CASE REPORT

Case of Primary Leptomeningeal Lymphoma Presenting with Papilloedema and Characteristics of Pseudotumor Syndrome

Mai Takagi^a, Hidehiro Oku^a, Teruyo Kida^a, Toshikazu Akioka^b, and Tsunehiko Ikeda^a

^aDepartment of Ophthalmology, Osaka Medical College, Osaka, Japan; ^bDepartment of Internal Medicine, Osaka Medical College, Osaka, Japan

ABSTRACT

The authors describe an immunocompetent, 50-year-old man who complained of a daily transient blurring of his vision with bilateral papilloedema. His visual acuity was 20/20 OU, and the blind spot was enlarged bilaterally. There was intracranial hypertension, but imaging for systemic and brain tumours were negative. These findings suggested a diagnosis of the pseudotumor syndrome. However, MRI showed leptomeningeal enhancement, and acetazolamide successfully resolved his visual symptoms and papilloedema. Cytology and flow cytometry of the CSF led to the final diagnosis of primary leptomeningeal lymphoma (PLML). Clinicians need to be aware that a case of PLML may be misdiagnosed as pseudotumor cerebri.

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Introduction

Primary central nervous system lymphomas (PCNSLs) account for approximately 5% of all brain tumours,¹ and the lymphocytes are restricted to the central nervous system (CNS), including the eye. PCNSL typically presents as a solitary parenchymal mass,^{2,3} but leptomeningeal dissemination can also be seen.³ In cases with ocular involvement, the lymphocytes usually invade the uvea, retina, and vitreous, i.e., intraocular lymphomas.⁴ In these cases, the signs and symptoms often masquerade as steroid-resistant ocular inflammation.⁴ In other cases, the lymphocytes invade the optic nerve, causing optic neuropathy.⁵

The intracranial pressure can be increased in PCNSL, causing papilloedema. However, without a detection of a brain mass, other examination procedures are necessary to determine the exact cause of the papilloedema. Primary leptomeningeal lymphoma (PLML) without simultaneous parenchymal brain lesions or systemic involvement is a rare variant of PCNSL that accounts for 7% of all PCNSL.⁶ We describe a case of PLML with signs and symptoms of pseudotumor syndrome that is characterised by intracranial hypertension without a mass lesion and ventriculomegaly.⁷

Case report

A 50-year-old man complained of transient blurred vision in his right eye on awakening in the morning for 1 week prior to the visit to our hospital. At the initial examination, his visual acuity was 20/20 OU, and he did not complain of headaches or retrobulbar and orbital pain. He was not obese (170 cm in height, 58 kg in weight, body mass index [BMI] = 19.9 kg/m²) and had not been given any medication that is known to increase intracranial pressure (e.g., tetracycline, vitamin A, etc.).⁸ Visual field tests revealed an enlargement of the blind spots bilaterally (Figure 1). No signs of inflammation were detected in the anterior chamber or the vitreous. Fundus examination showed a swelling of the optic disc, i.e., papilloedema, in both eyes (Figure 2A). A relative afferent pupillary defect was not present. The intraocular pressure (IOP) was 17 mm Hg OD and 14 mm Hg OS. Because of the papilloedema, examinations were performed to rule out an intracranial mass or a systemic malignancy.

Brain magnetic resonance imaging (MRI) with gadolinium enhancement did not show any parenchymal space-occupying lesion and clear ventriculomegaly (Figure 3A). However, there was

CONTACT Hidehiro Oku, MD, PhD hidehirooku@aol.com Department of Ophthalmology, Osaka Medical College, 2-7 Daigaku-machi, Takatsuki, Osaka 569-8686, Japan.

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Figure 1. Visual fields of a patient with leptomeningeal lymphoma. Blind spots are enlarged bilaterally, but the visual fields are not constricted and a central scotoma is not present.

Figure 2. Fundus changes of the patient with leptomeningeal lymphoma. (A) At the initial examination. The optic discs are swollen in both eyes, i.e., papilloedema. (B) After taking acetazolamide for 3 months. Note the decrease in the papilloedema.

leptomeningeal gadolinium enhancement around the cavernous sinus and ventral surface of the pons (Figure 3B). The roots of the cranial fifth and sixth nerves and the inner ear were also enhanced bilaterally (Figure 3B). However, the abduction movements were not limited, and there was no sensory hearing loss in both ears. Other neurological deficits were also not found.

