Evaluation of sixteen children with pseudotumor cerebri

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Pseudotumor cerebri (PTC) is a clinical condition characterized by signs and symptoms of increased intracranial pressure, such as headache and papilledema. A total of 16 patients diagnosed with PTC [12 (75%) female; 4 (25%) male] were included in the study. The age of onset of symptoms was 123.4±34.3 months (range: 60–168 months). Obesity was found in four (25%) of them. Two patients had venous sinus thrombosis, two had corticosteroid withdrawal, and one had posttraumatic PTC. The most common symptom was headache, recorded in 93.8% of the patients. All patients were treated medically. Two patients in our group also required a lumboperitoneal shunt. In conclusion, PTC in children is rare. Both papilledema and sixth nerve palsy resolved rapidly with treatment. However, children can sustain loss of visual field and visual acuity despite treatment.

Key words: pseudotumor cerebri, treatment, children.

Pseudotumor cerebri (PTC) is characterized by signs and symptoms of increased intracranial pressure, such as headache and papilledema, absence of an intracranial mass lesion or ventricular dilatation, usually normal findings on neurological examination except for papilledema, and an occasional abducens nerve palsy.

The annual incidence of PTC in the general population is 1 per 100,000[1]. PTC in children is rare and has different characteristics from that in adults. Although secondary causes for PTC are less commonly identified in adults (most of whom are obese), 53.2-77.7% of pediatric cases have been associated with identifiable conditions, the most common of which include endocrine abnormalities, trauma, drugs, and infections[2-4].

The prognosis seems to be better in children than in adults. Spontaneous remission may occur even following the diagnostic lumbar puncture. PTC is possibly an under-recognized disorder in children and adolescents.

The aim of this study was to determine the clinical characteristics of PTC in children.

Material and Methods

We reviewed patient charts from the Pediatric Neurology Clinic with respect to those diagnosed with PTC over the past 10 years. Diagnosis of PTC was made according to the modified Dandy criteria (Table I)[5]. Each patient's chart was reviewed to collect the following clinical information: age, sex, weight, medical history, presenting symptoms, imaging results, and treatment. Obesity was defined as a body weight percentile ≥95% for age.

All patients underwent a complete general, neurological and ophthalmologic examination, including Snellen visual acuities, ophthalmoscopy and Goldmann kinetic perimetry when age permitted. All underwent brain computed tomography (CT) scanning or magnetic resonance imaging (MRI). Magnetic resonance venography (MRV) was done in 14 patients. To obtain pressure measurements and a sample of the cerebrospinal fluid (CSF) for cellular, chemical and microbiological examination, a lumbar puncture (LP) was performed. To establish underlying causes of secondary PTC, extended laboratory work-up was done, including screening for anemia, chronic infection and endocrine abnormalities.

Results

Sixteen patients, 12 females (75%) and 4 males (25%), were identified with a confirmed

Table I. Modified Dandy Criteria for PTC

1. Signs and symptoms of increased intracranial pressure
2. No localizing neurological signs except for unilateral or bilateral cranial nerve VI palsy
3. Increased cerebral spinal fluid opening pressure but otherwise normal cytologic and chemistry values
4. Normal symmetric ventricles must be demonstrated by neurological imaging

diagnosis of PTC based on the modified Dandy criteria. Mean age was 123.4±34.3 months (range: 60–168 months).

The most common symptom in our patients was headache, which was noted in 93.8%. The clinical symptoms of our patients are shown in Table II. Papilledema was found in 15 patients. In the neurological examination, 6 patients (37.6%) had abducens nerve palsy and 2 patients (12.4%) had oculomotor nerve palsy with abducens nerve palsy. Obesity was present in 4 of the 16 children (25%), and all of them were female.

Eleven patients were accepted in the primary PTC group as no probable precipitating cause could be identified; 4 patients had obesity. The remaining 5 of the 16 patients were in the secondary PTC group. Two of them had venous sinus thrombosis on MRI/MRV, and one of these children had nephrotic syndrome. Two patients had PTC resulting from corticosteroid withdrawal. These patients had been using oral corticosteroid for familial Mediterranean fever (FMF) and juvenile rheumatoid arthritis (JRA) in recent years. Another patient had posttraumatic PTC. The mean CSF opening pressure was 450.8±12.7 mm H_2O (range: 320–700 mm H_2O).

All patients were treated with acetazolamide. In addition, 5 of them were given oral corticosteroid, 2 took furosemide, 2 took topiramate, 2 took enoxaparin sodium for venous sinus thrombosis, and 2 were treated for FMF and JRA. Lumboperitoneal shunts were placed in 2 patients as they continued to deteriorate despite medical therapy. Two patients received anticoagulation with enoxaparin sodium for venous sinus thrombosis, and all demonstrated substantial or complete thrombus resolution on follow-up imaging studies.

Table II. Clinical Symptoms of Our Patients

	Number (n = 16)	%
Headaches	15	93.8
Visual loss	7	43.7
Diplopia	6	37.5
Nausea and vomiting	5	31.3
Vertigo	1	6.25

The mean duration of medical treatment was 6.5±2.3 months (range: 4–12 months). Patients were seen by an ophthalmologist and a pediatric neurologist at four-week intervals. All patients were under follow-up at least one year. In 15 patients, the visual field grade improved, while in one patient it worsened.

