The Canadian Journal of Neurological Sciences (2024), 1–2
doi:10.1017/cjn.2024.334

Canadian Journal of Neurological Sciences
Journal Canadien des Sciences Neurologiques

Letter to the Editor: New Observation

Asymptomatic Optic Disc Oedema due to Haematologic Malignancy

Samira Jafari[1,2], Suradech Suthiphosuwan[3] and Jonathan A. Micieli[1,2,4]

[1]Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, ON, Canada, [2]Kensington Research Institute, Kensington Vision and Research Centre, Toronto, ON, Canada, [3]Department of Medical Imaging, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada and [4]Department of Ophthalmology and Vision Sciences, St. Michael's Hospital, Unity Health, Toronto, ON, Canada

Papilledema, the swelling of the optic disc due to increased intracranial pressure, is a critical finding that can indicate serious underlying pathology, including central nervous system (CNS) involvement of lymphoproliferative disorders. These disorders, such as Waldenström's macroglobulinemia (WM), also known as lymphoplasmacytic lymphoma (LPL), are rare haematologic malignancies that can present with various ocular manifestations, including optic disc oedema.[1]

This case report discusses two patients diagnosed with CNS involvement of lymphoproliferative disorders after incidental findings of optic disc oedema during routine eye exams. Both patients were asymptomatic.

Case 1: A 75-year-old woman with a history of breast cancer presented with asymptomatic bilateral optic disc oedema found during an annual optometry exam. Her examination revealed best corrected visual acuity of 20/40 in the right eye and 20/25 in the left eye. The anterior segment was unremarkable, but fundoscopy showed optic disc oedema, more pronounced in the left eye. The thickness of the retinal nerve fibre layer (RNFL) was 118 micrometres in the right eye and 216 micrometres in the left eye. The Humphrey 24-2 SITA-Fast visual fields (VFs) were normal. She was diagnosed with bilateral optic disc oedema with preserved visual function, consistent with papilledema. An urgent workup was arranged, suspecting optic nerve sheath involvement and leptomeningeal disease. MRI of the orbits with gadolinium revealed perioptic enhancement along the intra-orbital and intracanalicular segments of both optic nerves (Figure 1). Lumbar puncture (LP) showed negative CSF culture, WBC count zero, glucose 3.3 mmol/litre and protein 0.31 grams/litre. Opening pressure could not be measured. CSF cytology, along with peripheral blood and bone marrow biopsies, confirmed the diagnosis of indolent B-cell lymphoma with plasmacytoid differentiation and kappa light chain restriction. A Positron Emission Tomography scan revealed no evidence of disease elsewhere. At her two-month follow-up, the optic disc oedema had resolved spontaneously, and she remained asymptomatic with normal VF and RNFL Optical Coherence Tomography (OCT). She was then started on zanubrutinib to prevent CNS complications.

Case 2: A 53-year-old man with no significant medical history was found to have mild, incidental optic disc oedema in both eyes during a routine examination. His visual acuity was 20/20 in both eyes, with OCT RNFL measurements of 137 µm in the right eye and 113 µm and in the left eye. His Humphrey 24-2 SITA-Fast VFs were normal. MRI of the brain and spine with gadolinium revealed bilateral optic and multiple cranial nerve enhancements, along with mild dilatation of the optic nerve CSF spaces and flattening of the posterior sclera (Figure 2). The differential diagnoses at this stage included inflammatory, neoplastic and infectious aetiologies. An urgent LP and neurology, rheumatology, haematology and infectious disease consultation were requested. An LP showed an opening pressure of 31 cm of water, protein 3.23 grams/litre (elevated), glucose 4.2 grams/litre and WBC count zero. On repeat LP, flow cytometry of the CSF showed an aberrant population of

