LONG-TERM EVOLUTION OF PAPILLEDEMA IN IDIOPATHIC INTRACRANIAL HYPERTENSION

Observations concerning two cases

Elcio Juliato Piovesan, Marcos Cristiano Lange, Liciane do Rocio Maia Piovesan, Sergio Monteiro de Almeida, Pedro André Kowacs, Lineu Cesar Werneck

ABSTRACT - Chronic headaches, associated with papilledema and pulsatile tinnitus without any neuroradiologic, cytobiochemical or cerebrospinal fluid abnormalities are suggestive of idiopathic intracranial hypertension (IIH). However the absence of the papilledema does not rule out this diagnosis. The reason why some patients do not develop papilledema in IIH is ignored, however there are some hypotheses concerning the structure of the optical nerve. In this study we described two female patients that presented diagnosis of IIH with papilledema, with subsequent resolution of papilledema without the due resolution of intracranial hypertension. The long-term behavior of the optic nerve (ON) facing an increased intracranial pressure was evaluated through repeated measurements of the intracranial pressure. We concluded that the ON submitted to high intracranial pressure for a certain length of time can adapt itself with subsequent disappearance of the papilledema. The presence or not of papilledema in IIH can be related to the period in which the diagnosis is accomplished.

KEY WORDS: headache, intracranial pressure, papilledema, pseudotumor cerebri.

Avaliação do comportamento do papiledema na hipertensão intracraniana idiopática: a propósito de dois casos

RESUMO - Cefaléias com características crônica, diária, acompanhadas de edema de papila e tinnitus pulsátil, sem nenhum achado neuroradiológico ou citobioquímico no líquor, são altamente sugestivas de hipertensão intracraniana idiopática (HII). Entretanto a ausência do papiledema não invalida o seu diagnóstico. A razão pela qual alguns pacientes não desenvolvem papiledema na HII é desconhecida, porém algumas hipóteses relacionadas com propriedades intrínsecas da bainha do nervo óptico têm sido propostas. Neste estudo relatamos dois pacientes do sexo feminino que apresentaram diagnóstico de HII com papiledema, evoluindo para resolução do papiledema sem a devida resolução da HII. O comportamento do nervo óptico (NO) frente ao aumento da pressão intracraniana foi avaliado neste estudo a partir de um monitoramento intermitente criterioso da pressão intracraniana. Concluímos que o NO submetido a um período de hipertensão intracraniana pode adaptar-se a este ambiente promovendo uma resolução do papiledema para normalidade papilar. A presença ou ausência de papiledema na HII pode estar relacionada ao período no qual seu diagnóstico é realizado.

PALAVRAS-CHAVE: cefaléia, pressão intracraniana, papiledema, pseudotumor cerebral.

Idiopathic intracranial hypertension (IIH), also known as pseudotumor cerebri or benign intracranial hypertension, is associated to a group of symptoms in which the headache prevails over the others\(^1\). This headache in considered not to be associated with vascular intracranial disorders, and is accompanied or not by papilledema\(^2\). Several mechanisms may lead to the increase of the intracranial pressure, however all break of the dynamics of several intracranial structures leading to nociceptive stimulation and to a headache that presents with peculiar features\(^3\).

The presence of papilledema makes the diagnosis easier, however, its absence, much less frequent, it has been reported in several papers\(^2\). In this study we have followed-up two patients with the diagnosis of IIH for a period of 36 months. We have demonstrated that papilledema may subside during the course of this disease even without the remission of the intracranial hypertension.

METHOD

Study design

Two patients with diagnosis of IIH were appraised and accompanied by a period of 36 months. The initial evalu-
ation consisted of clinical and neurological examination and laboratorial work-up. All the patients were submitted to laboratorial evaluation of serum calcium, thyroid and parathyroid function tests, blood count, glucose, erythrocyte sedimentation rate (ESR), Kvein test and angiotensin-converting enzyme. Both patients underwent computerized axial tomography (CAT) and magnetic resonance imaging (MRI) of the head, cerebral angiography (CA) and fluorescein angiography (FG). To obtain pressure measures and a sample of the cerebro-spinal fluid (CSF) for cellular, cytological, chemical, and bacteriological examination a lumbar puncture (LP) was carried out. The patients were also appraised by a physician, an ophthalmologist, an endocrinologist and a neurologist.

