Idiopathic intracranial hypertension after 40 years of age: Clinical features in 23 patients

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PURPOSE. *Idiopathic intracranial hypertension (IIH) is a well-recognized disorder of unknown etiology associated with elevated intracranial pressure (ICP), normal neuroimaging, and normal cerebrospinal fluid (CSF) composition, found mostly among obese females of childbearing age. The aim of this study is to investigate the clinical features of IIH in patients older than 40 years.*

METHODS. *This is a retrospective chart review (1998–2007) of all consecutive patients older than 40 years who were diagnosed with IIH based on the Modified Dandy Criteria.*

RESULTS. *Twenty three of the 200 IIH patients in the institutional database fulfilled study entry criteria. They included 22 females and one male whose mean age was 51.4 years (range 41–79). Coexisting systemic arterial hypertension was found in 13 (56.5%) patients. Seventeen patients (73.9%) had symptoms attributable to elevated ICP. The most common presenting symptoms were visual; mainly blurred vision and transient visual obscuration (15/17 patients, 88.23%). Eleven patients (64.7%) complained of headache, and another 4 (23.5%) of pulsatile intracranial noise. The average follow up period was 21.8 months.*

CONCLUSIONS. *The findings indicate that IIH among individuals older than 40 years of age may be underreported. These patients are more likely to present with systemic hypertension and with more visual disturbances, but with fewer complaints of headache than the younger IIH population. (Eur J Ophthalmol 2008; 18: 989-93)*

KEY WORDS. *Idiopathic intracranial hypertension, Pseudotumor cerebri, Visual symptoms, Late onset*

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INTRODUCTION

Idiopathic intracranial hypertension (IIH, also known as pseudotumor cerebri) is a well-known disorder associated with elevated intracranial pressure (ICP) >25 cm H_2O, with normal neuroimaging and a normal cerebrospinal fluid (CSF) composition, for which no causative factor can be identified (1). Dandy (2) was the first to describe diagnostic features of the disorder in 1937, and a set of diagnostic criteria was provided by Smith in 1985 (3). Recent advances in neuroimaging technology have led Friedman and Jacobson (4) to provide updated diagnostic criteria for IIH, which include the following:

1. Symptoms/signs, if present, may only reflect those of generalized intracranial hypertension or papilledema
2. Documented intracranial hypertension, measured in the lateral decubitus position
2. Normal CSF composition
4. No evidence of hydrocephalus, mass, structural or vascular lesion on magnetic resonance imaging (MRI) or contrast-enhanced computerized tomography (CT) for typical patients, and MRI and MR venography (MRV) for all others
5. No other identified cause of intracranial hypertension

IIH has long been recognized as being typically prevalent among the young population. It occurs most commonly

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among women of childbearing age who are typically obese but otherwise healthy. Specifically, the reported annual incidence is 1 in 100,000 in the general population, but this figure increases 19-fold among obese women aged 20–44 years (5). Previous studies reported a mean age of 30 years for first onset of IIH symptoms (17, 25). Although IIH has been described in men (6, 7) as well as in the pediatric population (8-10), our literature search yielded only one report on the clinical features of IIH diagnosed in older patients. Bandyopadhyay and Jacobson (11) reported a series of 14 patients who were diagnosed with IIH at 44 years of age or older and reported some differences from the typical patients with respect to clinical presentation and visual outcome.

We present the clinical features, risk factors, and visual outcome in patients who were first diagnosed with IIH after the age of 40 years in our institution. We arbitrarily chose the cutoff of 40 years as being representative of patients older than the typical ones at IIH presentation.

METHODS

We retrospectively reviewed the institutional medical records of 200 consecutive patients who fulfilled Friedman and Jacobson's criteria (4) for IIH. At the time of data collection for our study, retrospective collection of data from charts was exempt from IRB approval at our institution. All the patients had been evaluated by a single neuro-ophthalmologist (A.K.) during the years 1998 to 2007. Specific questions were asked regarding the presenting complaints, with attention paid to presence of visual symptoms, headache, and intracranial noise. The standard neuro-ophthalmologic evaluation included formal visual field testing, assessed at least twice with the 30-2 Humphrey perimeter, and neuroimaging, i.e., gadolinium-enhanced MRI. Subsequent lumbar puncture procedure was performed in the lateral decubitus position for measurement of the CSF opening pressure and analysis of CSF composition. Body mass index (BMI) was calculated in all cases. Data were collected on the presence of recognized risk factors, mainly uremia (12, 13) and thyroid disease (14, 15), as well as on the use of medications, such as vitamin A derivatives (16, 17), antibiotics (18, 19), and hormonal medications (17, 20).

All patients who were 40 years of age or older at the time of diagnosis, defined as first onset of symptoms at age older than 40 years, were selected to comprise our current study population.

