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Original Article

Long-Term Follow-up of Pseudotumor Cerebri Syndrome in Prepubertal Children, Adolescents, and Adults

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ABSTRACT

Purpose: Pseudotumor cerebri syndrome can have a recurrent course. We compared the long-term disease course, recurrences, and final visual outcomes in prepubertal children, adolescents, and adults.
Methods: In this retrospective observational study, patients were divided into prepubertal children (group A) adolescents (group B), and adults (group C).
Results: Sixty-five patients (56 females, nine males) were included, 26.2% in group A, 24.6% in group B, and 49.2% in group C. Age at diagnosis was 8.6 ± 2.0 years, 14.3 ± 1.5 years, and 31.9 ± 9.7 years for the prepubertal children, adolescents, and adults, respectively. Medical treatment duration was similar (2.4 to 3.3 years, $P > 0.05$). Recurrences were observed in 23.5% of prepubertal children, 50% of adolescents, and 28.1% of adults. Recurrences occurred within 1.3 ± 0.6 years from treatment cessation in the prepubertal group compared with 3.8 ± 5.1 years in adolescents and 2.7 ± 2.0 years in adults ($P = 0.267$). Optic neuropathy was evident in 41% of group A, 31% of group B, and 87.5% of group C ($P < 0.001$). Obesity and cerebrospinal fluid opening pressures were unassociated with either relapsing rates or final visual outcomes in all groups.
Conclusions: Pseudotumor cerebri syndrome exhibits a relapsing course in a third of cases. Recurrences tend to occur within one year after treatment cessation in prepubertal children, and within three years in older patients, revealing the importance of longer follow-up, especially in adults. Optic neuropathy was more common in adults along with a tendency for visual decline. Longer treatment times were associated with fewer recurrences.

Introduction

Pseudotumor cerebri syndrome (PTCS) is a disorder of cerebrospinal fluid (CSF) circulation.[1] The term *PTCS* is used to include both primary (when no clear cause for intracranial hypertension is observed) and secondary intracranial hypertension.[2] There is a trend in the medical literature to use either the term primary or the term secondary intracranial hypertension. However, because this study includes only the primary causes of PTCS, we will solely use the term PTCS for simplicity. PTCS is defined as elevated intracranial hypertension (higher than 25 cm H_2O in adults and 28 cm in children or higher than 25 cm if the child is not sedated and not obese) together with normal neuroimaging, CSF composition, and neurological examination except for cranial nerve abnormalities with either papilledema or abducens nerve palsy,[2] in the absence of other known etiologies. PTCS primarily affects young obese females and potentially causes severe headaches,[3] pulsatile tinnitus, and several visual disturbances, such as transient visual disturbances (TVO), blurred vision, and diplopia.[4] The principal consequence of PTCS is visual loss if not treated promptly.[5-7] The annular incidence of PTCS in adults is reported to be between 0.9 and 2.36 per 100,000

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persons, whereas in the pediatric population it is 0.63 per 100,000 persons.[8]

PTCS is highly associated with obesity,[9] which is present in more than 70% of the diagnosed patients. Obesity and weight gain are also considered well-known risk factors related to PTCS development, progression, and recurrences in adults[10,11] as well as in adolescents.[12-14] However, in prepubertal children, PTCS is less strongly associated with obesity.[12,15] Some studies have demonstrated body mass index (BMI) to be associated with CSF opening pressures[16,17] and weight reduction to be strongly associated with a decrease in intracranial pressure.[18]

The data concerning the clinical course in prepubertal patients with PTCS are limited. Some previous reports have shown a relatively benign course in children when compared with adults,[19] whereas others describe a much more severe visual loss.[20] Although PTCS of prepubertal children and adults involves heterogeneous groups, a comparative study between them may demonstrate whether the disease course, recurrence rates, and final visual outcomes are similar or not. We therefore conducted a study aiming to characterize these groups in terms of their disease progression, symptom presentation, and long-term follow-up outcomes.

