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ORIGINAL ARTICLE

Sixth Nerve Palsy in Paediatric Intracranial Hypertension

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ABSTRACT

The purpose of this study was to report the incidence and describe the characteristics of sixth cranial nerve (CN VI) palsy in paediatric patients with intracranial hypertension (IH). A retrospective chart review of central Ohio children diagnosed with IH over the 3-year period from 2010 to 2013 was conducted. IH without identifiable cause was defined as idiopathic intracranial hypertension (IIH), whereas IH with identifiable pathologic aetiology was deemed secondary intracranial hypertension (SIH). A subset of patients with CN VI palsy was identified. Data collected included patient age, gender, past medical history, aetiology of SIH, ophthalmic examination, lumbar puncture results, neuroimaging results, and response to treatment. Seventy-eight children with intracranial hypertension were included in the study. Nine (11.5%) children (four males, five females; median age 14, range: 3–18) were found to have a unilateral (n = 2) or bilateral (n = 7) CN VI palsy. Five children had IIH; the remaining four had SIH from cerebral venous sinus thrombosis (n = 2) and infection (n = 2). The mean lumbar puncture opening pressure for the nine patients with CN VI palsy was 40 cm H_2O (range: 21–65 cm H_2O). Papilloedema was present in 8/9 (89%) patients. One patient required a lumboperitoneal shunt, and two others required optic nerve sheath fenestrations in addition to medical management. All cases of CN VI palsy resolved with treatment. In our primary service area, the incidence of CN VI palsy is approximately 12% among paediatric IH patients. The majority of cases with CN VI palsy presented with papilloedema and all cases resolved with treatment of intracranial hypertension.

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Introduction

Paediatric intracranial hypertension (IH) can be idiopathic or secondary. The list for secondary intracranial hypertension (SIH) causes is long and growing. Some of the more important causes to consider are cerebral venous abnormalities, drugs, endocrine abnormalities, and infectious causes.[1] Paediatric idiopathic intracranial hypertension (IIH) has been further divided into childhood and adolescent forms. In the childhood form, males and females are affected in similar percentages and there is at best a weak association with obesity.[1] The adolescent form has been compared to the adult form because there is a female predominance and strong association with obesity.[1,2] As childhood obesity becomes more prevalent, there may be a similar increased prevalence of paediatric IIH.[3]

Aside from papilloedema, sixth nerve (CN VI) palsy is the most common neurologic examination finding in paediatric IIH.[1,4] This occurs because of elevated intracranial pressure (ICP), which results in a downward displacement of the brainstem that stretches CN VI as it crosses over the petrous ridge and enters Dorello's canal. Approximately 12% of adults with IH develop sixth nerve palsy.[5] It has been suggested that CN VI palsy occurs more frequently in children with IH, but the reported incidence has ranged widely, from 9% to 59%.[4,6–12] One study found cranial nerve palsies, including CN VI, to be more common in children aged 11 or younger.[7] The incidence of CN VI palsy in paediatric IH therefore remains variable and somewhat uncertain.

We sought to report the incidence and describe the characteristics of CN VI palsy in paediatric patients with IH, including association with papilloedema and response to treatment. We also aimed to look at differences between patients

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with SIH and IIH as well as differences between patients with the childhood and adolescent forms.

