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Spectrum of benign intracranial hypertension in children and adolescents

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Abstract. A review of the most recent 23 cases of benign intracranial hypertension (BIH), admitted to the War Memorial Children's Hospital in London, Ontario, provided a compendium of the clinical manifestations of this disorder in children and adolescents. Although CT scanning lets one feel more secure in making such a diagnosis, pitfalls still exist. The sex ratio was 11 males to 12 females. Age groupings were: 0–6 years (2 patients); 7–12 years (10); 13–17 years (11). No postviral etiologies were encountered in patients more than 13 years of age. In only 6 cases could no definite etiology be established. Of great importance was the recognition of the condition in 12 patients who did not have papilledema. Elevated intracranial pressure was proven in 8 of these by lumbar CSF pressure monitoring, in 1 by lumbar punctures and in 1 infant with split cranial sutures. Absence of papilledema was confirmed by ophthalmological examination. Transient visual obscurations were very common in this group. In 6 patients, persistent signs and symptoms in spite of vigorous drug therapy prompted lumboperitoneal shunting, with immediate relief of symptoms in all. In only 1 case has the diagnosis of BIH proven to be in error. A warning leak from an aneurysm caused papilledema and headache, and a normal CT scan supported the diagnosis until the patient had a major hemorrhage weeks later. BIH has a variety of causes in children and adolescents, and papilledema is not a prerequisite for diagnosis.

Key words: Benign intracranial hypertension – Papilledema – Etiology.

Benign intracranial hypertension (BIH), also known as pseudotumor cerebri, is still a mysterious ailment, its pathophysiology elusive. In the past, the diagnosis has been based upon the complaint of chronic and severe headache; absence of intracranial pathology on cerebral angiography or air contrast studies and, more recently, CT scans and papilledema. Recognition that papilledema is not a criterion for diagnosis has been fairly recent [8, 14, 16]. Specific associations between BIH and ingestions of certain drugs, hematologic disorders, endocrine disturbances, ear infections, head trauma, obesity, and preceding viral infestations seem established, but such recognition has thrown little light upon the mechanisms of the disorder. The studies of Johnston [7] and, more recently, of Janny et al. [6] and Sklar et al. [15] lend support – in our minds, at least – to the idea that outlet resistance to the egress of cerebrospinal fluid (CSF) through the arachnoid granulations is somehow increased. The fact that lumbar drainage or lumbar-peritoneal CSF shunting relieves the headache and the papilledema supports this view. What is not understood is the failure of the ventricles to dilate in the presence of an increased volume of intracranial fluid. Something of importance is being missed with respect to the genesis of so-called communicating hydrocephalus, but what that something is has so far escaped detection.

Clinical data

All patients were under the immediate or consultative care of a neurologically expert person, and in those where papilledema was not seen, of a consultant ophthalmologist.

There was no sex predominance. Eleven of the cohort were boys, 12 girls. In the general BIH population, women are said to predominate by a substantial margin [2].

The established etiological associations for this cohort are listed in Table 1. These results indicate that an etiology

Table 1. Etiologies

Association	Patients	
	N	%
None	6	26
Trauma	5	22
Virus	6	26
Antibiotic	3	13
Subarachnoid hemorrhage	1	4
Obesity	1	4
Blood dyscrasia	1	4

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for the BIH can be discerned in about 75% of cases, in the young.

Trauma was felt to be the precipitating factor in 5 cases; 4 of these were males. In no instance did the injury produce coma. The typical story was provided by a 13-year-old boy who whacked the top of his head sharply on an overhead rack in a school bus. Two weeks later, his progressive headache syndrome began. One might speculate that a small amount of subarachnoid blood spilled in such an event might act as an irritant within the arachnoid granulations, inducing inflammation, perhaps fibrosis, and increased resistance to CSF outflow.

Viral illness antecedents to the onset of BIH (6 cases) were flulike in 5. In 1 child, there was a CSF lymphocytosis of 300 cells/mm^3, and he was judged to have had a mild viral meningitis. There were no postviral cases in any patient past the age of 13.

The antibiotics implicated were amoxicillin (Amoxil) and co-trimoxazole (Bactrim) in 1 case, trisulfaminic in 1, and tetracycline in 1. Upon stopping the drug, the syndrome receded in all cases, with the adjunctive therapy of digoxin in 1, acetazolamide and steroids in 1, and steroids in 1.

