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Review

An update on the management of pseudotumor cerebri

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ABSTRACT

Pseudotumor cerebri, or benign intracranial hypertension, is characterized by intracranial hypertension of unknown etiology typically in obese women <45 years of age, and can be disabling secondary to headaches and visual disturbances. Medical management includes pharmaceuticals that reduce cerebrospinal fluid (CSF) production and lumbar punctures that reduce the CSF volume, both aimed at reducing intracranial pressure. When medical management fails, surgical CSF diverting procedures are indicated. Recently it has been demonstrated that dural sinus stenosis or thrombosis can be responsible for this disease and treated with endovascular venous stent placement. The intent of this educational manuscript is to review the clinical presentation of pseudotumor cerebri patients and discuss the medical, surgical, and endovascular treatment options for this disease. After reading this paper, the reader should be able to: (1) understand the pathophysiological basis of pseudotumor cerebri, (2) describe its presenting signs and symptoms, and (3) discuss the medical, surgical, and endovascular treatment options.

Contents

1. Introduction

Pseudotumor cerebri (PTC), or benign intracranial hypertension, is a syndrome in which patients have the signs and symptoms of elevated intracranial pressure but have no radiographic evidence of a mass lesion in the brain. It was first described by a German physician named Quincke in the 1890s [1]. He described a neurological condition whereby many of the symptoms of a brain tumor were present, but without an actual mass lesion to account for them. Dr. Dandy, one of the pioneers of neurosurgery, proceeded to describe the clinical course of 22 patients he encountered with this particular condition over a 7 year period in the 1920s and 1930s [2]. All patients in this series complained of symptoms consistent with intracranial hypertension: headaches, blurred vision, and vomiting. Fundoscopy in all cases revealed papilledema and in many cases retinal hemorrhages were also present, indicative of

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long-standing severe intracranial hypertension, confirmed by elevated pressures on lumbar puncture or ventricular tap. Ventriculography however, excluded a significant mass lesion in all cases. Many of these patients were treated surgically by subtemporal decompression with surprisingly good results. Interestingly, Dandy noted that the craniectomy flaps of patients would often fluctuate between flat and tense within a period of minutes suggesting that the pressure elevations experienced by PTC patients were intermittent and often rapid in onset. Dandy felt that this rapid and intermittent rise in intracranial pressure was better explained by dynamic changes in the vasomotor vascular bed rather than more static problems such as CSF malabsorption or venous sinus occlusion [3].

There has been an additional subset of patients with PTC whereby an overt cause, or strong association, is identified and described as secondary PTC [4]. This occurs in approximately 10% of PTC cases [4]. Although PTC traditionally occurs in young obese females, one's suspicion for the "secondary" form of this entity heightens if the demographics of the presenting patient are out of the ordinary, such as in males, non-obese women, pre-pubertal children, and those refractory to classical treatments. Some potential contributing factors to PTC include certain metabolic or endocrine derangements, ingestion or withdrawal of specific substances, systemic illness (such as thyroid dysfunction, hematological disease, lupus, and chronic renal failure) [5], and cerebral venous sinus obstruction. A very small subset of patients with PTC present with a fulminant course resulting in a brisk decline in vision [6–8]. This is best treated initially with a lumbar drain until a more definitive CSF diverting procedure can be undertaken.

Contemporary descriptions of PTC have changed little since Dandy's time. Although ventriculography has been supplanted by more modern imaging techniques, PTC remains a diagnosis of exclusion. Fortunately, the symptoms of PTC are not life-threatening and usually self-limiting. In fact, many patients with PTC respond to conservative treatments such as diuretics and weight loss. Those patients who continue to have headaches and vision loss despite conservative management are often considered for surgical treatment. While Dandy performed subtemporal decompression to alleviate the symptoms, nearly all medically refractory PTC patients are now treated using CSF diversion or optic nerve fenestration with varying results. Recently, there has been debate as to the cause and effect relationship of dural sinus obstruction in regards to PTC. In a subset of PTC patients with dural sinus obstruction noted as a potential etiology, endovascular stenting of the sinus stenosis has been shown to be safe and effective for symptomatic relief [9–11].

