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Ischemic Retinopathy Associated With Mantle Cell Lymphoma–Induced Vascular Occlusion

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Abstract

Purpose: To describe a patient with bilateral ischemic retinopathy, likely attributable to vascular occlusion induced by mantle cell lymphoma. **Methods:** A case and its findings were analyzed. **Results:** A 54-year-old man presented with an 11-month history of significant vision loss in both eyes. His medical history was significant for mantle cell lymphoma with no signs of intraorbital involvement on magnetic resonance imaging. At presentation, the visual acuity was 20/400 OD and counting fingers OS, with an unremarkable anterior segment examination. On funduscopy, optic nerve pallor, sclerotic blood vessels, and cotton-wool spots were seen. Profound retinal nonperfusion and inner retinal layer loss were confirmed with fluorescein angiography and optical coherence tomography, with no signs of macular edema at the time of presentation. **Conclusions:** This report represents the first instance of bilateral ischemic retinopathy, likely originating from mantle cell lymphoma, presenting predominantly with ischemic retinal features and resulting in profound vision loss. With few cases documenting retinal involvement in mantle cell lymphoma, this report provides a better understanding of this rare pathology and its effect on retinal health.

Keywords

mantle cell lymphoma (MCL), ischemic retinopathy, retinal vascular occlusion

Introduction

Mantle cell lymphoma is a rare but aggressive B-cell non-Hodgkin lymphoma. It accounts for approximately 10% of all cases of non-Hodgkin lymphoma and has a higher incidence in men.[1] Mantle cell lymphoma is incurable, and the treatment goal is to achieve a longer remission and to prolong survival.[1] Ocular involvement is a rare feature of this lymphoma, with most cases in the literature describing ocular adnexal manifestations.[2] To date, few cases have been reported that describe the rare retinal involvement of mantle cell lymphoma.[3–6]

Here, we report a case of bilateral ischemic retinopathy, which was likely attributable to mantle cell lymphoma–induced vascular occlusion, that resulted in profound vision loss.

Case Report

A 54-year-old White man with a history of sudden vision loss in both eyes presented to the Duke Eye Center, Durham, NC, USA, in August 2023 for a second opinion. He had been symptomatic for the previous 11 months and had initially been treated at a local ophthalmology clinic. He received intravitreal (IVT) bevacizumab injections for bilateral cystoid macular edema (CME) that was linked to suspected central retinal vein occlusion in the right eye and hemiretinal vein occlusion in the left eye (Figure 1).

In November 2022, a complete blood cell count with differential showed a pronounced lymphocyte-predominant increase in white blood cells of $128.1 \times 10^3/\mu L$. The patient denied having B symptoms, such as fever, night sweats, or unintentional weight loss, and was subsequently sent to the emergency department and for further management by the hematology and oncology service. Stage IV mantle cell lymphoma was ultimately confirmed on a bone marrow biopsy. Phenotypically, there was expression of CD5, CD20, cyclin D1, and BCL2; however, lymphoma cells were negative for CD3, CD10, BCL6, CD21, LEF1, p53, or Sox11. The proliferative rate by Ki67 was low (20%). Computed tomography of the chest, abdomen, and pelvis showed no lymph node involvement. Magnetic resonance imaging (MRI) of the brain showed no evidence of intracranial or orbital lymphoma. A systemic bendamustine–rituximab immunochemotherapy regimen was started, and the patient ultimately completed 6 cycles of therapy, with the last round in May 2023.

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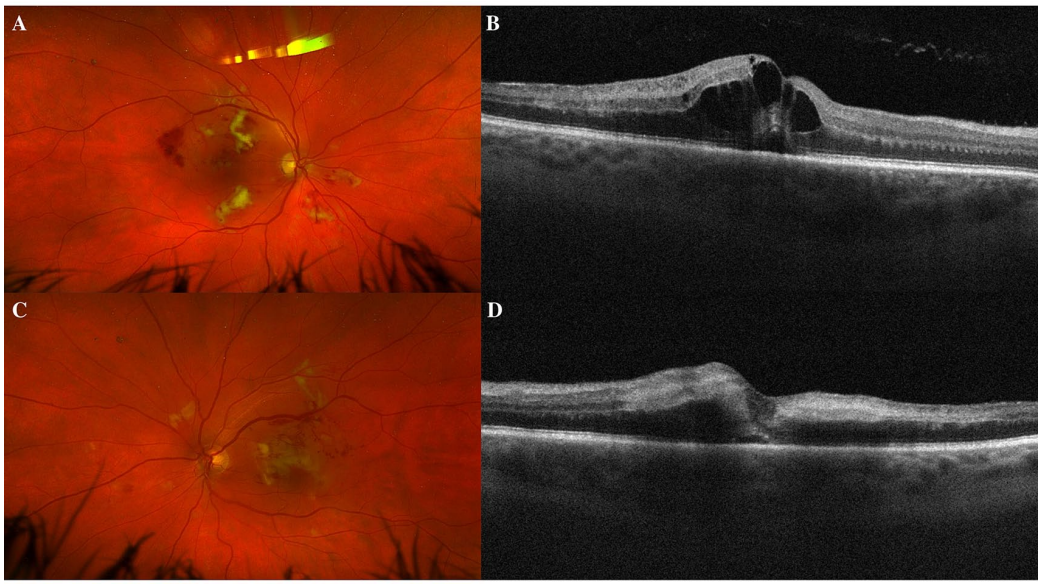

