Research Article

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Secondary pseudotumor cerebri in the pediatric population: clinical features, treatment, and prognosis

Pediatrik popülasyonda sekonder psödotümör serebri: klinik özellikler, tedavi ve prognoz

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Abstract

Purpose: Pseudotumor cerebri syndrome (PTCS) is characterized by elevated intracranial pressure (ICP) without intracranial mass, hydrocephalus, or abnormalities in cerebrospinal fluid (CSF) composition. In secondary PTCS (sPTCS), there is a reason that increases the CSF pressure. The aim of this study is to evaluate the diagnosis, treatment, and follow-up of pediatric patients diagnosed with sPTCS.

Materials and methods: This is a retrospective study conducted in a single-center tertiary pediatric hospital. We included patients aged 1-17 years who were diagnosed with sPTCS in a tertiary hospital between 2018 and 2023 and met the current diagnostic criteria for PTCS. We evaluated the complaints, etiology, ophthalmological evaluations, and treatment results of the cases.

Results: Seventeen patients with a diagnosis of PTCS were included in the study. The mean age was 9.82 (±4.6). Of the patients, 9 (56.2%) were male and 8 (43.7%) were female. The most common symptoms were headache in 10 patients (62.5%), nausea/vomiting in 6 patients (37.5%), and double vision in 5 patients (31.2%). All patients had papilledema and 7 (43.7%) patients had sixth nerve palsy. Recurrence was observed in 3 (16%) patients. Optic nerve fenestration was performed in three patients as a second-line treatment.

Conclusion: In cases that do not respond to medical treatment, optic nerve sheath fenestration may be a good treatment option.

Keywords: Optic nerve, pseudotumor cerebri, child.

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Öz

Amaç: Psödotümör serebri sendromu (PTSS), intrakranyal kitle, hidrosefali veya beyin omurilik sıvısı (BOS) bileşiminde anormallikler olmadan yüksek kafa içi basıncı (KİB) ile karakterizedir. İkincil PTSS'de (sPTSS), BOS basıncını artıran bir neden vardır. Bu çalışmanın amacı sPTSS tanısı alan pediatrik hastaların tanı, tedavi ve takiplerinin değerlendirilmesidir.

Gereç ve yöntem: Bu çalışma tek merkezli üçüncü basamak bir pediatri hastanesinde gerçekleştirilen retrospektif bir çalışmadır. 2018 ile 2023 yılları arasında üçüncü basamak bir hastanede sPTSS tanısı konan ve PTSS için mevcut tanı kriterlerini karşılayan 1-17 yaş arası hastaları dahil ettik. Olguların şikayetleri, etiyolojisi, oftalmolojik değerlendirmeleri ve tedavi sonuçları değerlendirildi.

Bulgular: Çalışmaya PTSS tanısı alan 17 hasta dahil edildi. Ortalama yaş 9,82 (±4,6) idi. Hastaların 9'u (%56,2) erkek, 8'i (%43,7) kadındı. En sık görülen semptomlar 10 hastada (%62,5) baş ağrısı, 6 hastada (%37,5) bulantı/kusma, 5 hastada (%31,2) çift görme idi. Hastaların tamamında papilödem, 7 (%43,7) hastada ise altıncı sinir felci vardı. 3 (%16) hastada nüks görüldü. Üç hastaya ikinci basamak tedavi olarak optik sinir fenestrasyonu uygulandı.

Sonuç: Medikal tedaviye yanıt alınamayan durumlarda optik sinir kılıfı fenestrasyonu iyi bir tedavi seçeneği olabilir.

Anahtar kelimeler: Optik sinir, psödotümör serebri, çocuk.