Here, we will review the historical and contemporary perspectives of the diagnosis and treatment of PTC and discuss existing controversies regarding its pathophysiology and treatment.

2. Pseudotumor cerebri: the syndrome

By definition, all patients with PTC will have signs and symptoms of elevated intracranial pressure. The "Modified Dandy Criteria" are used to aid diagnosis [12]:

(1) Cranial CT and/or MRI confirming the absence of radiographic hydrocephalus or mass lesion.
(2) Elevated CSF opening pressure upon ventricular or lumbar spinal tap with normal CSF fluid profile.
(3) Intact neurological exam with the exception of visual disturbances, sixth cranial nerve palsy, and papilledema.

The most common presenting symptoms are headache, vomiting, and blurred vision. Pulsatile tinnitus is also common and may be related to flow disturbances in the cerebral venous system [13]. Like other high-pressure headaches, PTC headaches tend to be most severe upon awakening. Often, patients have tried other headache remedies, including prescription medication, without significant relief. Although papilledema is present in the vast majority of PTC patients, its absence is not an exclusionary criterion. The grading system used to describe the severity of papilledema is called the "Frisen Scale" [14]. This classification system distinguishes the fundoscopic appearance of the optic disc into various stages, from normal appearing to severe papilledema (Table 1).

Transient visual loss is second only to headache as the most commonly presenting symptom, and is the major morbidity in PTC [15–17]. In the most typical situation, visual loss is gradual, but there are described cases where the onset is rather abrupt. This particular patient population with rapidly progressive visual loss, usually have a more fulminant course and less chance of visual recovery [6–8]. More commonly, PTC patients experience transient obscurations of vision (TOV) [16]. They typically are precipitated by postural changes and can occur several times throughout the day. One of the theories behind TOV is transient ischemia of the optic disc caused by optic nerve swelling. The most feared complication of PTC is permanent vision loss [18,19].

The physical and neurological exam should be normal with the exception of the fundoscopic exam. With rare exception, all PTC patients have papilledema, a hallmark of subacute intracranial hypertension. The absence of papilledema or the presence of focal neurological deficits should put the diagnosis of PTC in doubt. It should be noted that isolated abducens nerve palsies in the setting of PTC, presumably related to compression of the nerve as it exits Dorello's canal, have been reported in the literature as well [20]. Formal visual field testing will generally reveal enlargement of the blind spot as well as loss of the inferior peripheral fields.

3. Pseudotumor cerebri: proposed pathophysiology

The pathophysiology of PTC is largely speculative. Although most neurosurgeons treat PTC using diuretics or CSF diversion to lower the intracranial pressure, it is still uncertain whether PTC is caused by derangements in CSF hydrodynamics (such as excess production or malabsorption) or other etiologies. Dandy's theory of dynamic changes in the vasomotor vascular bed may certainly hold true in many cases. What must be kept in mind however, is that PTC is a clinical entity without a clear cause, and that the clinical presentation may be a common aftermath of different pathophysiological processes of the central nervous system.

Despite several theories regarding the pathophysiology of PTC, the common thread is a high incidence in obese females of childbearing age. One of the earliest proposed mechanisms of PTC was cerebral edema. In one case series, this actually had pathologic support [21]. Subsequent pathological and MRI studies however, have not supported cerebral edema as a cause of PTC [22–25]. There have been reports of PTC occurring in conjunction with vitamin A intoxication [26,27]. Some studies have reported higher vitamin A, retinol, and retinol binding protein levels in the CSF of the PTC population when compared to controls [28–30]. In regards to these findings, it has been suggested that excess retinol binding protein or excess retinol itself in the CSF may actually interfere with spinal fluid absorption.

