Idiopathic intracranial hypertension

Idiopathic intracranial hypertension is characterized by symptoms and signs of raised intracranial pressure in the absence of a space-occupying lesion or hydrocephalus. It is associated with obesity and although visual loss is the most serious complication, patients are often more worried about headache. Idiopathic intracranial hypertension is the currently preferred term, superseding previous names such as pseudotumour cerebri and benign intracranial hypertension. The word 'benign' is misleading given the potential for severe and permanent visual loss with the condition, and 'pseudotumour' has potentially alarming connotations for patients.

Epidemiology

Idiopathic intracranial hypertension is primarily a condition of young (<45 years), obese women. Although it can occur in men, there is a striking (9:1) female predominance (Kosmorsky, 2014). The majority of patients are overweight or obese and some report rapid weight gain over the months preceding diagnosis (Szewka et al, 2013). The annual incidence in the UK is 1.56 per 100 000, rising to 12 per 100 000 in obese women (Raoof et al, 2011). Given the increasing obesity epidemic, it is likely that the incidence of idiopathic intracranial hypertension will rise (Karnik and Kanekar, 2012).

Pathophysiology

The pathophysiology of idiopathic intracranial hypertension is unclear. Increased CSF production does not appear to be a feature, thus current hypotheses focus on increased resistance to CSF outflow and/or venous hypertension. Some authors suggest that venous sinus stenoses result in venous hypertension and therefore reduced CSF absorption which in turn causes raised intracranial pressure and worsening of the sinus stenosis, creating a vicious cycle. Given the striking association between idiopathic intracranial hypertension and obesity, others have suggested that cytokines and hormones secreted by adipose tissue play a crucial role in the pathogenesis of the condition (Wakerley et al, 2015).

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How patients present

Headache

Headache is the most common presenting feature of idiopathic intracranial hypertension and is almost always present. The character of headache in idiopathic intracranial hypertension is variable, and may not always be a 'classic' raised intracranial pressure headache. Patients frequently complain of a throbbing headache associated with nausea or vomiting, photophobia and phonophobia and thus may be confused with migraine headaches. The headache may be exacerbated by changes in posture such as bending forward.

Patients with idiopathic intracranial hypertension are at risk of developing a secondary medication overuse headache as a result of regular use of analgesics and thus details of prescribed and over-the-counter medication use should be sought repeatedly. It is important to remember that some drugs used for headache treatment, such as tricyclic antidepressants, may cause weight gain and can therefore hinder attempts at weight loss.

Visual symptoms

Many patients complain of transient visual obscurations. These are a temporary loss or darkening of vision in one or both eyes, often when bending forward or standing up, and are thought to reflect temporary optic nerve ischaemia. Although transient visual obscurations are alarming for both patients and doctors, their presence and frequency do not correspond to the severity of papilloedema or the likelihood of permanent visual loss (Corbett et al, 1982; Wakerley et al, 2015).

Other focal symptoms

Over half of patients with idiopathic intracranial hypertension also complain of tinnitus or 'whooshing' in the ears, another feature of raised intracranial pressure. Numerous cranial nerve palsies have been described with idiopathic intracranial hypertension (Davenport et al, 1994), but sixth (abducens) nerve palsies as a false localizing sign of raised intracranial pressure are the most common, resulting in diplopia.

Asymptomatic

Some patients with idiopathic intracranial hypertension present following the identification of papilloedema following a routine eye check, or because they have undergone fundoscopy for another reason.

Examination

The typical patient is young, female and obese. Papilloedema will be present and is usually symmetrical although it can be unilateral. Although identifying papilloedema is often straightforward, there are circumstances in which patients are wrongly identified as having papilloedema and are therefore subjected to unnecessary investigations. Differentiating between papilloedema and pseudopapilloedema can be difficult and if there is uncertainty, the input of an experienced neuro-ophthalmologist may be required. Mollan et al (2014) describe the potential pitfalls in diagnosing papilloedema further.

The remainder of the neurological examination is usually unremarkable, aside from the possibility of unilateral or bilateral sixth cranial nerve palsies caused by raised intracranial pressure.