Figure 1. Multimodal imaging of bilateral ischemic retinopathy associated with mantle cell lymphoma–induced vascular occlusion at baseline. Color fundus photographs of (A) the right eye and (C) the left eye show multiple cotton-wool spots and scattered intraretinal hemorrhages at the posterior pole. (B and D) Optical coherence tomography highlights inner retinal layer thickening with diffuse hyperreflectivity combined with cystoid macular edema and mild subretinal fluid in both eyes.

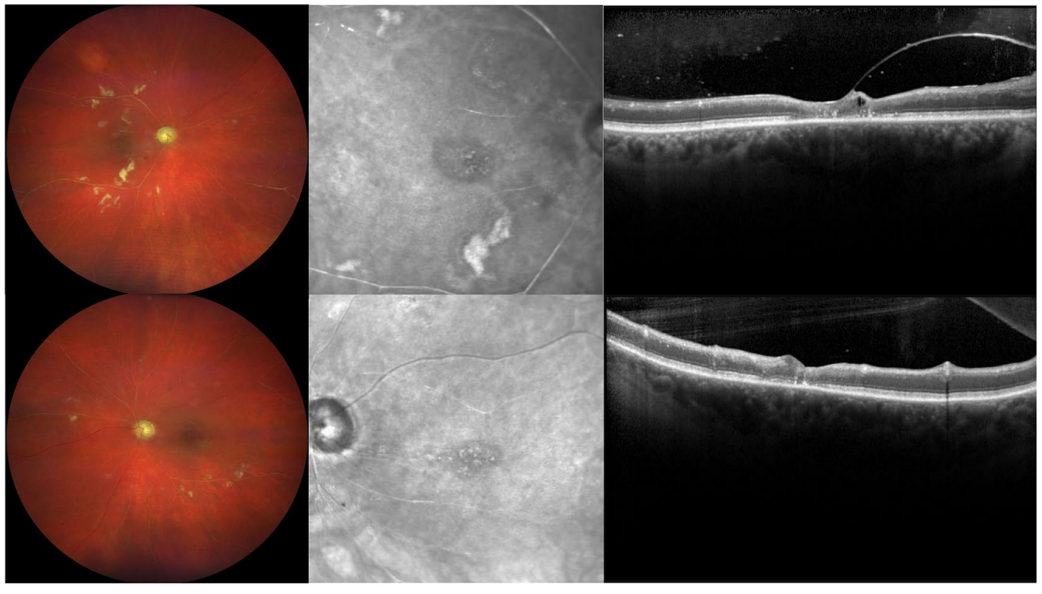

Figure 2. Multimodal imaging of bilateral ischemic retinopathy associated with mantle cell lymphoma–induced vascular occlusion after 11 months. Color fundus photographs of the right eye (top row) and the left eye (bottom row) illustrate optic nerve pallor, arteriolar narrowing, sclerotic blood vessels, and multiple cotton-wool spots. Optical coherence tomography shows vitreomacular traction in the right eye (top row) and disturbed retinal lamination with pronounced inner retinal layer loss in both eyes (top and bottom rows).

At presentation to our clinic, the patient's best-corrected visual acuity (VA) was 20/400 OD and counting fingers OS. A slitlamp examination of the anterior segment was grossly unremarkable (ie, showed only early cataracts). A fundus examination of both eyes was characterized by optic nerve pallor, severe arteriolar narrowing, sclerotic blood vessels, and scattered multiple cotton-wool spots (Figure 2). Optical coherence tomography (OCT) documented vitreomacular traction in the right eye and disturbed retinal lamination with pronounced inner retinal layer loss without evidence of ME in both eyes (Figure 2).

