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Systemic lymphoma masquerading as Vogt-Koyanagi-Harada syndrome: Report of a case with multimodal imaging and histopathology

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ABSTRACT

Purpose: To report a case of systemic diffuse large B cell lymphoma presenting with ocular manifestations and neurologic findings resembling Vogt-Koyanagi-Harada syndrome.

Observations: A 51-year-old Caucasian man presented with headache, ear pain, and blurry vision in both eyes. He was found to have bilateral exudative retinal detachments. After a short period of initial improvement with high dose systemic corticosteroid, his condition significantly worsened. An extensive work-up, including a kidney biopsy, led to a diagnosis of systemic diffuse large B cell lymphoma. He had excellent recovery following treatment with appropriate chemotherapy.

Conclusions and Importance: Systemic malignancy may present with ocular manifestations and may masquerade as another diagnosis. An unexpected clinical course may suggest an alternative diagnosis. A broad systemic work-up including an evaluation for malignancy should be considered for patients presenting with unexplained exam or systemic findings.

1. Introduction

Ocular involvement in systemic lymphoma usually includes the choroid.[1] Rarely, it can present with vitreoretinal involvement.[2–12] We report a unique case of systemic lymphoma presenting with neurologic symptoms and bilateral exudative retinal detachments suggestive of Vogt-Koyanagi-Harada (VKH) syndrome, expanding the spectrum of ocular manifestations of systemic lymphoma.

2. Case report

A 51-year-old Caucasian man presented to the Massachusetts Eye and Ear Emergency Department (ED) with blurry vision in both eyes (OU). He reported flu-like symptoms commencing three weeks prior to presentation, followed by headache, ear pain, and blurry vision. In addition, he reported transient weakness in his extremities. Visual acuity (VA) was 20/80 in the right eye (OD) and 20/40 in the left eye (OS). Intraocular pressures were normal OU. No cells were noted in the anterior chamber or anterior vitreous OU. Dilated fundus exam was notable for multiple exudative retinal detachments OU. Multimodal imaging findings are presented in Fig. 1. Fluorescein angiography (FA) showed multiple pinpoint areas of hyperfluorescence with leakage and pooling OU. Optical coherence tomography (OCT) showed choroidal thickening and subretinal fluid OU. He declined an evaluation by the neurology service. He was diagnosed with Vogt-Koyanagi-Harada (VKH) syndrome and treated with oral prednisone 60 mg daily. He returned two days later with dizziness and confusion and was admitted to the neurology service. Magnetic resonance imaging (MRI) of the brain showed areas of hyperintensities in the subcortical white matter (Fig. 2A), which were thought to be consistent with VKH. He was treated with a 3-day course of intravenous methylprednisolone 1g daily. His neurologic symptoms improved, VA improved to 20/25 OU and the subretinal fluid improved OU. He was discharged with oral prednisone 60 mg daily.

One week later, he returned with altered mental status and worsening vision. Repeat retinal imaging showed further accumulation of