RESULTS

Our search of the hospital database yielded 27 suitable patients: complete follow-up data were available for 23 patients, and they comprised our study group. There were 22 females and one male whose mean age at the time of diagnosis was 51.4 years (range 41–79). The average follow-up period was 21.8 months (range 3–54). Fourteen (60.8%) were considered significantly overweight, defined by a BMI > 30. Thirteen (56.5%) patients had systemic arterial hypertension warranting chronic use of oral antihypertensive agents. Thyroid disease and diabetes mellitus coexisted each in three patients.

Seventeen patients (73.9%) had symptoms attributable to elevated ICP. Visual symptoms, mainly blurred vision and transient visual obscuration, were the most common presenting symptoms, reported by 15/17 (88.23%) patients. Visual symptoms were the only presenting symptoms in 5/15 patients. Another 6/15 patients also had headache associated with the visual symptoms, and another 4/15 had associated intracranial noise. Eleven patients (11/17, 64.7%) complained of headache: it was associated with visual symptoms in six of them, another three had visual symptoms and intracranial noise, and another two headache only. The categories of symptoms are listed in Table I. The other six patients (26%) who were asymptomatic were diagnosed with IIH after completion of evaluation due to a physical finding of papilledema. All 23 patients had bilateral swollen optic disc upon presentation, while 14 (60%) also had splinter hemorrhages. None had severe papilledema, nor associated exudates. One patient

TABLE I - DISTRIBUTION OF PRESENTING SYMPTOMS AMONG OUR PATIENTS

Category	Number of patients
Visual symptoms	15
Associated with headache	6
Visual symptoms only	5
Associated with headache and intracranial noise	3
Associated with intracranial noise	1
Headache	11
Associated with visual symptoms	6
Associated with visual symptoms and intracranial noise	3
Headache only	2
Asymptomatic	6

had coexisting old branch retinal vein occlusion. Importantly, none had signs of hypertensive retinopathy.

At baseline, visual acuity (VA) levels were in the range of 6/30 to 6/6, with an average of 0.18 (LogMAR). Visual field testing as part of the diagnostic workup detected a visual field abnormality in 11 patients (47.8%). Visual field test demonstrating an enlarged blind spot was interpreted as normal. All visual fields were reliable. A visual field defect involving the nasal hemifield was found in 6/11 (54.5%) patients, one of which was attributed to a coexistent branch retinal vein occlusion. A slight visual field constriction was found in one eye of one patient, and severe visual field constriction was found in 4/11 patients. The average mean deviation (MD) was –5.32 dB.

The mean CSF opening pressure during the initial examination was 33.26 cm H_2O (range 25–50 cm H_2O).

Brain MRI was performed in 19 patients; 6 patients also underwent MRV with special attention paid to signal changes of venous sinus narrowing or thrombosis. Brain MRV revealed narrowing of the transverse cerebral sinus in these 6 patients (31.57%). There were no remarkable findings on the other 13 MRI evaluations. Four patients did not undergo brain MRI: three due to morbid obesity and one patient who refused to perform the scan. All four had undergone contrast-enhanced brain CT that was unremarkable, and had consistently normal findings on neurologic examination during at least 30 months of follow-up.

Three patients had possible associated risk factors for elevated ICP: two had been treated with progesterone as hormone replacement therapy and the third received oral tetracycline for a dental infection a few months prior to being diagnosed with IIH.

All 23 study patients were treated with oral acetazolamide. One patient developed allergic rash that required prompt discontinuation of the drug: she was prescribed oral topiramate. Another patient underwent temporary deterioration in vision and was given a course of steroids, which were gradually tapered down after remission was achieved. No patient required a lumboperitoneal shunt or optic nerve sheath fenestration.

At their last follow-up examination, all 23 patients had corrected VA levels in the range of 6/10 to 6/6, with a mean LogMAR of 0.08. All patients had reliable visual filed testing. Seventeen patients had normal visual field, while visual field abnormality persisted in six: a nasal loss in one eye was attributed to a coexistent branch vein occlusion, and a mild defect involving one quadrant persisted in one eye of the other five patients. The average MD was –4.14 dB. Two eyes developed optic atrophy that was suspected as being attributable to IIH.

DISCUSSION

IIH is more frequently present among younger populations (5). We describe the clinical characteristics of 23 patients who first showed signs and symptoms of IIH after the age of 40 years. For the most part, the typical patient in our series was an obese, hypertensive female first presenting with visual symptoms and, less often, headache and intracranial noise. Notably, headache is the most common presenting symptom among younger patients with IIH (9, 21, 22), and so our findings suggest that it may not similarly alert to IIH for older ones. The reported frequency of visual disturbances as the initially presenting symptoms of IIH in the young population is in the range of 30–68% frequency, a similar figure to our 65%. Visual symptoms, however, were most common among our symptomatic patients, having been reported by up to 88% of them.