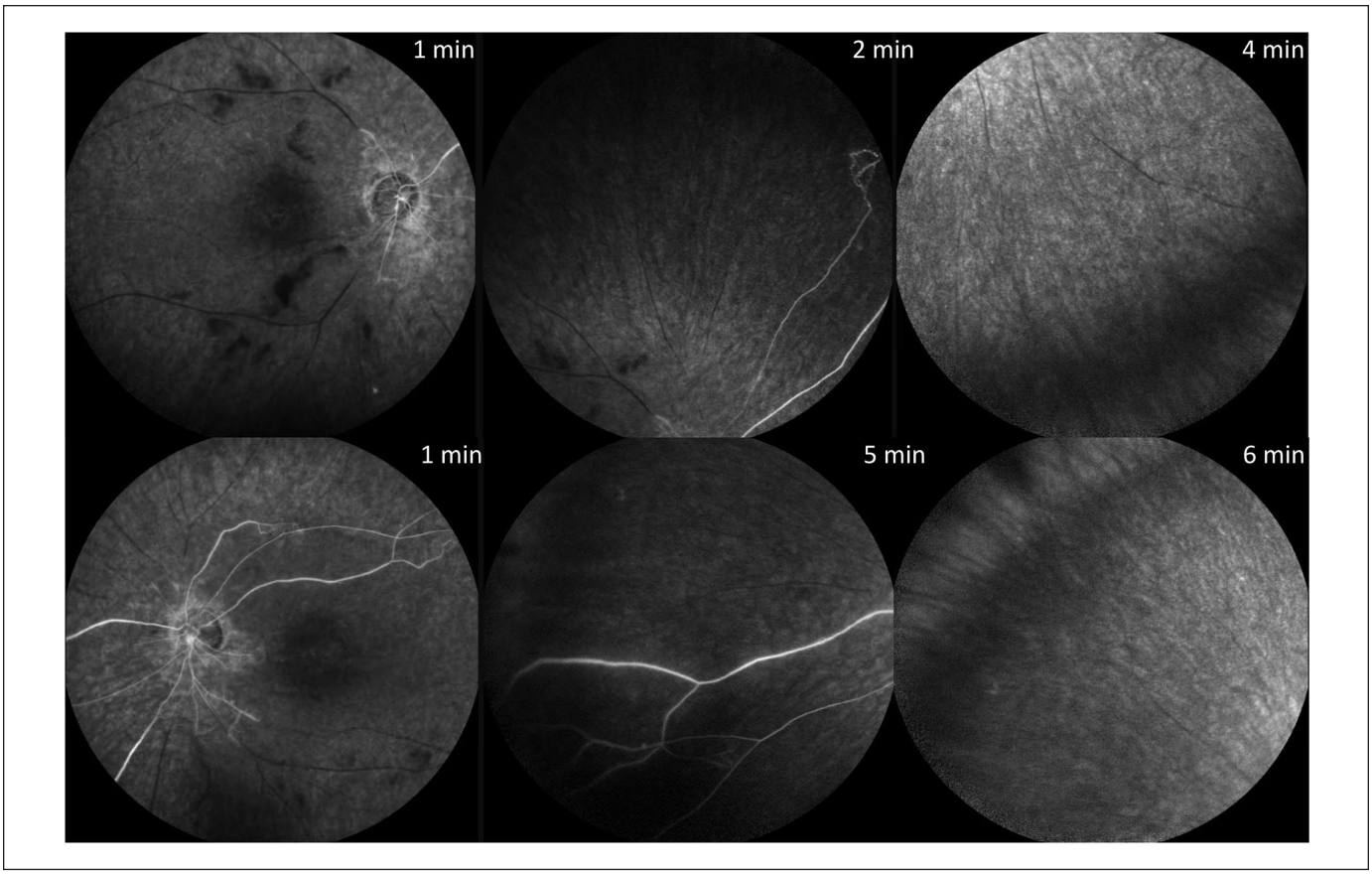

Figure 3. Angiography study of bilateral ischemic retinopathy associated with mantle cell lymphoma–induced vascular occlusion. Fluorescein angiography with peripheral sweeps shows delayed filling and profound retinal nonperfusion extending to the periphery in the absence of retinal neovascularization in both eyes. The right eye is depicted in the top row, and the left eye is depicted in the bottom row.

Fluorescein angiography showed delayed filling, profound retinal nonperfusion in the absence of retinal neovascularization (NV), and perivascular leakage (Figure 3).

An improvement in vision since the onset of the patient's symptoms was not reported. Low vision rehabilitation was recommended as well as close follow-up to monitor for the development of NV and its complications, including vitreous hemorrhage and neovascular glaucoma.