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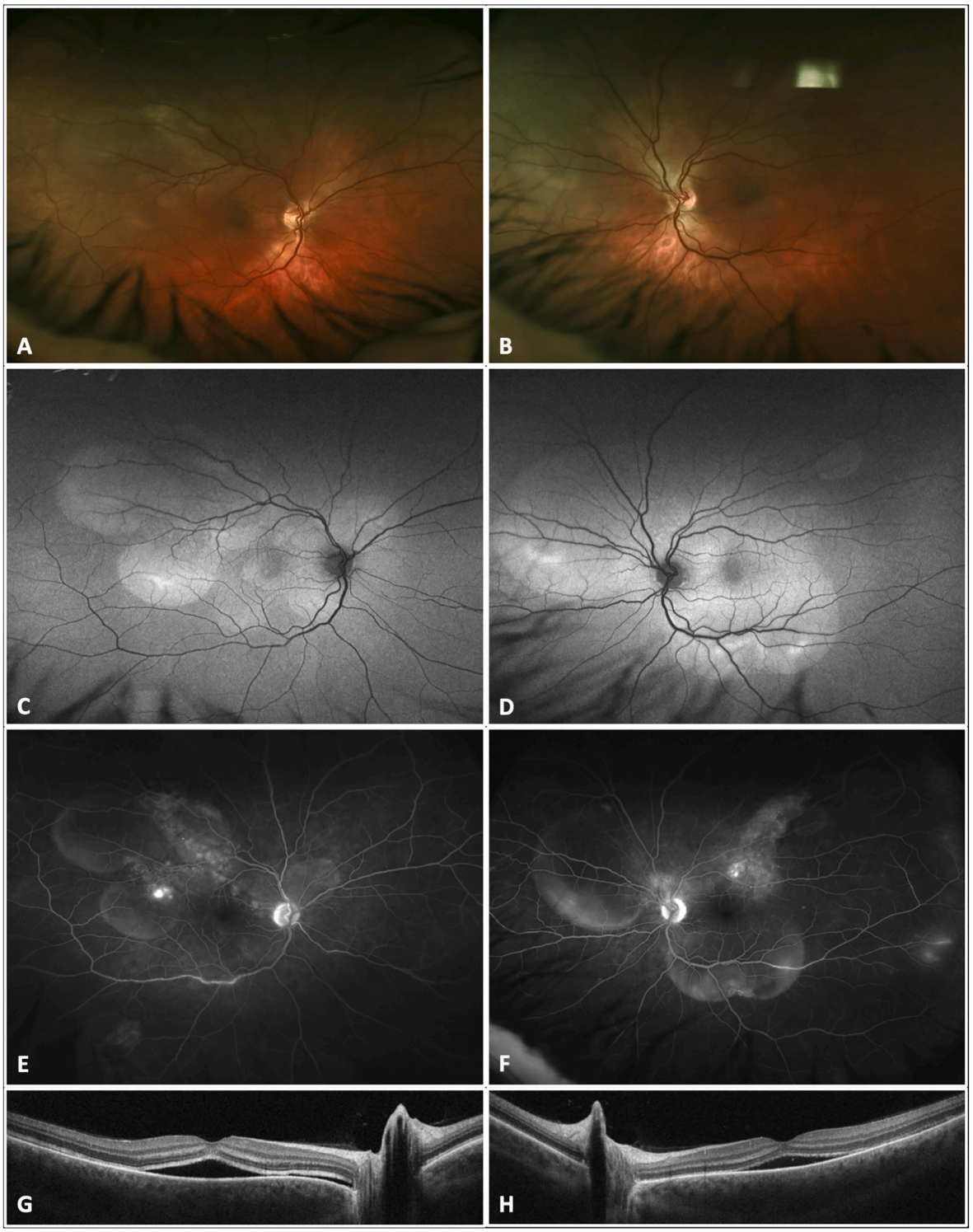

Fig. 1. Color fundus photographs of the right eye (A) and left eye (B) reveal exudative retinal detachments. Fundus autofluorescence shows hyperautofluorescence in the areas of exudative retinal detachment in the right eye (C) and left eye (D). Fluorescein angiography shows pinpoint areas of leakage and associated pooling in the right eye (E) and left eye (F). Optical coherence tomography reveals a thick choroid and subretinal fluid involving the macula in the right and left eyes (G and H, respectively). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

subretinal fluid suggesting progression of disease. Repeat MRI of the brain showed progression of the hyperintensities in the subcortical white matter and new foci of hemorrhage (Fig. 2B). Given the atypical course while being actively immunosuppressed, a brain biopsy was performed, which showed only an inflammatory infiltrate. Whole body and brain position emission tomography-computed tomography showed increased uptake in both adrenal glands and kidneys. Given the non-diagnostic brain biopsy, a renal biopsy was performed, which showed infiltration of the kidney with lymphoma cells and a diagnosis of diffuse large B cell lymphoma was made (Fig. 3).

He was treated with a chemotherapy regimen consisting of rituximab, cyclophosphamide, hydroxydaunorubicin hydrochloride,