One 12-year-old boy was admitted with 3 days of increasingly severe headache and papilledema. A CT scan with contrast was normal. In 7 days, his headache and papilledema were receding, and he was discharged with a diagnosis of BIH of unknown etiology. Four weeks later, his mother found him having a seizure in bed. He was drowsy and irritable. A repeat CT scan showed a small left basal frontal clot, and angiography revealed an anterior communicating artery aneurysm. At operation, old staining of cortex was seen, implying that the BIH previously diagnosed was in fact a manifestation of a warning leak from the aneurysm sac. This case was the sole example of inaccurate diagnosis, but it shows that pitfalls still exist in making the diagnosis of BIH, even with CT scanning.

Headache was a dominant complaint in all patients. Almost always it was pancephalic or frontal, and severe enough to interfere with daily routines. Eleven of the cohort had experienced attacks of vomiting in association with the headache bouts. Features that suggested high-pressure headaches were: accentuation with any Valsalva-like maneuver, increase in intensity with bending over, occurrence in the early morning, and associated vomiting. Visual obscurations occurred in 9 and in 7 of these, the fundi were not abnormal.

The visual obscurations were described usually as a "dimming" or "browning-out" of vision, sometimes as a severe "fuzziness." One girl had as many as 10 or 12 such episodes daily. Seldom did the attacks last more than several seconds and most commonly they were very brief. Why the history of visual obscurations was obtained almost exclusively from patients without papilledema in this group of patients is unknown. Nevertheless, such a symptom in a patient with headaches that resemble high-pressure headaches strongly suggests the diagnosis of BIH, even when papilledema is not found.

It is fair to say that in the patients without papilledema, spontaneous venous pulsations were not seen. Perhaps in this situation, the loss of spontaneous venous pulsations represents very early choking of the discs.

All patients had CT scans. In 21, the scan was normal, in 2 the ventricles were described as smaller than normal. Of 9 EEG examinations, 6 were normal and 3 had posterior slowing. Five patients had normal cerebral angiograms. Early on, 3 patients without papilledema underwent fluorescein angiography of the retina, normal in every case. The role of lumbar puncture and of lumbar CSF pressure monitoring is discussed below. Some of the patient data are summarized in Table 2.

Patients without papilledema

This group of patients deserves additional comment. Table 3 summarizes some of the pertinent data. The etiologies of the BIH in this group were varied.

The 15-month-old boy (case 1) had widely split cranial sutures and no intracranial mass lesions. He was bright

Table 2. Patient data

Age group	Males	Females	Etiologies	Papilledema	Resolved	Lumbo-peritoneal shunt
0–6	2	0	Trauma (1) Viral (1)	1	2	
7–12	4	6	Idiopathic (2) Viral (5) Antibiotics (1) Subarachnoid hemorrhage (1) Blood dyscrasia (1)	7	10	1
13–18	5	6	Idiopathic (4) Trauma (4) Antibiotics (2) Obesity (1)	3	11	5

Table 3. Cases without papilledema

Case	Age	Sex	Etiology	Visual obscuration	Lumbar puncture pressure	CSF pressure monitoring
1	1.3	M	Trauma	?	–	–
2	9.9	F	Viral	No	↑↑	–
3	12.9	M	Viral	No	↑	–
4	12.0	M	None	No	–	Positive
5	15.11	F	None	Yes	–	Positive[a]
6	15.11	F	None	Yes	–	Positive[a]
7	16.6	F	Trauma	Yes	–	Positive[a]
8	17.3	F	None	Yes	–	Positive[a]
9	13.5	M	Trauma	Yes	–	Positive[a]
10	16.1	M	Trauma	Yes	–	Positive[a]
11	13.0	M	Antibiotics	No	–	Positive[a]
12	15.6	F	None	Yes	↑↑	–