Diagnostic criteria and exclusion of secondary causes of raised intracranial pressure

The diagnostic criteria for idiopathic intracranial hypertension are outlined in *Table 1*; alternative causes of raised intracranial pressure must be excluded. Several drugs have been reported to cause raised intracranial pressure, and tetracyclines, nitrofurantoin and retinoids such as vitamin A have all been linked with the condition and should be stopped if idiopathic intracranial hypertension is diagnosed (Wakerley et al, 2015). Anaemia and renal failure can also result in raised intracranial pressure and must be excluded. Neuroimaging is essential to exclude secondary causes of raised intracranial pressure.

Table 1. Diagnostic criteria for idiopathic intracranial hypertension

Papilloedema
Normal neurological examination except for cranial nerve abnormalities
Hydrocephalus, structural lesion, or venous sinus thrombosis or other structural lesion excluded with neuroimaging
Normal CSF constituents
Elevated (>25 cm water) opening pressure on lumbar puncture

adapted from Friedman et al (2013); Mollan et al (2014)

Investigations

Figure 1 outlines the diagnostic pathway for patients who present with papilloedema. The presence of headache, along with other symptoms of raised intracranial pressure, and the finding of papilloedema on examination in a patient who fits the phenotype of young, female and obese will usually result in a diagnosis of idiopathic intracranial hypertension. However, all patients must undergo radiological exclusion of secondary causes of raised intracranial pressure before this diagnosis can be reached (*Figure 2*). The imaging of choice is magnetic resonance of the head and orbits with magnetic resonance venography; however, a computed

Figure 1. Idiopathic intracranial hypertension diagnostic pathway for patients who present with papilloedema.

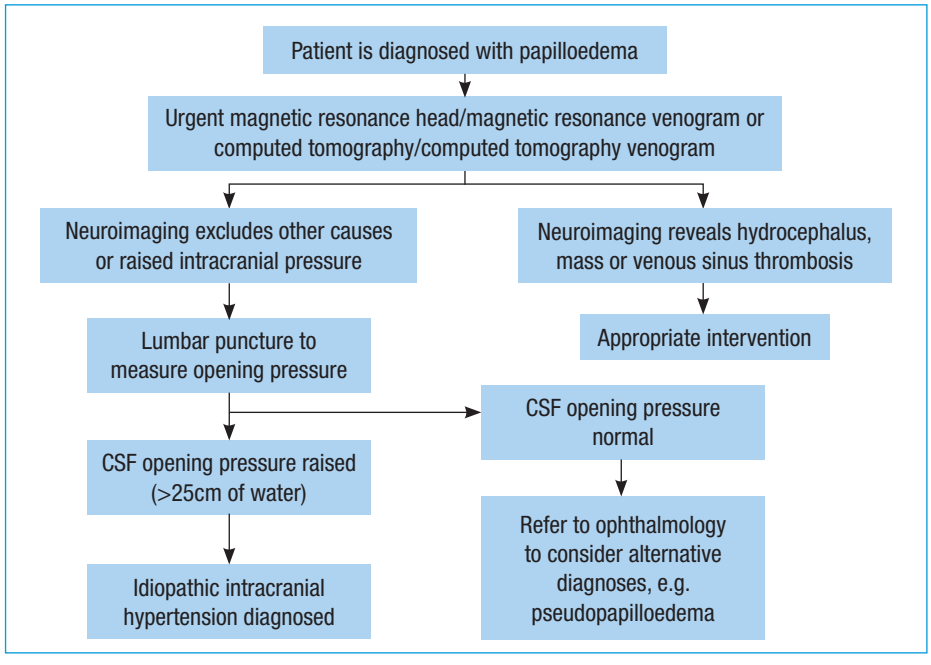
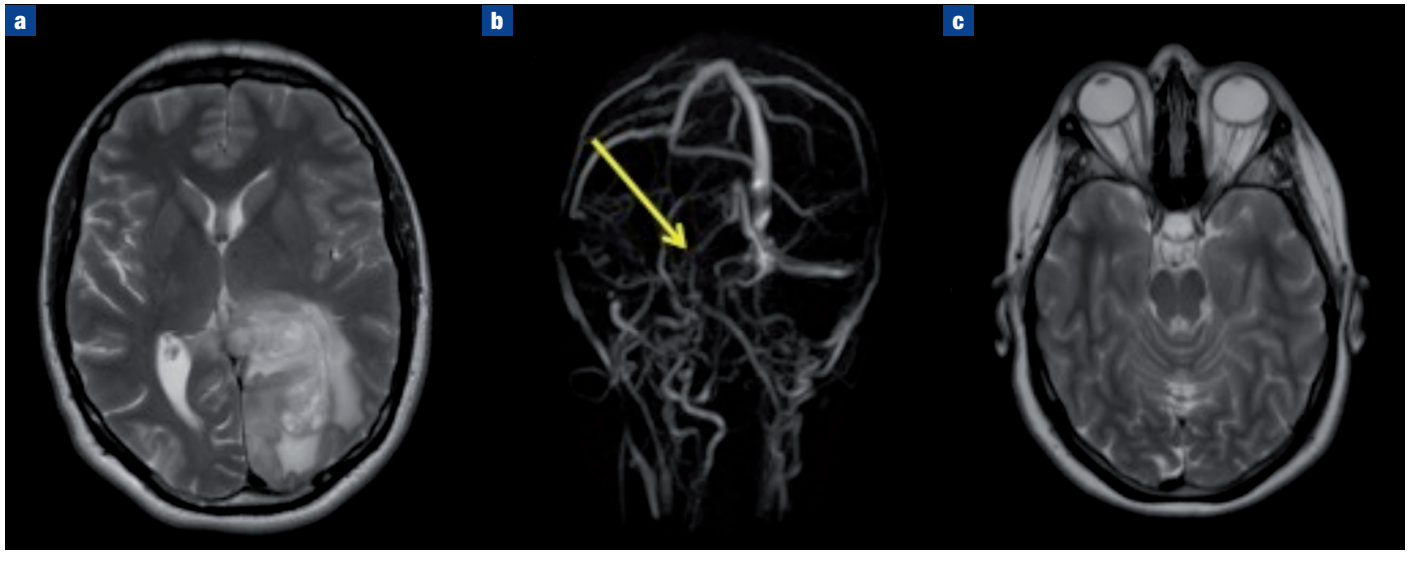


