clinical course of papilledema from IIH in asymptomatic individuals.

Objectif: On définit l'hypertension intracrânienne idiopathique (HII) comme une élévation de la pression intracrânienne (PIC) en présence d'un volume normal de liquide céphalorachidien et en l'absence d'une cause identifiable. Les patients ressentent souvent des symptômes typiques d'une élévation de la PIC (p. ex., des céphalées); cela dit, il existe un sous-groupe de patients dont la PIC est élevée et qui présentent un œdème du disque optique, sans aucun autre symptôme connexe. La littérature médicale compte peu d'articles sur ce type de patients. Nous avions donc pour objectif, par l'entremise de la présente étude, de déterminer les caractéristiques cliniques initiales de ces patients asymptomatiques, de même que leurs résultats visuels pendant le suivi.

Méthodes: Nous avons réalisé une revue rétrospective de l'ensemble des patients qui ont été adressés au service de neuro-ophtalmologie du Baylor College of Medicine en vue de l'évaluation d'un œdème papillaire entre janvier 2012 et juin 2020. Les dossiers médicaux de 139 patients consécutifs qui présentaient un œdème papillaire ont ainsi été passés en revue. Les patients qui répondaient aux critères d'inclusion (diagnostic d'HII, œdème bilatéral du disque optique et absence de symptômes d'une élévation de la PIC) ont été inclus dans notre analyse.

Résultats: Sur les 139 dossiers examinés, 5 patients répondaient aux critères d'inclusion. Il s'agissait de 5 femmes dont l'âge moyen se chiffrait à 25,2 ans (fourchette : 13 à 48 ans). Leur indice de masse corporelle moyen s'élevait à 36,3 kg/m^2 (fourchette : 31,5 à 40 kg/m^2), et la durée moyenne du suivi était de 3 ans (fourchette : 12 mois à 5 ans).

Conclusion: Les résultats démontrent que chez les patients dont l'HII est asymptomatique, l'évolution peut être variable et, malgré l'absence initiale de symptômes, avoir des effets oculaires non négligeables. Au fil du temps, l'affection peut devenir symptomatique ou entraîner un œdème continu ou une pâleur persistante du disque optique, même si le patient prend un médicament en vue d'abaisser sa PIC. Il s'agit, que l'on sache, de la toute première étude rétrospective à se pencher sur l'évolution clinique de l'œdème papillaire secondaire à l'HII chez des sujets asymptomatiques.

Idiopathic intracranial hypertension (IIH) or pseudotumour cerebri syndrome is defined as elevated intracranial pressure (ICP) with normal cerebrospinal fluid (CSF) content in the absence of an identifiable cause. A confirmed diagnosis of IIH requires fulfillment of the following criteria: (*i*) papilledema, (*ii*) normal neurologic examination aside from cranial nerve palsies, (*iii*) normal neuroimaging, (*iv*) lumbar puncture (LP) opening pressure >250 mm H_2O in adults with normal CSF composition, and (*v*) no other identifiable cause for increased ICP.[1]

Patients with IIH present with optic disc edema from high ICP (papilledema) that can lead to severe and irreversible visual loss if left untreated.[2–5] Although the etiology of IIH is unknown, several risk factors for elevated ICP have

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been identified and include female sex, obesity and weight gain, endocrine disorders, steroid withdrawal, hypervitaminosis A, and certain medications.[6] Patients may experience a variety of symptoms, including headache, transient visual obscurations (TVOs), back pain, pulsatile tinnitus, dizziness, photophobia, neck pain, visual loss, and double vision.[7–10] However, a subgroup of patients with elevated ICP may have optic disc edema without any associated symptoms. There are limited data about this subgroup in the literature, likely because patients are not routinely screened for IIH. Considering the rising rate of obesity and the association of obesity with IIH, characterization of this group is particularly important.[11]

In this retrospective review, we assessed asymptomatic patients who were referred to the neuro-ophthalmology service at Baylor College of Medicine (BCM) from January 2012 to June 2020 owing to an incidental finding of papilledema on routine eye examination. Our aim was to characterize the initial clinical findings and visual outcomes over the follow-up period in this group of asymptomatic patients.