Methods

We performed a retrospective observational cohort study at two tertiary medical centers, Kaplan Medical Center and Schneider Medical Center. Individuals diagnosed from January 1983 and January 2003, respectively, until December 2014 were included. The study followed the tenets of the Declaration of Helsinki, and approval was obtained from the hospital administrations and local ethics committees.

Patients

We included newly diagnosed patients with PTCS, who were evaluated and followed by two neuro-ophthalmologists from the two tertiary medical centers and were treated by the neuro-ophthalmology clinics. The minimal follow-up period was five years (Fig). All patients underwent complete neuro-ophthalmologic examinations including visual acuity, color vision, pupillary function assessment, extraocular eye movement examination, slit-lamp examination with dilated fundoscopy, and visual field testing by either a Humphrey automated visual field test or confrontation in younger and less cooperative patients. In addition to a lumbar puncture, computed tomography or magnetic resonance imaging were performed to rule out sinus vein thrombosis and intracranial-space-occupying lesions. All patients were diagnosed according to the revised diagnostic criteria for PTCS in adults and children as outlined by Friedman et al. in 2013.[2] Data regarding height and weight (kilograms) were used to calculate BMI or *z* scores. In adults, overweight was defined as a BMI above 25.

Exclusion criteria included all identifiable secondary medical conditions that may be associated with increased intracranial pressure due to underlying neurological, systemic, or metabolic diseases or cases that were secondary to the use of medications. In addition, we excluded all those who did not complete a follow-up of at least five years.

Outcome measures

Patients were categorized into prepubertal children (younger than 12 years, group A), adolescents (aged 12 to 17 years, group B), and adults (18 years or older, group C).

Patients' medical records were reviewed for demographic data, past ocular and systemic medical history, type of treatment, and response and recurrence rates. Special attention was given to the age of onset; presenting signs and symptoms such as headaches, TVO, tinnitus, diplopia, and cranial nerves palsies; duration of symptoms; CSF opening pressures; visual acuities; visual fields; and final visual outcomes. Primary outcomes were treatment duration during first and following episodes, recurrence rates, and final visual outcomes.

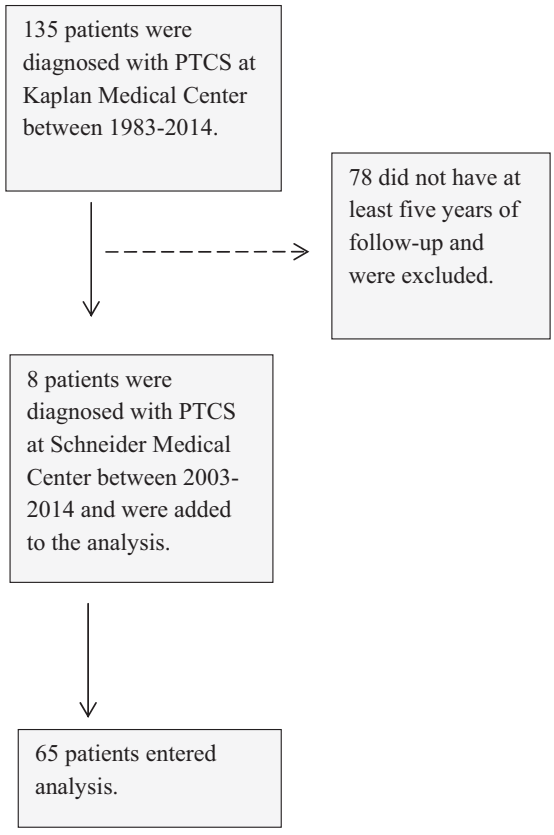

FIGURE. Flowchart of the patients included in the analysis.

Secondary outcomes were recurrence duration, response to therapy, and recurrence-free time.

Outcome definitions

Remission was defined as a period of at least six months without medical treatment, without headaches (if they were part of the complaint), and improvement in optic nerve functions. In addition to improvement or no deterioration of the visual fields, resolution of papilledema was also considered remission if it was documented.

Recurrence was defined as secondary appearance of a new disc edema or new sixth cranial nerve palsy in conjunction with elevated intracranial pressure by lumbar puncture in combination with the clinical symptoms for recurrences, which were defined as the presence of headaches and diplopia, after being free of symptoms and signs for at least six months.