Obesity and its complications have been looked at in regards to the pathophysiology of PTC. It is well-known fact that sleep apnea is a frequent consequence of obesity. This particular entity, specifically in men, may play a role [31,32]. A case report whereby a patient with PTC had intracranial pressure monitoring simultaneously with oximetry, showed episodic apneic events were associated with significant elevations in ICP [33]. These elevations

Table 1
Papilledema grading system (Frisen Scale) [14].

Stage 0	Normal optic disc	Blurring of nasal and temporal disc borders by overlying nerve fiber bundles in inverse proportion to the disc diameter. Pattern of the peripapillary nerve fiber bundles is strictly radial, without tortuosity. Rarely, a major vessel may be obscured, usually in the upper pole.
Stage 1	Very early papilledema	Excessive blurring of the nasal border of the optic disc, with disruption of the normal radial arrangement of never fiber bundles. Normal temporal disc margin. Subtle grayish halo along the circumference of the optic disc, with a temporal gap.
Stage 2	Early papilledema	Elevation of the nasal circumference of the nerve head, and blurring of all of the temporal margin. Halo now surrounds the disc completely.
Stage 3	Moderate papilledema	Elevation also of the temporal circumference, and a clearly increased diameter of the nerve head. The elevated borders now totally obscure one or more segments of the major retinal vessels. The circumpapillary halo has an irregular outer fringe with finger-like extensions.
Stage 4	Marked papilledema	Elevation of the entire nerve head in combination with obliteration of the optic cup, or compression of the cup to a slit, or total obscuration of a segment of the central retinal artery or vein.
Stage 5	Severe papilledema	Anterior expansion of the nerve head now dominates over sideways expansion. Nerve head assumes smooth, dome-shaped protrusion, with a narrow and smoothly demarcated halo. Major retinal vessels climb steeply over the dome surface. Segments may be totally obscured by overlying swollen tissue.

in ICP are likely from vasodilatation secondary to hypercapnea from apneic episodes. Central obesity in and of itself is also thought to be a contributing factor in PTC. In particular, the central abdominal fat distribution results in elevated intra-abdominal, cardiac filling, pleural, and central venous pressure, which all potentially contribute to elevated intracranial venous pressures [34]. Some of the work by Karahalios has looked at measurements such as right atrial pressure, in patients with suspected pseudotumor cerebri. His group found that five patients with normal dural venous sinus anatomy actually had elevated right atrial pressures. These elevated intra-cardiac pressures are subsequently transmitted to the intracranial venous sinuses [35]. Nadkarni looked at two obese middle-aged females and were examined for pseudotumor cerebri. Intracranial venography in these patients revealed elevated intracranial dural venous sinus pressure, in addition to increased right atrial pressure. It is postulated that the elevated right atrial pressures are in fact attributable to the patients' obese body habitus. These two patients subsequently underwent bariatric surgery in order to achieve weight loss. Approximately one year later, clinical evaluation of these patients showed that their pseudotumor had resolved. Repeated measurements of intracranial dural venous sinus pressures had shown that they returned to normal. In relation to PTC, the result of bariatric surgery is a decrease in right atrial pressure, leading to decreased intracranial venous sinus pressure, and ultimately to lowered intracranial pressure [36].

The most accepted pathophysiological theory of PTC is obstruction of intracranial venous drainage. However, it is heavily debated whether obstructed venous drainage is the primary mechanism or secondary to another pathological process. Flow-related abnormalities can be quite difficult to differentiate from pathological venous sinus stenosis. Non-contrast magnetic resonance venography can depict flow-related artifacts that can be mistaken for venous sinus stenosis. Intracranial venous sinus abnormalities in the PTC population should still be considered with caution.

A specific entity called the Chiari pseudotumor cerebri syndrome, has been used in the literature to describe a specific subset of patients with Chiari I malformations that respond poorly to posterior fossa decompression, and appear to have elevated CSF pressures with small ventricles [37]. The etiology of this association is not clear, but it is postulated that posterior fossa surgery in the setting of abnormal anatomy and potentially anomalous CSF flow dynamics contributes to CSF malabsorption and resultant PTC [37].