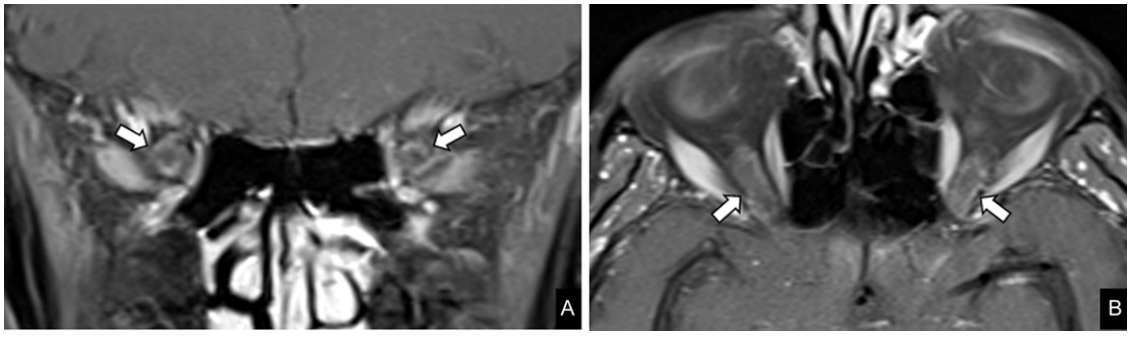

Figure 1. MRI of the orbit. Coronal (A) and axial (B) post-gadolinium T1-weighted Turbo-Spin-Echo (TSE) with fat saturation of the orbit show perioptic enhancement along the intra-orbital segments of bilateral optic nerves (arrows in A and B).

Corresponding author: Jonathan A. Micieli; Email: jonathanmicieli@gmail.com

Cite this article: Jafari S, Suthiphosuwan S, and Micieli JA. Asymptomatic Optic Disc Oedema due to Haematologic Malignancy. *The Canadian Journal of Neurological Sciences*, https://doi.org/10.1017/cjn.2024.334

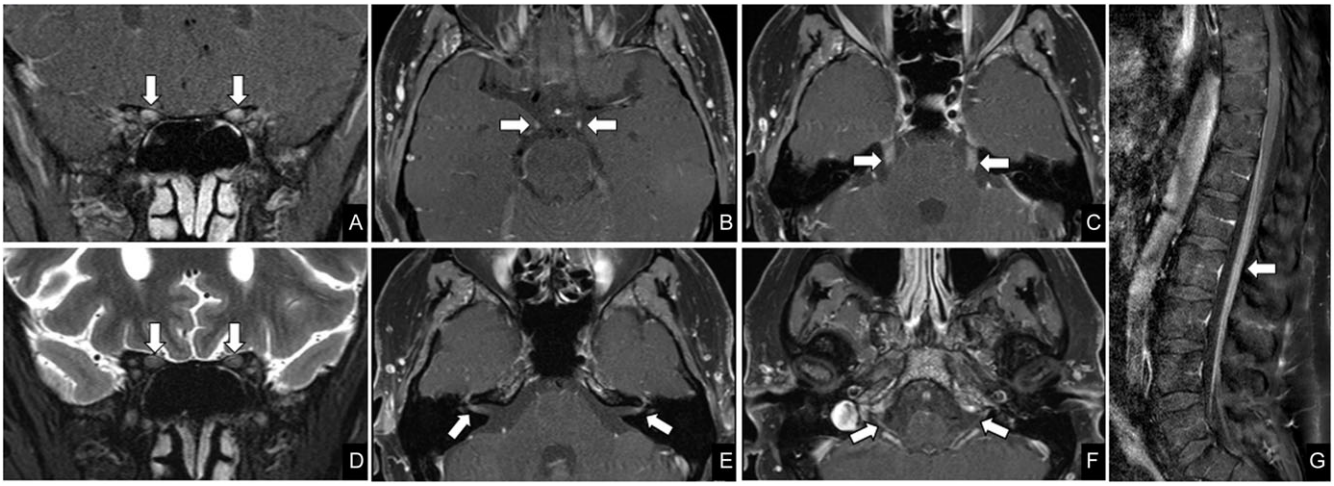

Figure 2. MRI of the brain, orbit and lumbar spine. Coronal post-gadolinium T1-weighted Turbo-Spin-Echo (TSE) with fat saturation (A) and coronal T2-weighted TSE (D) of the orbit show abnormal T2 hyperintensity and enhancement of bilateral optic nerves (arrows in A and D). Axial post-gadolinium T1-weighted TSE with fat saturation at the level of the posterior fossa (B, C, E and F) shows diffuse cranial nerve enhancement involving bilateral oculomotor nerves (arrows in B), trigeminal nerves (arrows in C), facial and vestibulocochlear nerve complexes (arrows in E) and vagus nerves (arrows in F). Sagittal post-gadolinium T1-weighted TSE with fat saturation of lumbar spine (G) shows diffuse smooth thickening and enhancement of the cauda equina nerve roots (arrow in G).