Optic neuropathy was defined as reduction in visual acuity below 20/27, any remaining visual field defects, color vision defects, or the appearance of an afferent pupillary defect, when compared with the disease onset.

Treatments

Treatment regimens included dietary recommendations for weight loss and the initially accepted pharmaceutical treatments

such as acetazolamide, furosemide, and topiramate either alone or in combination. In the majority of cases, acetazolamide was first given according to weight, with dose increases as needed, in addition to follow-up of electrolyte imbalances. In individuals who were intolerant of acetazolamide, the other two drugs were introduced. Gradual discontinuation was usually initiated after six months of treatment, unless symptoms or edema persisted, then the tapering started with cessation of the symptoms or according to the appearance of the optic nerve. The tapering was done gradually, with usually a quarter of the received dose being initially reduced, and again another quarter after three months, and so on. If symptoms reappeared, the dose was increased once more.

Patients with a more malignant course with progressive damage to visual fields and acuity despite maximal tolerable therapy underwent CSF shunting procedures.

Follow-up

During an acute episode, the patients were hospitalized and were followed daily for about a week, depending on the severity. Upon improvement, they were followed once a week for the first few months, and with further improvement, follow-up was extended to once a month. Thereafter, the patients were followed for every three months to one year. Every visit usually included an automated visual field test.

Statistical analysis

Statistical analysis was performed using SPSS software for windows version 22.0 (IBM, Armonk, NY, USA). *P* values less than 0.05 on a two-sided test were considered statistically significant. We conducted $\chi 2$ tests for categorical variables. Clinical parameter distributions were tested for normality by the Shapiro–Wilk test. Independent and paired t tests were conducted for continuous variables with a normal distribution, and Wilcoxon signed-rank test and Mann–Whitney U test were conducted for variables with a non-normal distribution. Unless otherwise specified, values are mean ± S.D.

Results

Sixty-five patients (56 females, nine males) were included and were categorized into 17 prepubertal children (14 females and three males, group A), 16 adolescents (11 females and five males, group B), and 32 adults (31 females and one male, group C). Clinical and demographic parameters are detailed in Table 1. The mean age of diagnosis was 8.6 ± 2.0 (range: five to 11) in the prepubertal group, 14.3 ± 1.5 (range 12 to 17) in the adolescent group, and 31.9 ± 9.7 years (range: 18 to 56) in adults. Mean duration of follow-up was 8.8 ± 4.5 years (8.2 ± 1.9 for group A, 9.3 ± 6.4 for group B, and 8.9 ± 4.4 for group C, $P > 0.05$). Mean BMI in the adolescent group was 33.45 ± 7.5 kg/m^2 and in the adult group was 36.4 ± 8.1 kg/m^2 ($P = 0.269$). In the prepubertal children group, the weight-for-age *z* score was 1.19 ± 1.4 (mean percentile: 76.6% ± 32%).

Presenting symptoms

All patients presented with papilledema, whereas the presenting symptoms for PTCS were varied. The presenting symptoms were headaches in 83% of cases (54 of 65), TVO in 51% (33 of 65), pulsatile tinnitus in 12% (eight of 65), and diplopia in 9% (six of 65). Nine percent (six of 65) of the patients were asymptomatic (12% [two of 17] from group A, 25% [four of 16] from group B, and 0%