Methods

We performed a retrospective review of all patients who were referred to the neuro-ophthalmology service at BCM for evaluation of papilledema between January 2012 and June 2020. The study design was approved by the BCM Institutional Review Board. All patients provided informed consent for photography and completed a screening questionnaire that included an extensive review of systems checklist. Medical records of 139 consecutive patients with papilledema were reviewed. Patients were excluded from analysis if they had no disc edema when evaluated by the neuro-ophthalmologist, symptoms of elevated ICP, unavailable or abnormal neuroimaging, or no CSF studies. Additionally, patients with normal LP opening pressure, abnormal CSF composition, or an identifiable etiology for elevated ICP were excluded from analysis. Of note, all were evaluated for papilledema by a single neuro-ophthalmologist at their initial presentation and follow-up examinations.

Patients included in this study fulfilled the IIH diagnostic criteria. In addition, no patient had any visual symptoms (including diplopia, transient or fixed visual loss, or metamorphopsia) or symptoms of elevated ICP (e.g., headache, pulsatile tinnitus).

Results

Between January 2012 and June 2020, 139 patients presented for evaluation of papilledema. Of those, 5 patients met the inclusion criteria for IIH and were asymptomatic (Table 1). All 5 patients were female with a mean age of 25.2 years (range, 13–48 years). The mean body mass index (BMI) was 36.3 kg/m^2 (range, 31.5–40 kg/m^2), and the mean follow-up period was 3 years (range, 12 months–5 years). The following is a summary of each patient's clinical course (Table 2).

Patient 1

A 48-year-old female with a BMI of 40.1 kg/m^2 and hypertension, treated with hydrochlorothiazide, presented for a routine eye examination and was found to have trace bilateral optic disc edema in the absence of symptoms. Her neuroimaging studies were unremarkable, and LP opening pressure 25 cm H_2O with normal CSF content. Given the trace optic disc edema and lack of symptoms of elevated ICP, weight loss was suggested as an initial treatment for IIH. In a subsequent follow-up visit 11 months after her initial presentation, her BMI had decreased by 2% (10 pounds), but she reported experiencing TVOs on occasion. The optic disc edema appeared to be stable, and optical coherence tomography of the retinal nerve fibre layer (RNFL) was unchanged compared with prior visits. Acetazolamide was recommended, but the patient preferred to manage symptoms with weight loss only.

Patient 2

A 16-year-old female with a BMI of 33 kg/m^2 was noted to have grade 2 optic disc edema bilaterally in the absence of symptoms of elevated ICP. Her neuroimaging studies were unremarkable, and the LP opening pressure was 31 cm H_2O with normal CSF content. She was started on 750 mg acetazolamide per day, and her optic disc edema improved initially. However, during her 5-year follow-up period, she experienced several episodes with worsening papilledema and began experiencing headaches and TVOs about 12 months after initial presentation. This was likely aggravated by her occasional noncompliance with acetazolamide. Four years after her initial presentation, she stopped taking acetazolamide, and her BMI increased to 42 kg/m^2. She subsequently developed frequent blackouts in each eye and was found to have grade 3 disc edema in both eyes as well as elevated RNFL measures. She was restarted on 2 g acetazolamide daily, and her symptoms and disc edema had

Table 1—Characteristics and clinical course of 5 asymptomatic patients with idiopathic intracranial hypertension

Patient	Age (y), sex	BMI (kg/m^2)	LP opening pressure (cm H_2O)	Follow-up duration	Treatment
1	48, F	40.1	25	12 mo	Weight loss
2	16, F	33	31	5 y	Acetazolamide
3	23, F	37.7	42	3.5 y	Acetazolamide
4	13, F	38.9	41	18 mo	Acetazolamide
5	26, F	31.6	30	4 y	Acetazolamide

Table 2—Ophthalmic findings of 5 asymptomatic patients with IIH hypertension

Patient	Initial ophthalmic findings				Final ophthalmic findings			
	VA_{cc}(OD, OS)	Disc edema (OD, OS)	HVF MD(OD, OS)	OCT global (OD, OS)	VA_{cc}(OD, OS)	Disc edema(OD, OS)	HVF MD(OD, OS)	OCT global(OD, OS)
1	20/20, 20/20	Grade 1, 1	+0.59, +1.44	120, 128	20/20, 20/20	Grade 1, 1	+1.89, +1.72	121, 128
2	20/20, 20/20	Grade 2, 2	−4.6, −8.44	94, 93	20/20, 20/20	Grade 2, 2	−5.33, −6.73	185, 194
3	20/20, 20/20	Grade 2, 2	−3.16, −5.63	354, 483	20/20, 20/20	Grade 1, 1	−2.72, −2.67	85, 92
4	20/20, 20/20	Grade 1, 1	−3.62, −3.80	131, 120	20/20, 20/20	Grade 1, 1	−3.55, −5.06	126, 117
5	20/20, 20/20	Grade 1, 1	−1.35, −2.25	141, 193	20/25, 20/25	None, none	−2.04, −3.22	105, 106

improved on the most recent follow-up examination, 5 years after her initial presentation.

