

Pseudotumor cerebri in pediatric age: role of obesity in the management of neurological impairments

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Pseudotumor cerebri occurs quite rarely in the pediatric population and its clinical features differ from adults in many ways. Intracranial hypertension with papilledema should obviously be treated promptly to avoid permanent visual damage, but various more or less invasive options have been proposed over the years, from bariatric surgery for obesity to optic nerve sheath fenestration. We report a prospective study on a group of 15 children, aged 3–16 years, with clinical and instrumental diagnosis of pseudotumor cerebri. All the patients were treated simply by external lumbar cerebrospinal fluid drainage with a mean volume of 10 ml/h for 3–5 days, with hypocaloric diet and with appropriate dosages of acetazolamide. All had immediate relief of headache, a considerable reduction in papilledema and marked improvement of both visual loss and cranial nerve palsies within 2 months. None of the patients relapsed during the follow-up period, ranging from 12–48 months.

Keywords: Pseudotumor cerebri, idiopathic intracranial hypertension, papilledema, obesity

Introduction

Idiopathic intracranial hypertension or pseudotumor cerebri is a pathological condition characterized by intracranial hypertension, with pressure values of more than 20 cmH₂O, and normal cerebrospinal fluid (CSF) composition, in the absence of intracranial lesions or other underlying systemic causes. Its occurrence is quite rare in the pediatric population. The syndrome is typically found in young obese females with long-lasting headache, papilledema and visual impairment at neurological examination.^{1,2} Neuroimaging is characterized by normal or small ventricular size with signs of intracranial hypertension, particularly enlargement of the suprasellar

cisterns (empty sellae), reversal of the optic nerve head and optic nerve sheath tension.^{2–4} In obesity-related pseudotumor, weight loss by dieting or by bariatric surgery has been associated with resolution of marked papilledema⁵ and of idiopathic intracranial hypertension.^{6–10} Pseudotumor in pediatric patients presents some atypical features. Younger children with idiopathic intracranial hypertension are less likely to be obese than are older children or adults.^{11–13}

Relief of headache and preservation of visual function are the main treatment goals. The approach to pseudotumor cerebri management includes medical and surgical options. Acetazolamide is the first-line drug used to lower intracranial pressure by decreasing CSF production; steroids are also helpful in continuing and enhancing the effect of acetazolamide.^{5,14} When medical treatment fails, a surgical solution is required, provided by ventriculoperitoneal or lumboperitoneal shunts or by optic nerve sheath fenestration. When signs and symptoms are serious

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and the risk of visual loss is high, medical treatment does not rapidly lower intracranial hypertension, especially in small children, who do not seem to respond easily to medication.¹⁵

The need for immediate treatment to lower intracranial hypertension in children with severe papilledema and visual loss, while avoiding major surgery, has only been sporadically reported in literature.^{12,16}

We decided to adopt a protocol of extensive external lumbar cerebrospinal fluid drainage in order to test the efficacy of this technique not only in emergent situations but also in definitive treatment of this rare, still unclear pathology.

Patients and methods

During the last 5 years, 15 pediatric patients with a suspected diagnosis of pseudotumor cerebri or

idiopathic intracranial hypertension were enrolled in this study (Table 1). Four were females and 11 males; their age ranged from 3–16 years and all came to our attention for visual loss and/or papilledema at fundus oculi examination.

In a 3-year-old female (patient no. 12), irritability and weight loss were the cause of hospital admission. In one 11-year-old boy (patient no. 3), ophthalmoplegia of sudden onset with IV and VI nerve palsy bilaterally was the first sign of intracranial hypertension. Patient no. 9 had been diagnosed with pseudotumor some months previously due to headache and was receiving medical treatment. He was brought to our attention after the onset of ptosis in the right eye.