Discussion

Pseudotumor cerebri (PTC) in children is rare and its clinical profile differs greatly from the adult type. Babikian et al.[6] found that most children (60%) with PTC were older than 10 years of age. In our patients, the mean age was 10 years. Although the range of normal intracranial pressure in a child is unknown, a pressure of 200 mm H_2O may not be elevated in a crying child. However, opening pressures in all our patients were ≥200 mm H_2O and were obtained in a relaxed child, as described above.

According to the literature, there are many conditions associated with PTC in children, as shown in Table III[7]. Tibussek et al.[8] described a secondary cause of PTC in 37.7% of the 53 children with PTC. Kesler et al.[3] reported the etiology of PTC in 14.8% of the 27 patients. In their series, the only condition found that may be associated with PTC was drug use. Furthermore, overweight or obesity was found in 16 (59%) patients. In our study, five patients were in the secondary PTC group. Two patients had venous sinus thrombosis, two had corticosteroid withdrawal, and one had posttraumatic causes. The association of PTC with obesity and overweight was more pronounced in the pubertal age group. Tibussek et al.[8] reported obesity in 16.9% of 53 with

Table III. Classification of Pseudotumor Cerebri in Children

1. Primary pseudotumor cerebri
No recognized cause (idiopathic pseudotumor cerebri)
2. Secondary pseudotumor cerebri
A. Pseudotumor cerebri associated with neurological disease:
Dural venous sinus thrombosis (associated with otitis media, mastoiditis, or head trauma)
Altered CSF composition (meningitis)
Arteriovenous malformation draining into a venous sinus Gliomatosis cerebri
B. Pseudotumor cerebri secondary to systemic disease:
Malnutrition
Systemic lupus erythematous
Addison disease
Severe anemia (aplastic or iron deficiency)
C. Pseudotumor cerebri secondary to ingestion or withdrawal of exogenous agents:
Corticosteroid withdrawal
Tetracycline or minocycline therapy
Vitamin A intoxication
Nalidixic acid (used in treatment of urinary tract infection)
Thyroxine replacement in hypothyroidism
Danazol, Danocrine (used for endometriosis or autoimmune hemolytic anemia)

PTC. Obesity was found in four patients (25%) in our group.

In PTC, while headache, nausea and vomiting are known classic symptoms, patients may complain of blurry vision, diplopia and stiff neck as well. Other reported symptoms include photophobia, anorexia, retro-orbital pain, light-headedness, myalgia, and head tilt[2,9].

Headache is the most common complaint among children with PTC and has been documented in 62-91% of cases. Distelmaier et al.[10] described 12 patients (66.7%) who presented with headache. In the majority of our cases, the most common symptom was headache, which was noted in 93.8% of patients. It was the presenting symptom of the patients. Papilledema has generally been regarded as a hallmark physical finding of PTC. Most often the papilledema is bilateral, although it can be asymmetric or unilateral as well. Tibussek et al.[8] found papilledema in 86.7% of the 53 patients. In another series, Distelmaier et al.[10] reported that papilledema was present in all cases. We detected papilledema in 15 patients. Sixth nerve palsy is the most common diagnostic feature with PTC and has been reported in 9-48% of the pediatric population[6]. Additionally, palsies of cranial nerves III, IV, VII, IX, and XII have also been noted in children[3,6]. In the series of Phillips et al.[11], children younger than 11 years were more likely to have cranial nerve deficits (59%) compared with older children (39%). We found that six patients had abducens nerve palsy and two patients had oculomotor nerve plus abducens nerve palsy in our series. In our patients, six patients (37.5%) had diplopia that was caused by oculomotor nerve palsy, which is very unusual in adults. Visual loss has been reported in 17 to 33% of childhood PTC[9,12]. We found visual loss in 43.8% of our patients.

After diagnosis of PTC, treatment is directed toward decreasing intracranial pressure, which can be achieved by either medical or surgical therapy. The treatment aims of PTC are the relief of symptoms and the preservation of visual function. Acetazolamide was the drug of choice for the initial treatment. Other treatment agents are furosemide, prednisone and topiramate[8,13]. All patients were treated with acetazolamide. In our group, two patients were taking acetazolamide and topiramate together. These patients who took topiramate had a substantial weight loss. Modification of

therapy was based on a combination of the patient's symptoms, visual-field examinations and changes in papilledema. As a result, when medical treatment remains ineffective and visual function deteriorates, surgical treatment should be considered.

Orssaud et al.[14] described PTC in 22 children. Medical treatment was successful in seven children; however, the remaining 15 patients required a lumboperitoneal shunt because of elevated intracranial pressure, no response to the medical therapy, or threatened vision. Tibussek et al.[8] treated two of 53 children with PTC with lumboperitoneal shunt.

In our group, only three patients developed a progressive papilledema and visual function deterioration, despite the modification of treatment. Therefore, two of the three patients finally underwent successful ventricular–peritoneal shunting, which could be done without complication. The other patient was referred to the surgery center for optic nerve sheath fenestration, but the parents refused this therapy. After six months, the patient was admitted to hospital and optic atrophy was established on the right eye. We want to emphasize the favorable outcome in our children; only one patient lost visual acuity.

In this retrospective study, medical therapy appeared successful in treating pediatric PTC in most patients. Permanent optic atrophy is a severe complication when patients do not respond to medical and surgical treatment. Nevertheless, despite adequate treatment, children can sustain loss of visual field and acuity rarely; thus, prompt diagnosis and management are important.

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