Figure 2. Neuroimaging including a venogram must be performed on any patient presenting with bilateral papilloedema before a lumbar puncture is undertaken in order to exclude life-threatening structural causes of raised intracranial pressure. Other possible causes of raised intracranial pressure include **(a)** a brain tumour and **(b)** venous sinus thrombosis. **c.** The scan will be largely normal in idiopathic intracranial hypertension, although features of raised intracranial pressure (such as papilloedema or empty sella syndrome) may be evident.



KEY POINTS

- The most common clinical features of idiopathic intracranial hypertension are headache, transient visual obscurations and pulsatile tinnitus.
- Take a careful and detailed headache history – migraine and medication overuse headaches frequently co-exist in patients with idiopathic intracranial hypertension.
- A normal computed tomography and computed tomography venogram or magnetic resonance imaging and magnetic resonance venogram are essential investigations before a patient with papilloedema undergoes a lumbar puncture.
- Treatment options are controversial because of the paucity of evidence; weight loss remains the mainstay of management, but is difficult to achieve.
- In the small subset of idiopathic intracranial hypertension patients with rapid visual loss, surgical procedures such as CSF shunting or optic nerve fenestration may be necessary.

tomography scan of the head and computed tomography venogram are an adequate alternative depending on local availability. Blood tests should be performed to exclude anaemia and renal failure. Recording height and weight in clinic is useful, particularly to monitor subsequent weight loss.

If imaging excludes a venous sinus thrombosis or space-occupying lesion, a lumbar puncture should be performed with the patient lying on his/her side so that the pressure can be measured accurately. If the pressure is raised above 25 cmH_2O (Whiteley et al, 2006) and the CSF constituents (cell count, protein and glucose) are normal, then the diagnosis of idiopathic intracranial hypertension can be made. It is advisable to have a spare manometer for the procedure so that if the opening pressure is greater than 40 cmH_2O the pressure can still be measured accurately. Patients with idiopathic intracranial hypertension should undergo measurement of visual acuity and colour vision, and formal visual field testing.

Management

Visual loss is the most serious complication of idiopathic intracranial hypertension and treatments are aimed at preventing or reversing deteriorating visual acuity. One study estimated that 1–2% of patients newly diagnosed with idiopathic intracranial hypertension develop permanent visual loss within the year (Best et al, 2013). However, for patients, headache is usually the most troublesome symptom.