TABLE 1.
Clinical Characteristics of Patients With PTCS

Variable	Pre-pubertal		Adolescents		Adults		*P* Value (Prepubertal vs Adults)	*P* Value (Adolescents vs Adults)
	N (S.D.)	%	N (S.D.)	%	N (S.D.)	%		
Number	17	26.2	16	24.6	32	49.2		
Age	8.65 (2.0)		14.3 (1.5)		31.9 (9.7)		<0.001	<0.001
BMI[a] /z score[b], percentile[c]	1.19 (1.4)[b], 76.6% ± 32%[c]		33.45 (7.5)[a]		36.4 (8.1)[a]		-	0.269
Overweight*			13	86.7	22	91.7	-	0.617
Female gender	14	82.4	11	68.8	31	96.9	0.077	0.005
Opening pressure (cm H_2O)	33.7 (9.5)		34.7 (8.2)		32.7 (13)		0.775	0.597
BCVA right eye (LogMAR)	0.062 (0.1)		0.070 (0.14)		0.075 (0.16)		0.753	0.911
BCVA right eye	20/23		20/23		20/24			
BCVA left eye (LogMAR)	0.078 (0.1)		0.059 (0.12)		0.054 (0.090)		0.411	0.858
BCVA left eye	20/24		20/23		20/23			
Visual field defects	7	46.7	9	60.0	27	84.4	0.007	0.066
TVO	8	47.1	6	37.5	19	59.4	0.409	0.153
Tinnitus	2	11.8	2	12.5	4	12.5	0.940	1.00
Headache	15	88.2	12	75.0	27	84.4	0.713	0.433
Diplopia	1	5.9	16	100	5	15.6	0.310	0.095
Asymptomatic	2	11.8	4	25.0	0	0.0	0.048	0.003
Overweight etiology	17	100	14	87.5	31	97	0.461	0.206
Treated with diet	7	41.2	12	75.0	24	75.0	0.019	1.00
Treated with Diamox	16	94.1	15	93.8	27	84.4	0.322	0.355
Treated with furosemide	1	5.9	0	0.0	5	15.6	0.322	0.154
Surgery was performed	3	17.6	2	12.5	4	12.5	0.624	1.00
Follow-up time (years)	8.2 (1.9)		9.3 (6.4)		8.9 (4.4)		0.521	0.828

Abbreviations:
BCVA = Best corrected visual acuity
BMI = Body mass index
PTCS = Pseudotumor cerebri syndrome
TVO = Transient visual obscuration
Demographics of 65 patients with PTCS.
[a]BMI, [b]Z score, [c]percentile.
* BMI > 25, or *z* score > +1 S.D.

[zero of 32] from group C, $P < 0.05$). Comparison of the presenting symptoms between the groups is detailed in Table 1. Prepubertal children had a significantly lower incidence of visual field defects upon presentation with a 47% incidence (seven of 15) with two of the children not being able to perform the examination, compared with approximately 84% (27 of 32) seen in adults ($P = 0.029$). Adolescents had similarly low rates of visual field defects compared with adults (nine of 16, 60%, vs 27 of 32, 84%, $P = 0.066$). All groups had similar rates of tinnitus, diplopia, TVO, and headaches (all $P > 0.05$, Table 1).

Mean presenting visual acuity was 20/23 (0.066 ± 0.11 LogMAR) and was similar between the groups (prepubertal group: 20/23 (0.070 ± 0.11 LogMAR), adolescent group: 20/23 (0.065 ± 0.13 LogMAR), adults group: 20/23 (0.065 ± 0.12 LogMAR, $P > 0.05$, Table 1).

Opening pressures

The mean CSF opening pressure was 33.7 ± 9.5 cm H_2O in group A, 34.7 ± 8.2 cm H_2O in group B, and 32.7 ± 13 cm H_2O in group C ($P > 0.05$). The mean CSF opening pressure in the surgically treated patients was 38.0 ± 8.2 cm H_2O (in all groups) compared with the pharmacologically treated group, in which the pressure was 33 ± 9.5 cm H_2O ($P = 0.978$). No statistical correlation was found between the opening pressures and age (Spearman r = −0.003, $P = 0.969$), BMI (Spearman r = 0.057, $P = 0.568$), relapse rates (Spearman r = 0.039, $P = 0.716$), or final visual acuity (Spearman r = −0.103, $P = 0.302$).