Methods

A retrospective chart review of central Ohio children diagnosed with IH over the 3-year period from 2010 to 2013 was conducted. The study was approved by the institutional review board and conducted in compliance with the Health Insurance Portability and Accountability Act (HIPAA). Inclusion criteria consisted of the following: (1) new diagnosis of IH based on elevated lumbar puncture (LP) opening pressure (OP) or cerebral sinus venous thrombosis on magnetic resonance (MR) venogram and clinical examination consistent with elevated intraocular pressure (ICP); (2) age 0 to 18 years; (3) fundus examination with indirect ophthalmoscopy by a paediatric ophthalmologist within 1 day of IH diagnosis; and (4) from our hospital's primary service area. Using the prepubertal primary intracranial hypertension criteria,[1,13] in which the normal opening pressure limits are adjusted for age, IH was defined as an LP with OP >25 cm H_2O and if younger than 8, OP >18 cm H_2O in the presence of optic disc oedema. If the OP was recorded as being "greater than" a certain value (because it was greater than the length of the manometer), it was converted to 1 cm above the "greater than" value (i.e., OP >55 was converted to OP of 56). IH without identifiable cause was defined as IIH, whereas IH with identifiable pathologic aetiology was deemed SIH. The subset of patients diagnosed with CN VI palsy based on the presence of a new abduction deficit and/or esotropia worse in lateral gaze was reviewed in depth. Specific outcomes for these patients included the presence of papilloedema and response to treatment. In addition, patient age, gender, body mass index (BMI) and BMI percentile for age, past medical history, aetiology of SIH, ophthalmic examination, lumbar puncture results, and neuroimaging results were recorded. Subjects were further categorized based on whether their IH was idiopathic or secondary to another cause. Patients were classified as having the prepubertal disease form if they were 11 or younger and the pubertal disease form if they were older than 11 years.[14,15] All eye examinations occurred within 1 day of diagnosis, with the majority (8/9) completed the day prior to or day of diagnosis.

Results

Seventy-eight patients with IH were included in the study and 9/78 (11.5%) patients (4 males, 5 females; median age 14, range: 3–18) were found to have a unilateral (n = 2) or bilateral (n = 7) CN VI palsy (Table 1). More specifically, the incidence of CN VI palsy was 13.0% (3/23) among patients with the childhood form and 10.9% (6/55) among patients with the adolescent form. The median BMI was 29.6 kg/m^2 and median BMI percentile was 96.5. Five children had IIH; the remaining four had SIH from cerebral sinovenous thrombosis (n = 2) and infection (n = 2; one meningitis and one Rocky Mountain spotted fever). The median opening pressure among all patients was 40 cm H_2O (range: 21–65 cm H_2O). Papilloedema was present in 8/9 (89%) patients. All cases of CN VI palsy resolved within days to weeks of initiating treatment. Treatment of elevated ICP consisted of medical management in all but one patient with IIH who required a lumboperitoneal shunt upon failure of medical management. Two patients, both with IIH, underwent optic nerve sheath fenestration due to concern for vision loss.

Median BMI was higher among IIH patients (30.2 kg/m^2 as opposed to 22.6 kg/m^2 in SIH patients) and adolescent patients (34.4 kg/m^2 as opposed to 15.8 kg/m^2 in younger patients). This is demonstrated in Table 2. The median opening pressure was highest among the IIH and adolescent groups (43 and 46 cm H_2O, respectively).

In the 69 patients with IH but without CN VI palsy, the median BMI was 25.1 kg/m^2 (Table 3). These patients had a median opening pressure of 36 cm H_2O.

Discussion

Our incidence of CN VI palsy in paediatric IH patients is at the lower end

of the previously reported range and is similar to what has been reported in adult IH patients.[5] We had no cases of unresolved CN VI palsy within this study set. In our experience, most cases of CN

Table 1. Demographic data of patients presenting with IH and CN VI palsy.

Subjects	9 (4 males, 5 females) of 78 patients with IH
Age, median	14 years (range: 3–18)
BMI, median	29.6 kg/m^2 (range: 15.3–45.9)
BMI percentile for age, median	96.5 (range: 0.12–100.0)
Aetiology	
Idiopathic	5
Cerebral sinovenous thrombosis	2
Infection	2
Intracranial pressure, median	40 cm H_2O (range: 21–65) (measured in 8 patients)
Eye examination timing (relative to diagnosis)	
−1 to 0 days	8
1 day	1
CN VI palsy	
Unilateral	2
Bilateral	7
Papilloedema	8 (89%)
Treatment	
Diamox	8
Lumboperitoneal shunt	1
Optic nerve sheath fenestration	2

VI palsy related to IH resolve with medical management.

In comparing the different IH groups with CN VI palsy, the median BMI and BMI percentile for age was higher amongst the IIH and adolescent groups, which supports the known role of obesity in development of adolescent IIH. In addition, all three patients requiring more than just medical management had IIH, so perhaps this reflects an overall higher disease severity in IIH compared with SIH patients. The IIH and adolescent groups had the highest mean ICP as well. Further studies with larger subsets of IH patients are needed to reliably uncover differences.

