

Idiopathic intracranial hypertension in adolescents with severe visual impairment: Long-term outcome and the beneficial effects of weight loss and psychological support.

Garoufi Anastasia^a, Georgouli Helen^a, Vartzelis George^a, Eliades Andreas^b, Velissariou Joanna^a, Kossiva Lydia^{a,*}

^aDepartment of Pediatrics 'P&A Kyriakou' Children's Hospital, Athens University, Athens, Greece

^bPediatric Intensive Care Unit, University Hospital of Patras, Patras, Greece

Abstract. The aim of this manuscript is to evaluate retrospectively, the symptoms, treatment and long-term outcome of idiopathic intracranial hypertension (IIH) in adolescents with severe visual impairment, particularly in relation to body weight and compliance to treatment. We reviewed the clinical notes of adolescent patients treated in our department for IIH through a one-year period. From January 2004 to Feb 2005 four patients, aged between 12 and 13 years were diagnosed with IIH. Inclusion criteria were cerebrospinal fluid (CSF) opening pressure greater than 250 mmH₂O, normal CSF composition, severe visual impairment, normal brain imaging and nonfocal neurological examination except for sixth nerve palsy. All patients were followed for a minimum of 3 years. All patients were either overweight or obese. The sex distribution was 3 girls, 1 boy. The most common presenting symptom was headache. Visual field abnormalities were present in all cases with severe visual loss. All patients were treated with acetazolamide while two of them received steroids in conventional dose and one needed high-dose methylprednisolone. The use of transcranial Doppler (TCD) was available only after treatment with minimum impact on results. Adolescents represent an age group with special emotional and biological needs leading in difficulties when compliance to specific treatment is necessary. Although IIH in adolescents is rare, it could lead in permanent visual loss. Especially in obese patients, successful weight management in combination with good compliance to treatment seems important for a favorable long-term outcome.

Key words: Adolescents, pseudotumor cerebri, treatment, vision, weight loss

1. Introduction

Idiopathic intracranial hypertension (IIH) is a diagnosis of exclusion characterized by intense headache, raised cerebrospinal fluid (CSF) pressure in the absence of an intracranial mass lesion or ventricular dilatation, normal spinal

fluid composition, normal findings on neurological examination except for papilledema and an occasional VI nerve palsy with normal level of consciousness (1). It is relatively uncommon in childhood with an incidence of one case per 100.000 (2,3). This syndrome can cause significant visual loss and impairment of quality of life, thus early recognition is important as timely intervention may preserve vision and alleviate symptoms (4). Obesity has been proposed as a predisposing factor that can lead to IIH possibly due to increased intra-abdominal pressure, increased right heart filling pressure and subsequently increased central venous pressure (5). We report four cases of either overweight or obese adolescents that presented with IIH and severe visual impairment in a large tertiary centre

*Correspondence: Dr. Kossiva Lydia
Pediatrician, Lecturer of the Second Department of Pediatrics 'P&A Kyriakou' Children's Hospital, Athens University, Athens, Greece
Address: Thevon & Levadias str, 11527, Athens, Greece
Tel: + 30 2132009261
Fax: + 30 210 7774383
E-mail: lydiakossiva@hotmail.com
Received: 20.09.2011
Accepted: 27.06.2012

over a one-year-period in terms of diagnosis, management and 3 - year outcome (6).

2. Materials and methods

Adolescent patients with severe visual loss, normal brain magnetic resonance imaging (MRI with MR venous angiography), intracranial opening pressure greater than 250 mm H₂O with normal spinal fluid content, edema of the optic disc and no focal neurological signs except for sixth nerve palsy were included in this retrospective study. Patients with other pathologies such as dural sinus thrombosis, brain hemorrhage or other autoimmune, clotting or infectious diseases were excluded from the study as well as hypothyroidism. Patients were classified either as overweight (BMI: body mass index, for age and sex > 85th percentile) or obese (BMI for age and sex > 95th percentile). A thorough neurological examination of all cranial nerves was performed as well as ophthalmological examination with fundoscopy and measurement of visual acuity upon admission and during the 3-year follow up.

Four patients met the inclusion criteria (3 girls, 1 boy). The girls were classified as overweight and the boy as obese. Patients' data are displayed in Table 1.

All of our patients exhibited severe headache and visual impairment with patients 1 and 4 having only light perception while diplopia was noticed in 3 patients [1,2,4]. Papilledema of both eyes was diagnosed in all cases with normal pupillary responses. Visual field abnormalities were detected in all patients with visual acuity ranging from light perception to 0.1.

