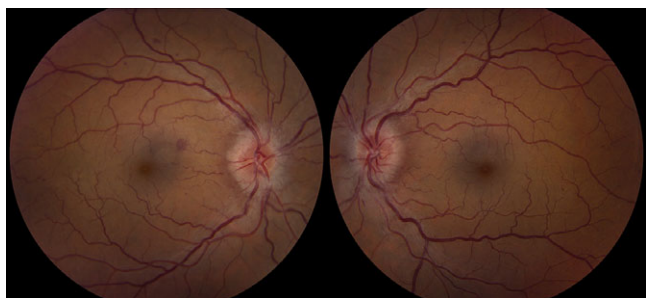


**LETTER TO THE EDITOR****To THE EDITOR****Primary Leptomeningeal Lymphoma: A Rare Mimicker of Idiopathic Intracranial Hypertension**

**Keywords:** Primary leptomeningeal lymphoma, Intracranial hypertension, Primary central nervous system lymphoma, Papilledema

A 46-year-old Caucasian woman was seen in neuro-ophthalmology consultation for bilateral optic disc edema. She had a past medical history of obesity (body mass index 38 kg/m<sup>2</sup>), hypertension, and dyslipidemia. She developed back pain 3 months prior to presentation that was unresponsive to over-the-counter medications. One week prior to presentation, she developed holocephalic headaches and intermittent nausea. She also reported transient visual obscurations and pulsatile tinnitus. She presented to the emergency department and had a CT scan of the head, which was reported as normal. Ophthalmological examination revealed a visual acuity of 20/20 in both eyes, normal Humphrey visual fields, and bilateral optic disc edema with several dot retinal hemorrhages in both eyes (Figure 1). Ocular motility and alignment were normal. Neurological examination was normal. Because of concern for papilledema and raised intracranial pressure, she underwent MRI of the brain, which was initially reported as normal, but on further review showed diffuse sulcal fluid attenuated inversion recovery (FLAIR) nonsuppression with leptomeningeal enhancement within the posterior fossa (Figure 2). There were no parenchymal lesions or ventriculomegaly. MRI of the spine showed diffuse enhancement along the cauda equina nerve roots with possible leptomeningeal enhancement along the spinal cord. The differential diagnosis included leptomeningeal carcinomatosis, infectious or inflammatory leptomeningitis. She underwent a lumbar puncture (LP) that revealed an opening pressure of 32 cmH<sub>2</sub>O with 2000 nonerythroid cells, 16 erythroid cells, protein greater than 2 g/L, and glucose of 1.2 mmol/L. Cerebrospinal fluid (CSF) cytology and flow cytometry showed a monotypic B-cell population consistent with large B-cell non-Hodgkin's lymphoma. CSF culture and polymerase chain reaction for the detection of viruses were negative.

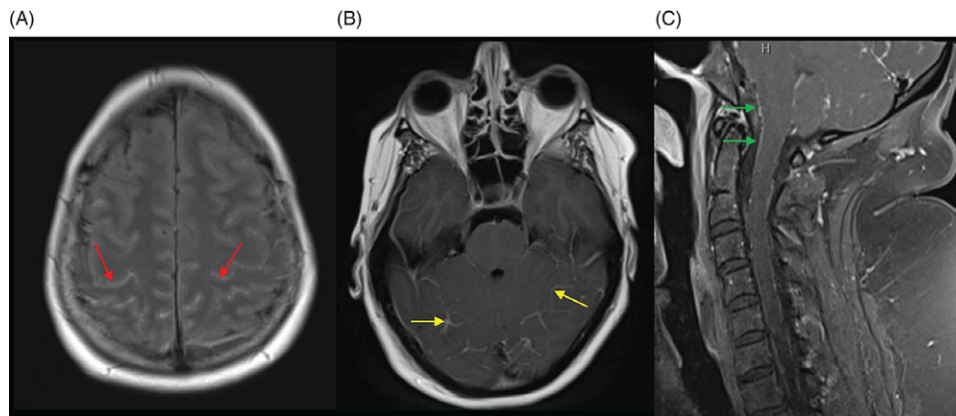


**Figure 1:** Fundus photos at presentation revealing bilateral optic disc edema with small, dot hemorrhages in the retina.