4. Differential diagnosis of pseudotumor cerebri

The clinical presentation and features of PTC can vary from one patient to the next, and are non-specific. A thorough fundoscopic exam looking for papilledema is essential in the identification of this pathological entity. Papilledema suggests elevated intracranial pressure, however, optic disc swelling, either unilateral or bilateral, may have a similar appearance to papilledema and may be caused by different etiologies. Other causes of elevated intracranial pressure (such as tumor or other mass lesions) must be ruled out prior to making the diagnosis of PTC. One particular type of tumor, a choroid plexus papilloma, may significantly increase the ICP by overproducing CSF and give a similar presentation to that of PTC. Adhesions of the arachnoid granulations from infection or subarachnoid hemorrhage may impede CSF reabsorption and subsequently cause elevated ICP. Obstructive hydrocephalus from a mass or aqueductal stenosis should be considered in the differential diagnosis. Intracranial venous sinus obstruction, whether from neck surgery, sinus thrombosis, or jugular venous compression, must also be investigated with imaging studies.

5. Epidemiology and risk factors

PTC is uncommon with a reported incidence between 1 and 5 cases per 100,000 people in the general population [38,39]. PTC is independent of age, but is ten times more common in women than men, and obesity increases the risk of PTC 20-fold [17]. In men who do have PTC, black men are at the greatest risk of loss of vision [40]. Pediatric cases are divided into pre-pubertal and pubertal forms based on the development of secondary sexual characteristics [12]. The use of tetracycline antibiotics – particularly minocycline, has been reported to cause PTC in humans and is often used in animal models to induce intracranial hypertension [41]. Excess vitamin A and the use of retinoid drugs has also been reported to induce intracranial hypertension [42]. Certain primary hematological disorders put individuals at risk for dural venous obstruction, such as Protein C and S deficiency, Factor-V Leiden, and Prothrombin gene mutations [43]. No genetic markers for PTC have been identified yet.

6. Treatment options

6.1. Medical management

When PTC is suspected, imaging studies should be performed to rule out mass lesion followed by lumbar puncture (LP) to check

for intracranial hypertension, collect CSF for cytology and microbiology, and to identify those patients whose vision and headaches improve with CSF drainage. Imaging studies and LP are helpful when evaluating a patient for PTC and before considering any type of treatment for PTC.

In most cases PTC is a benign and self-limiting condition. The primary goal of treatment is symptom relief and vision preservation. In patients with mild headaches and stable vision, non-invasive management is often adequate and in obese patients includes weight loss alone. Anecdotal evidence and small case series have shown that even a 6% weight loss can result in reversal of papilledema [44]. For patients with stable vision and mild headaches this may be a reasonable option, as most cases of PTC resolve spontaneously. In non-overweight patients or in those with more severe symptoms this approach may not be appropriate mandating more aggressive therapy.

The current theories suggesting that PTC is the result of abnormal CSF hydrodynamics, treatment generally aims to modify CSF production and flow. The carbonic anhydrase inhibitor acetozolamide (Diamox) and to a lesser extent, furosemide (Lasix) inhibit the production of CSF and consequently reduce the intracranial pressure [45,46]. A long-term follow up study was done in PTC patients using a carbonic anhydrase inhibitor and demonstrated that 60% of patients experienced multiple recurrent episodes over a mean observation period of 6.2 years, but none of the recurrences occurred while maintained on acetazolamide [47]. In addition to acetazolamide decreasing CSF production from a biophysical perspective, it is also diuretic. It may also treat PTC by lowering intra-cardiac right atrial pressures by this diuretic effect [36]. A recent case report using the loop-diuretic similar to furosemide, called bumetanide, also showed promising results in the treatment of PTC. In this particular case, a 13 year-old obese female with PTC refractory to trials with acetazolamide and furosemide, had essentially complete resolution of signs and symptoms, including papilledema, with bumetanide [48]. The specific physiological action of bumetanide is to inhibit the mechanism of glial cell volume regulation. PTC is classically associated with small ventricular size on radiographic imaging suggesting that alterations in CSF production may not be as significant as alterations in glial cell volume. This would imply that bumetanide potentially may treat PTC by reducing glial cell volume, instead of CSF volume.

