Diagnosis and management of benign intracranial hypertension

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Benign intracranial hypertension (BIH) is a headache syndrome characterised by (1) raised cerebrospinal fluid (CSF) pressure in the absence of an intracranial mass lesion or ventricular dilatation; (2) normal spinal fluid composition; (3) usually normal findings on neurological examination except for papilloedema and an occasional VI nerve palsy; and (4) normal level of consciousness. The appellation “benign” means not fatal. The syndrome can, however, disrupt normal life and cause significant visual failure. It is an uncommon condition in childhood presenting about once or twice a year in a large referral hospital. Early recognition is important as timely intervention may preserve vision and enables the doctor to start the appropriate treatment to control headaches. Children as young as 4 months can be affected; sex distribution is equal.1,2

Which intracranial compartment is primarily responsible for raising CSF pressure in the absence of ventricular dilatation is still unclear. Theories of BIH pathophysiology have been based on neuroradiological studies on patients with BIH (computed tomograms, magnetic resonance imaging (MRI), magnetic resonance diffusion scans, and radioisotope cisternography) and CSF hydrodynamic studies. These include increased venous sinus pressure, decreased spinal fluid absorption, increased spinal fluid secretion, increased blood volume, and brain oedema.3,4

Since the first large report on childhood BIH in 1967, reports subsequently show a changing clinical picture over time in terms of possible aetiology and clinical presentation.5,6 Diagnosis is not always simply achieved. BIH can occur in the absence of papilloedema; a “normal resting” CSF pressure does not exclude the diagnosis in the presence of suggestive symptoms and signs.7,8 Review of our cases over the past 10 years confirms the wide clinical spectrum of this condition. Of the 22 cases seen, 15 presented with the classical picture of headaches, papilloedema, and a raised CSF pressure of more than 20 cm CSF; four patients showed an increased CSF pressure in the absence of papilloedema, and three patients showed fundoscopic evidence of papilloedema with “normal” to “borderline” CSF pressures of 7–13 cm CSF.

On the basis of our experience we have developed a standard and logical approach to diagnosis and treatment of children with BIH.

Diagnosis

Diagnostic process is one of exclusion based on clinical symptoms, neurological, ophthalmic, radiological, and CSF findings.

Symptoms

Symptoms in BIH are non-specific and are those of increased intracranial pressure. Headaches, nausea/vomiting, and visual disturbances are the most common presenting symptoms.9 Headaches are predominantly frontal in location, become worse on lying down, and may wake the child at night. Increased intracranial pressure can exacerbate migraine. Some with a “mixed headache syndrome” are able to differentiate between the continuous daily headache of BIH which is worse on awaking from associated more severe, but intermittent, migraine headaches.

Children describe a variety of visual disturbances—diplopia, transient visual loss/blurring of vision, photophobia, and “shimmering lights with coloured centres”. Other symptoms include lethargy and tiredness, dizziness, mood change, and intracranial buzzing sounds. Sleep and behaviour disturbances are often reported by parents in the young preverbal child. In contrast with patients with an intracranial mass lesion, the level of consciousness and intellectual functioning remains normal in BIH.

Neurological examination

By definition, the neurological examination is normal apart from papilloedema or a sixth nerve palsy. Sixth nerve palsy is the most common neurological abnormality reported in 9–48% of children with BIH.9 Like others, we have seen an occasional III or IV nerve paresis. Other neurological abnormalities reported have included facial paresis, neck pain, seizures, hyperreflexia, bruit, hypoglossal nerve palsy, nystagmus, and choreiform movements.10,11 but these features are sufficiently rare that diagnosis of BIH should seriously be considered only after exclusion of an underlying intracranial mass lesion, an infectious or inflammatory process.