[a] Patient underwent lumbo-peritoneal shunting

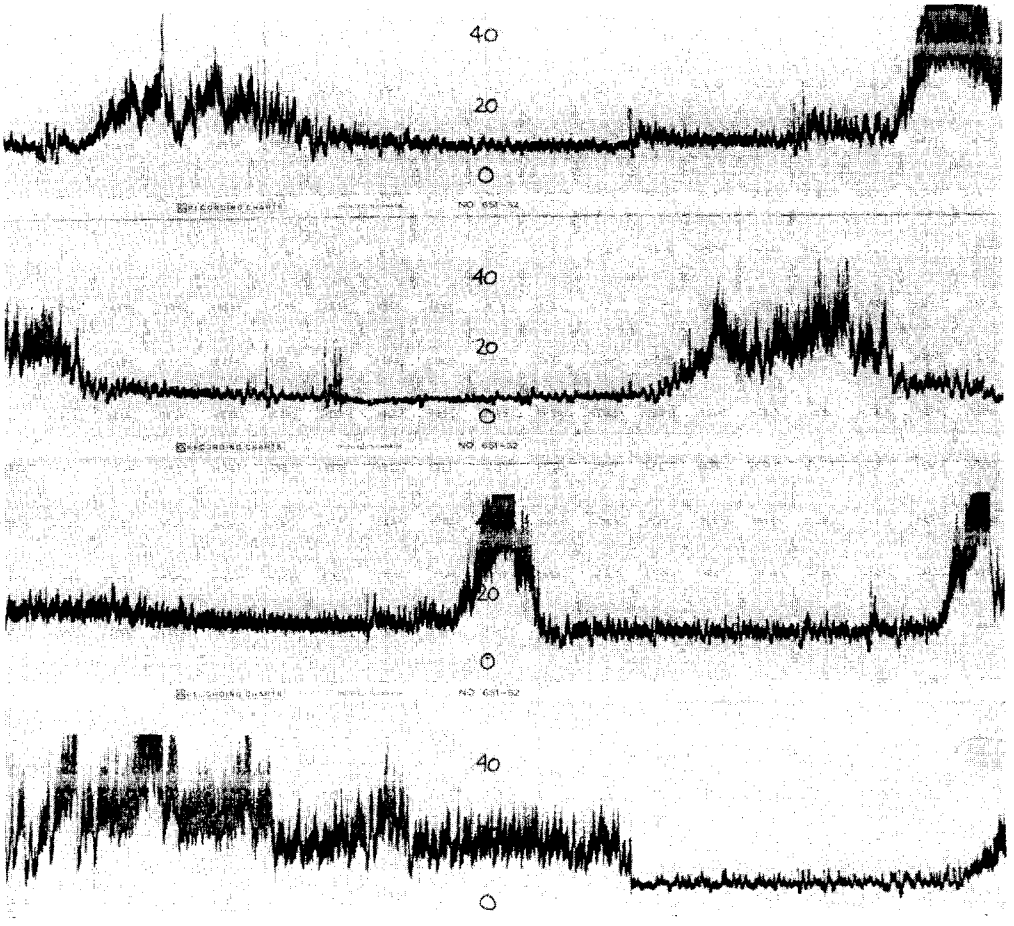

Fig. 1. Ten-hour tracing of CSF pressure from lumbar subarachnoid catheter. Pressure calibration is in torricelli. Paper speed is 2.5 mm/min

and alert, but vomited excessively. This fundi were normal, except for absent spontaneous venous pulsations. The syndrome cleared with 2 weeks, and the cranial sutures became normal.

Cases 2, 3, and 12 had high resting CSF pressures at lumbar puncture (in excess of 300 mm H_2O in each case) in quiet, cooperative patients. In each of these cases, the syndrome settled quickly, following a single lumbar puncture. All had had increasingly severe headache for at least 2 weeks. Perhaps a continuing CSF leak from the lumbar puncture site provided a continuous decompression for CSF while the underlying pathophysiology was resolving. Two of these children had suffered viral antecedent illnesses, and in 1 no cause was obvious.

Cases 4–11 underwent CSF pressure monitoring to prove the diagnosis. Under local anesthesia, a sterile plastic catheter was introduced into the lumbar theca via a No. 14 Toohy needle. A Hewlett-Packard strain gauge

was set at the level of the foramen of Monro, and a continuous tracing of intracranial pressure obtained on a Hewlett-Packard paper recorder moving at 2.5 mm/min. Tracings were done continuously for 24–36 h. Patient cooperation was excellent and observation by nursing staff was continuous. The patients remained in the supine position throughout.

Figure 1 is an example of a CSF pressure tracing obtained by this technique. It is typical of the group so monitored and is clearly abnormal. In this particular boy (case 4), the pressure waves were accompanied by headache. Much of the time, the baseline intracranial pressure was normal, but runs of pressure waves lasting from 10 min to 1.5 h were prominent. During some of these episodes, mean intracranial pressure reached 40 mmHg. His symptoms came under control very rapidly with acetazolamide therapy.