Treatment

The mean treatment duration for the initial event was 2.7 years (2.4 ± 2.2 years for the prepubertal children, 2.5 ± 2.2 years for the adolescents, and 3.3 ± 3.3 years for the adults, $P > 0.05$, Tables 2 and 3). The average treatment duration was similar between the relapsing and the nonrelapsing diseases (in prepubertal children 1.8 ± 1.1 years for the relapsing disease and 2.6 ± 2.5 years for the nonrelapsing disease, $P = 0.117$; in adolescents 1.9 ± 1.7 years compared with 3.3 ± 2.6 years, $P = 0.254$; and in adults 2.7 ± 4.7 years compared with 3.6 ± 2.5 years, $P = 0.515$). Longer treatment times at first admission were associated with a lower number of recurrences (Spearman r = −0.335, $P = 0.012$).

All patients were initially treated with standard monotherapy or combination therapy (acetazoleamide, topiramate, or furosemide). Nine patients who continued to deteriorate (i.e., progressive visual acuity loss or visual field defects) despite maximal tolerated pharmaceutical therapy underwent surgical intervention (three of 17 in group A, two of 16 in group B, and four of 32 in group C, $P > 0.05$, Tables 2 and 3), within a mean of 3 ± 2.3 years (range: three months to seven years) after initial diagnosis, either a CSF ventriculoperitoneal shunt (two of three in group A, one of two in group B, and all four in group C) or an optic nerve sheet fenestration (one of three in group A, one of two in group B, and none in group C), whereas all others remained on pharmacologic treatment. During the follow-up period, bariatric surgery was performed on two patients from group B, which led to their improvement. No single treatment, including acetazoleamide, furosemide, an optic nerve sheet fenestration, or ventriculoperitoneal shunts, and diet changes had a significant correlation with either recurrence rates or time to recurrence (all $P > 0.05$).

Visual outcomes

Mean visual acuity at last follow-up was on average 20/26 (0.109 ± 0.23 LogMAR). A nonsignificant tendency for worse acuity in the adult group was seen (prepubertal group: 20/24 [0.076 ± 0.07 LogMAR], adolescent group: 20/22 [0.052 ± 0.1 LogMAR], and adults group: 20/29 [0.170 ± 0.3 LogMAR], $P = 0.027$ comparing prepubertal children with adults and $P = 0.056$ comparing adolescents with adults, Tables 2 and 3).

In the prepubertal and adolescent groups there was practically no change in visual acuity from the first admission to the last follow-up (prepubertal: 0.066 ± 0.11 LogMAR to 0.076 ± 0.07 LogMAR, $P = 0.550$, adolescent: 0.064 ± 012 LogMAR to 0.052 ± 0.1 LogMAR, $P = 0.808$), whereas in the adult group, a tendency for deterioration was observed (0.065 ± 0.11 to 0.17 ± 0.3 LogMAR, $P = 0.065$). Optic neuropathy was observed in at least one eye in 62% patients (40 of 65). It was significantly less prevalent in prepubertal children with an incidence of 41.2% (seven of 17) and

TABLE 2.
Clinical Outcomes of Prepubertal Children Compared With Adults With PTCS

Variable	Prepubertal		Adults		*P* Value
	N (S.D.)	%	N (S.D.)	%	
Number	17	26.2	32		
At least one recurrence	4	23.5	9	28.1	0.729
At least two recurrences	0	0.0	0	0.0	-
Number of recurrences	0.18 (0.4)		0.28 (0.5)		0.427
Recurrences within one year	3	75	3	33.3	0.310
Visual field defects upon recurrence	6	35.3	24	75	0.007
Improvement trend under initial treatment	14	82.4	28	87.5	0.624
BCVA right eye at discharge (LogMAR)	0.047 (0.1)		0.176 (0.3)		0.027
BCVA right eye at discharge	20/22		20/30		
BCVA left eye at discharge (LogMAR)	0.053 (0.1)		0.165 (0.4)		0.140
BCVA left eye at discharge	20/23		20/29		
Optic neuropathy	7	41.2	28	87.5	0.001
Initial treatment duration (years)	2.4 (2.2)		3.3 (3.3)		0.355
Time to recurrence (years)*	1.3 (0.6)		2.7 (2.0)		0.267
Second treatment duration (years)	3.3 (3.2)		2.5 (2.4)		0.662
Time to second recurrence (years)*	NA		NA		
Time to shunt placement (years)*	1.8 (1.5)		2.8 (3.0)		0.634

Abbreviations:
BCVA = Best corrected viasual acuity
PTCS = Pseudotumor cerebri syndrome
Clinical outcomes of 49 prepubertal and adult patients with PTCS.
* Calculated since treatment cessation.