Bone marrow biopsy, CT scan of the chest, abdomen, and pelvis, and positron emission tomography-CT (PET-CT) from vertex to mid-thigh demonstrated no systemic involvement. She started treatment with high-dose methotrexate induction chemotherapy, rituximab, and temozolomide, followed by intrathecal cytarabine. Follow-up 9 months after initial presentation demonstrated normal visual function and no optic disc edema. She relapsed 18 months after initial presentation and died 3 months later.

Primary leptomeningeal lymphoma (PLML) is a type of primary central nervous system lymphoma (PCNSL), a rare neoplasm that arises as solitary or multifocal lesions in the cerebral hemispheres in 60% of cases.<sup>1,2</sup> While most leptomeningeal lymphomas are metastatic from another primary lymphoma,<sup>3,4</sup> PLML without parenchymal or systemic disease accounts for 7% of all PCNSLs.<sup>1</sup> The largest case series of PLML comprised 48 patients and found that most PLMLs, like other PCNSL, are non-Hodgkin's lymphoma of B cell lineage.<sup>3</sup> Most patients with PLML present with multifocal symptoms, ranging from cranial nerve palsies, lumbosacral radiculopathies, to less common ones like headaches and ataxia.<sup>3</sup> Isolated intracranial hypertension was not described in this case series.<sup>3</sup> Because of its wide range of presentations, PLML is commonly misdiagnosed as stroke, meningitis, polyradiculopathies, and rarely idiopathic intracranial hypertension (IIH).<sup>5</sup>

Our patient was an obese woman who presented with headache, nausea, transient visual obscurations, and papilledema, which suggested IIH.<sup>6</sup> Symptoms and signs of IIH, if present, may only reflect those of generalized elevated intracranial pressure.<sup>7</sup> However, in our patient, there were several atypical features that favored another diagnosis, including the rapid onset of symptoms, dot hemorrhages in the retina outside of the peripapillary area, and MRI findings of leptomeningeal enhancement. The MRI findings were not obvious and required expertise in interpreting the images. Five previously published cases of PLML have reported symptoms of intracranial hypertension.<sup>8-12</sup> In these cases, PLML caused a clinical syndrome consistent with IIH, which is defined as intracranial hypertension without mass lesions, dural venous sinus thrombosis, or other secondary cause.<sup>13</sup> Our case was unique since previous cases reported papilledema and intracranial hypertension in men,<sup>8,9,11</sup> had significant associated neurological symptoms such as obtundation,<sup>10</sup> significantly compromised visual function,<sup>12</sup> or the main location of disease was in the spine.<sup>9</sup> Patients may present with only blurred vision without headache<sup>5</sup> and initial MRI brain may be normal.<sup>6</sup> The importance of CSF studies in cases atypical for IIH including male patients was emphasized by a case where a 49-year-old man with 6 weeks of headaches and transient visual obscurations with a normal MRI brain underwent transverse sinus stenting without LP.<sup>6</sup> It was only 2 years later when he represented with seizures, balance problems, and progressive vision loss that the diagnosis of PLML was established. These cases demonstrate how difficult this condition can be to diagnose and the importance of contrast-enhanced MRI and CSF in these atypical cases for IIH. The Friedman-Jacobson criteria also include elevated intracranial pressure in lateral decubitus position, normal CSF composition,



**Figure 2:** Magnetic resonance imaging (MRI) of the brain at presentation. (A) FLAIR images showing diffuse sulcal FLAIR nonsuppression (red arrows). T1-post gad MRI images of the brain (B) and cervical spine (C) showing linear posterior fossa sulcal enhancement of the extra-axial spaces (yellow and green arrows, respectively).

and no evidence of hydrocephalus, mass, structural, or vascular lesions on MRI or contrast-enhanced CT for diagnosis of IIH.<sup>14</sup>

To diagnose PLML, a combination of MRI, serial CSF studies, and/or meningeal biopsy must be used. Leptomeningeal enhancement on MRI was found in 74% of patients with PLML, most commonly in the spinal cord and nerve roots.<sup>3</sup> Patients with PLML usually have high protein and low glucose on CSF studies.<sup>3</sup> CSF detection of PLML can be increased by doing a combination of cytology (malignant lymphocytes in 67% of PLML cases), flow cytometry (monoclonal population in 80% of cases), and receptor gene rearrangement studies (positive in 71% of cases).<sup>3</sup> Serial LPs are indicated in patients who are suspected of PLML as initial CSF studies can be negative.<sup>9,11</sup> If CSF remains nondiagnostic, a leptomeningeal biopsy is required.<sup>3</sup> PLML is usually a diagnosis of exclusion, and it was ruled in for our patient after PET-CT scan showed no systemic involvement, MRI of brain found no parenchymal involvement, and bone marrow biopsy was negative for lymphoma.