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Introduction

The definition of pseudotumor cerebri syndrome includes both primary and secondary PTCS. IIH (idiopathic intracranial hypertension) is synonymous with primary PTCS and its etiology is unknown. sPTCS has a known cause and its treatment may differ from PTCS [1, 2]. When all diagnostic criteria are met, PTCS is called definite primary/secondary PTCS. When all diagnostic criteria are not met, it is classified as possible primary/secondary PTCS. In the pediatric population, some of the most common causes of sPTCS are intracranial tumor, sinus venous thrombosis, intracranial hemorrhage, hydrocephalus, CNS (central nervous system) infection, severe anemia from drug use, discontinuation of chronic corticosteroids, use of antibiotics such as synthetic growth hormone and tetracycline [3]. There are cases of sPTCS occurring as a result of the discontinuation of corticosteroid therapy. Accordingly, it suggests that abnormal glucocorticoid metabolism plays a role in the pathophysiology of PTCS. Cortisol level may play a triggering role for PTCS by affecting the 11-β-hydroxysteroid dehydrogenase type 1 and 2 (HSD1 and HSD2) enzyme complex in the choroid plexus, which regulates the functions of cortisol. Headache is the most common symptom of primary and sPTCS. Acetolzamide, topiramate, prednol are given in medical treatment. Optic nerve sheath fenestration (ONSF) and ventriculoperitoneal shunt (VPS) are used in surgical treatment. Most importantly, lowering ICP and revealing its etiology requires a multidisciplinary approach [4, 5].

Materials and methods

Between January 2018 and 2023, 17 pediatric patients with sPTCS, aged 1-17 years, were included. The causes of secondary PTCS included in the study are infectious, endocrinological diseases and drug exposure, more rarely hematological diseases, trauma, arachnoid cyst rupture, some syndromic diseases, and chronic renal failure (CRF). The body mass index (BMI) of the patients was recorded. We classified the patients into age groups 0-14 years and 15-17 years. We evaluated the patients according to their phenotype, age, gender, comorbidities, and BMI status. IIH is diagnosed according to the ICHD-III criteria and revised Friedman criteria [6]. Papilledema scores were categorized as mild, moderate, and severe, respectively (mild degree 0-1), (moderate degree 2-3), (severe degree 4-5). Visual impairment was defined as mild (visual acuity 20/40-20/80) or severe (visual acuity <20/80). Patients who met the updated diagnostic criteria for PTCS and were found to have a cause for high ICP were included in the study [6]. Despite medical or surgical treatment, mild or severe visual impairment and optic atrophy were considered unresponsive to treatment. This study was approved by the Pamukkale University Non-Interventional Clinical Research Ethics Committee.

Statics

IBM SPSS 21.0 software was used for data analysis. Mean ± standard deviation was calculated for continuous variables. Two-way analysis of variance (ANOVA) was employed to compare continuous variables among groups. Discrete variables were compared using the appropriate Pearson chi-square test or Fisher's test. A *p*-value <0.05 was considered statistically significant.

Results

There were 17 children with sPTCS in our study, 8 females and 9 males. The underlying causes were infection in 3 patients (17.6%), drug exposure in 3 patients (17.6%), endocrine disease in 4 patients (23.5%), and less common causes are summarized in Table 1. The median age of the cases is 10.7 (2.6 between 17.6). Headache was the most common symptom 10 (58.8%), nausea or vomiting in 6 patients (35.2%), diplopia in 5 patients (29.4%), blurred vision in 5 patients (29.4%), and the patient (11.7%) had tinnitus. Papillary edema was present in all patients. Opening CSF pressure was 38±4.7 H_2O. There was no difference in prognosis, incidence, and etiology between adolescent and non-adolescent children. Papilledema was detected in all patients at the time of diagnosis. There was 7 (41.1%) abducens paralysis (5 unilateral, 2 bilateral). All patients received primary and/or secondary treatment. Primary treatment was acetazolamide in 13 (76.4%) patients and topiramate in 4 (23.5%) patients. Secondary treatment was applied to 3 of the cases and ONSF was applied to all of these cases. No complications were observed

Table 1. Clinical features of children with secondary pseudotumor cerebri syndrome