TABLE 3.
Clinical Outcomes of Adolescents Compared With Adults With PTCS

Variable	Adolescents		Adult		*P*Value
	N (S.D.)	%	N (S.D.)	%	
Number	16		32		
At least one recurrence	8	50	9	28.1	0.135
At least two recurrences	2	12.5	0	0.0	0.106
Number of recurrences	0.63 (0.7)		0.28 (0.5)		0.049
Recurrences within one year	4	50	3	33.3	0.486
Visual field defects upon recurrence	5	31.2	24	75	0.003
Improvement trend under initial treatment	14	87.5	28	87.5	1.00
BCVA right eye at discharge (LogMAR)	0.059 (0.1)		0.176 (0.3)		0.056
BCVA right eye at discharge (Snellen)	20/23		20/30		
BCVA left eye at discharge (LogMAR)	0.045 (0.1)		0.165 (0.4)		0.251
BCVA left eye at discharge (Snellen)	20/21		20/29		
Optic neuropathy	5	31.2	28	87.5	<0.001
Initial treatment duration (years)	2.5 (2.2)		3.3 (3.3)		0.426
Time to recurrence (years)*	3.8 (5.1)		2.7 (2.0)		0.561
Second treatment duration (years)	2.3 (1.4)		2.5 (2.4)		0.870
Time to second recurrence (years)*	1.2 (1.4)		N/A		-
Time to shunt placement (years)*	1.5 (0.7)		2.8 (3.0)		0.597

Abbreviations:
BCVA = Best corrected visual acuity
PTCS = Pseudotumor cerebri syndrome
Clinical outcomes of 48 adolescent and adult patients with PTCS.
* Calculated since treatment cessation.

adolescents (31.2%, five of 16) compared with adults in which it was seen in 87.5% of cases (28 of 32) ($P < 0.001$).

Color vision was relatively preserved (14/15 of the Ishihara color vision test) in all groups upon admission, and a trend toward slight improvement was observed during follow-up.

Owing to the retrospective nature of the study, the Frisen scale could not be reported. At presentation, moderate to severe visual impairment (less than 20/40) was observed in only three patients (one from group A and two from group B) who all later improved (more than 20/25) toward their last examination. Conversely, only four patients (exclusively from group C) had visual function deterioration (20/45 to counting fingers) despite proper medical therapy.

Recurrences

The main clinical outcomes are detailed in Tables 2 and 3. Prepubertal children had similar recurrence rates as adults (23.5% vs 28.1%, respectively, $P = 0.729$), whereas adolescents showed slightly higher rates (50%, eight of 16). This is during a similar follow-up period for all groups (8.2 ± 1.9, 9.2 ± 6.4, and 8.9 ± 4.4 years, respectively, $P > 0.05$).

Time to recurrence was also similar between the groups with a mean of 1.3 ± 0.6 years of remission in prepubertal children, which showed a slight tendency to occur earlier compared with 3.8 ± 5.1 years in adolescents and 2.7 ± 2.0 years in adults. However, the difference was not statistically significant ($P = 0.267$). Most recurrences in prepubertal children happened within a year of medical treatment cessation (three of four, 75%) compared with a minority in the adult group (three of nine, 33.3%, $P = 0.310$) and half in the adolescent group (four of eight, 50%). Most of the recurrences in the adult group occurred within three years (12 of 17, 71%).

Secondary analysis: comparing prepubertal children to all older patients

A comparison of clinical outcomes between prepubertal children and all older patients is presented in Table 4. Mean recurrence-free survival in prepubertal children was 9.3 ± 0.8 years (95% confidence interval: 7.8 to 10.8), and in older patients, it was 14.9 ± 1.5 years (95% confidence interval: 11.8 to 17.8). A log-rank (Mantel–Cox) test revealed the difference to be nonsignificant ($P = 0.557$). Recurrences in prepubertal children showed a trend for higher incidence of visual field defects compared with older patients (64.7% vs 39.6%, $P = 0.074$). Treatment times upon recurrence were similar between the groups (3.3 ± 3.2 vs 2.4 ± 1.9, $P = 0.486$).

