Secondary pseudotumour cerebri syndrome in children: clinical characteristics and long-term outcomes

Pseudotumour cerebri syndrome (PTSC) is characterized by elevated intracranial pressure (ICP) with the absence of an intracranial mass, hydrocephalus, or abnormalities in cerebrospinal fluid composition. PTSC can be primary (also known as idiopathic intracranial hypertension) or secondary. We recently published an article summarizing the clinical characteristics and visual outcomes for primary PTSC in children.[1] The purpose of this correspondence is to report the clinical characteristics and long-term outcomes in a concomitant cohort of children with secondary PTSC from the same institution over the same time period.

This was a retrospective cohort study conducted at a single tertiary care pediatric hospital. The methods were similar to the recently published study on primary PTSC.[1] We used the same database over the same time period (January 2009–December 2020) to identify pediatric patients (from birth to 18 years of age) with secondary PTSC. The causes of secondary PTSC that were included in the study were cerebral venous abnormalities (e.g., cerebral venous sinus thrombosis), medications and exposures (e.g., vitamin A and retinoids), and medical conditions (e.g., renal failure).[2] Papilledema severity was categorized as mild (Frisén grades 0–1), moderate (Frisén grades 2–3), or severe (Frisén grades 4–5). Visual impairment was defined as mild (visual acuity 20/40–20/80 or a mean deviation of −3 to −7 on a 24-2 Humphrey visual field) or severe (visual acuity <20/80 or a mean deviation of less than −7 on a 24-2 Humphrey visual field). All patients were required to have recognition visual acuity testing, but visual field testing was not required in patients who were too young to perform testing reliably. Patients were included in the study if they met the updated diagnostic criteria for PTSC and an underlying cause for elevated ICP was identified.[2] In addition to cases of "definite PTSC," cases of "likely PTSC" also were included if there was a clear clinical presentation and known underlying cause (lumbar puncture was considered diagnostically unnecessary in these cases).[2] The primary outcome was poor visual function, irreversible structural pathology, or failure of conservative management, which were defined as mild or severe visual impairment, optic atrophy, or a surgical procedure to lower ICP, respectively. The statistical analysis was performed using STATA statistical software version 14 (StataCorp, College Station, Tex.). Clinical characteristics were analyzed using nonparametric statistical tests. Median age at diagnosis between groups was compared using the Kruskal–Wallis test with the Bonferroni adjustment for multiple comparisons.

There were 48 children (24 females, 24 males) with secondary PTSC. The underlying cause was cerebral venous abnormalities in 22 (46%), medications or exposures in 18 (38%), and medical conditions in 8 (17%; Table 1). The median age at diagnosis was 10.3 years (range, 2.6–17.6 years). The median age was significantly higher in the medications or exposures group (13.1 years) than in the cerebral venous abnormalities group (7.7 years, $p = 0.005$) and the medical conditions group (8.1 years, $p = 0.03$). The most common presenting symptoms were headache in 38 patients (79%), nausea or vomiting in 19 (40%), diplopia in 9 (19%), blurred vision in 9 (19%), and tinnitus in 6 (13%). Only 4 patients (8%) were asymptomatic at presentation. All patients had papilledema at diagnosis, and 11 (23%) had a cranial nerve VI palsy (6 unilateral, 5 bilateral).

Of the 48 patients, 43 (90%) had active treatment to decrease ICP. Primary treatment was acetazolamide in 40 (83%) and topiramate in 3 (6%). Secondary treatment was required in 4 patients, with 2 (4%) given a second-line medication and 2 (4%) undergoing ventriculoperitoneal (VP) shunting. In this cohort, no patients underwent optic nerve sheath fenestration or venous sinus stenting. The median duration of follow-up was 17 months. There was complete resolution of the papilledema in 46 patients (96%) after a median duration of 4.8 months (range, 1.0–25.1 months). The other 2 patients (4%) had chronic papilledema that was stable for more than a year with no active treatment.

At final follow-up, a total of 9 patients (19%) were categorized as having a poor long-term outcome, which was due to visual impairment in 5 (10%), optic atrophy in 6 (13%), and (or) VP shunt surgery in 2 (4%; Table 2). All 5 patients with visual impairment had a mild loss of visual field. No clinical characteristics (underlying cause, age at diagnosis, severity of papilledema, or duration of papilledema) were found to be significantly associated with a poor long-term outcome.

