Review Article

Pseudotumor cerebri: An update on treatment options

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Aims: The aim was to identify Pseudotumor cerebri treatment options and assess their efficacy. **Setting and Design:** Review article. **Materials and Methods:** Existing literature and the authors' experience were reviewed. **Results:** Treatment options range from observation to surgical intervention. Weight loss and medical treatment may be utilized in cases without vision loss or in combination with surgical treatment. Cerebrospinal fluid shunting procedures and/or optic nerve sheath decompression is indicated for severe vision loss or headache unresponsive to medical management. The recent use of endovascular stenting of transverse sinus stenoses has also demonstrated benefit in patients with pseudotumor cerebri. **Conclusion:** While each treatment form may be successful individually, a multimodal approach is typically utilized with treatments selected on a case-by-case basis.

Key words: Idiopathic intracranial hypertension, pseudotumor cerebri, treatment

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Pseudotumor cerebri (PTC), also known as idiopathic intracranial hypertension (IIH), is a condition that usually affects obese women of childbearing age. Because many cases formerly thought to be idiopathic may have an identifiable cause (see below), we will use the term PTC in this review. By definition, PTC is characterised by signs and symptoms of raised intracranial pressure (ICP), elevated opening pressure on lumbar puncture, and normal cerebrospinal fluid (CSF) studies and imaging. The exact etiology of the disease remains unclear in many cases, and there are no formal guidelines regarding management and treatment. Case series and clinical experience determine current practice patterns. Treatment options for this potentially blinding disease are discussed below, including management of transverse sinus stenosis.

Treatment Approaches

Treatment of PTC ranges from observation to emergent surgery. A team approach amongst the patient's neurologist, ophthalmologist, primary care physician, and neurosurgeon is essential.

The goals of treatment in an individual with PTC are twofold: Preservation of vision, and reduction of symptoms (usually headache). Multiple factors should be considered when selecting both the form of treatment and its relative urgency. The presence and degree of symptoms (i.e. headache, vision loss), the severity of vision loss, and any apparent progression are all crucial factors in deciding on urgency of treatment. The first step in treating any PTC patient is to identify and ameliorate conditions such as anaemia, causative medications, obesity, obstructive sleep apnea, and venous sinus thrombosis.[1] Factors consistent with poor visual prognosis such as high-grade papilledema, macular oedema, venous sinus thrombosis, and systemic hypertension may support a more aggressive form of treatment.[2] Immediate aggressive management is often advocated in cases of severe or rapidly progressive vision loss, and in cases at higher risk of rapid progression (male sex, black race) regardless of disease severity.[3,4]

"Conservative" Management

As obesity and/or recent weight gain are the main identifiable PTC risk factors in most patients, a defined weight loss program should be initiated regardless of disease severity. Observation without medical or surgical intervention may be indicated in an asymptomatic patient who presents with papilledema and understands the importance of clinical monitoring for progression. The precise relationship between weight gain or obesity and raised ICP is not clear, but the benefits of weight reduction have been demonstrated repeatedly. In a study of 25 obese women, weight reduction was associated with reduction of headaches, papilledema, and ICP.[5] In addition, in individuals whose PTC is in remission, prevention of weight fluctuation has been shown to be critical in prevention of recurrence.[6] Studies have demonstrated that loss of approximately 6% of body weight is associated with a reduction in papilledema and discontinuation of systemic treatment.[7,8] To most effectively assist a patient in weight loss, the help of a registered dietician or nutritionist should be enlisted. If weight loss through diet and exercise fails, bariatric surgery has been shown to positively benefit IIH, although this is clearly more invasive and carries risks of anastomotic leaks, small bowel obstruction, malabsorption, and gastrointestinal bleeding.[9-11]

Medical Management

Medical treatment is indicated in the setting of good vision when a patient's primary symptom is headache. Carbonic anhydrase inhibitors (CAI) are the treatment of choice, although no prospective data confirm their effectiveness.[12] A pilot trial by Ball *et al.* highlighted difficulties with recruitment of patients as well as poor compliance with acetazolamide.[13] The IIH

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treatment trial is a multicenter, double-blind, placebo-controlled North American clinical trial that is currently enrolling patients to evaluate the benefit of acetazolamide versus placebo in the setting of a structured weight loss program.

Acetazolamide (diamox) and methazolamide (neptazane) inhibit carbonic anhydrase in the choroid plexus, ostensibly decreasing CSF production. They also act as mild diuretics. Acetazolamide in adult patients is usually started at 1 g daily (250 mg QID or 500 mg BID), with a maximum recommended daily dose of 4 g. Side-effects include paraesthesias, lethargy, and altered taste and may limit dosage. Although non-CAI diuretics (i.e. furosemide, chlorthalidone, spironolactone) have been used in the treatment of PTC, their efficacy in reducing ICP is unclear. Hypokalemia may occur with any of these agents, and blood electrolytes should be monitored.