Discussion

We studied 65 patients with definite PTCS and compared three age groups, prepubertal children, adolescents, and adults. There are several important findings. (1) PTCS recurs in approximately a third of the cases. (2) Most of recurrences occurred within one year in prepubertal children and within three years in adults. (3) The number of recurrences and the time to recurrence were similar. (4) Presenting symptoms were similar apart from visual field defects, which were less common in prepubertal children. (5) Optic neuropathy was more common in adults, who also showed a tendency for visual decline. (6) Longer treatment times were associated with fewer recurrences. These are important findings as they directly compare the different age groups and could help in assessing the expected clinical course and prognosis.

Previous studies that have focused on the clinical course of PTCS demonstrated inconsistent results. Disease progression in these studies ranged from a short benign self-limiting syndrome to an aggressive disease that progressed to blindness within a short period of time. However, data regarding PTCS in prepubertal children with long-term follow-up are sparse, with no major direct comparison with adults performed so far.[5-7,18,21,22]

In adults, the reported female to male ratio ranges between 4.3:1 and 15:1,[23-25] whereas in children, no sex predilection was observed.[7,11,15] Surprisingly, in the present study, we found female gender to be prominent in all groups. One possible explanation is sample bias owing to the smaller number of prepubertal individuals. This might also be due to different gender distributions in our study. A larger study is necessary to confirm this.

Unlike adults, children tend to present with normal body weight.[14,15] In our study, the children tended to be overweight with a mean weight percentile of 77%.[26] There is still debate about the correlation between body weight and the clinical course and visual outcome in children. Steibel-Kalish et al.[27] found that the

TABLE 4.
Clinical Outcomes of Patients With PTCS

Variable	Pre-pubertal		Adolescent and Adult		*P* Value
	N (S.D.)	%	N (S.D.)	%	
Number	17	26.2	48	73.8	
At least one recurrence	4	23.5	15	31.2	0.548
At least two recurrences	0	0.0	2	4.2	0.393
Number of recurrences	0.18 (0.4)		0.40 (0.6)		0.150
Recurrences within one year	3	75	7	41.2	0.413
Visual field defects upon recurrence	11	64.7	19	39.6	0.074
Improvement trend under initial treatment	14	82.4	42	87.5	0.597
BCVA right eye at discharge (LogMAR)	0.047 (0.1)		0.137 (0.3)		0.161
BCVA right eye at discharge	20/22		20/27		
BCVA left eye at discharge (LogMAR)	0.053 (0.1)		0.125 (0.3)		0.386
BCVA left eye at discharge	20/23		20/27		
Optic neuropathy	7	41.2	33	68.8	0.045
Initial treatment duration (years)	2.4 (2.2)		3.0 (3.0)		0.457
Time to recurrence (years)*	1.3 (0.6)		3.3 (3.7)		0.392
Second treatment duration (years)	3.3 (3.2)		2.4 (1.9)		0.486
Time to second recurrence (years)*	NA		1.3 (0.3)		NA
Time to shunt placement (years)*	1.8 (1.5)		2.4 (2.5)		0.742

Abbreviations:
BCVA = Best corrected visual acuity
PTCS = Pseudotumor cerebri syndrome
Clinical outcomes of 65 prepubertal and pubertal patients with PTCS.
* Calculated since treatment cessation.

recurrence rate is fivefold higher among obese children compared with normal weight children, whereas Soiberman et al.[5] did not find a correlation between body weight in children and their final visual outcome. Our findings appear to be in agreement with those of Soiberman et al. as we observed no correlation between body weight and any clinical outcome. It is important to emphasize that weight loss is still considered a major factor for reducing the recurrences of PTCS and may reduce the risk for visual impairment by lowering central venous pressure or by a tentative endocrinological mechanism.[28]