More recently, topiramate (Topamax) too, has been shown to decrease CSF production with the added benefit of inducing weight loss [49–51]. Mannitol has also been used to successfully treat PTC symptoms in some patients [52]. Unfortunately, topiramate and mannitol are not effective in all patients and the side-effects of these drugs, such as excessive urination and mild cognitive dysfunction, can be intolerable.

Previously, corticosteroids were recommended to treat PTC, but are now avoided because of undesirable side effects such as steroid withdrawal and weight gain. Steroid withdrawal can cause significant rebound intracranial hypertension, and the potential for weight gain itself is counterintuitive to the mantra of weight loss as effective treatment in the majority of this patient population [53].

6.2. Cerebrospinal fluid diversion

Once an intracranial mass lesion has been ruled out with imaging studies, serial high volume LP's can be safely performed for therapeutic purposes and to augment the effect of the medications on an as-needed basis. This procedure not only allows for the rapid reduction of intracranial hypertension and its symptoms, but also allows the physician to check the progress of the medical treatments by measuring CSF opening pressures. As with any invasive procedure, there are risks during high volume LP's including meningitis, subdural hematoma, sixth cranial nerve palsy, and brainstem herniation. These risks are small, however, and this procedure is generally considered safe and effective for the management of intracranial hypertension in the setting of PTC. Unfortunately, serial high volume LP's may be impractical in some patients whose symptoms respond well to this intermittent CSF drainage. For instance, CSF re-accumulation may occur so rapidly that even daily lumbar punctures are insufficient for prolonged symptomatic relief. Additional complicating factors include: (1) obese PTC patients in whom lumbar puncture can be technically challenging, time consuming, and require the radiological assistance; (2) refusal of serial LP's by the patient due to discomfort and anxiety experienced during the procedure. Nevertheless, serial LP's can be useful for reducing intracranial hypertension in the acute phase until the symptoms resolves or a more definitive CSF diverting procedure is offered. Of note, LP is the preferred treatment of PTC during pregnancy given the pharmacological contraindications, the risk of performing a surgical ventriculoperitoneal shunt procedure on a pregnant woman, and the chance that the symptoms will resolve after delivery [54,55].

6.3. Surgical intervention

Despite the fact that PTC is usually self-limiting, 25% of patients will continue to have visual deterioration and headaches despite medical and LP management [53]. These refractory patients should be considered for surgical treatment. In Dandy's original series, PTC patients were treated successfully with unilateral subtemporal decompressive craniectomy, albeit high surgical risk and a poor cosmetic result. Contemporary surgical management is accomplished by optic nerve fenestration and cerebral spinal fluid shunts, each of which has its own set of benefits and risks. Recently, PTC has also been attributed to intracranial dural venous sinus stenosis in a subgroup of patients who respond to venous sinus stenting. In the sections that follow herein, we will discuss surgical options in greater detail.

6.4. CSF diversion

The most common neurosurgical procedure for the treatment of PTC is shunt placement [56]. Unlike patients with hydrocephalus, PTC patients have small ventricles that can be difficult to cannulate with a ventricular catheter using standard techniques. While accessing the ventricles is possible with stereotactic planning, most neurosurgeons will avoid this unnecessary risk by placing a lumbar-peritoneal shunt (LPS) instead. Lumbar-peritoneal shunts (LPS) differ from ventricular shunts in that the former accesses not only the intracerebral ventricles, but also the subarachnoid space. Technically simple with a low complication rate, LPS is 80% effective in the treatment of PTC. While serious complications are possible and include paralysis, brainstem herniation, and iatrogenic Chiari-1 malformation, they are rare. The development of secondary Chiari malformations has been suggested, supported mainly by literature looking at babies with valveless LP shunts. Additionally, LPS is associated with a lower infection rate (1%) than VPS (7–15%) but at the cost of a higher failure rate (50%/2 years for LPS compared to 20%/2 years for VPS) requiring surgical revision [57]. The associated obese body habitus of many PTC patients is likely a cause for the high failure rate of LPS. However, the term "shunt failure" in a pseudotumor patient must be carefully used. Some patients with PTC do develop chronic daily headaches, and this may be mistaken for a malfunctioning shunt. In addition, ventricular size does not routinely change in this patient population with shunt failure. This points to the fact that intracranial pressure should always be confirmed prior to revising a shunt in a pseudotumor patient [58]. Recently, advanced technologies such as endoscopic assisted