All patients underwent ophthalmological examination adapted to the child's age, with visual acuity testing, optic disc evaluation, visual field evaluation and ocular motility testing (Fig. 1). Patients then underwent MRI and MR-

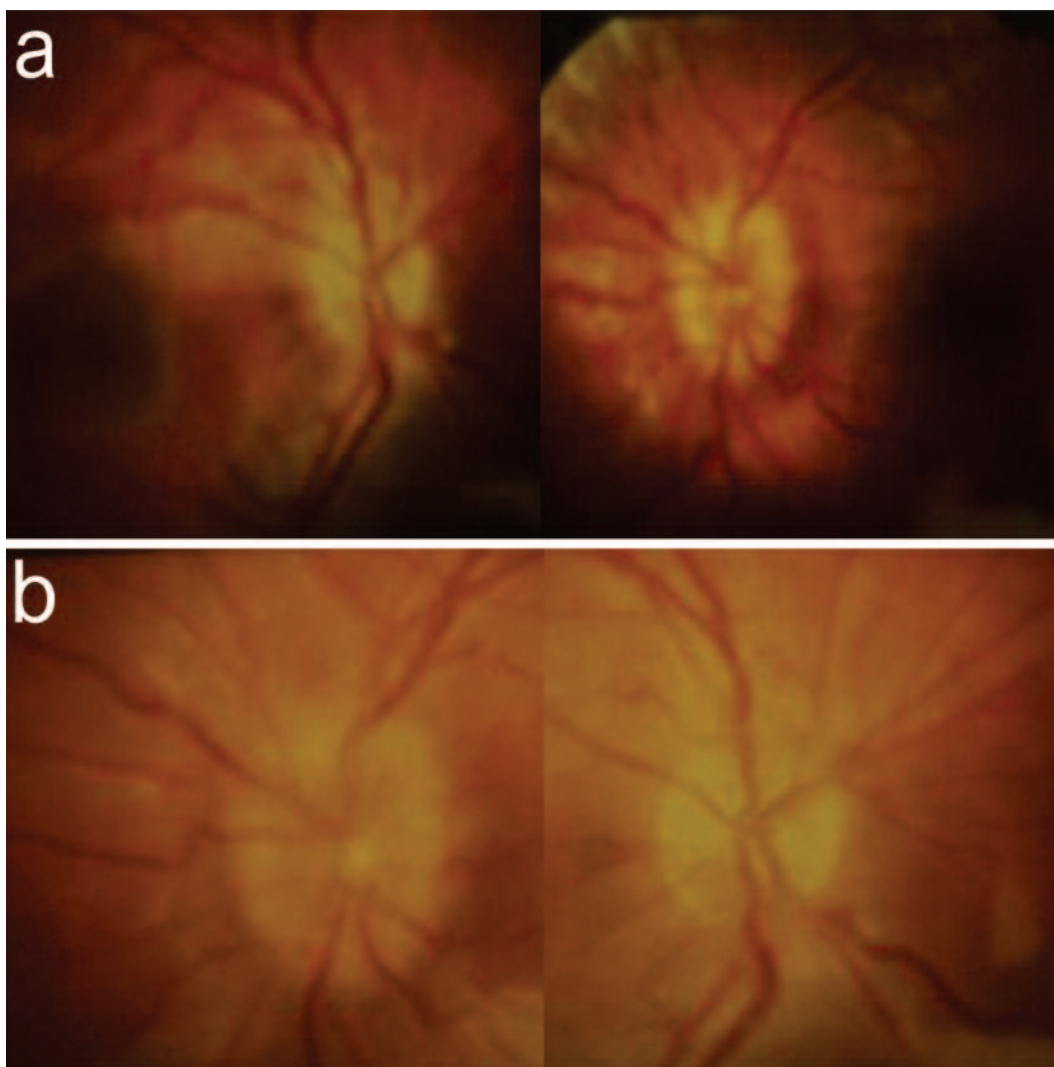


Figure 1 Patient 3. (a) Pre-operative ophthalmological evaluation with bilateral papilledema at optic disc evaluation. (b) Postoperative ophthalmological evaluation at 2-month follow-up: resolution of the papilledema in the left eye and significant reduction of the papilledema in the right eye

Table 1 Results of CSF lumbar draining in 15 pediatric patients with pseudotumour cerebri showing persistence of tension in the optic nerve sheaths

