Pseudotumor Cerebri (2008)

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Pseudotumor cerebri syndrome (PTCS), also known as idiopathic intracranial hypertension, was described by Heinrich Quincke over 100 years ago. This syndrome has well-established clinical features, but our progress is still poor on pathophysiology and treatment. The symptoms and signs are those of raised intracranial pressure, with headache the leading symptom. The common symptoms are headache, nausea, visual dysfunction and diplopia, while the common signs are papilledema, restriction of visual fields, reduced visual acuity and VI nerve palsy. It is common also for patients to experience tinnitus. Obscurations of vision occur frequently, and are typically very short-lived episodes. The blurry vision of migraine is generally not as profound or as brief as the obscurations of PTCS.

All new headache patients should have their optic disks examined, as papilledema may be the only sign of this syndrome, and PTCS can occur without any symptoms at all - for instance, ophthalmologists can incidentally pick up papilledema. Considering a diagnosis of PTCS means looking for secondary causes of intracranial hypertension. MRI brain imaging and an MRV to rule out venous sinus thrombosis are warranted. Friedman and Jacobson have updated diagnostic criteria for PTCS, referenced at the end. Symptoms are not needed, but if present, should only represent those of intracranial hypertension. The pressure of cerebrospinal fluid (CSF) should be greater than 250mm of water, and values between 200mm and 250mm of water are non-diagnostic; a point I have found particularly useful. Failure to place the patient in a relaxed position, straightening the neck and legs, may result in a higher CSF pressure, and this becomes particularly important in those with borderline readings. One must be particularly cautious concerning mildly elevated pressures and no papilledema.

There are many secondary causes of intracranial hypertension including long-term tetracyclines and vitamin A with its derivatives such as tretinoin. There are many factors that are thought to impart a very small increased risk, such as pregnancy and thyroid disease. Intracranial hypertension can be reliably produced with massive intake of vitamin A.

Brain imaging of the PTCS patient may be entirely normal, but it is not uncommon to find an empty sella, or smaller ventricles and effaced sulci. It has still not been worked out whether PTCS is associated with an increase in CSF volume or not. The predominant risk group is overweight pre-menopausal women. PTCS does occur outside this demographic, but less commonly, and there are no excuses for missing a case in younger women. Children do get PTCS, albeit less commonly, and with no female preponderance. Pseudotumor cerebri occurs at a rate of at least 1 per 100,000 people per year.

The treatment plan should focus on treating symptoms, namely headache, and most importantly, protecting vision. The most critical feature to follow is not headache but visual function, and formal visual fields are needed. Clearly the day-to-day management involves treating headache also. The headache of PTCS does not have any distinctive features; hence, a presentation may be confused with migraine.

Management revolves around weight loss for those who are obese; acetazolamide, which reduces CSF secretion by as much as 50%; other diuretics like furosemide; lumbar puncture (sometimes multiple), and. for those which more severe symptoms, surgical interventions like lumbo/ventriculoperitoneal shunts and optic nerve sheath fenestration (ONSF). Most patients are started on acetazolamide initially, and side effects include paresthesias, which may be very bothersome. Topiramate is occasionally used to treat PTCS as well. Steroids also reliably reduce CSF production, but chronic therapy has troubling side effects, and withdrawal is very often associated with increased symptoms. There are differing opinions on what surgical options are preferred, but they all generally prevent deterioration in vision, and may improve vision in those more severely affected. Complications from surgical options are common, including rare instances of severe visual loss with ONSF. Significant weight loss for the obese patient is

associated with improvement and recover,y but is often not attained. The rising prevalence of obesity in the U.S. predicts that more diagnoses of PTCS will be made.

Patients easily accept the idea that there is increased pressure causing headache, but management may in the future involve headache which may or may not be related to intracranial pressure; hence the treatment can have an added level of complexity. Patients with PTCS are just as entitled to have primary headache as anyone else, and possibly more so. Those patients with predisposing genes to primary headache are more likely to manifest prolonged headache symptoms.

The natural history of PTCS is variable. Shah and colleagues reviewed the records of 20 patients; 11 demonstrated a stable course, without worsening in papilledema or visual field, and 9 patients worsened after a stable course, 6 of whom experienced delayed worsening (28-135 months after initial presentation). Three patients had recurrence after resolution of papilledema, 12-78 months after symptoms were initially controlled.

Cerebrospinal fluid, the composition of which should be normal in PTCS, is not merely an ultra filtrate of blood plasma, but is created by active transport of different ions and other substances with the passive passage of water, driven by an ionic gradient. Reduced CSF absorption is likely a critical part of the pathophysiology of PTCS, for reasons that are not clear. Classic teaching states that the CSF is absorbed through the arachnoid villi, but this appears far from the full story, as considerable amounts may be absorbed at the spinal level and even through the cribriform plate involving nasal lymphatic channels. The absorption of CSF may be under the influence of female hormones, given that most adult patients are premenopausal women.

The topic of stenosed intracranial venous sinuses as possibly etiologic to PTCS has featured in recent literature. Raised intracranial pressure appears to compress the venous sinuses, and this can be relieved with reduction in intracranial pressure. Whether focal sinus stenosis can cause PTCS is still a matter of debate, as is stenting of the venous sinuses.

Criteria for diagnosing idiopathic intracranial hypertension from Friedman and Jacobson:

1. If symptoms are present, they may only reflect those of generalized intracranial hypertension or papilledema.

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3. Documented elevated intracranial pressure measured in the lateral decubitus position.

4. Normal CSF composition.

5. No evidence of hydrocephalus, mass, structural or vascular lesion on MRI or contrast-enhanced CT for typical patients, and MRI and MR venography for all others.

6. No other cause of intracranial hypertension identified

Friedman DI, Jacobson DM (2002). “Diagnostic criteria for idiopathic intracranial hypertension”. Neurology 59(10): 1492-1495

Shah et al. (2008). Long-term follow-up of idiopathic intracranial hypertension. Neurology;70:634-640