Therapeutic measures

Table 4 is a summary of the successful therapies for the entire cohort.

Neither child in the 0–6 age group had lumbar punctures or specific treatment, and the symptoms receded over 2–3 weeks. Three children in the 7–12 age group required no specific therapy for their symptoms. One of these had apparent idiopathic BIH, 1 was postviral, but the 3rd was the case of inaccurate diagnosis. His syndrome had been caused by an undetected warning leak from an aneurysm.

The 3 children successfully treated by a single lumbar puncture have been discussed above. A boy of 13.5 years gained no relief from daily lumbar punctures over a 2-week period. He did not have papilledema. When presented with further treatment options, the boy and his parents declined all drug therapy, choosing instead a lumboperitoneal shunt. His symptoms receded immediately, only to recur in several weeks when the shunt blocked. Reestablishment of shunt patency once again abolished the headache. One year later, he suffered from low-pressure headaches, prompting removal of the shunt. He has been asymptomatic since.

Three lumbar punctures and correction of severe iron-deficiency anemia cured BIH in an 11-year-old girl. Lumbar punctures with adjunctive acetazolamide therapy were successful in one. A girl of 8, with severe papilledema, failed to respond to a month's trial of twice weekly lumbar punctures and acetazolamide. A lumboperitoneal shunt cured her, the symptoms abolished from the 1st postoperative day.

Acetazolamide therapy alone cured 4 patients over time courses of 2–4 weeks. Two patients in whom this therapy failed opted for lumboperitoneal shunts, which were immediately successful in both. No headache relief had been obtained in either of these children after 2 months of drug therapy. In successful cases, drug therapy provides gradual and increasing relief from the outset.

Various combinations of acetazolamide, digoxin, and steroids failed to control symptoms in 2 of 3 patients. Digoxin alone and steroids alone controlled the disorder in 1 patient, respectively. In 1 girl of 16.5 years, steroids provided some relief for 1 month, but symptoms recurred promptly upon steroid withdrawal. A lumboperitoneal shunt was successful in controlling her headache. She developed low-pressure headaches, undoubtedly the signal that her BIH had receded, but has steadfastly refused to have her shunt removed.

Lumboperitoneal shunts have been inserted into 6 patients, in all cases after failure of one or more other therapeutic modalities. The spectacular abatement and total control of symptoms by this procedure lend credence to the opinion that BIH is in some way closely related to abnormal CSF absorption mechanisms [6, 7, 15]. Although some might regard a lumboperitoneal shunt as radical therapy for BIH, others – ourselves included – consider this surgical procedure as much more conservative than prolonged steroid use in children and adolescents. Symptoms disappear immediately [5].

The development of low-pressure headaches several months to 1 year following shunting has prompted shunt removal in 3 patients, without recurrence of symptoms. Presumably, the onset of a chronic low-pressure headache signals the disappearance of the BIH disorder. Two patients remain shunt-dependent more than 3 years following insertion.

Table 4. Successful therapies for the entire cohort

Mode	Number of treatments	
	Tried	Successful
None	5	4[a]
Lumbar punctures	4	3
Lumbar punctures, correct anemia	1	1
Lumbar punctures, diamox	2	1
Diamox	6	4
Diamox, digoxin	1	0
Diamox, steroid	1	1
Diamox, steroid, digoxin	1	0
Digoxin	1	1
Steroid	2	1
Lumboperitoneal shunt	6	6

[a] One failure, case of subarachnoid hemorrhage (see text)

Discussion

We agree with Johnston [7] that the term "benign intracranial hypertension" to describe this disorder should be scrapped. There is nothing "benign" about a condition that incapacitates patients with headache and often threatens vision. In a sobering review of 57 patients followed from 5

to 41 years from the time of diagnosis, Corbett et al. [2] found that 14 patients had permanent and severe visual loss (25%). Often, the visual loss was not apparent for months, even years, from the time of diagnosis. Twenty-four eyes in 14 patients were blind or severely impaired. Six patients had legal bilateral blindness. A further 29 eyes showed moderate visual loss. Yet in at least one major textbook of pediatrics, the entire syndrome receives extremely little attention [4].