Patient	Age	Sex	Weight (kg)	VISUS (/10)	Edema papilla	ICP (cmH ₂ O)	Fundus (at 60 days)	VISUS (/10) (at 60 days)	Weight (kg, at 1 month)
1	13	M	77	OO 7	OO	27	NO	OO 8	-4 ^a
2	6	M	25	OD 5, OS 6	OO	25	NO	OD 7, OS 8	-4 ^a
3	11	M	61	OD 2, OS 6	OD>OS+ VI-VI nerves palsy bilateral	30	NO	OO 8	-2 ^a
4	7	F	34	OD 7, OS 9	OD>OS	24	NO	OD 8, OS 10	-2 ^a
5	15	M	100	OO 10	OS>OD	26	NO	OO 10	-0 ^a
6	12	M	71	OO 6	OD>OS	22	NO	OO 8	-5 ^a
7	13	M	60	OO 10	OO	21	NO	OO 10	-4 ^a
8	14	F	79.5	OD 5, OS 6	OO	28	NO	OD 7, OS 9	-5 ^a
9	10	M	48	OD 7, OS 7 Ptosid dx	OO	25	NO	OD 8, OS 8	-3 ^a
10	16	F	100	OD 3, OS 2.1	OO	26	NO	OD 7/8, OS 8/9	-7
11	13	M	94	OD 10, OS 8	OS	22	NO	OD 10, OS 10	-4
12	3	F	10	OO 4	OO	22	NO	OO 8	-4
13	5	M	24	OD 5, OS 9	OD	30	NO	OD 8, OS 9	-4
14	9	M	39	OO 7	OO	32	NO	OO 8	-4
15	7	M	35	OD 7, OS 3	OS>OD	26	NO	OD 9, OS 8	-4

^aIndicates -5% of body weight.

venography to exclude thrombosis of dural sinuses. Neuro-imaging was significant for the presence of tension of the optic nerve sheaths, reversal of the optic nerve head and empty sellae (Fig. 2). Intracranial pressure was measured for 12 h during the night with a lumbar catheter: all patients had a mean pressure of over 20 cmH₂O.

Only 9 out of 15 patients were obese; notably, the older patients were more obese. The six patients with normal weight were aged 3–9 years, and a 3-year-old child among these was underweight.

The treatment protocol consisted of:

1. Positioning a lumbar drainage with a CSF flow of 10 ml/h.
2. Medical treatment with acetazolamide: the dose was regulated according to body weight, up to a maximum of 1.5 g/day. Medical treatment was continued in all patients for at least 1 month.
3. The diet for the obese or overweight patients, focused on the loss of 5% of body weight in the first month and then continued gradually until reaching the ideal body weight for that age.

Patients were followed clinically and with a fundus oculi examination after 14 days, 30 days and 2 months. MRI was performed 2 months after discharge.

Results

Response to treatment was immediate and substantial in all patients. All had relief of severe headache just a

few hours after the start of cerebrospinal fluid removal. The lumbar drainage was kept in place for 3 days for all children; in just two cases, it was kept for two more days because of the persistence of slight, but not severe, headache on the third day.

We treated 15 children aged 3–16 years, 8 children of prepubertal age and 7 of pubertal age. The prepubertal group, composed of patients aged 3–11 years, with a male:female ratio of 6:2, and only 2 out of 8 children were overweight or obese. One 3-year-old child was underweight and was admitted to hospital because of irritability with anorexia. One 11-year-old boy (patient no. 3) presented with bilateral ophthalmoplegia due to IV and VI cranial nerve palsy and marked visual loss in his right eye (2/10). In addition to medical treatment, another patient with a previous diagnosis of pseudotumor (no. 9) was brought to our attention because of the onset of ptosis of his right eye. The initial symptom in the other 5 young children was headache. All the patients presented papilledema and visual loss.