surgery, have resulted in improved success rates for ventricular catheter placement into the small ventricles of these patients. In rare instances when a LPS and VPS cannot be placed, cisterna magna shunting is an option but are associated with a higher complication rate than other forms of shunting [59]. In short, most shunted PTC patients require multiple revision surgeries during their lifetime.

Reported outcomes for CSF diversion are somewhat mixed. Some range from above 95% with visual stabilization or complete remission while others report progressive worsening despite shunting [60–64]. In regards to headaches after shunting, one series reported symptomatic relief shortly after the procedure, but sustainability at three years post-operatively was poor, despite a functioning shunt [57].

6.5. Optic nerve sheath fenestration (ONSF)

A non-neurosurgical treatment for PTC includes optic nerve sheath fenstration. Ophthalmologists treat PTC by making slits in the ONS to reduce the local pressure around the optic nerves. The exact mechanism by which this procedure has its effect is uncertain [65]. One hypothesis is that the naturally occurring fibrous trabeculations partially block the flow of CSF between the intracranial subarachnoid space and the optic sheath, thereby reducing the transmission of high intracranial pressure to the optic apparatus. Interestingly, in approximately 50% of cases, a unilateral ONSF will result in the resolution of visual symptoms in both eyes [65]. This phenomenon can be explained within the framework of the above hypothesis when one considers that both ONS's are essentially connected at the optic chiasm. Experimental data from animal models and clinical observations suggest that resolution of visual symptoms is usually not associated with lower intracranial pressure [65,66]. This means that some patients will continue to have symptoms of high intracranial pressure – headaches, nausea, or diplopia, despite resolution of their papilledema [65,66]. In those patients a shunt would likely be the better treatment modality than ONSF. Some reserve ONSF only for those who present with visual symptoms and no headaches.

Regardless of its mechanism, ONSF has been shown to be safe and effective in follow-up studies spanning out to ten years [65,67]. Unlike shunting procedures where multiple revision surgeries are the rule, ONSF typically needs to be performed only once per eye and does not require the implantation of foreign bodies, the latter of which increase susceptibility to infection and device failure. Furthermore, a technique for endoscopic ONSF via the trans-nasal route with no external incisions has been described, making this procedure the most cosmetically benign pseudotumor surgery. ONSF has also been shown to preserve vision in cases where vision deteriorates despite a functioning shunt [65,68,69].

6.6. Bariatric surgery

The role of bariatric surgery in obese PTC patients remains unclear. Bariatric surgery can lead to rapid and substantial weight loss and theoretically result in reduced intracranial pressure. In fact, the literature is peppered with accounts of the PTC patient who was cured after his or her gastric bypass [70,36,71]. However, not all PTC patients are medically or psychologically ready to accept the commitment needed to undergo successful gastric bypass or banding procedures, particularly when time is of the essence because of progressive visual deterioration. Additionally, there currently is no means of identifying whose symptoms will respond well to weight loss and undergoing bariatric surgery purely for PTC is currently not supported in the literature. Furthermore, intra-abdominal adhesions after bariatric surgery make future CSF-diverting procedures more difficult with higher risk of abdominal organ injury. Until the benefit/risk ratio is better defined, it currently seems premature to recommend bariatric surgery solely as a treatment option for PTC.