Patient 3

A 23-year-old female with a BMI of 37.7 kg/m^2 presented with bilateral 2+ optic disc edema detected during a routine eye examination. Her neuroimaging studies were unremarkable, and the LP opening pressure was 42 cm H_2O with normal CSF content. She was treated with 1 g acetazolamide daily and did not develop any symptoms of elevated ICP during her 3.5-year follow-up period. During this time, her optic disc edema remained stable, including on measures of the RNFL by optical coherence tomography.

Patient 4

A 13-year-old female with a BMI of 38.9 kg/m^2 was found to have grade 1 papilledema bilaterally. Her neuroimaging studies were unremarkable, and the LP opening pressure was 41 cm H_2O with normal CSF content. She was started on 1 g acetazolamide daily. During a follow-up period of 18 months, her RNFL measures stayed consistently elevated in both eyes despite her poor compliance with medication. At her most recent follow-up visit about 18 months after initial presentation, she reported a 20-pound weight gain, and her RNFL measures had increased, although she continued to be asymptomatic.

Patient 5

A 26-year-old female with a BMI of 31.6 kg/m^2, bilateral keratoconus, and hypothyroidism on levothyroxine and oral contraceptives presented with mild grade 1 optic disc edema. Her neuroimaging studies were unremarkable, and the LP opening pressure was 30 cm H_2O with normal CSF content. She was started on 500 mg acetazolamide daily. During her 4-year follow-up period, the optic disc edema improved initially, and she continued to be asymptomatic. Given her response to treatment, the decision was made to gradually wean her off acetazolamide. However, her RNFL measures increased on cessation of the medication, and she was started back on 250 mg daily. Her only symptom related to elevated ICP was persistent pulsatile tinnitus that started about 30 months after her initial presentation.

Conclusions

IIH can have a highly variable clinical presentation leading to delays in diagnosis.[12,13] Up to 94% of patients report experiencing headaches, and up to 72% report visual disturbances, particularly unilateral or bilateral TVOs.[12,13] In patients who lack associated symptoms, diagnosis is particularly challenging.

In a retrospective study, the incidence of papilledema in the absence of symptoms was 24%. This study included all patients with an initial diagnosis of IIH in the Detroit Medical Center during a 17-year period. Of the 77 patients who fit the diagnostic criteria, the vast majority (92%) were female with a mean age of 34 years. Additionally, 88% of patients were characterized as obese. Nineteen patients (24.7%) were asymptomatic, all of whom were found to have papilledema during routine eye examinations. The clinical course of these patients was not characterized.[14]

Our results demonstrate that the disease course for patients who present with asymptomatic IIH can be variable, yet still visually significant. Despite the absence of symptoms, patients can progress to symptomatic disease or experience persistent optic disc swelling or pallor despite the use of medication to lower ICP. Patients also may experience relapses associated with changes in weight or medication compliance, as seen in patient 2 in our study. Additionally, our study did not demonstrate a correlation between BMI and clinical variability or disease progression. We hypothesize that asymptomatic IIH falls into a spectrum of the disease before progressing into the classic symptoms. For these reasons, we recommend continued assessment for patients found to have IIH, even in the absence of symptoms, to avoid potential visual loss related to papilledema.

We recognize that our study has several limitations. Our sample size is small; therefore, our findings and the generalizability of our results may be limited. Additionally, patients included in this study were referred after an incidental finding of papilledema during routine eye examination; hence, we acknowledge the possibility for referral bias. Lastly, some

patients with papilledema from IIH were excluded from the study because of a lack of follow-up; therefore, there may be a higher number of patients with asymptomatic IIH whom we failed to include due to insufficient data.

To our knowledge, this is the first retrospective study characterizing the clinical course of papilledema from IIH in asymptomatic individuals. We found that individuals with asymptomatic or previously undiagnosed papilledema can have highly variable presentations, response to treatment, and overall disease progression. Given the possibility for visual loss due to optic disc swelling, we believe that these patients would still benefit from continued assessment despite the absence of symptoms. Additional research may be necessary to further characterize this group of patients and identify the optimal management approach.

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Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

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