The pubertal group, composed of patients aged 12–16 years, a male:female ratio of 5:2, and all were overweight or obese. Headache was the main disturbance in all, with visual loss in 5; papilledema was always present. Hence, in accordance with the literature, our prepubertal patients had atypical features of pseudotumor, *i.e.* the pathology was not related to female gender or obesity,^{13,17} and isolated oculomotor palsy was the only symptom in some cases.¹⁸ By contrast, our series differed from those in the literature in its predominance of pubertal males,

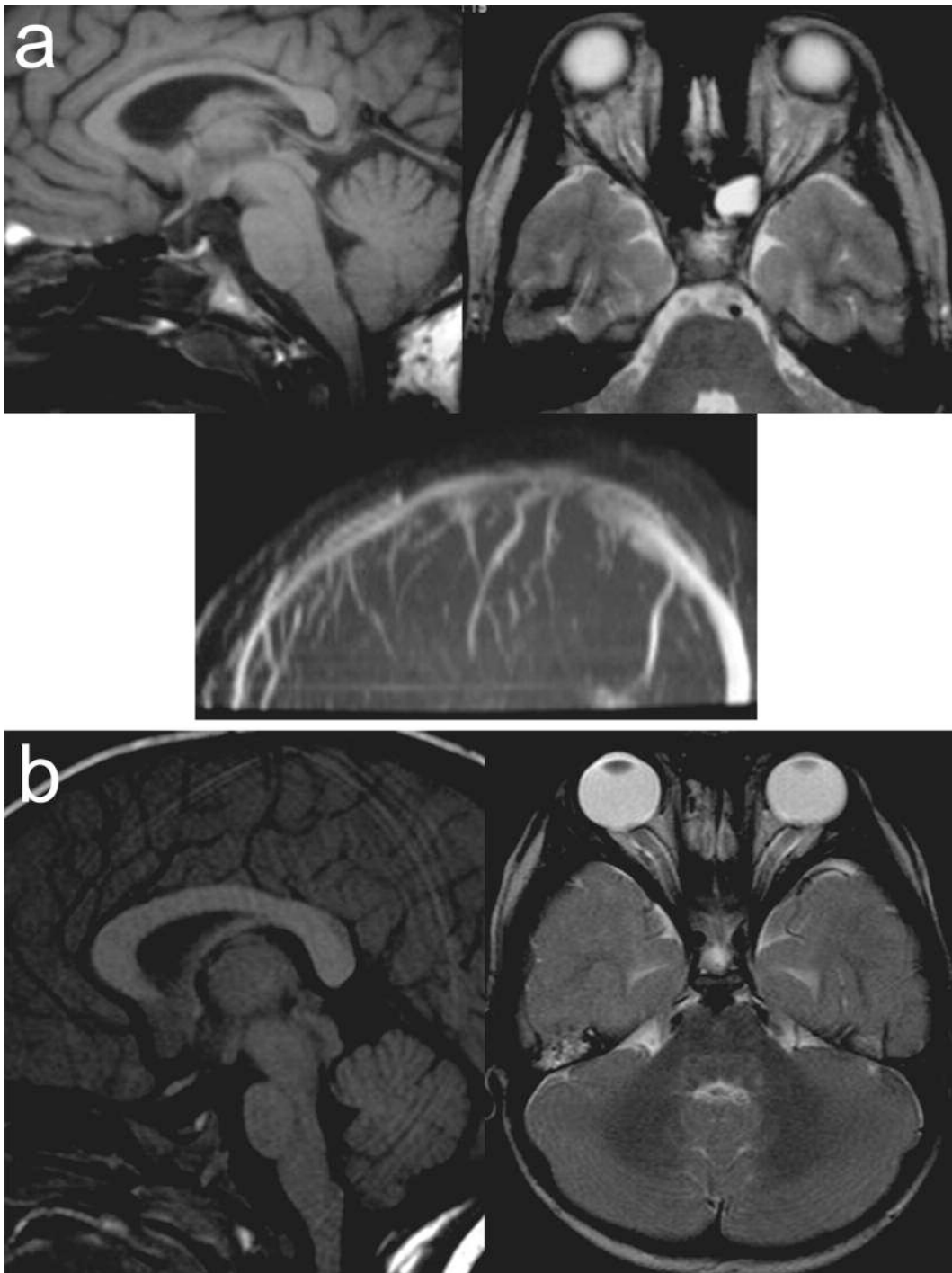


Figure 2 Patient 3. (a) Pre-operative MRI sagittal T1- and axial T2-weighted images revealing empty sellae, enlarged optic nerve sheaths and reversal of the optic nerve head. MR-venography does not show any dural sinuses thrombosis. (b) Postoperative MRI: sagittal T1-weighted images showing the reduction of tension in the suprasellar cisterns and axial T2-weighted images

although the small size of our population precludes analysis of statistical significance.