Corticosteroids are not generally recommended for routine use in PTC, although they will lower ICP acutely. Corticosteroid withdrawal is associated with a rebound increase in ICP, and the long-term side-effects, including weight gain and fluid retention, are even less desirable in PTC patients. Intravenous corticosteroid may reduce acute optic disc swelling in fulminant disease, while an urgent surgical procedure is arranged.[2]

Topiramate also has been used in treatment of PTC. Many patients have headache that is separate from the ICP and thus benefit from topiramate's action on migraine. An open-label study comparing topiramate and acetazolamide demonstrated equivalence in reduction of papilledema and headache, and topiramate use was associated with greater weight loss.[14] Octreotide, an inhibitor of growth hormone and insulin-like growth factor 1, is not routinely used, but is being research and has been shown to reduce ICP.[15]

Surgical Management

Initial surgical treatment of PTC is indicated when there is severe optic neuropathy, either acute or rapidly progressive, or medical treatment failure. CSF diversion (ventriculoperitoneal [VP], ventriculoatrial [VA], or lumboperitoneal [LP] shunting) and optic nerve sheath decompression (ONSD) are most commonly performed, with subtemporal decompression reserved for extreme cases. The decision between CSF diversion procedures and ONSD depends on the availability of local resources and on the patient's particular signs and symptoms. Both procedures may be required.

Cerebrospinal fluid shunting is the most widely performed surgical treatment for PTC,[3] and it is useful in the treatment of papilledema, headache, and visual loss. Shunting results in rapid normalization of the ICP, resolution of papilledema, and improvement of vision. All shunt procedures have a high long-term failure rate and often need revision because of obstruction or failure. In a case series and literature review by Abubaker *et al*., the failure rate was higher for VP shunts (14%) than LP shunts (11%), but the revision rates were higher for LP shunts (60%) than VP shunts (30%).[16] VA/VP shunting may be more effective than LP shunting in relieving headache,[17] but it is more technically challenging to place the catheter into the typically normal or small ventricles of PTC patients. Stereotactic guidance should be used if available.

Optic nerve sheath decompression effectively treats patients with papilledema and severe visual loss but does not improve headache in most patients. ONSD rapidly reduces papilledema on the operated side and occasionally on the contralateral side as well.[18] Bilateral improvement in visual function is seen in many cases.[19] The procedure probably has little effect on ICP, but clinical improvement is likely due to local reduction in pressure on the nerve by lowering the intrasheath pressure. Long-term effectiveness may be due to fibrous scar formation between the dura and the optic nerve, thus creating a barrier that protects the anterior optic nerve from ICP. Patients with improvement or apparent remission after ONSD should remain under close follow-up, as long-term visual decline may still occur.[20]

Venous Sinus Stenting

Focal stenosis of the distal transverse sinus may be seen in the majority of PTC patients and is absent in obese controls.[21] While in some cases, the stenosis is a consequence of elevated ICP, several studies have demonstrated that a pressure gradient may persist across the stenotic segment even after ICP is normalized by lumbar or cervical puncture.[22-25] In such cases, the stenosis may be the cause of ICP elevation, and endovascular stenting may be pursued if medical management is inadequate to relieve headache or papilledema.[26-29]Numerous reports of stent placement for sinus stenosis suggest tremendous success with 100% reduction of the intracranial sinus pressure.[25]

In a recent report from our institution, we described in detail the visual outcomes in 12 patients who underwent venous sinus stenting for PTC after failing maximal tolerated medical therapy.[29] A manometric gradient of >4 mmHg was found in all patients (range 5-28 mmHg) with reduction or resolution after stenting. Eleven of 12 patients had visual improvement or stability, and headache either resolved or improved in 7 patients. Pulsatile tinnitus also remitted in the 11 patients in whom it was present. We did identify 2 patients who developed a new stenosis proximal to the stent, and we postulate that the triangular anatomy of the venous sinus may contribute to collapse of the segment immediately proximal to the cylindrical stent. Future modification of stent size may prevent this occurrence. Based on our data and those of others, we obtain contrast-enhanced magnetic resonance venography in all PTC patients and consider stenting in appropriate cases.

Potential complications of venous stenting include stent migration, venous sinus perforation, in-stent thrombosis, subdural hemorrhage, and recurrent stenosis proximal to the stent.[26,27] As in our experience, Kumpe *et al*. reported persistent headache following stent placement in 10 of 12 female patients with headache prior to the procedure.[25] Poststenting headache is often different in character than that caused by elevated ICP, resolves gradually, and is likely due to local irritation of the meninges following stent placement.

Pseudotumor Cerebri in Pregnancy

Pseudotumor cerebri may be unrecognized before pregnancy or associated with excessive weight gain; worsening of existing PTC in pregnancy has been described.[30] Acetazolamide is rated as class C by the US FDA and is typically used if needed after 20 weeks gestation. A recent retrospective study showed no adverse effects from its inadvertent use earlier in gestation, but could not establish the safety of doing so.[31] There is no contraindication to pregnancy in individuals with PTC. If vision deteriorates acutely, corticosteroids may be used. In addition,

ONSD or CSF shunting can be performed, though the shunt may obstruct as the uterus enlarges.

Conclusion

Treatment of PTC must be tailored to the patient's presenting symptoms, vision, and comorbidities. A multidisciplinary team and often multiple treatment forms are necessary. While no clear recommendations exist, a careful consideration of a patient's particular presentation can lead a clinician to the most effective and appropriate treatment.

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