Although there are no case-control studies of aetiology in paediatric benign intracranial hypertension, various case studies have reported a number of associated conditions. Drug related cases and several endocrine abnormalities in children are among the most

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common reported associations. Treatment with tetracycline and isotretinoin for acne, nitrofurantoin prophylaxis for urinary infection, oral contraceptives (which are now given at younger and younger ages), and corticosteroid withdrawal including topical use for eczema have all been implicated. Hypothyroidism, hyperthyroidism, thyroid replacement, and chronic hypocalcaemia secondary to vitamin D deficiency or hypoparathyroidism need to be considered in selected cases.

OPHTHALMIC FINDINGS
The hallmark of BIH is papilloedema which may be bilateral, asymmetrical, or even unilateral. One of the main difficulties in diagnosis is differentiation of papilloedema from pseudopapilloedema. Optic nerve drusen, or an anomalously raised disc, in the presence of headaches can mimic papilloedema leading to a mistaken diagnosis of BIH. To add to the confusion, transient visual loss, haemorrhage on the disc, and visual field defects can be seen with drusen. We have seen drusen associated with papilloedema. Fluorescein angiography can help clarify the diagnosis, as in papilloedema the disc leaks diffusely, but with drusen there may be spots of autofluorescence before fluorescein is injected and no diffuse leakage is seen. These finer ocular subtleties clearly require the expertise of an ophthalmologist who must be involved early as an integral member of the team.

IMAGING
Normal imaging is a prerequisite for the correct diagnosis of BIH. Computed tomography and MRI confirm one of the pathognomonic features of BIH: undilated ventricles in the presence of intracranial hypertension. A computed tomogram and MRI imaging can supply important and predictive information about the state of the optic nerves in BIH. Thin section computed tomogram sections of the orbits may show hydrops of the optic nerve sheath and reversal of the optic nerve head. Severe visual loss in BIH patients is correlated with more frequent and more severe reversal of the optic nerve head.12 Because of the risk of radiation damage to the lens, however, high resolution images of the optic nerves are no longer used as widely as they once were. Hydrops of the optic nerve is also visible on MRI (fig 1). Orbital ultrasound is said to be another useful investigation in assessing the diameter of the optic nerve in relation to the CSF pressure.13 Magnetic resonance venography (MRV) is the procedure of choice for diagnosis of dural venous sinus thrombosis in BIH. Limited intracranial thrombosis, typically of the transverse sinus can present with BIH without localising neurological signs. It is important to establish the presence or otherwise of clot in the venous sinuses as steroid treatment in this situation may exacerbate the condition. Venous sinus thrombosis may be the presenting feature of a hypercoagulable state or may be caused by adjacent infection which may require treatment in its own right.

CSF FINDINGS IN BIH—WHAT IS NORMAL CSF PRESSURE IN CHILDREN?
Increased intracranial pressure with normal CSF chemical and cellular analysis confirms the diagnosis of BIH. Obtaining reliable CSF pressure readings in children requires skill and often sedation. CSF pressure measurement via the lumbar route is always done after imaging has excluded a mass lesion. As there may be a wide diurnal fluctuation in CSF pressure, establishing an increased pressure is not always straightforward.14 For this reason, “normal” levels can be recorded in patients with elevated optic discs. In this situation, we advocate repeating the lumbar pressure measurement. When clinical suspicion is sufficiently strong, prolonged pressure monitoring may be indicated. The optimum technique for this is arguably the Camino catheter in the subarachnoid space is invasive, a catheter in the lumbar subarachnoid space connected to a pressure transducer may be less reliable. The upper limit of what may be regarded as a normal CSF pressure in children is not well defined. Data on normal values of CSF pressure in children are sparse and little is known of the characteristics of an intracranial pressure recording in healthy people. Most reviews on BIH in children consider 20 cm CSF as the upper limit of normal. Studies on intracranial pressure in infants, however, report that the upper limit of normal intracranial pressure is 7.5 cm CSF below the age of 2 years and 13.5 below the age of 5 years.15 16 The only controlled study on intracranial pressure found the upper limit of normal CSF pressure ranged between 20–25 cm CSF in normal non-obese and obese adults, whereas the majority of patients with acute BIH showed concentrations above this range.17 The age at which transition occurs to the pressure appropriate to that of adults is unknown.