In 13 out of 15 cases, the initial resolution of papilledema was already present at fundus oculi examination 14 days after treatment. Papilledema was considerably reduced in all children at 2-month follow-

up. There was marked regain of visual function at 2 months in all 13 patients with a visual defect at the time of admission. The highest recovery was in patients with the worst visual acuity at baseline (patient nos. 3, 10, 12 and 15). The two children with ophthalmoplegia recovered completely in 1 month (patient nos. 3 and 9).

MRI performed 2 months after discharge showed improvements in 11 out of 15 patients. At 2-month MRI, only two patients (nos. 4 and 12) presented complete resolution of the signs of intracranial hypertension: dilatation and tension of the optic nerve sheaths and suprasellar cisterns was no longer evident. In 9 children, the MRI improved to different degrees of normalization (Fig. 2). In 4 patients (nos. 5, 6, 8, 10) there was no, or very little, improvement, besides the clinical success. All four patients were obese, and were aged from 12–16 years. Improvement was substantial only in the MRI performed 6 months after treatment, and slowly continued at subsequent follow-up examinations.

The 9 obese or overweight patients followed a diet from the start of treatment. Seven managed to lose 5% of their body weight in the first month, but only 5 were able to achieve the ideal weight for their age in a mean time of 20 months. The other two were still overweight after 12 months. Two obese patients failed to lose 5% of body weight in the first month (patients nos. 3 and 5), and one did not lose any weight in the first 3 months, although headache and papilledema were resolved. This patient's MRI did not change at all in the first month, and we observed a slight improvement in optic nerve sheath tension only 6 months later.

None of the 15 patients presented any relapse of signs and symptoms of intracranial hypertension during the clinical follow-up period, ranging from 12–48 months. Neuro-imaging follow-up clearly improved in 11 out of 15 patients, and slightly improved, but did not worsen, in four.

Discussion

Idiopathic intracranial hypertension is a pathological condition caused by raised intracranial pressure of unknown origin.¹⁹ The pathophysiology consists of increased resistance to cerebrospinal fluid outflow at the arachnoid granulations due to increased venous pressure.²⁰ The syndrome is typically found in young obese females with long-lasting headache.^{1,2}

The link between obesity and raised intracranial pressure is probably due to high central venous pressure that increases the pressure in the intracranial dural sinuses. Severe venous stasis develops as a result of increased intra-abdominal pressure typical of obesity.^{7,21} Diagnostic cerebral venography with measurement of pressures in both the right atrium and cerebral venous sinuses has been part of the routine examination in obese-related pseudotumor in recent studies.⁷ In obesity-related pseudotumor, weight loss

by dieting or by bariatric surgery has been associated with resolution of marked papilledema⁵ and of idiopathic intracranial hypertension.^{6–10}

Pseudotumor in pediatric patients presents some atypical features. Younger children with idiopathic intracranial hypertension are less likely to be obese than are older children or adults.^{11–13} In particular, in the prepubertal population, idiopathic intracranial hypertension does not occur predominantly in females and is not associated with obesity.^{13,17} Patients of prepubertal age, including patients aged less than 11 years, are also atypical because they do not respond to medical treatment as promptly as do patients in pubertal age or adult patients.¹⁵

Treatment of pseudotumor is symptomatic and includes different pharmacological and surgical strategies. First-line treatment includes acetazolamide,^{5,14} corticosteroids and diet, where obesity is present. Refractory syndromes are treated with lumbo-peritoneal shunts or optic-nerve-sheath fenestration. Severe visual loss, severe papilledema and ophthalmoplegia need urgent treatment. Medical treatment is effective, but not immediate.