Before the advent of CT scanning, common teaching was that as many as 20% of patients initially assigned to the BIH grab bag would turn up later with obvious mass pathology. In this cohort, the incidence to date has been one of 23 patients (4%). That is sufficient to support the caveat that one does not make a diagnosis of BIH, then promptly forget the patient.

As mentioned previously, the pathogenesis of this disorder remains elusive. Recently, Donaldson [3] has summarized current concepts relating to pathogenesis. With respect to CSF dynamics, one or more of five mechanisms must be operative.

1. There is a reduced or reversed gradient between subarachnoid space and the great venous sinuses. Normally, this gradient favors the CSF. Not infrequently, sinograms show total or incomplete occlusion of the great venous sinuses [1]. Such a situation increases venous pressure in the outlet channels from the head, reducing the subarachnoid space-great venous sinuses gradient.

2. There is an increase in resistance to absorption of CSF, for reasons that are not clear. That this occurs in at least some patients has been demonstrated beyond controversy [6, 7, 15]. It is reasonable to speculate that arachnoid granulations inflamed by blood or reactive white blood cells might be less amenable to bulk transport of CSF across narrowed and tortuous channels. However, why, for example, obesity [12] and sudden change in adrenocorticotropic hormone levels [7, 9] should induce an elevation in resistance to CSF absorption is a mystery.

3. A couple of studies have suggested an increase in cerebral blood volume in patients with "BIH" [10, 11]. Where venous sinus obstruction is a factor, this fact is not surprising. The cerebral venous bed is a capacitance system because of vein distensibility. Most of the cerebral blood volume at any one instant is within the cerebral veins and sinuses; to cause an appreciable and symptom-producing increase in intracranial pressure would require an increase in CBV of 23% or more [11]. It is difficult to imagine that such a mechanism can account for every case of "BIH."

4. Reid et al. [12, 13] have described a group of patients with "BIH" where ventricular volume has been reduced to subnormal values. Increased interstitial water content of the brain [11] could account for such a feature. The fascinating thing about the follow-up studies of Reid et al. [13] is that some patients who responded to therapy for "BIH" showed an increased ventricular volume or subsequent CT scans, while patients who remained symptomatic did not.

5. Donaldson [3] has suggested that some patients with "BIH" may be oversecreting CSF, beyond the capacity of the arachnoid granulations to absorb the CSF. Aside from his studies, no one has ever shown CSF oversecretion to be a physiological fact in the absence of a papilloma of the choroid plexus. Even if one were to agree that an increased blood flow through the choroid plexus might induce an increased outpouring of CSF, the studies of Raichle et al. [11] dispute that assumption. They found that while there was an increased cerebral blood volume in patients with BIH, cerebral blood flow in fact was diminished.

It is our opinion, all facts considered, that the strength of the argument lies with reduced CSF absorption for whatever reason. Reports that CSF diversionary procedures immediately relieve symptoms support this view [2, 5, this report]. We cannot explain why ventricular enlargement does not occur. It is a fact that BIH is unusual in the very young and in patients beyond the age of 40 years. Perhaps some intrinsic property of brain elastance at these ages causes the brain to react differently when CSF absorption dynamics are altered at the anatomical level of the arachnoid granulations.

A major thrust of this report from the clinical perspective has been that a very significant group of patients with the BIH syndrome do not have papilledema. Of our original cohort of 9 patients with the BIH syndrome but without papilledema, 5 had not attained the age of 18. This report contains 12 such preadult patients, and our current experience in the adult population adds a further 3 cases. This means that we have encountered 18 patients over a time-frame of 5 years who have had the BIH syndrome in the absence of papilledema. Our CSF pressure-monitoring technique has shown that the majority of such patients have normal intracranial pressures most of the time, yet they have significant periods of raised ICP, especially at night – episodes that would be missed entirely by so-called diagnostic lumbar punctures. It is obvious that the clinical history of raised intracranial pressure is far more reliable than fundoscopic examination.

Conclusion

This cohort of children and adolescents with the BIH syndrome supports the following observations: (1) in children and adolescents, the sex ratio is even; (2) papilledema is *not* a prerequisite for diagnosis; (3) in the absence of papilledema, a history evoking the BIH syndrome accompanied by a history of visual obscurations is very suggestive; (4) there is usually a demonstrable etiology; (5) CSF pressure-monitoring [1] is of great value in doubtful cases; (6) lumboperitoneal shunts will abolish the persistent BIH syndrome.

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