6.7. Endovascular dural venous sinus stent placement

The etiology and significance of intracranial venous sinus stenosis as a cause of PTC remains uncertain. Anatomical studies have demonstrated a considerable amount of congenital asymmetry between the transverse sinuses with the right one being dominant up to 73% of the time, and partial or total agenesis of the transverse sinus seen in up to 23% [72]. So its significance in PTC is uncertain. The rationale for endovascular venous stenting for PTC comes from the observation that the transverse sinus of some PTC patients is narrowed and resembles partial recanalization after sinus thrombosis. Others have suggested that increased ICP is the cause of venous sinus obstruction via extrinsic mechanical compression of the sinus walls rather than the result of impeded venous drainage [71,74]. Studies have shown dural venous sinus obstruction resolves after CSF removal [75–77]. Others believe that it is a cause of PTC given that in a few particular studies, venous sinus thrombosis had persisted despite normalization of intracranial hypertension [78].

In any case, stenting of stenotic venous sinuses for PTC has shown promising results recently. Bussière et al. published a series of PTC patients treated with dural venous sinus stenting showing significant symptomatic relief and resolution of papilledema [73]. When severe, dural venous sinus obstruction reduces venous outflow from the brain resulting in increased intracranial pressure. The mechanism for elevated ICP from venous obstruction is two-fold in this situation: (1) venous outflow obstruction induces interstitial edema of the brain parenchyma, increasing the total brain tissue volume; (2) venous obstruction increases the pressure within the superior sagittal sinus retarding CSF reabsorption via the pressure dependent valves, called arachnoid granulations. By increasing brain volume and reducing CSF reabsorption, venous sinus obstruction can result in abnormally high intracranial pressure. Revascularization of the intracranial venous sinus obstruction with an endovascular-placed stent across the lesion, can improve venous drainage from the brain thereby reducing intracranial pressures by the mechanisms described previously.

Not every PTC patient is a candidate for venous stenting. Determination of potential benefit from stent placement is first determined by the presence of a venous sinus stenosis and secondly by transvenous manometry across the stenosis. The latter requires catheter-based venography that is often performed with femoral aterial access used for visualization of the venous system, and femoral venous access to navigate the catheter across the stenosis and venous manometry. In most cases the site of venous stenosis is at the transverse-sigmoid sinus junction [79]. Once the site of stenosis is identified, venous sinus manometry is performed through a catheter navigated across the stenosis. Venous sinus manometry is performed proximal and distal to the lesion and the differential pressure is measured using a standard pressure transducer attached to the catheter. The theory is that a hemodynamically significant stenosis will be associated with a large pressure differential, with the pressure proximal to the stenosis being higher than distal. A differential pressure greater than 10 mm of mercury suggests hemodynamic significance and a higher likelihood of a good response from venous stenting ultimately resulting in improved CSF drainage into the dural sinuses and relief of PTC. In one study with ten patients that demonstrated a pressure gradient across the stenosis greater than 10 mmHg, all reported resolved or significantly improved headaches, and either a gradual or immediate relief of symptoms following stent placement [73].

When deemed appropriate for venous sinus stenting, antiplatelet agents are administered preferably 7–14 days before

Table 2
Study outcomes of IIH patients treated by transverse sinus stenting (modified and reprinted from Bussière et al. [73]).

Atrophy	Stenting		Pressure gradient		Follow-up duration (months)	Headache			Papilledema		
	Unilateral	Bilateral	Before (mmHg)	After (mmHg)		No change	Resolved or impreoved	Worse	No change	Resolved or improved	
Higgins et al. [80]	10	2	8–37	2–15	7–26	5	7	0	2	4	3
Owler et al. [81]	4	0	12–25	0–1	5–12	0	4	0	0	4	2
Ogungbo et al. [11]	1	0	25	ns	6	0	1	0	0	1	0
Rajpal et al. [82]	1	0	25	ns	6	0	1	0	0	1	0
Rohr et al. [83]	1	0	39	1	0.25	0	1	0	0	0	0
Donnet et al. [84]	9	1	14–34	ns	6–36	2	8	0	0	10	2
Paquet et al. [85]	1	0	15	ns	ns	0	1	0	0	1	0
Bussière et al. [73]	10	0	11–50	2–23	4–60	0	10	0	0	9	1
Total	37	3	8–50	0–23	0.25–60	7	33	0	2	30	8