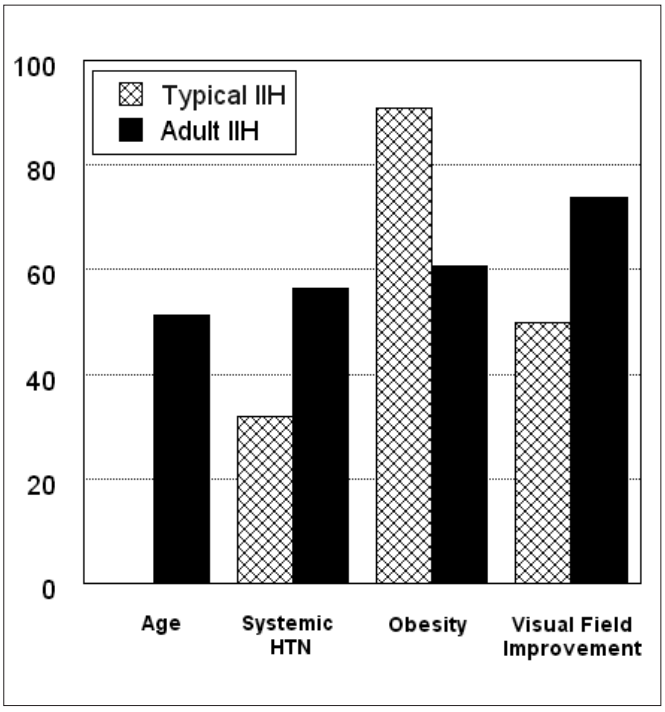

Fig. 1 - *Diagram showing comparison of rate of associated systemic arterial hypertension, obesity, and visual field improvement over time between our adult idiopathic intracranial hypertension (IIH) patients and typical IIH patients. Data were adopted from references 21 and 23-25.*

The rate of associated systemic arterial hypertension reported for younger IIH patients was reported in the range of 14–32% (21, 24-26); it was 56.5% for our older study group (Fig. 1). Although that prevalence of systemic hypertension in our series was higher than the reported prevalence (29–33%) in the general white population aged 40–59 years (27, 28), it is not clear whether this finding implies a true pathophysiologic association between IIH and systemic hypertension or if it merely reflects a higher incidence of elevated blood pressure in an obese adult population. Coexisting systemic hypertension had been suggested to confer a poor visual prognosis in younger patients with IIH (29, 30). Systemic HTN did not influence the visual prognosis in our patients. However, the small number of patients in our series limits analysis of difference in the visual outcome between IIH patients with coexisting systemic HTN in comparison with those without it.

Only 14 of our patients (60.8%) were obese compared to the reported 88–94% significantly overweight patients in the typical younger IIH population (23) (Fig. 1).

The natural history of IIH may be one of severe visual loss, with reported rates of severe visual impairment in the range of 17.6–24.6% for typical IIH patients (30, 31), and a 50% chance of improvement of visual field as assessed with Humphrey perimeter (21). For our older patients it was good, with all of them emerging with pre-IIH visual acuity after treatment and most (17/23, 73.9%) with corrected visual field results on the last examination.

Our search of the English literature yielded only one published report on the clinical features of late-onset IIH, that by Bandyopadhyay and Jacobson (11). Similar to our results, the 14 patients in their series with late-onset IIH were more often men, less often obese, and less often symptomatic. They reported being able to identify the likely causes of intracranial hypertension in 4 (29%) patients, and suggested that nonidiopathic causes of intracranial hypertension in older age groups may be overlooked by strict adherence to the Modified Dandy Criteria. As such, they proposed further expanding those criteria to account for factors such as necessity of excluding other causes of intracranial hypertension (e.g., medications or toxins) in older patients. Although we were not able to pinpoint the underlying possible cause for intracranial hypertension in more than 13% of our patients (two patients taking hormonal replacement therapy and another patient receiving oral tetracycline treatment), we support Bandyopadhyay and Jacobson's (11) suggestion to consider changing modified Dandy's criteria accordingly. Finally, their reported visual prognosis was generally good, as was ours.

Our study has several limitations. First, our results depend on historical controls and therefore may be biased by different inclusion criteria, different disease severity, and different methods of data collection and prognostic information in particular. We recognize that it is not possible to arrive at firm conclusions based on the findings of a study group as small as ours. Twenty-three out of 200 patients, however, represents a prevalence of 11.5% and, given that IIH in older patients has rarely been addressed in the literature (11), we believe that larger studies are warranted to validate our results, especially in light of the good prognosis that can be expected with appropriate management in this population.

In conclusion, our results suggest that IIH should also be considered in the differential diagnosis of older patients complaining of visual symptoms, especially when they are associated with headache, and that the condition may be more prevalent among individuals above the age of 40 years than previously believed. The frequent association of systemic hypertension with IIH in our series may indicate that it is a risk factor for IIH, in addition to obesity, but that this risk factor does not necessarily pose a worse prognosis. Further studies are needed to confirm a true pathophysiologic predisposition.

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