Magnetic resonance imaging and venous angiography were normal in all cases thus brain lesions, hemorrhage or dural sinus thrombosis were excluded. Patient 3 exhibited dilatation of both optic nerve sheaths. Lumbar puncture was

performed in all patients. The spinal fluid content was normal but the opening pressure was significantly elevated (ranged from 320 to 1000 mmH₂O).

All patients were treated with acetazolamide (dose 1gr/day) and 3 patients (case 1, 3, 4) received combined therapy with acetazolamide and oral corticosteroids (prednisone 2mg/kg/day) with gradual tapering. Only one patient (case 4) received methylprednisolone pulse therapy (30mg/kg/day for 3 days) followed by oral corticosteroids. During the long-term follow up, the patients underwent a detailed ophthalmological and neurological examination and compliance to treatment was evaluated. Interestingly, the girls had severe emotional instability and although they received the appropriate treatment, they did not manage to lose weight and in two cases (pt 1, 3) the vision was significantly deteriorated in long-term follow up. Specifically, in case 3, due to enlargement of optic nerve sheaths during relapse, a surgical approach was proposed but the patient refused it. Although patient 2 was still overweight, she managed to lose weight and her vision was normal in 3-year follow up. Outcome of the male patient was excellent in terms of body weight as he lost 25 kg with absolute normalization of visual acuity in long-term follow up. Interestingly, all of our patients were advised to visit a psychologist but only the boy consented to our suggestion.

Transcranial Doppler was applied after the first lumbar puncture in all cases and during relapse in case 2. Initial measurements were within normal values [pulsatility index (PI) <1, resistance index (RI) <0.6 in all cases] while during relapse in case 2 these values were elevated before lumbar puncture (PI: 1.1, RI: 0.65) and returned to normal after CSF drainage (15ml) and medical treatment.

Table 1. Symptoms, clinical examination, treatment, compliance, outcome

Pt	Sex	Age	Assoc. Factors	Symptoms	Visual Acuity		Treatment			Compl.	Vis. Rec.	Relapse
					RE	LE	Acet	Cort	T4			
1	F	13	Ovw	H, V, D, N	LP	0.1	+	+	+	G	+	+
2	F	12	Ovw, Thyr	H, D, N, NR, N	0.1	0.1	+	-	+	P	-	+
3	F	12	Ovw	H, NR, V, N	EONS 0.1	EONS 0.1	+	+		G	+	-
4	M	13	Ob	H, D, N	EONS LP	EONS LP	+	+				

H: Headache, V: Vomiting, D: Diplopia, N: Facial numbness, LP: Light perception, P: Poor, G: Good, NR: Nuchal rigidity, EONS: Enlargement of optic nerve sheath, Ob: Obese, Ovw: Overweight.

3. Discussion

Although initial reports describe an equal incidence of IIH through all age groups, it is more likely that this condition occurs more frequently in adolescents in comparison to younger patients (7). Furthermore, it is supported that IIH in younger children is distinct from the IIH of adolescents. More specifically IIH in younger children is characterized by equal sex occurrence and little if any relation to body weight while IIH in adolescents occurs more frequently in obese female individuals (8,9). All our patients comply with the currently accepted criteria for IIH and represent typical cases of the adolescent group of patients in terms of symptoms, signs and prognosis (1). With regards to long-term outcome for two of our patients had significantly impaired vision that caused a considerable restraint to their daily living.

As suggested by others, it is still unclear which factors predispose to permanent visual loss; visual outcome is not apparently related to the degree of papilledema, the presence of visual obscurations, or the incidence of recurrent increased intracranial pressure. Frank visual loss at the onset of the disease is the one factor which can predict visual outcome and indeed in our cases, those with the poorest outcome were the ones with the worst visual loss at diagnosis with the exception of case 4 (4). Weight loss in this group of overweight adolescents, seems to have significant importance for a favorable long-term outcome along with good compliance to treatment. Especially with regards to relapses, it is supported that these occur mainly to adolescents who regain the weight, they lost at the beginning of the treatment (10).

Three of four patients were obese and one was overweighted at diagnosis. It is useful to notice only the male patient managed to reduce his weight successfully and he was the only patient with the best outcome overall and the patient with close psychological follow up. The beneficial effect of weight loss in children with IIH is still under investigation, in women however it is well documented, as it has been demonstrated to reduce papilledema and lower CSF pressures. Furthermore, recent weight gain has been associated with relapses of IIH in women and, indeed in our cohort, case 1 responded to initial treatment but relapsed subsequently having gained almost 20 kg (10,11).