Patients

Patient 1. A 31 years-old white female, 155 cm of height and 76 kg of weight, had been seen by the same neurologist because of migraine an year before. Migraine had started when the patient was 13 and increased in intensity, duration and frequency in the preceding 6 months, evolving to a daily chronic headache (transformed migraine). In this occasion the neurological examination and the CAT were normal. For the treatment of the migraine propranolol 40 mg/day was prescribed for 60 days. Amitriptyline 50 mg/day and divalproex sodium (Depakote(R) 500 mg/day) were also tried without results. At the appointment in which IIH was suspected, the intensity of the headache had increased, associated with transient visual abnormalities (photopsias) and noises in both ears (pulsatile tinnitus). Bilateral papilledema was observed. A second CAT was normal. Intracranial pressure was 430 mmH2O (graphic-1) and the cerebrospinal fluid (CSF) was normal. Blood lab were normal. Fluorescein angiography (FG) revealed bilateral papilledema (Fig 1-A). Acetazolamide 250 mg b.i.d. was started. Fifteen days later the headache had improved without resolution of the papilledema, but a new LP revealed an intracranial pressure of 530 mmH2O (Fig 2). Forty-five days after acetazolamide was started the papilledema had remitted. At this time, the frequency of the throbbing headaches was twice a week. They were bilateral, associated to nausea and vomiting. Six months later the patient presented no papilledema (Fig 1-B), photopsias or headaches. A new LP revealed an intracranial pressure of 320 mmH2O (Fig 2). During the following 24 months the patient continued without papilledema but with episodic headaches. Thirty months after the first evaluation the daily headaches had recurred. There was no papilledema and an ophthalmological evaluation was normal. A new LP was carried out, disclosing an intracranial pressure of 460 mmH2O (Fig 1-B) without papilledema. The patient refused a lumbo-peritoneal shunting. Currently the patient persists with chronic daily headache, without papilledema.

Patient 2. A 40 years-old, white female, 161 cm of height and 70 Kg of weight, presented with a six month history of chronic daily headaches with pressing quality, bilateral location, mild to moderate intensity, increasing slowly during the day. Occasionally this headache increased in intensity, becoming throbbing and associated with nausea and/or vomiting. At the time of the appointment the patient also revealed myalgia, pulsatile tinnitus in both ears and low fever in the last five days. Bilateral papilledema was observed. The CAT revealed a left maxillary sinusitis. Intracranial pressure was 330 mmH2O (Fig 3) and the cerebrospinal fluid (CSF) revealed 26 leukocytes (95% polymorphonuclear), glucose of 64 mg/ml and 122 mg/ml of protein. Culture for fungus and virus were negative. For fifteen days she received only symptomatic medication for the treatment of viral meningitis. Thirty days after completing therapy the

![Fig 1. The behavior of the optic nerve during different phases of the intracranial idiopathic hypertension. During the first phase the patient revealed papilledema, some months later the patient improved and revealed no more papilledema (patient 1).](image-url)
The patient was still presenting papilledema and pulsatile tinnitus but her headache had improved. A new CSF examination disclosed normal results but intracranial pressure was 350 mmH2O (Fig 3). A MRI of the head revealed persistence of the left maxillary sinusitis and a CA was normal. During ten days the patient received floxacilin. The headache disappeared three months later, but not the papilledema. A new CAT of the facial sinus was normal. Another LP was carried out revealing a normal CSF but the intracranial pressure was 420 mmH2O (Fig 3). There was an elevated serum thyroid-stimulating hormone (TSH-12.5yU/m), and reduced triiodothyroine (T3-30ng/dl) and tetraiodothyronine (T4-2.3g/dl). Synthetic L-thyroxine 100 mg/day was prescribed. Fluorescein angiography (FG) revealed bilateral papilledema. Acetazolamide 250 mg b.i.d. was also prescribed. Six months after the treatment for the IIH and for the hypothyroidism the papilledema and the headache had disappeared. After one year the patient stopped the medication. Fifteen days later the pulsatile tinnitus and the headache reappeared without associated papilledema. The intracranial pressure was 380 mmH2O (Fig 3) and the CSF was still normal. Fluorescein angiography (FG) revealed papillary pallor without papilledema. Again acetazolamide 250 mg b.i.d. was started with improvement of the symptoms after twenty days. A new LP revealed intracranial pressure of 250 mmH2O and a normal CSF (Fig 3). For thirty six months we followed up the patient. During this period three new episodes of headache were observed, when the intracranial pressure measurements were 340, 290 and 510 mm H2O (Fig 3) respectively. The patient did not agree to be submitted to a lumboperitoneal shunting.

**DISCUSSION**

Intracranial pressure can be increased through out different mechanisms and several disorders. Those disorders may be either primary, secondary or atypical. The syndrome of IIH occurs predominantly in obese women of childbearing age. Definitive diagnosis cannot be made without excluding brain tumours and other intracranial mass lesion, infections, hypertensive encephalopathy, pulmonary encephalopathy, and obstruction of the cerebral ventricles.