Carcinomatous meningitis and inflammatory meningitis, such as that due to sarcoidosis, were also considered as possible causes of the

leptomeningeal gadolinium enhancement. Thus, whole-body fluorodeoxyglucose (FDG) positron emission tomography (PET) was performed, but uptakes of FDG were not observed in any organ or lymph node. Whole-body enhanced computed tomography (CT) did not show any neoplastic lesions. All inflammatory and cancer markers were negative in the blood. Human immunodeficiency virus (HIV) infection was also negative, and he had no other significant clinical history. Lumbar puncture was suggested, but he refused

Figure 3. Axial brain (A, B) and sagittal spine (C) T1-weighted MR images with gadolinium enhancement. (A) There is no parenchymal mass lesion or clear ventriculomegaly in the brain. (B) Mass lesions are not present in the posterior fossa, and the fourth ventricle is not dilated. Leptomeningeal enhancement is seen around the cavernous sinus and roots of the fifth nerve and inner ear on both sides (arrows). (C) Extensive leptomeningeal enhancement of the lumbar and cauda equine can be seen (arrow).

further examination because of his business schedule.

Oral acetazolamide (500 mg two times daily) was started to treat the papilloedema. The dosage was scheduled to increase with an increment of 250 mg every week up to a maximum dosage of 2.0 g twice daily.⁹ However, acetazolamide of 500 mg twice daily had improved his blurred vision and the initial dosage was maintained. Actually, the optic disc swelling gradually decreased and disappeared 3 months later (Figure 2B). However, he developed kidney calculi, and the urologist advised him to stop taking acetazolamide 4 months from his initial visit to our hospital. During the interval, no neurological deficits appeared and he continued with his regular schedule. After discontinuing the acetazolamide for 1 month, a cognitive dysfunction appeared and he was hospitalised when the papilloedema reappeared.

He agreed to receive lumbar puncture at this time. Examination of the cerebrospinal fluid (CSF) showed a clear CSF with an increased opening pressure of 220 mm H₂O and pleocytosis of 126 cells/mm³ with lymphocytic predominance (73.5%). Atypical and large lymphocytes were found by cytology. Flow cytometry revealed that 38.4% of the cells were CD19 and 50.6% were CD20 positive. The ratio of κ/λ was 20.54, and the CSF protein (163.9 mg/dL) and glucose (61 mg/dL) were not elevated.

The CSF findings led us to examine the cauda equine lesion. MRI with gadolinium enhancement of the spine revealed an enhanced lesion at the cauda equine (Figure 3C). This finding is known

to be characteristic of a spinal involvement in PCNSL¹⁰ and led us to diagnose the patient with diffuse large B-cell PCNSL.

Injection of methotrexate (4.8 g/day) into the medullary cavity and R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy were started. The treatments led to a remission of his condition, and the papilloedema and cognitive dysfunction recovered. We have followed this patient for 16 months, and no recurrences have occurred.

Discussion

This case presented with bilateral papilloedema with leptomeningeal gadolinium enhancement. CSF cytology and flow cytometry determined the condition as diffuse large B-cell lymphoma. Systemic and CNS parenchymal involvement was absent. In addition, he was immunocompetent with no history of lymphomas or immune-suppression treatments. Thus, his findings were in good agreement with the diagnostic criteria of primary leptomeningeal lymphoma (PLML),¹¹ although some of the signs suggested pseudotumor cerebri.

Pseudotumor cerebri generally presents with the signs and symptoms specific to intracranial hypertension. Although the intracranial pressure is increased, the composition of the CSF is normal, and neuroimaging does not detect any abnormalities.¹² Our case did have extensive abnormalities in the neuroimages and CSF. However, the transient visual blurring is a typical symptom of papilloedema,¹³ and the papilloedema

was the only sign suggesting pseudotumor cerebri. Johnston et al. have broadened the characteristics of pseudotumor cerebri and framed the term pseudotumor syndrome, which is caused by disturbed CSF circulation and is characterised by intracranial hypertension without a mass lesion or ventriculomegaly in the brain.⁷ Thus, the pseudotumor syndrome could be a possible diagnosis in our case.

Similar cases of PLML that had signs of pseudotumor cerebri or pseudotumor syndrome have been reported.^{14,15} We suggest that an increase in the intracranial pressure can occur in PLML without other neurological deficits. The absorption of the CSF by the arachnoid may be impaired in PLML, which would then disturb the CSF circulation and cause an intracranial hypertension. Asymptomatic lumbosacral root infiltration of lymphocytes has been reported in PLML.¹⁵ Although the cause for the infiltration without any signs or symptoms was not stated, our case had leptomeningeal gadolinium enhancement around the cavernous sinus and the roots of the cranial fifth, sixth, and eighth nerves without these neuropathies.

It is important to note that negative CSF findings are not uncommon in CNS lymphomas and repeated punctures are warranted.¹¹ In addition, MRI is often performed without gadolinium enhancement, which can yield negative findings. In cases with negative findings in CSF cytology and plain MRI, intracranial hypertension due to PLML can be misdiagnosed as pseudotumor cerebri or idiopathic intracranial hypertension. The finding that acetazolamide was effective in our case supports this idea.

In conclusion, papilloedema with signs and symptoms specific to intracranial hypertension can be indications for PLML. Ophthalmologists should be aware of this rare condition, and neuroimaging with enhancement and lumbar puncture need to be performed for an accurate diagnosis.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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