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Topical Review

Pediatric Intracranial Hypertension

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ABSTRACT

Primary (idiopathic) intracranial hypertension has been considered to be a rare entity, but with no precise estimates of the pediatric incidence in the United States. There have been attempts to revise the criteria over the years and adapt the adult criteria for use in pediatrics. The clinical presentation varies with age, and symptoms tending to be less obvious in younger individuals. In the prepubertal population, incidentally discovered optic disc edema is relatively common. By far the most consistent symptom is headache; other symptoms include nausea, vomiting tinnitus, and diplopia. Treatment mainstays include weight loss when appropriate and acetazolamide. Furosemide may exhibit a synergistic benefit when used in conjunction with acetazolamide. Surgical interventions are required relatively infrequently, but include optic nerve sheath fenestration and cerebrospinal fluid shunting. Pain and permanent vision loss are the two major complications of this disorder and these manifestations justify aggressive treatment. Once intracranial hypertension has resolved, up to two thirds of patients develop a new or chronic headache type that is different from their initial presenting headache.

Keywords: pseudotumor cerebri, intracranial hypertension, pediatric, headache

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History

Primary intracranial hypertension (idiopathic intracranial hypertension, pseudotumor cerebri) is generally considered to be a rare entity. Although the annual incidence in the United States adult population is estimated at 0.9 per 100,000, there are no precise incidence estimates in the pediatric population.[1] In Germany the annual pediatric incidence is estimated to be 0.47 per 100,000, and in Croatia, 1.2 per 100,000.[2,3] In the provinces of Nova Scotia and Prince Edward Island, the annual incidence was 0.9 per 100,000 in children two to 15 years of age between 1979 and 1994.[4] Surprisingly, in the same population from 1997 to 2007, the annual incidence fell to 0.6 per 100,000 in children aged two to 16 years, despite increased rates of childhood obesity during this period.[5]

The original description of intracranial hypertension by Quincke appeared in 1897. He described the clinical findings in a series of patients with increased intracranial pressure in the context of normal cerebrospinal fluid (CSF) and labeled this condition "meningitis serosa."[6] In the 120 years following Quincke's publication, the condition has gone by many different names, including serous meningitis, otitic hydrocephalus, toxic hydrocephalus, and hypertensive meningeal hydrops. In 1904, "pseudotumor cerebri" was coined by Nonne to reflect the similarities in presentation to patients with an intracranial mass.[7] In 1955, Foley suggested the condition be renamed "benign intracranial hypertension" to avoid the negative connotation associated with a "pseudocancer" diagnosis.[8] In the 1980s, following a series of reports describing permanent visual dysfunction, the syndrome was renamed idiopathic intracranial hypertension.[9,10]

Today, pseudotumor cerebri and idiopathic intracranial hypertension remain the two common terms among both practitioners and the lay public. There remains confusion with both terms, and practitioners still often misdiagnose pseudotumor cerebri despite the identification of a direct cause of the increased pressure. There have been recent attempts to clarify the terminology surrounding the ambiguity in these terms. Some have attempted to use a broader

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designation of "pseudotumor cerebri syndrome," which still includes the designation of idiopathic when a cause is not found.[11-13] We prefer the use of the terms primary intracranial hypertension (PIH) and secondary intracranial hypertension (SIH).[14] In cases where a clear precipitant of increased intracranial pressure is not found, individuals would be labeled as primary instead of idiopathic. Although they may have risk factors for increased intracranial pressure, such as female gender, postpubertal status, obesity, or polycystic ovarian syndrome, these conditions do not fully explain increased pressure. The concept of SIH is reserved for individuals whose intracranial hypertension is the direct result of another condition, such as cerebral sinus venous thrombosis or minocycline use.

Diagnostic criteria

The diagnostic criteria for adult PIH stems from a series of 22 patients reported by Dandy in 1937.[15] His report resulted in the initial criteria bearing his name, although he did not propose the criteria in this paper. The main limitation of the Dandy criteria is that imaging was at that time limited to pneumoencephalography, which sometimes provided evidence of an intracranial mass by distortion or compression of the ventricles. This method did not allow the identification of nonmass causes such as a sinus venous thrombosis. In 1985, Smith proposed modernization of the criteria into what is now accepted as the "modified" Dandy criteria to include additional imaging criteria.[16] These revised criteria include: (1) signs and symptoms of raised intracranial pressure (e. g. headache, nausea, vomiting, transient visual obscurations, or papilledema), (2) absence of localizing neurological signs with the exception of unilateral or bilateral abducens nerve palsy, (3) CSF opening pressure of more than 25 cm H_2O with normal composition, (4) normal to small ventricles as demonstrated by computed tomography (CT) study (today magnetic resonance imaging is the modality of choice).