BIH WITHOUT PAPILLOEDEMA
Various reports have confirmed that BIH can occur in the absence of papilloedema in adults and children. Recognition of this important headache syndrome has therapeutic implications in that these headaches respond to
pressure lowering treatment, including lumbo-peritoneal shunting. To date, there is no evidence that BIH without papilloedema is a threat to vision. Again, if clinical suspicion is sufficiently strong, repeat lumbar puncture is justified if the initial CSF pressure is normal.

Management

It is not possible to make evidence-based recommendations for the management of BIH because there are no randomised, controlled, double blind prospective studies of treatment, the natural history of the untreated condition is still unknown, and the underlying pathophysiology remains elusive. Although recovery is often gauged as resolved papilloedema, and is thought to be synonymous with the return of CSF pressure to normal, CSF pressure can be persistently increased for years after the initial episode of BIH which implies that BIH is a chronic condition. In addition, asymptomatic papilloedema with progressive visual loss has been reported months to years after the initial episode of increased intracranial pressure, thus emphasising the lack of a direct relation among papilloedema, symptoms of headache, visual disturbances, and increased CSF pressure. Therefore, at present, it is difficult to make rigid recommendations on how treatment is best assessed.

The various treatment modalities used in children have included corticosteroids, acetazolamide, frusemide, repeated lumbar punctures, and surgery. Most cases respond to nonsurgical management. The goals of treatment are symptom relief and preservation of vision. Acetazolamide, a carbonic anhydrase inhibitor, is perhaps the most commonly used drug of first choice. In adult patients, an oral dose of 1 g/day has been shown to resolve papilloedema and 4 g/day to decrease CSF pressure. Side effects are dose related, which may limit its use if high doses are required. These include gastrointestinal upset, perioral and digital tingling, loss of appetite, acidosis and electrolyte imbalance, and rarely nephrocalcinosis. Continuous medication may result in “low” pressure headaches, which are initiated or exacerbated by moving from the lying position to sitting or standing. In the absence of papilloedema, a trial of medication may help to clarify the situation.

Steroids

Evidence of the effectiveness of steroids in treating BIH relies on retrospective clinical analysis of patients with this condition. Clinical experience has shown that decrease of symptoms and resolution of papilloedema can be expected in the first two weeks of treatment. Our practice is to use steroids in those unresponsive or intolerant to acetazolamide treatment. Symptomatic relief occurred in three patients out of the eight treated with steroids.

Repeated Lumbar Punctures

Although lumbar puncture can be used to lower CSF pressure, this has a short lived effect. CSF pressure can return to pretap concentrations within one to two hours. Spinal taps may be technically difficult and distressing to the child, especially if done repeatedly. This, together with the theoretical risk of developing intraspinal epidermoid tumours and the low back pain after the procedure, has discouraged us from using this option of treatment except as a temporary measure in a child with severe headaches.

Surgery

Surgical management is indicated in those with deteriorating visual function and/or severe incapacitating headaches interfering with daily activities despite vigorous medical management. Currently, lumboperitoneal shunting (LPS) and optic nerve sheath fenestration (ONSF) are the two surgical procedures employed.

Lumboperitoneal Shunting

LPS effectively lowers intraventricular pressure and relieves headaches and papilloedema. Unfortunately, it is fraught with problems. Shunt obstruction and low pressure headaches are the most common complications. Other complications include acquired cerebellar tonsillar herniation, syringomyelia, lumbar radiculopathy, and infection. The development of a lumboperitoneal catheter with a fixed resistance may prevent low pressure headaches or cerebellar tonsillar herniation. In addition, LPS has failed to halt progressive vision loss in documented cases. It may, however, be a treatment option in the patient whose documented increased intracranial pressure fails to respond to medical management. The long term outcome of visual function after LPS has not been reported. Our experience showed that headaches and visual function improved after LPS in all five of our patients who failed to respond to medical management.