IIH occurs at a frequency of about 1 case per 100 000
per year in the general population and of 19.3 cases per 100 000 per year in obese women aged 20-44 years. The pathophysiology of IIH is unknown, but some postulated hypothesized mechanisms are proposed: increase of the volume of the cerebral blood or of the CSF; increase of the cerebral blood flow; intracelular or extracelular edema; abnormalities of the cerebral microvascular structures producing an increase in the amount of tissue water; absorption disturbances of the CSF secondary to an increase of the pressure in the superior sagittal sinus.

The most commom symptoms are: headache, otalgia, diplopia, photopsia, vomiting, mialgia, dizziness and pulsatile tinnitus. The typical characteristic of headache in the IIH are: severe intensity (93%); pulsating quality (83%); bilateral location (50%); associated to nausea and/or vomiting (57%); photophobia and phonophobia (30%) and photopsias (20%) with a daily frequency (73%) and lasting from four days to three years. The mechanisms that produce these symptoms can be related to traction of the nociceptores located in the intracranial vessels; transitory herniation of the hipocampal uncus; traction of cranial nerves (triplet and branches of C1, C2 and C3).

The pulsatile tinnitus presents a duration of seconds to days being unilateral in 62% of the cases. They are reported by the patients as “falls of a ray”, “beat of a breeze”, “heart pulsing in the ear” or eventually “blows in the hear”. The patients can also present photopsias (presence of sparkles or flashes of light of variable duration, from seconds to hours). Less frequently, the patients refers pain in the shoulders and in the arm (probably due to dilation of the spinal roots). Bilateral retro ocular pain, occuring during movements of the head, are reported by 20% of the pacientes.

The main abnormality disclosed by examination is papilledema, occasionally with hemorrhagic exsudates. However, its absence does not exclude IIH. Paralysis of the abducent nerve, trochlear and facial paralysis are also common findings. Less frequently nystagmus, bilateral intranuclear ophthalmoplegia, dissociation of pupillary reflex and limi-
tation of the upper gaze may occur. Rarely the patient may reveal ataxia and the presence of a Babinski sign.

Grant, follow-up 79 children with IIH, showed that papilledema disappeared in 48% of the cases after 2 months, in 54% after 6 months, in 67% after one year, in 75% after two years, in 85% after 3 years and in 86% after 10 years. The optic atrophy was only observed respectively in two patients two and four years after the beginning of the treatment. The most frequent sequelae of IIH is the loss of visual sharpness. However many patients even with intracranial hypertension do not present papilledema. Why there is no papilledema in cases of intracranial hypertension is not known. Congenital or acquired optic nerve sheath defects, IIH with resolution of papilledema, or early idiopathic intracranial hypertension are alternative explanations. Unilateral papilledema from IIH is an infrequent and rare situation. The possible mechanisms that have been considered responsible for lack of papilledema in IIH include: an anomaly in the orbital optic nerve sheaths, an abnormality in the venous sinuses; difference in the lamina cribosa between the two optic disc that results in reduced transmission of the intracranial pressure to the optic nerve in the scleral canal; axoplasmic blockage at the level of the lamina cribosa induced by experimental elevated intracranial pressure.

In both patients herein described, improvement of the papilledema was verified even in the presence of intracranial hypertension with daily chronic headache and pulsatile tinnitus. As seen in the first case, the patient presented with symptoms of daily chronic headache and the papilledema that, could had developed during the course of the disease, remitting afterwards. This observation has lead us to hypothesize that the optic nerve can behave in different ways during the evolution of this pathology, beginning without papilledema, with further development of papilledema that resolves later on. We believe that this pattern might be related to the fact that the retrograde axoplasmatic flow and anterograde axoplasmatic flow of the optic nerve behave distinctly during the different phases of this condition, mainly when oscillations of the intracranial pressure occur.

We believe that the finding or not of papilledema in IIH might reflect only the phase in which diagnosis of IIH is done. In this condition, the presence of the papilledema can be transitory.

REFERENCES
11. Johnston I, Hawke S, Haimagyi M, Teo C. The pseudotumor syn-
16. Schoenen J, Noordhout AM. Headache. In Wall PD, Melzck R (eds) Text-
17. Giuseffi V, Wall M, Siegel PZ, Rojas PB. Symptoms and disease asso-
20. Spence JD, Amacher AL, Willis NR. Benign intracranial hypertension without papilledema: role of 24 hour cerebrospinal fluid pressure moni-
23. Lessel S. Pediatric pseudotumor cerebri (Idiopathic intracranial hyper-
30. Tso MOM, Hayreh SS. Optic disc edema in raised intracranial pres-