Unfortunately, 3 months after the patient presented to our clinic, he developed retinal NV with associated preretinal and vitreous hemorrhage as a result of severe ischemia in both eyes. Further therapeutic intervention was planned that included IVT antivascular endothelial growth factor (anti-VEGF) agents and panretinal photocoagulation.

Conclusions

Predominantly retinal involvement in mantle cell lymphoma, including intraretinal, subretinal, and optic disc lymphomatous infiltration, together with intraocular hemorrhage, has been described in only a few reports.[3–6]

Our patient's unique clinical presentation involved solely profound bilateral ischemic retinal changes, most likely stemming from significant combined retinal artery and vein occlusions precipitated by the accumulation of atypical lymphocytes within retinal vessels. This was supported by the initial OCT findings of bilateral inner retinal layer thickening and diffuse hyperreflectivity combined with ME. Remarkably, MRI of the brain showed no indications of orbital lymphoma and the patient did not exhibit mantle cell lymphoma–associated end-organ vasculitis at any phase of the disease, likely because of the early and aggressive ocular involvement and prompt treatment for the systemic aspect (unfortunately, not ocular) of the disease.

The abnormal elevation in lymphocyte-predominant white blood cells and the simultaneous occurrence of bilateral retinal ischemic findings strongly suggest substantial vascular compromise attributable to mantle cell lymphoma. Paraneoplastic hypercoagulability may be an additional occlusive culprit. Noninfectious retinal vasculitis, in the case of many underlying malignancies, appears to be a frequent cause of retinal pathology. Clinical findings on funduscopic examination can include vascular sheathing, cotton-wool spots, intraretinal hemorrhages, retinal infiltrates, and ME, and both arteries and veins may be involved.[7–9] In these instances, vascular occlusion and retinal ischemia are believed to be thrombotic or obliterative and secondary to inflammatory cell infiltration.[10–12]

Our case is noteworthy because of pronounced late ischemic features presumably associated with mantle cell lymphoma in the absence of significant retinal vasculitis, which to our knowledge has not been previously reported. In our patient, the retinal findings and VA did not improve after aggressive immunochemotherapy with bendamustine and rituximab, which may be explained by the delayed initiation of the treatment, at least for the eye. In addition, initial treatment with IVT anti-VEGF agents may have prevented early-onset NV secondary to pronounced ischemia. However, it is possible that anti-VEGF therapy simultaneously led to a further decrease in retinal perfusion by way of anti-VEGF–induced vasoconstriction, decreased blood flow velocity, and increased platelet aggregation.[13,14] Thus, anti-VEGF treatment may have closed off thread-like blood vessels providing vital perfusion, resulting in worsening retinal ischemia and affecting potential visual recovery. However, rare cases of retinal vasculitis with improvement in VA after administration of IVT anti-VEGF agents have been reported.[15,16]

In this case, the similarity in retinal presentation with Purtscher-like retinopathy is notable given the concurrent presence of multiple cotton-wool spots/Purtscher flecken and scattered intraretinal hemorrhages at the posterior pole in both eyes.[17] Purtscher-like retinopathy is also characterized by retinal vascular occlusion and retinal ischemia, often associated with trauma or systemic disease (eg, pancreatitis, renal failure, and autoimmune disorders).[18–20] However, to our knowledge the existing literature does not report any known association between mantle cell lymphoma and Purtscher-like retinopathy.

Finally, it has been documented that in nearly two thirds of reported cases of mantle cell lymphoma involving the eyes, ocular or periocular manifestations were the initial presenting signs of lymphoma. Most of these patients were diagnosed with stage III or stage IV disease at the time of ophthalmic presentation, which resembles our patient's case.[21,22] Furthermore, less than one third of patients with mantle cell lymphoma exhibit B symptoms at the time of presentation.[23]

In summary, the range of ophthalmic complications associated with mantle cell lymphoma has been broadened to include bilateral ischemic retinopathy, likely attributable to mantle cell lymphoma–induced vascular occlusion. Our findings provide a better understanding of this rare pathology and how it affects retinal health. Although this lymphoma is uncommon, it is imperative for clinicians caring for these patients to remain vigilant regarding any reported visual symptoms or observed retinal findings.

Ethical Approval

This case report was conducted in accordance with the Declaration of Helsinki. The collection and evaluation of all protected patient health information were performed in a US Health Insurance Portability and Accountability Act–compliant manner.

Statement of Informed Consent

The patient provided informed consent for publication of this paper.

Declaration of Conflicting Interests

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