Optic Nerve Sheath Fenestration

ONSF is currently the favoured treatment for BIH in adults with deteriorating visual function despite medical management. The procedure successfully relieves papilloedema, rapidly reversing visual loss in most cases. The mechanism is not entirely clear, as pressure as measured by lumbar puncture in the immediate postoperative period is persistently increased. Despite this, two thirds of patients have improved headaches and few develop headaches requiring LPS after the procedure. The key to success with ONSF is early intervention and the appropriate expertise. Undoubtedly, better visual outcome is reported with ONSF after surgery for acute rather than chronic papilloedema. Thus, patients with BIH and vision threatening papilloedema should be offered ONSF without delay. Results are favourable in terms of visual outcome, there is an infrequent need for repeated surgery, and in expert hands the procedure is safe with few intraoperative or postoperative complications and no reported mortality. Eyes that have more than one ONSF, however, rarely stabilise or improve after surgery. Presently, there are no large reports
Figure 2  Flow chart of results of treatment in our 22 patients with BIH.

on ONSF treatment in children. More data are needed to determine the optimal operative technique, the complication, and success rate in the childhood population.

In the light of the above evidence, decisions regarding which treatment to employ in a particular patient must be individualised. ONSF may be the treatment of choice in patients with rapid visual loss, whereas LPS may be the favoured procedure in patients with intractable headaches and less threatening visual loss.

MONITORING VISION

Loss of visual function is the only serious permanent complication of BIH. Visual field loss or decreased visual acuity in children has been reported in 13–27%. This may be visible at presentation, progress during treatment, or recur late in the course of the disorder.20 21 One factor which may complicate visual acuity measurement is a hysterical visual loss, which may be difficult to detect particularly if superimposed on an organic loss. Suspicion is raised in those manifesting a precipitous deterioration in the visual acuity, which is unaccompanied by significant changes in the visual field or optic disc appearance. The most common visual field change is an enlargement of the blind spot, which usually improves with resolution of the optic disc swelling. Central scotomas, inferior nasal defects, and peripheral constriction are the next most common field defects.22 It is still unclear which factors predispose to permanent visual loss. Visual outcome is not apparently related to the duration of symp-
toms, the degree of papilloedema, the presence of visual obscurations, or the incidence of recurrent increased intracranial pressure.39 Frank visual loss at the onset of the disease is the one factor which can predict visual outcome.30

The above evidence shows that children and adolescents with BIH should be kept under close ophthalmic surveillance. This should start at the time of diagnosis and continue until the status of the visual acuity and the visual field is clear. At present, it is difficult to make firm recommendations on the length of surveillance as the natural history and the risk factors for poor visual outcome remain unknown.

Currently, our indicators of optic nerve neuropathy include visual acuity testing, serial visual field testing by static or kinetic perimetry, and relative afferent pupillary defect measurement. These tests, however, may detect optic nerve damage in patients with BIH only after one third of fibres have been lost.31 From the available tests, visual field testing remains the most sensitive indicator of incipient vision loss.32 Contrast sensitivity loss has also shown some encouraging results.33 Visual evoked potentials are an insensitive indicator of early vision loss as changes are infrequent and often occur late with severe vision loss.34 Testing young children requires patience and skill, and tests need to be adapted to the age and the ability of the child. Generally, children over the age of 7 years will cooperate with formal perimetry testing. Below this age, formal visual field testing is difficult. Sedation may be required to examine the fundus adequately. Fundus photographs or indirect fundoscopy may be useful in follow up assessment especially in the younger age group. We observed a transient visual loss in five out of the 22 children we followed up, and none had permanent visual impairment secondary to BIH.

Proposed management protocol

Having reviewed the various options, we offer our current schedule for management. While we would not claim that it is the best or even the most effective, it is at least consistent with what is known. We offer it as a base upon which others can improve. Figure 2 shows the result of treatment in our 22 patients.

(1) INVESTIGATIONS

Computed tomography/MRI are essential first investigations to exclude a mass lesion. MRV is done to exclude an occult venous sinus thrombosis if symptoms persist after initial lumbar puncture.