We used acetazolamide for many years, with unsatisfactory results – a too long period of time to obtain satisfactory results for both the headache and the papilledema. Only long-term therapies obtained some positive results, but very slowly. We have no experience with topiramate, although there is only one pediatric report on headache in the literature.²²

The choice of an invasive treatment was due to the presence of papilledema (15 out of 15 patients) and visual loss (14 out of 15 patients) and to the need to reduce the intracranial pressure as soon as possible. The use of acetazolamide was, therefore, associated with lumbar CSF drainage from the beginning of treatment in all patients, and was not the alternative in patients refractory to conservative treatments.

In the literature, there are sporadic descriptions of emergency treatment with a lumbar cerebrospinal fluid tap, with immediate improvement of symptoms and gradual recovery of visual acuity in the following days.^{12,16} In the case of visual loss and papilledema, surgical treatment is required if medical treatment is not immediately effective and neurological defects are not improving. In view of the benefits of the lumbar cerebrospinal fluid tap, we decided to adopt a lumbar catheter for constant, continuous lumbar cerebrospinal fluid drainage, with a CSF flow of 10 ml/h. A single spinal tap, with the removal of 30–40 ml of cerebrospinal fluid, is useful but it is at risk for relapse considering the CSF production (CSF production is

about 240–250 ml/day). The removal of 250 ml/day for 3–5 days can effectively decrease intracranial pressure and keep it at normal values for a few days, giving improvement to CSF hemodynamics which leads to an immediate and stable improvement of symptoms in patients. In our population, papilledema was slightly reduced at fundus oculi examination 14 days after treatment in 13 out of 15 cases, and considerable reduced in all patients 2 months later. Regaining visual function was marked at 2 months in all 13 patients with visual impairment at the time of admission. All patients immediately started acetazolamide therapy, which was administered for 1 month. Obese patients also went on a diet.

The lumbar drainage was well tolerated and resolved neurological signs and symptoms within 2 months. This prevented visual loss from worsening while adopting solely medical treatment, and shortened the length of acetazolamide therapy. No complications occurred.

The clinical improvement, with resolution both of the headache and of the papilledema, is probably due to the reduction of the values of intracranial hypertension, but not to the normalization of the values themselves, which probably will need more time: we expect normalization of MRI imaging will take years. Patients described above had an initial improvement only at the 6-month MRI follow-up, and further improvements at 12–18 months; the imaging we report is the first after clinical improvement, made only 2 months after discharge.

No relapses were observed on clinical and neuro-radiological follow-up examination held every 3 months for the first year and then once a year. The average follow-up time was 25 months.

None of the 15 children in this study underwent major surgery, such as VP or LP shunt or optic-nerve-sheath fenestration. Rapid and effective resolution of these pathological conditions also had a beneficial psychological effect on parents, who find it hard to tolerate long-standing medication of their children.

In the literature,²³ we found association of pseudotumor cerebri from sinus venous thrombosis with polycystic ovary syndrome and hereditary hypercoagulability.

Concerning the evidence of polycystic ovary syndrome, our female patients were only 4 out of 15, aged 3, 7, 14, and 16 years. Polycystic ovary syndrome was not detected in the two pubertal age girls.

Testosterone serum levels were on the average values in 13 out of 15 patients. Only in patients 5 and 11 (two obese patients) were testosterone serum values higher than normal.

On the exclusion of sinus venous thrombosis, all patients underwent MRI venography as protocol, and sinus venous thrombosis was always excluded. D-Dimer values and other hemocoagulative parameters were within normal ranges.

Conclusions

Pseudotumor cerebri in pediatric patients presents some atypical features. In particular, younger children with idiopathic intracranial hypertension are less likely to be obese than older children or adults.^{11–13} The younger the children, the less is the role of obesity in determining intracranial hypertension and more difficult is the management of neurological impairment. We are aware that predictive models are not applicable to such a small population, but the positive results of our minimally invasive management of pseudotumor cerebri with external lumbar drainage must be taken into consideration especially if neurological signs are present and severe, if there is no obesity to treat and if a rapid decision is required.

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