This study also confirms the similarity in symptoms in different ages. We found prepubertal children to present with similar symptoms to adolescents and adults and at similar decreasing frequencies (all $P > 0.05$): headaches, TVO, tinnitus, and diplopia. These results are in agreement with the findings of Kesler et al. regarding the prevalence of the different symptoms.[29]

When assessing recurrences, it is important to note that headaches often persist despite a normalization of intracranial pressure. Friedman et al. found that up to two-thirds still tend to have headaches even after the resolution of the intracranial hypertension. Therefore this symptom should be used cautiously when assessing illness resolution.[30,31]

Restoration of visual acuity and resolution of papilledema constitute the primary goal in PTCS management. Our study suggests that visual field defects appear to persist compared with visual acuity or color vision.[18,32] An interesting observation arising from this study is the apparent difference between the groups concerning visual field defects. Upon initial presentation, visual field defects had a lower incidence in prepubertal children (47% vs 77%, $P = 0.029$), whereas upon recurrence, the opposite was true (65% vs 40%, $P = 0.074$). It is possible that this is due to the difficulty in assessing visual fields in small children and that a higher percent of tests in this age group were performed using confrontation, suggesting perhaps that many field defects were left undiagnosed in this group.

With a similar follow-up period in all groups, our study detected an overall recurrence rate among adults of 28%, which is in the range of 8% to 38% previously reported by others, whereas adolescents had higher rates (50%).[5,33,34] Prepubertal children showed rates of 23%, which is similar to the reported 20%.[5,6,12,27,35]

Another surprising result is the relatively high recurrence rates seen in the prepubertal children group. One possible explanation is the makeup of our local population, which is primarily Mediterranean and Jewish. Another possible contributing factor is the long follow-up periods available in our dataset.

Similar to previous findings[5,21,29] our study did not find any correlation between the initial CSF opening pressures in either the medically or surgically treated groups to clinical outcomes. This is in contrast to Ravid et al.[6] who found an association between the opening pressures and visual impairment. In our study, we did not find any significant statistical correlation between CSF opening pressures and the relapsing rates, final visual acuity, or final visual field. These findings are similar to those described by Soiberman et al.[5] In addition to lower rates of visual field defects found among prepubertal children, the children had relatively good visual acuity and color vision, which tended to be preserved during follow-up. In addition, optic neuropathy was diagnosed at much lower rates among the prepubertal children, which may be related to the lack of complaints and lower cooperation to reach a proper diagnosis.

The limitations of our study include its retrospective nature, and therefore exact signs and symptoms of the disease were incomplete in some of the patients' charts. As weight change was not always available, it could not be used for the analysis of recurrences. In addition, as Tanner scores were not available for all the children and prediction of the exact age of puberty could not be determined, we used age 11 years as the puberty cutoff. However, this may not necessarily be true for all patients.

Further limitations included the absence of data on the types of visual field defects, predisease visual acuity, and color vision. It is worth mentioning that color vision was found to be 14/15 in all groups, and thus relatively preserved. The slight decrease may be related to the lack of cooperation or congenital reasons without deterioration. However, again due to the retrospective nature of the study some data were not available. Another limitation was the dissimilarity between the sizes of the prepubertal group, which was relatively small due to lower disease prevalence. The strengths and novelty of the study are the long-term follow-up together with a relatively large number of patients. Second, previous reports have described either children or adults, whereas this study compares

children, adolescents, and adults and discusses treatment course and outcomes for each group.

In conclusion, our study adds further information regarding the obscure clinical course in prepubertal children and also directly compares the clinical course to adults and adolescents. Our study also demonstrates that PTCS will present with a relapsing course in about a third of the cases. Most recurrences occurred within a year in prepubertal children and within three years in older patients. Prepubertal children showed similar presenting symptoms, with visual field defects more easily missed. Optic neuropathy was more common in adults who also showed a tendency for visual decline. Longer treatment times were associated with fewer recurrences. BMI and opening pressures were not associated with either relapsing rates or final visual acuity. Our results will hopefully assist the treating physician in clarifying the patient's expectations regarding the clinical course and outcome of PTCS in prepubertal children, adolescents, and adults.

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