It is probably due to the similarities between adolescents and adults with IIH that optimum weight management seems to be important for the successful treatment of adolescent patients under

the condition that they receive the proper medical treatment. However more research is required to establish the beneficial effect of weight loss in adolescents with IIH. The weight loss seems to be more difficult for female adolescents, due to emotional and endocrinological reasons. Thus the medical treatment of these patients should be assisted by psychological support and encouragement.

The diagnostic tools used in this case series are the ones that are widely accepted in this context, with the addition of TCD that has only recently started to appear in current literature, especially in adults with cerebral ischemia or children with sickle cell disease (1-4-11,12). It seems to be a useful adjunct to diagnosis and management of intracranial hypertension cases as it is non invasive and it may provide reproducible measurements of resistance and pulsatility associated with intracranial hypertension. In our cases, it was only used in remission therefore we cannot extrapolate any significant outcomes; however case 2 had a TCD prior to lumbar puncture that gave results suggestive of intracranial hypertension, as well as after CSF drainage where the same indices measured by TCD had significantly improved. It would seem that TCD should be investigated further in this context to evaluate its future use.

With regards to management, all cases received oral acetazolamide that is currently the first line treatment and none had any significant side effects from long-term administration of this regimen (4-13). Two girls received thyroxine as well at different stages of the disease as they were found to have some thyroid dysfunction. Hypothyroidism is a well documented cause of secondary IIH (1). In our cases we cannot hypothesize that hypothyroidism was the cause of IIH because free T3 and free T4 were only marginally low in case 1 and normal in case 2. Steroids were given to three of the cases with different regimes but the one that manifested the best outcome was the boy who received high dose methylprednisolone intravenously. The role of steroids in the treatment of IIH remains controversial; nevertheless a short course of high-dose corticosteroid therapy may be helpful for patients with acute visual loss resulting from fulminant papilledema, as the boy in our case (14).

In conclusion, adolescents with IIH, especially girls, consist a group with special biological and emotional needs. The long-term visual outcome of these patients appears to be guarded and early diagnosis and management may be helpful. Transcranial Doppler may serve as a useful, non-

invasive, tool for the initial assessment and follow up of the patients. Weight loss seems to be beneficial and preventive of significant visual impairment along with proper medical treatment and adequate psychological support, although more research is required in this field.

References

1. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. *Neurology* 2002; 59: 1492-1495.
2. Baker RS, Carter D, Hendrick EB, Buncic JR. Visual loss in pseudotumor cerebri of childhood. A follow-up study. *Arch Ophthalmol* 1985; 103: 1681-1686.
3. Grant DN. Benign intracranial hypertension. A review of 79 cases in infancy and childhood. *Arch Dis Child* 1971; 46: 651-655.
4. Soler D, Cox T, Bullock P, Calver DM, Robinson RO. Diagnosis and management of benign intracranial hypertension. *Arch Dis Child* 1998; 78: 89-94.
5. Sugerman HJ, DeMaria EJ, Felton WL, 3rd Nakatsuka M, Sismanis A. Increased intra-abdominal pressure and cardiac filling pressures in obesity-associated pseudotumor cerebri. *Neurology* 1997; 49: 507-511.
6. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000; 320: 1-6.
7. Gordon K. Pediatric pseudotumor cerebri: descriptive epidemiology. *Can J Neurol Sci* 1997; 24: 219-221.
8. Cinciripini GS, Donahue S, Borchert MS. Idiopathic intracranial hypertension in prepubertal pediatric patients: characteristics, treatment, and outcome. *Am J Ophthalmol* 1999; 127: 178-182.
9. Distelmaier F, Sengler U, Messing-Juenger M, et al. Pseudotumor cerebri as an important differential diagnosis of papilledema in children. *Brain Dev* 2006; 28: 190-195.
10. Rangwala LM, Liu GT. Pediatric idiopathic intracranial hypertension. *Surv Ophthalmol* 2007; 52: 597-617.
11. Mehta SR, Afenyi-Annan A, Byrns PJ, Lottenberg R. Opportunities to improve outcomes in sickle cell disease. *Am Fam Physician* 2006; 74: 303-310.
12. Razumovsky AY, Gillard JH, Bryan RN, Hanley DF, Oppenheimer SM. TCD, MRA and MRI in acute cerebral ischemia. *Acta Neurol Scand* 1999; 99: 65-76.
13. Binder DK, Horton JC, Lawton MT, McDermott MW. Idiopathic intracranial hypertension. *Neurosurgery* 2004; 54: 538-551.
14. Liu GT, Glaser JS, Schatz NJ. High-dose methylprednisolone and acetazolamide for visual loss in pseudotumor cerebri. *Am J Ophthalmol* 1994; 118: 88-96.