Pseudotumor Cerebri Syndrome Without Headache in an Obese Male With Eight Restricted Cerebrospinal Fluid (CSF) Oligoclonal Bands: A Case Report

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Abstract

Pseudotumor cerebri syndrome (PTCS) is a condition caused by an abnormal elevation of intracranial pressure (ICH), which may be primary (idiopathic intracranial hypertension) or because of an identifiable secondary cause. We present a rare case of an obese male who complained of gradual bilateral visual loss for one year without headaches and tinnitus. On fundoscopy, he had high-grade bilateral papilledema and, on lumbar puncture, he had an elevated intracranial pressure of 260 mmH2O. Cerebrospinal fluid (CSF) was unique for eight restricted oligoclonal bands while extensive other demyelinating workup was negative. He was started on acetazolamide initially and subsequently proceeded with bilateral optic nerve sheath fenestration (ONSF) with mild improvement in the right eye and no improvement in the left eye. Although the causative mechanism of PTCS is a matter of debate, immune-mediated processes are one of the proposed mechanisms that may play a role in the pathophysiology of PTCS, evidenced by the presence of oligoclonal bands (OCBs) and pro-inflammatory markers in CSF. PTCS diagnosed in men and patients with OCBs poses an increased risk of vision loss as this case and literature documented. Therefore, prompt treatment through therapeutic lumbar punctures, acetazolamide therapy concurrently with weight loss, and surgical intervention in severe or refractory cases are necessary.

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| Laboratory Test                        | Results         | Reference range          |
|---------------------------------------|-----------------|--------------------------|
| Complete blood count                  | Normal          | Normal                   |
| Basic metabolic panel                 | Normal          | Normal                   |
| Oligoclonal bands (common to CSF and Serum) | 2 paired bands | Negative                 |
| Anti-MOG IgG                          | Negative        | Negative                 |
| NMO/AQP4 autoantibodies IgG           | Negative        | Negative                 |
| CRP                                   | 29 ↑            | <=10.0 mg/Lite           |
| ESR                                   | 31 ↑            | 0 - 15 mm/Hr             |
| ANCA Screen                           | Negative        | Negative                 |
| ANA-IFA Screen                        | Negative        | Negative                 |
| SPEP                                  | Normal          | Normal                   |

**TABLE 1: Serum laboratory tests and results**

NMO: Neuromyelitis optica; MOG: Myelin oligodendrocyte glycoprotein; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; ANCA: Antineutrophil cytoplasmic antibodies; ANA (IFA): Antinuclear antibodies (immunofluorescence assay); SPEP: Serum protein electrophoresis

He was fully alert and oriented on neurological examination and had fluent speech and intact comprehensive abilities. There were no signs of meningeal irritation. Cranial nerve (CN) testing revealed 3-5 mm pupils equal in size and reactive to light and accommodation, intact extraocular movements with no nystagmus, saccadic movement, or skew. The facial sensation was similar on both sides, with a strong jaw opening and a midline tongue. In addition, the shoulder shrug was symmetrical and hearing was intact. The rest of his neurological examination, including motor function, sensation, reflexes, coordination, and gait analysis, was within normal limits.

Fundus examination of the right eye revealed blurring of the superior margins of the optic disc corresponding with grade 2 papilledema, and the left eye exhibited paleness of optic disc correlating with grade 3 papilledema. Visual acuity was limited to finger counting in both eyes. Humphrey’s vision test was significant for near to complete vision loss in the left eye.

Magnetic resonance imaging (MRI) of the brain and orbit didn't evidence any demyelinating disease; however, bilateral optic sheaths expansion, low lying cerebellar tonsils, empty sella, and stenosed transverse and sigmoid sinus on magnetic resonance venogram (MRV) correlated with elevated intracranial pressure. MRI cervical spine and thoracic spine were negative for structural abnormalities and demyelinating lesions. No abnormal enhancement was seen in either of the scans as mentioned above.

Lumbar puncture (LP) was done once and had an elevated opening pressure of 260 mmH20 (< 200 mmH20). CSF labs were relevant for eight CSF restricted oligoclonal bands, myelin basic protein elevation at 4.4 ng/mL, elevated immunoglobulin G (IgG) synthesis rate of 53.7 mg/day, high IgG index of 2.9, four nucleated cells, four red blood cells (RBCs), protein 41 mg/dL, glucose 79 mg/dL, and negative neuromyelitis optica (NMO) antibodies. In addition, in serum, anti-myelin oligodendrocyte glycoprotein (MOG) and neuromyelitis optica antibodies were negative as well (Table 2).
| Laboratory Test                | Result | Reference Values               |
|-------------------------------|--------|--------------------------------|
| Opening pressure              | 26 ↑   | 100-200 mm H2O                 |
| Oligoclonal bands (CSF only)  | 8 ↑    | Negative                       |
| Myelin basic protein          | 4.4 ↑  | 0.0 - 3.8 ng/mL                |
| IgG synthesis rate            | 53.7 ↑ | -9.9 TO +3.3 mg/day            |
| IgG index                     | 2.9 ↑  | 0.0 - 0.7                      |
| Alpha 1 Globulin              | 0.35 ↑ | 0.11 - 0.34 g/dL               |
| Nucleated cells               | 4      | 0 - 5 /mm3                     |
| RBC                           | 4      | Negative                       |
| Protein                       | 41     | 15.0 - 45.0 mg/dL              |
| Glucose                       | 79 ↑   | 40 - 70 mg/dL                  |
| CSF/Serum Albumin Index       | 4      | < 9 is correlated with intact blood-brain barrier |