When we compared IH patients with and without CN VI palsy, the CN VI palsy patients had a higher BMI and opening pressure. The role of obesity and opening pressure in the development of CN VI palsy in IH warrants further study.

We opted to use the more widely accepted criteria for opening pressure,[13] reasoning that the recently proposed stricter criteria for IH[16] would have excluded actual IH cases from our series. Commentaries by others in the field have raised similar concerns about the stricter criteria.[17–19] Due to the retrospective nature of our study, Tanner staging was not obtained on

Table 2. Comparison of idiopathic, secondary, childhood, and adolescent IH patients with CN VI palsy.

Characteristic	IIH	SIH	Childhood	Adolescent
Subjects	5 (2 males, 3 females)	4 (2 males, 2 females)	3 (1 males, 2 females)	6 (3 males, 3 females)
Age (years), median	13 (range: 3–18)	15 (range: 5–16)	5 (range: 3–7)	16 (range: 13–18)
BMI, median (kg/m^2)	30.2 (range: 15.8–39.2)	22.6 (range: 15.4–45.9)	15.8 (range: 15.6–17.04)	34.4 (range: 15.3–45.9)
BMI percentile for age, median	98.6 (range: 84.2–100.0)	77.2 (range: 0.12–99.9)	59.7 (range: 51.1–84.2)	99.2 (range: 0.12–100.0)
Intracranial pressure (cm H_2O), median	46 (range: 21–65)	36 (range: 29–44)	27 (range: 21–44)	46 (range: 29–65)
CN VI palsy				
Unilateral	0	2	1	1
Bilateral	5	2	2	5
Papilloedema	5 (100%)	3 (75%)	3 (100%)	5 (83%)
Treatment				
Diamox	5	3	3	5
Lumboperitoneal (LP) shunt	1	0	0	1
Optic nerve sheath fenestration (ONSF)	2	0	1	1
Aetiology				
Idiopathic	5	0	2	3
Cerebral sinovenous thrombosis	0	2	1	1
Meningitis	0	1	0	1
Rocky mountain spotted fever	0	1	0	1

Table 3. Comparison of BMI and OP in IH patients with and without CN VI palsy.

Characteristic	With CN VI palsy	Without CN VI palsy
Subjects	9	69
BMI, median	29.6 kg/m^2 (range: 15.3–45.9)	25.1 kg/m^2 (range: 14.5–61.8)
Intracranial pressure, median	40 cm H_2O (range: 21–65) (measured in 8 patients)	36 cm H_2O (range: 21.5–56) (measured in 66 patients)

each patient. Thus, we opted to use previously accepted cutoffs for puberty.[14,15] It is also unlikely that a member of our prepubertal group would have gone through puberty, given that the oldest patient in this group was 7 years old.

Strengths of our study included the total number of patients, restriction of patients to a geographic area (to avoid selection bias), and ophthalmic examination within 1 day of IH diagnosis. However, there are some important limitations. A larger portion of our IH patients (56) were adolescent—and thus had a form of the disease that was more similar to the adult form—whereas fewer patients (23) were age 11 or younger. Even though that age distribution mirrors that of paediatric IH in the general population, the smaller proportion of 11-and-under cases in our sample could underestimate the true incidence of CN VI palsy in this age group, since it has been suggested that CN palsies are more commonly found in younger paediatric patients. In addition, one patient with cerebral sinovenous thrombosis did not have ICP measured with an LP. This patient had signs of IH, including bilateral CN VI palsies, enlarged blind spots on Humphrey visual field testing, and moderate-severe papilloedema, so we would not expect inclusion or exclusion of this patient to change our study conclusions.

Our findings suggest an incidence of CN VI palsy in paediatric IH patients of approximately 12%. Papilloedema is often an associated finding, and complete resolution of the CN VI palsy with treatment is characteristic. Further studies to compare paediatric patients with different types of IH as well as those with and without CN VI palsy could uncover important differences.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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