Case	Year/ gender	Etiology	Papil edema	Field of vision	Treatment	Comorbodite	Result
1	15/M	Mastoiditis	Severe	None	Acetazolamide	CVT	Normal
2	11/M	CRY (cystinosis)	Mild	None	Topiramate/optic nerve sheath fenestration	IDA Hypertension	Chronic papilledema
3	7/F	Head trauma	Mild	None	Acetazolamide	None	Normal
4	14/M	Mastoiditis	Severe	Mild visual field loss	Acetazolamide/ONSF	CVT	Normal
5	10/M	Pansinusitis	Mild	None	Acetazolamide	CVT	Normal
6	16/F	Andersen-Tawil Syndrome	Mild	Mild visual field loss	Acetazolamide	Pernicious anemia	Normal
7	4/F	Hypothyroid	Mild	None	Topiramate	Obesity	Normal
8	15/F	Steroid stop	Mild	None	Topiramate	Obesity	Normal
9	7/F	Coats Plus Syndrome	Severe	Mild visual field loss	Acetazolamide/ ONSF	IDA	Normal
10	2/M	Achondroplasia	Moderate	None	Acetazolamide	None	Normal
11	8/M	Growth hormone treatment			Acetazolamide	None	Normal
12	16/M	Retinoic acid treatment	Mild	None	Topiramate	Obesity	Normal
13	5/F	Acute lymphoblastic leukemia	Moderate	None	Acetazolamide	Steroid stop	Normal
14	15/F	Arachnoid cyst rupture	Mild	Mild visual field loss	Topiramate/ ONSF	Obesity	Normal
15	7/M	Hypothyroid	Mild	None	Acetazolamide	IDA	Chronic papilledema
16	5/M	Hypothyroid	Severe	None	Acetazolamide	IDA	
17	10/F	Turner syndrome	Mild	None	Acetazolamide	None	Normal

M: Male F: Female, CVT: Cerebral venous thrombosis, IDA: Iron deficiency anemia, ONSF: optic nerve heath fenestration

in the patients who received ONSF. VP shunt was not applied to any patient. Papilledema was completely resolved in 15 patients (88.2%) after a mean follow-up of 4.5 months (1.0 between 27.1 months). The other 2 patients (11.7%) had chronic papilledema that did not progress for 13 months and was not treated. There was no patient whose visual impairment continued after treatment. The most common comorbidity associated with sPTCS in our population was anemia 5 (29.4%).

Discussion

In our study, infectious diseases, endocrinological pathologies, and drug exposure were found more frequently in the etiology of PTCS. This finding shows similar results to the literature. Secondary pseudotumor cerebri can cause mortality and morbidity if not diagnosed and treated early. Especially in the treatment of sPTCS, the etiologic cause should be treated as well as reducing the ICP [1, 2]. In children, approximately 20% of cases of sPTCS have a poor long-term prognosis. These include visual impairment and optic atrophy. In our study, 4 of 17 patients had a mild visual loss. There was no patient whose vision loss continued at the end of primary and secondary treatment. In studies, mild long-term visual impairment was found in 9-10% of patients with primary and sPTCS. In addition, surgical treatment was not common in PTCS cases in these studies [2]. In our study, optic nerve fenestration was performed in 3 of 17 patients with secondary PTCS to lower ICP and the results were quite good. Because we followed up our patients very frequently (2 days a week) and in case of non-response to medical treatment, we thought that our results could be good due to surgical treatment without wasting time. Optic nerve sheath decompression is a surgical procedure performed to relax the optic nerves and relieve papilledema, which causes visual impairment due to increased intracranial pressure. A study investigated the efficacy and complications of ONSF. In this study, 525 ONSF procedures were performed on 341 patients during the follow-up period of 42.3 months. Accordingly, they concluded that ONSF could reduce papilledema and improve vision. Papilledema improved in 95% of patients, visual acuity improved in 67%, and visual fields improved in 64%. However, the effect of ONSF in relieving headache was insufficient (41%). A second fenestration operation was required in 11% of the cases [7]. Our patients did not require a second surgical procedure. It may be due to our continued medical treatment after surgical treatment. In another study, visual acuity and visual fields improved in 95% of patients who underwent ONSF without reporting any intraoperative complications.