The biological basis of PLML is not currently understood, nor are prognostic factors or sites of relapse. Treatment of PLML can involve radiotherapy, systemic, and intrathecal chemotherapy, with 66% of patients receiving two or more modalities.<sup>3</sup> Most patients receive high-dose methotrexate as the main treatment. The median overall survival for patients with PLML is 24 months, and a subset may be cured.<sup>3</sup>

In conclusion, PLML is a rare CNS neoplasm that may present with symptoms of intracranial hypertension such as headache and visual obscurations. Careful fundus examination, contrast-enhanced neuroimaging, and CSF studies must be performed in cases atypical for IIH. To diagnose PLML, a combination of MRI, CSF studies, and leptomeningeal biopsy may be required with systemic disease being ruled out.

#### CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

#### STATEMENT OF AUTHORSHIP

Conception and design (J.P., J.M.), data retrieval (C.Y., J.M.), drafting of manuscript (C.Y., J.M.), critical appraisal (J.P., J.M.), and final approval (C.Y., J.P., and J.M.).

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#### REFERENCES

1. Lachance DH, O'Neill BP, Macdonald DR, et al. Primary leptomeningeal lymphoma: report of 9 cases, diagnosis with immunocytochemical analysis, and review of the literature. *Neurology*. 1991;41(1):95–100.
2. Bühring U, Herrlinger U, Krings T, et al. MRI features of primary central nervous system lymphomas at presentation. *Neurology*. 2001;57(3):393–6.
3. Taylor JW, Flanagan EP, O'Neill BP, et al. Primary leptomeningeal lymphoma: International Primary CNS lymphoma collaborative group report. *Neurology*. 2013;81(19):1690–96.
4. Fischer L, Martus P, Weller M, et al. Meningeal dissemination in primary CNS lymphoma: prospective evaluation of 282 patients. *Neurology*. 2008;71(14):1102–08.
5. Margarette de Vera Andal V. Primary leptomeningeal lymphoma presenting as low back pain and dementia: a case report. *Clin Neurol Neurosci*. 2018;2(2):33.

6. Thurtell MJ, Bruce BB, Newman NJ, et al. An update on idiopathic intracranial hypertension. *Rev Neurol Dis.* 2010;7(2–3):e56–68.
7. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. *Neurology.* 2002;59(10):1492–5.
8. Takagi M, Oku H, Kida T, et al. Case of primary leptomeningeal lymphoma presenting with papilloedema and characteristics of pseudotumor syndrome. *Neuro-Ophthalmology.* 2017;41(3):149–53.
9. Ahmed RM, King J, Gibson J, et al. Spinal leptomeningeal lymphoma presenting as pseudotumor syndrome. *J Neuroophthalmol.* 2013;33(1):13–16.
10. Kepes JJ, Maxwell JA, Hedeman L, et al. Primary diffuse malignant lymphoma of the leptomeninges presenting as “pseudotumor cerebri”. *Neurochirurgia (Stuttg).* 1971;14(5):188–96.
11. Manusow JS, Lee-Wing M, Rahman J, et al. Primary leptomeningeal lymphoma masquerading as pseudotumor cerebri. *Can J Ophthalmol.* 2009;44(3):e19–e20.
12. Kim HJ, Ha CK, Jeon BS. Primary leptomeningeal lymphoma with long-term survival: a case report. *J Neurooncol.* 2000;48(1):47–49.
13. Johnston I, Hawke S, Halmagyi M, et al. The pseudotumor syndrome: disorders of cerebrospinal fluid circulation causing intracranial hypertension without ventriculomegaly. *Arch Neurol.* 1991;48(7):740–47.
14. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology.* 2013;81(13):1159–65.