Recently there have been further revisions to the criteria for PIH and the requirements increased, although the basic requirements remain.[12] The major concern with these stricter criteria is that they will result in missed cases, and thus potential morbidity.[17-20] There has been debate about the application of the adult criteria to children. One area that has seen recent change is the normative values for CSF opening pressure. Adult normative values are well established but due to ethical considerations there have not been many pediatric studies sampling normal patients. Adult studies have consistently shown that the pressure must be in excess of 25 cm H_2O to be considered abnormal.[21-24] There has not been a correlation found to degree of obesity and opening pressure in normal patients.[21-23] Studies have shown that flexed positioning and changes in arterial carbon dioxide (CO_2) result in an increased opening pressure in pediatric patients.[25-27] One study compared readings in both the flexed and extended positions and found a statistically significant difference.[25] Although the authors state that this change is likely of little clinical significance, there were some patients who had a change of 5 cm H_2O or more. Lim and Lin[27] found that an increase of 1 kPa in end-tidal CO_2 resulted in an increase in CSF pressure of 3.5 to 12 cm H_2O.

Some practitioners use $\leq$18 cm H_2O for children younger than eight years and $\leq$25 cm H_2O for children eight years or older (mirrors adult normal subjects) as cutoffs based on previously published works.[28-30] Three recent articles have questioned these values.[31-33] Avery et al.[31] analyzed patients aged one to 18 years receiving lumbar punctures (LPs) at The Children's Hospital of Philadelphia. They observed a mean opening pressure of 19.8 cm H_2O and suggest an upper limit of normal (i.e., the 90th percentile) of 28 cm H_2O. Subanalysis showed a small positive relationship between opening pressure and body mass index (BMI) and no influence of age on opening pressure. In a separate analysis of 33 patients with verified optic nerve edema, they found an average opening pressure of 41.4 cm H_2O (range 22 cm to 56 cm).[32] Lee and Vedanarayanan[33] reviewed 44 patients aged 1.1 to 16.8 years who had undergone a sedated LP and found a mean of 20.3 cm H_2O. Both study groups included patients with demyelinating and white matter disease in their normal patient sample (discussion in the online appendix provided by Avery et al.). Lee and Vedanarayanan[33] conducted a separate analysis of patients with demyelinating disease, and found a mean opening pressure of 21.5 cm H_2O, which is higher than that of their total population (20.3 cm H_2O). The inclusion of patients with demyelinating disease as a normal patient does raise the concern for a falsely elevated average as other published studies have shown increased opening pressures in this population.[34-36] Narula et al.[36] found that 28% of children with demyelinating disorders had an elevated opening pressure using the cutoff of 28 cm H_2O previously proposed by one of the coauthors. The percentage of cases with elevated opening pressures likely would have been higher if examined with the older cutoffs.

Demographics

In pediatrics, PIH is often divided into prepubertal or pubertal groups. Pubertal patients have the same risk factors as adults, whereas sex and weight are not prominent risk factors in prepubertal patients. The pediatric female-to-male ratio ranges from 1:1 to 13:6, and concurrent obesity ranges from 10% to 78%, largely depending on whether or not patients are divided by pubertal status (Table 1).[3-5,37-41] Balcer et al.[42] found that obesity correlated with an increased risk of PIH in older children but not in those less than 11 years old. Bursztyn et al.[5] found a similar correlation in those greater than 12 years old. Aylward et al. examined pediatric cases enrolled in a large intracranial hypertension registry and found significantly higher BMI in postpubertal PIH patients (30.7 versus 21.6).[41] Rare reports of familial links with PIH can be found in the literature.[41,43-45] Many of these reports involve a parent and offspring relationship, although affected siblings have also been documented. Although this pattern suggests a dominant inheritance pattern, specific genetic links have not been found.

Signs and symptoms

The clinical presentation of intracranial hypertension in pediatric patients can vary with age, with symptoms tending to be less evident in younger individuals. In the prepubertal population, incidentally discovered optic disc