The average follow-up period of the cases was 18.7 months. Among the postoperative complications, ocular deviation was detected (6%) and corneal Dellen was detected [8, 9]. In another retrospective study, unilateral ONSF showed papilledema and bilateral improvement in vision [8, 10]. In the literature, it has been found that ONSF in IHH cases, and especially in cases with acute papilledema, papilledema regresses in more than 90% of the patients. Repeated fenestrations have been shown to provide significant improvement in visual function. In a recent study, 13 of 53 IIH patients with acute papilledema and vision loss were treated with ONSF. However, 11 of them required secondary or tertiary decompression treatments. As a result, visual fields improved [8, 11]. Publications on the long-term outcomes of sPTCS in children are limited, and usually primary and secondary cases have been evaluated together. There is more work in primary PTCS. In one study, primary and secondary cases were evaluated together. While the vision of all 12 sPTCS patients was normal, 2 patients did not respond to medical treatment and VP shunt was applied to one patient [12]. In another study, moderate visual field loss was found in only 1 (4%) of 23 patients with sPTCS [13].

The most common comorbidities accompanying the causes of sIH in our cases were obesity and anemia. Obesity is a well-known risk factor for both secondary and primary PTCS [2]. In a study evaluating obesity in the pediatric population, it was reported that the incidence of IIH was equal and there was no clear relationship with obesity [14]. In another study, obesity was evaluated as a risk factor [1]. In our study, we did not find a relationship with obesity in terms of prognosis. However, as the number of cases increases, there may be a significant difference between obesity. It is well-documented that corticosteroid withdrawal can induce sPTCS [15, 16]. In one study, eight of 15 subjects with sPTCS were induced after

discontinuation of corticosteroids. Anemia is thought to be a risk factor for sPTCS by increasing cerebral blood flow [17]. Anemia and tissue hypoxia alters cerebral hemodynamics, increasing cerebral capillary permeability and thus increasing ICP, which causes sPTCS [18]. The literature review did not find an answer to the question of how severe anemia should be, although anemia was considered a cause or possibly an additional risk factor for sPTCS. This is because there are different study methods and different criteria for anemia. Iron deficiency anemia and hemolytic anemia have been identified as the most common risk factors for PTCS, and we found anemia due to iron deficiency and B12 deficiency in our cases [2]. Cerebral venous thrombosis (CVT) can be seen in the comorbidity of patients with secondary PTCS. In their study on this subject, they reported that visual acuity decreased in 3 (7%) of 37 children with cerebral venous sinus thrombosis. Additionally, surgery was performed in 19% of children with decreased visual acuity [1, 19]. One of our patients with CVT underwent ONSF and vision loss was not permanent. Treatments for sPTCS and primary PTCS are different. Since the etiology is very diverse in the treatment of sPTCS, a multidisciplinary approach is essential. For example, anticoagulation therapy should be arranged by a pediatric stroke team for children with cerebral venous sinus thrombosis.

If sPTCS has developed due to drug use or exposure, once this agent is identified, necessary precautions should be taken. When treating the underlying cause of sPTCS, it is more important to lower ICP and monitor visual function and papilledema. If there are signs of advanced papilledema/visual impairment, direct treatment of ICP may be indicated. There are cases where papilledema does not subside despite treatment of the underlying etiology. For example, in some studies, 2 patients with cerebral venous sinus thrombosis required a VP shunt due to severe or chronic papilledema despite anticoagulation therapy [1].

Limitations, the small number of our cases, the lack of longer follow-up periods and the small number of patients who underwent surgical treatment may limit our evaluation of the prognosis.

Since sPTCS has many different causes, classifying all causes into a single group reduces the reliability of the study. This was due to the low number of cases due to specific causes and insufficient risk factors and subgroup analyses. Due to the small number of cases in each sPTCS group in our study, we could not establish a strong association between different risk factors and sPTCS. It is thought that a multidisciplinary study for surgical options of patients who do not respond to medical treatment. Multidisciplinary work with clinicians will increase awareness of possible risk factors for sPTCS and provide better treatment of patients.

Conflict of interest: No conflict of interest was declared by the authors.

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Authors' contributions to the article

O.G. constructed the main idea and hypothesis of the study. O.G and E.S.U. developed the theory and arranged/edited the material and method section. O.G., B.K.Y. and O.P. have done the evaluation of the data in the results section. Discussion section of the article written by O.G. and E.S.U. and, B.K.Y. and O.P. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.