In this series of secondary PTSC in children, approximately 1 in 5 patients had a poor long-term outcome (e.g., visual impairment, optic atrophy, and/or surgery). However, the risk of long-term vision loss was low. Only 5 of the 48 patients (10%) had evidence of visual impairment at final follow-up, and it was mild in all cases. The long-term visual outcomes for secondary PTSC patients were comparable to

Table 1—Underlying cause of secondary pseudotumour cerebri syndrome in children (N = 48)

Underlying cause	Total (%)
Cerebral venous abnormalities	22 (46)
Cerebral venous sinus thrombosis	22 (46)
Medications and exposures	18 (38)
Antibiotics (minocycline and doxycycline)	7 (15)
Vitamin A and retinoids	8 (17)
Hormones (growth hormone)	3 (6)
Medical conditions	8 (17)
Renal failure	8 (17)

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Table 2—Children with secondary pseudotumour cerebri syndrome who had a poor long-term functional or structural outcome

Case	Underlying cause	Age at diagnosis (y)	Severity of papilledema at diagnosis	Treatment of underlying cause	Duration of papilledema (mo)	Reason for poor outcome
1	CVST (otitis media)	4	Moderate	Amoxicillin (otitis media) Heparin/LMWH (CVST)	25	Optic atrophy VP shunt
2	CVST (mastoiditis)	8	Severe	Amoxicillin (mastoiditis) Heparin/LMWH (CVST)	4	Optic atrophy Mild visual field loss
3	CVST (mastoiditis)	10	Severe	Amoxicillin (mastoiditis) Heparin/LMWH (CVST)	2	Optic atrophy VP shunt
4	CVST (GPA)	14	Moderate	Methylprednisone, plasmapheresis, cyclophosphamide (GPA) Heparin/LMWH (CVST)	15	Optic atrophy
5	CVST (SLE)	13	Severe	Prednisone, cyclophosphamide (SLE) Heparin/LMWH (CVST)	Chronic	Mild visual field loss
6	Antibiotic (doxycycline)	15	Mild	Discontinue medication (doxycycline)	10	Optic atrophy Mild visual field loss
7	Antibiotic (minocycline)	16	Mild	Discontinue medication (minocycline)	2	Mild visual field loss
8	Hormone (growth hormone)	10	Mild	Reduce dose (growth hormone)	3	Mild visual field loss
9	Renal failure	10	Severe	Fluid intake and blood pressure management (chronic kidney disease)	1	Optic atrophy

CVST, cerebral venous sinus thrombosis; LMWH, low-molecular-weight heparin; VP, ventriculoperitoneal; GPA, granulomatosis with polyangiitis; SLE, systemic lupus erythematosus.

the long-term visual outcomes for primary PTSC patients at our institution. In the cohort of children with primary PTSC, 9% of the patients had evidence of mild long-term visual impairment compared with 10% of children with secondary PTSC. Surgical intervention was uncommon in all cases of PTSC; only 2 of 48 patients with secondary PTSC and 1 of 90 patients with primary PTSC underwent surgery to lower ICP.[1]

There are limited data on the long-term outcomes in secondary PTSC in children. Most existing studies have looked at primary PTSC exclusively or at PTSC as a group (both primary and secondary). Per et al.[3] reported on 42 patients with PTSC, including 12 with secondary PTSC. All 12 secondary PTSC patients had normal visual acuity, but 2 failed medical therapy and required a VP shunt. Değerliyurt et al.[4] reported on 53 children with PTSC, including 23 with secondary PTSC. Of the 23 secondary PTSC patients, all had normal visual function except 1 (4%) who had moderate visual field loss. There are also studies that have looked at specific causes of secondary PTSC. For instance, Sebire et al.[5] reported that 3 of 37 children (7%) with cerebral venous sinus thrombosis had reduced visual acuity, but they did not give details on severity.[5] In this cohort of children with secondary PTSC, 10% of the patients had mild visual impairment, and 19% had either visual impairment or optic atrophy or required a surgical procedure. This is comparable to the outcomes of the small cohorts that have been reported to date.

The treatment for secondary PTSC differs from that for primary PTSC in that it is crucial to address the underlying cause of elevated ICP, often in the context of a multidisciplinary team. For instance, children with cerebral venous sinus thrombosis need anticoagulation treatment, ideally by a subspecialty team (e.g., pediatric stroke team). If the underlying cause is a medication or exposure, the offending agent needs to be identified and then discontinued, reduced, or replaced. Patients with underlying medical conditions usually benefit from specialized care and may need adjusted medication dosing (e.g., acetazolamide in renal failure). While addressing the underlying cause of secondary PTSC should lower the ICP, it is still important to monitor visual function and papilledema. Treating the ICP directly may be indicated if the papilledema is severe or there are signs of visual compromise. There are also cases in which treating the underlying cause is not curative. For instance, 2 patients with cerebral venous sinus thrombosis in this study had severe or chronic papilledema despite anticoagulation therapy and ultimately required VP shunting.

This study has several limitations. Secondary PTSC has several distinct causes, so grouping all causes into a single cohort may have falsely exaggerated the homogeneity of this condition. In addition, the number of patients with each specific cause was small, limiting risk factor and subgroup analysis.

In conclusion, we report the long-term outcomes for a cohort of children with secondary PTSC. Approximately 1 in 5 patients had a poor long-term outcome. However, only 1 in 10 had evidence of long-term visual impairment, and it was mild in all cases.

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