(2) PRESSURE MEASUREMENT

After MRI/computed tomography, lumbar CSF pressure is measured carefully in the sedated child on spinal tap by manometry/pressure transducer. We recognise that volume loss to fill the manometer may lower the final pressure reading. Connecting the spinal needle to a pressure transducer is a counsel of perfection. If the pressure is increased, sufficient fluid is removed lower CSF pressure to 12–15 cm
CSF. This is done as a two step procedure if initial pressure > 30 cm CSF.

(3) NO TREATMENT
If headaches improve within 24 to 48 hours no further treatment is required. Four of our 22 patients had long term relief of symptoms after “diagnostic” lumbar puncture and required no further treatment. Identification and correction of presumed or overt predisposing factors may result in resolution of BIH. Lumbar puncture may be repeated if papilloedema persists for more than one month. Medication is started in those whose headaches, loss of visual function, or diplopia persist after initial lumbar puncture.

(4) OPHTHALMIC SURVEILLANCE
Visual acuity and visual fields are measured at presentation and followed up regularly by an ophthalmologist.

(5) ACETAZOLAMIDE
If symptoms persist after the initial spinal tap and pressure is increased, acetazolamide is started at 25 mg/kg/day and is increased by 25 mg/kg/day until clinical response or a maximum dose of 100 mg/kg/day or 2 g/day. Regular blood gases and electrolytes are monitored and acidosis is corrected by sodium bicarbonate supplements. Renal ultrasound is done if the patient is on acetazolamide treatment for more than six months to exclude nephrocalcinosis. A repeat lumbar CSF pressure measurement is taken if symptoms do not improve after one week of treatment. The patient should be taken off acetazolamide for a trial period if low pressure headaches are suspected due to over medication.

(6) STEROIDS
Prednisolone is started at a dose of 2 mg/kg/day in those patients intolerant or unresponsive to a maximum dose of acetazolamide. This is given for two weeks and weaned over the next two weeks. Blood pressure, electrolytes, and urine glucose are monitored regularly. With this regimen, we did not observe any significant side effects.

(7) SURGERY
Surgery becomes necessary if intractable headaches and increased CSF pressure persist despite medical treatment or evidence of deteriorating visual function. LPS may be the preferred choice in those with intractable headaches and optic nerve sheath decompression in those with rapidly deteriorating visual function.

(8) RECURRENT
Children with a recurrence may be treated as new cases.

(9) PARENT INFORMATION
Parents are involved in the surveillance process by information on the condition. This is an essential step in the management process as recurrence of BIH can occur months or years after the first presentation and unrecognised recurrence could result in irreversible visual loss.

(10) ANTIMITRAINE TREATMENT
Persistent headaches with stable visual function may respond to antimigraine medication especially in those with a mixed headache syndrome.

(11) WEIGHT REDUCTION
Loss of weight has been shown to improve symptoms in adult patients.

(12) INDICATION FOR CSF—PRESSURE MONITORING
Preoperative evaluation of the very young child with persistent symptoms should be undertaken when visual fields cannot be tested.

Preoperative evaluation of children with unremitting symptoms in the absence of papilloedema who are unresponsive to medication should also be undertaken and they should be taken off the medication for a trial period. This process is essential in order to exclude low pressure headaches.

Conclusion
The correct diagnosis of BIH relies on the recognition of the typical symptoms, radiological exclusion of a mass lesion, and recognition of the possible diagnostic pitfalls. Visual impairment does occur in children and can occur at any stage. The incapacitating effect of headaches which interfere with the child’s daily activity cannot be ignored, however. Both factors have to be considered when deciding on the best treatment strategy. At the moment, it is difficult to make recommendations on how long to follow up children with BIH. This is because we do not understand the natural history of the condition and which factors predispose to a poor visual outcome. Meanwhile, all children regardless of age or ability to cooperate need careful neurological and ophthalmic follow up with the aim of preventing secondary optic atrophy. Future prospective studies on treatment will provide a scientific basis for a rational treatment plan for this condition.