B-lymphocytes, with detailed antibody testing consistent with a B-cell lymphoproliferative neoplasm. He was diagnosed with LPL or WM with cranial nerve involvement, also known as Bing–Neel syndrome, an extremely rare neurological complication of WM. He was started on high-dose methotrexate. His six-month ophthalmology follow-up showed normal visual acuity, OCT RNFL and ganglion cell complex measures.

Diagnosing lymphoproliferative disorders with CNS involvement through ocular findings is rare but essential. Both of our cases involved asymptomatic optic disc oedema detected during routine exams, highlighting that even subtle ocular findings can indicate systemic disease. While previous reports describe symptomatic cases of WM with visual complaints, our cases are the first to suggest that asymptomatic optic disc oedema alone may warrant further investigation. Pinna et al. reported a case of WM presenting with two months of blurred vision and bilateral optic disc swelling as the initial symptoms.[1] Other ocular manifestations of WM include central retinal vein occlusion, hyperviscosity-related retinopathy and serous macular detachment, reflecting the varied ways retinal and optic nerve involvement can occur.[2,3] Lai and Chang's report on serous macular detachment emphasises the risk of significant ocular morbidity in WM and the importance of early detection and treatment.[2] Dammacco et al. further documented the ophthalmic manifestations of WM, including optic disc oedema, retinal haemorrhages and vein occlusions, underscoring the variability of ocular presentations in this disease.[4]

Optic disc oedema in LPL and WM can result from several mechanisms. Malignant cells may infiltrate the meninges, obstructing CSF flow and increasing intracranial pressure (ICP), causing papilledema. Direct infiltration of the optic nerve can cause localised oedema, while hyperviscosity from excess monoclonal IgM in WM can impair blood flow, leading to optic disc swelling. Additionally, autoimmune and inflammatory responses can disrupt the blood-brain barrier, increasing vascular permeability. In some cases, lymphomatous deposits in the brain can compress optic pathways, further contributing to papilledema.[1,2,4] Understanding these mechanisms is essential for diagnosing and managing papilledema in LPL or WM. We suspect that the optic disc oedema in case 1 was due to direct infiltration of the optic nerve/optic nerve sheath complex, while in case 2, it was likely a result of malignant cells obstructing the CSF flow and increasing ICP.

In conclusion, optic disc oedema can be an early indication of CNS involvement in lymphoproliferative disorders such as WM and LPL, even without visual or systemic symptoms. These two cases emphasise the importance of conducting comprehensive diagnostic evaluations for unexplained optic disc oedema, regardless of the patient's symptomatology. As reported in the literature, the diverse ocular presentations of these disorders highlight the need for a multidisciplinary approach to diagnosis and management. Early recognition and prompt intervention are crucial, as timely and accurate diagnoses enable targeted treatments, ultimately improving outcomes and preserving patients' quality of life.

Acknowledgements. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines. Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

Author contributions. Samira Jafari: Writing – original draft, methodology, validation, investigation, preparation, visualisation.

Suradech Suthiphosuwan: Validation, reviewing and editing.

Jonathan A. Micieli: Supervision, conceptualisation, validation, reviewing and editing.

Funding statement. None.

Competing interests. None.

References

1. Pinna A, Dore S, Dore F, et al. Bilateral optic disc swelling as the presenting sign of Waldenström's macroglobulinaemia. *Acta Ophthalmol Scand*. 2003; 81:413–5. DOI: 10.1034/j.1600-0420.2003.00106.x.
2. Lai CC, Chang CH. Hyperviscosity-related retinopathy and serous macular detachment in Waldenström's macroglobulinemia: a mortal case in 5 years. *Eur J Ophthalmol*. 2022;32:NP109–14. DOI: 10.1177/11206721211002066.
3. Avashia JH, Fath DF. Bilateral central retinal vein occlusion in Waldenström's macroglobulinemia. *J Am Optom Assoc*. 1989;60:657–8.
4. Dammacco R, Lisch W, Kivelä TT, et al. The spectrum of ocular manifestations in patients with Waldenström's macroglobulinemia. *Ocul Immunol Inflamm*. 2022;30:1659–68. DOI: 10.1080/09273948.2021.1933068.