**TABLE 2: CSF laboratory tests and results**

RBC: Red blood cell; CSF: Cerebrospinal fluid; NMO: Neuromyelitis optica; IgG: Immunoglobulin G

The patient was initially treated with acetazolamide 500 mg/twice a day, started by his primary neurologist, and titrated weekly up to 1500 mg/twice a day. Unfortunately, his visual symptoms did not subside, and on our recommendation, he first underwent right eye optic nerve sheath fenestration (ONSF), and, after one month, left eye ONSF. As a result, his peripheral vision improved in the right eye, but no improvement in the left eye so far has been reported.

**Discussion**

Pseudotumor cerebri syndrome (PTCS) or idiopathic intracranial hypertension (IIH) in men is rare, with a prevalence of 9% [1]. PTCS in men poses a twofold risk of developing visual loss compared to females [1]. As per the idiopathic intracranial hypertension treatment trial [2], secondary causes for increased intracranial pressure need to be ruled out comprehensively when considering PTCS in men and patients without headache and pulse synchronous tinnitus. There is a consensus regarding CSF opening pressure of ≥250 mmH2O in adults and ≥280 mmH2O in children (obese and sedated) to diagnose PTCS considering other clinical symptoms, including headache associated with PTCS [3-4]. We used Friedland’s revised standards as published in Neurology, Journal of the American Academy of Neurology, while identifying and discussing PTCS in this case (Table 3) [3].
Diagnostic criteria for PTCS

A. Papilledema

B. Normal neurologic examination except for cranial nerve abnormalities

C. Neuroimaging: Normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion and no abnormal meningeal enhancement on MRI, with and without gadolinium, for typical patients (obese women), and MRI, with and without contrast, and MRV for others; if MRI is unavailable or contraindicated, contrast-enhanced CT may be used

D. Normal CSF composition

E. Elevated lumbar puncture CSF opening pressure (≥250 mmH20 in adults and ≥280 mmH20 in children [250 mmH20 if the child is not sedated and not obese]) in a properly performed lumbar puncture

Diagnosis of pseudotumor cerebri syndrome without papilledema

In the absence of papilledema, a diagnosis of pseudotumor cerebri syndrome can be made if B–E from above are satisfied, and in addition, the patient has a unilateral or bilateral abducens nerve palsy. In the absence of papilledema or sixth nerve palsy, a diagnosis of pseudotumor cerebri syndrome can be suggested but not made if B–E from above are satisfied, and in addition at least 3 of the following neuroimaging criteria are satisfied:

1) Empty sella, 2) Flattening of the posterior aspect of the globe, 3) Distention of the perioptic subarachnoid space with or without a tortuous optic nerve, 4) Transverse venous sinus stenosis

**TABLE 3:** A diagnosis of pseudotumor cerebri syndrome is definite if the patient fulfills criteria A–E. The diagnosis is considered probable if criteria A–D are met but the measured CSF pressure is lower than specified for a definite diagnosis

| PTCS: Pseudotumor cerebri syndrome | ICP: Intracranial pressure | MRI: Magnetic resonance imaging | CT: Computerized tomography | CSF: Cerebrospinal fluid |

Our patient had elevated CSF pressure of 260 mmH2O with MRI brain showing pathognomonic signs of elevated intracranial pressure, i.e., enlarged bilateral optic nerve sheaths (Figure 1), empty sella turcica (Figure 2), and low-lying cerebellar tonsils (Figure 3) [5].
FIGURE 1: T2-weighted magnetic resonance (MR) image (axial view) showing bilateral expanded optic sheaths (normal range 5.17±1.34 mm to 3.55±0.82 mm) with optic nerve tortuosity (cyan arrow) and posterior globe flattening (magenta arrow), more prominent in the left eye.
MRV visualized stenosed left transverse and sigmoid sinus [5]. Anti-MOG (myelin oligodendrocyte glycoprotein) and NMO (Neuromyelitis optica) antibodies were negative. There are no demyelinating lesions or abnormal enhancements in the MRI brain, cervical, and thoracic spine. All mentioned findings ruled out secondary causes of raised intracranial pressure, including tumors, strokes, infections, multiple sclerosis.
Pseudotumor cerebri syndrome’s exact pathophysiology is unknown. However, evolving data regarding multiple inflammatory markers found in CSF also suggest immunological involvement in PTCS pathogenesis. Males with PTCS can present without headache and tinnitus and overall have a higher propensity toward visual loss, making early ophthalmological exams crucial for a better prognosis. Future trials of OCB-positive PTCS patients may help prove an association of OCB with the duration and severity of the disease.

Conclusions
Pseudotumor cerebri syndrome’s exact pathophysiology is unknown. However, evolving data regarding multiple inflammatory markers found in CSF also suggest immunological involvement in PTCS pathogenesis. Males with PTCS can present without headache and tinnitus and overall have a higher propensity toward visual loss, making early ophthalmological exams crucial for a better prognosis. Future trials of OCB-positive PTCS patients may help prove an association of OCB with the duration and severity of the disease.

Additional Information
Disclosures

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