stent placement to reduce the risk of venous sinus thrombosis from the stent. Typically Aspirin 325 mg and Clopidogrel 75 mg given daily are the preferred antiplatelet agents and continued for at least six to twelve weeks after stenting and aspirin often for life thereafter, although this regimen varies. The standard technique for dural venous sinus stenting is similar to other types of intracranial stents. Currently, no stent is FDA approved for use in the dural venous sinuses, so they are being used "off-label" for PTC. An appropriately sized stent can be placed across the lesion using a standard endovascular delivery system followed by post-stent venous sinus manometry to confirm that the lesion has been adequately treated.

The experience with venous stenting in patients with PTC has largely been successful with a high frequency of resolved or improved symptoms such as headache and papilledema (Table 2). Choosing which PTC patient will benefit from transverse sinus stenting will remain controversial until a randomized clinical trial is performed that evaluates its efficacy. Therefore, this treatment option is currently best reserved for PTC patients with radiographic and manometric evidence of hemodynamically significant transverse sinus stenosis refractory to conventional treatment.

6.8. Subtemporal decompression

Subtemporal decompression was the preferred treatment for PTC prior to the introduction of CSF shunting procedures. The largest series of subtemporal decompressions for PTC was published by Dandy [2]. Of his reported 22 patients with PTC, 19 were treated surgically by subtemporal decompression with clinical good outcomes. All 14 patients with post-operative follow-up examinations had resolution of papilledema, there were no deaths and no one required a second operation for PTC. A recent series of eight pseudotumor patients treated by subtemporal decompression published in 1998 reconfirmed Dandy's excellent clinical outcomes [3]. Within one month of treatment, deterioration in visual fields and acuity resolved in all eight patients. Five of eight patients required CSF diversion to control headaches, but no patient experienced recurrent permanent visual deterioration after subtemporal decompression [3].

Interestingly, Dandy observed that the fullness of the craniectomy flaps in most patients fluctuated, reflecting changes in intracranial pressure in these patients, often over the course of minutes and in many cases these fluctuations coincided with physical and mental stress. Dandy felt that the changes in the intracranial pressure were too rapid to be accounted for by changes in the CSF volume or interstitial edema. He concluded that vasomotor changes in the vascular bed caused induced changes in the brain blood volume thereby altering intracranial pressure. Of note, Dandy did not think that dural sinus obstruction was a likely cause of PTC since none of his patients had a positive Queckenstedt test.

Since subtemporal decompression is effective and long lasting, one might wonder why it fell out of favor. One factor is that a subtemporal decompression is considered to be a more invasive and cosmetically displeasing operation than a shunt or optic nerve fenestration. Also, despite Dandy's observations, most clinicians attribute PTC to a defect in CSF absorption, thus making a CSF diverting procedures a more logical choice.

7. Conclusion

Pseudotumor cerebri has a complex pathophysiological mechanism that is not yet fully understood and may in fact have multiple etiologies, each preferentially responding a specific treatment option. Diagnosing PTC must include imaging studies of the brain to confirm no mass lesion followed by spinal tap to check CSF pressure and test response to CSF drainage. Initial treatment is typically aimed at medically reducing CSF production and serial removal of CSF, unless there is rapid loss of vision in which case optic nerve fenestration alone should be considered, or if headaches are the primary complaint with or without papilledema, then CSF diverting shunts are more effective at treating both symptoms. CSF diverting procedures have supplanted subtemporal craniectomy first described by Dr. Dandy, since the risks are smaller and more cosmetically pleasing. Venous sinus stent placement is an option but without any good studies reported, should be reserved for PTC patients with radiographic evidence of venous sinus stenosis, positive manometry testing, and response failure to other modes of medical and surgical therapy. The true etiology of PTC first described in the 1950s by Dr. Dandy remains elusive, the efficacy of various treatment options needs further investigation.

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