Patients with idiopathic intracranial hypertension are best managed by a neurologist and/or ophthalmologist with an interest in neuro-ophthalmology, as careful monitoring of vision is required. The evidence base for idiopathic intracranial hypertension treatments is limited and is outlined below.

Weight loss

For overweight patients with idiopathic intracranial hypertension, weight loss is associated with reduced intracranial pressure and reversal of papilloedema (Sinclair et al, 2010); indeed it is the only intervention supported by reasonable evidence. However, weight loss is notoriously difficult to achieve and maintain; a dietetics referral and suggested diet plan can support patients in losing weight steadily, thereby avoiding crash diets following which patients are prone to rebound. The role of bariatric surgery remains uncertain.

Drug therapy

Acetazolamide is a carbonic anhydrase inhibitor and traditionally has been widely used as the first-line drug in the management of idiopathic intracranial hypertension (Kosmorsky, 2014; Wakerley et al, 2015). Despite this, there is no convincing evidence that it works, and many patients are unable to tolerate it, with common adverse effects including tingling peripheries, anorexia and a metallic taste. In a randomized controlled trial that investigated the efficacy of acetazolamide, over half of patients in the treatment arm were unable to tolerate it (Ball et al, 2011). It is teratogenic and female patients should be counselled on avoiding pregnancy. Compliance may be improved if started at a dose of 250–500 mg twice daily and slowly titrated up, with final doses of between 1 and 2 g/day. Using a sustained release formulation may also improve tolerability.

Other drugs such as topiramate and loop diuretics (e.g. furosemide) are sometimes used as they also affect carbonic anhydrase activity and these can be used in addition to acetazolamide. Many patients with idiopathic intracranial hypertension continue to suffer from headaches as their CSF pressure is lowered. Many of these headaches are characteristic of chronic migraine or medication-overuse headache. Topiramate can be a useful drug in patients with idiopathic intracranial hypertension as it can induce weight loss and lower intracranial pressure, and can be effective in chronic migraine (Mollan et al, 2014).

Therapeutic lumbar punctures

Given that many patients experience a rapid amelioration in symptoms soon after the removal of a significant volume of CSF during a diagnostic lumbar puncture, 'therapeutic' lumbar punctures may be performed in very symptomatic patients while other treatments are initiated. There are no guidelines on the volume of CSF to be removed or a targeted closing pressure during therapeutic lumbar punctures, but the authors recommend removing 15–20 ml of CSF at a time.

Surgery

In patients with deteriorating visual acuity despite medical therapy, more invasive procedures are sometimes considered. CSF shunting is a technique in which a neurosurgeon places either a ventriculoperitoneal or lumboperitoneal shunt in order to lower intracranial pressure via CSF diversion. The operation of choice depends on local preference as there are no trial data comparing the two methods. Whereas shunt insertion is thought to be an effective method of reducing intracranial pressure and is therefore potentially a sight-saving procedure, shunts are prone to failure and may require revision, as well as complications such as infection. Over half of patients who undergo shunt insertion will need to undergo at least one revision procedure in the future (Sinclair et al, 2011). Over-drainage can also occur which results in low-pressure headaches.

Optic nerve sheath fenestration is a procedure in which part of the optic nerve sheath is opened surgically in order to relieve pressure on the optic nerve. Optic nerve sheath fenestration is effective in preserving vision and appears to have a lower complication rate than CSF shunt insertion (Banta and Farris, 2000), but it has little effect on intracranial pressure

and is less effective at improving headache symptoms than shunting.

Some centres have used venous sinus stenting for patients with idiopathic intracranial hypertension refractory to medical therapy. Its use remains controversial, as thus far there are only case series to support its use; the long-term effects are unclear and it is not without risk of significant complications.

Conclusions

Patients who present with papilloedema require urgent assessment and investigation. Given that most patients with idiopathic intracranial hypertension complain of headache, this emphasizes the importance of fundoscopy for all patients with headache. Life-threatening causes of raised intracranial pressure must be excluded with brain imaging before a lumbar puncture is performed. Management is controversial and should be undertaken jointly between neurologists and ophthalmologists. **BJHM**

Conflict of interest: none.

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