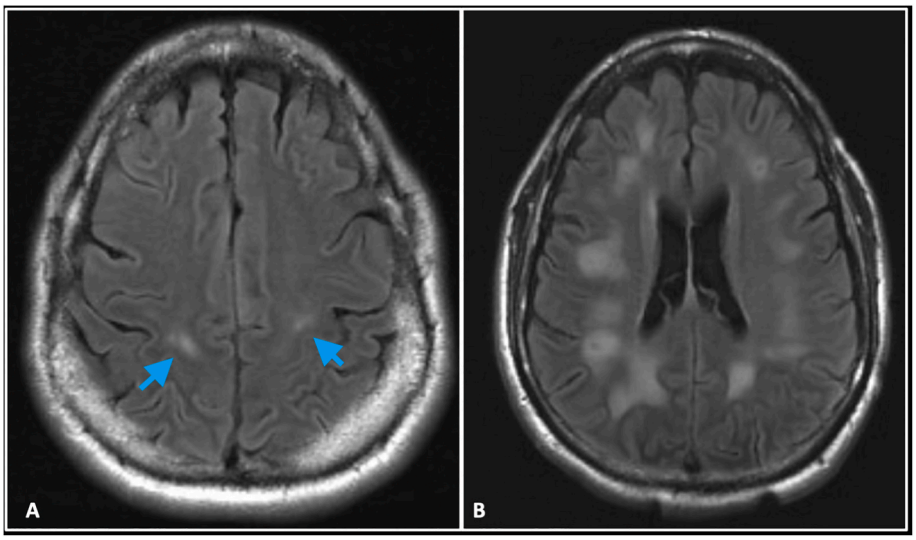

Fig. 2. A. Hyperintensities in the subcortical white matter (blue arrows) are noted on T2 fluid-attenuated inversion recovery magnetic resonance images of the brain. 2B. MRI brain demonstrates significant progression of disease consistent with a hemorrhagic leukoencephalopathy. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

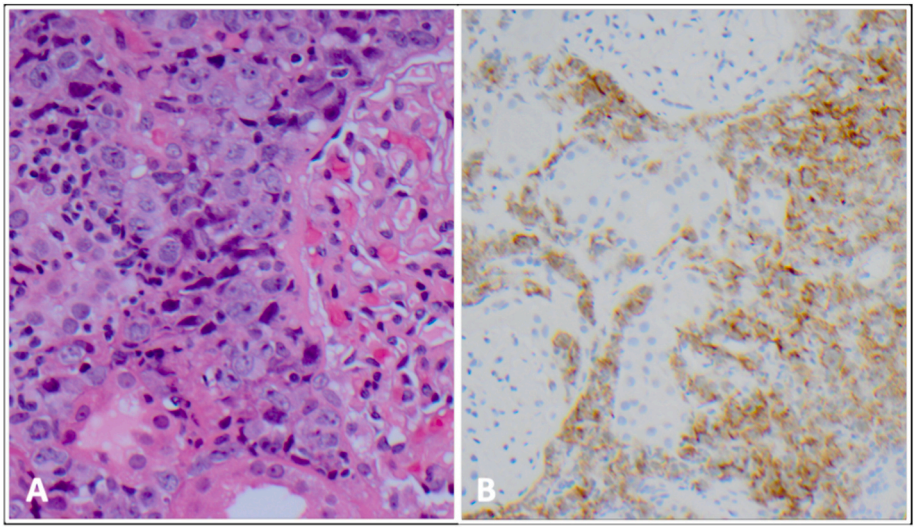

Fig. 3. Kidney biopsy. (A) H&E stain, 40× magnification, show a dense infiltrate of cytologically malignant cells in aggregates and sheets. Most of the neoplastic cells are large with irregular, occasionally lobulated nuclei, vesicular chromatin, prominent nucleoli, and scant to moderate amounts of cytoplasm, highly suggestive of large cell lymphoma. (B) CD20 stain, 20X magnification, shows large neoplastic cells positive for CD20.

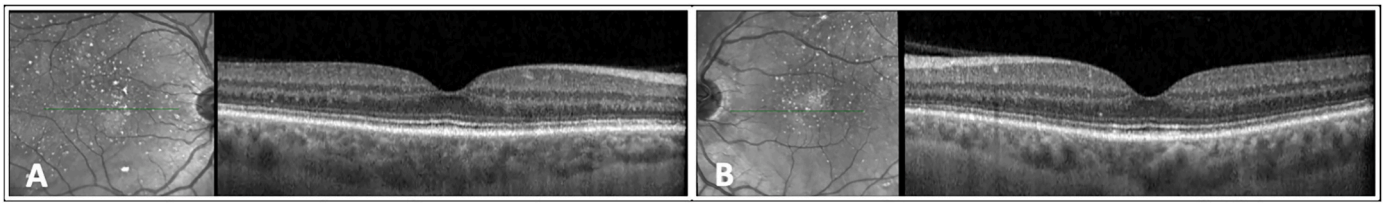

Fig. 4. Optical coherence tomography reveals resolution of submacular fluid and normalization of choroidal thickness in the right and left eyes (A and B, respectively).

vincristine, and prednisone. At last follow-up 20 months after initial presentation, VA was 20/20 OU with resolution of subretinal fluid (Fig. 4). His cancer remains in remission.

3. Discussion

The differential diagnosis for exudative retinal detachments is wide and includes inflammatory diseases such as VKH syndrome, sympathetic ophthalmia, and posterior scleritis; neoplastic diseases such as choroidal metastasis, choroidal melanoma, leukemia, and paraproteinemias; and

other entities such as uveal effusion syndrome and multifocal central serous chorioretinopathy. Several features in this case overlap with features of VKH: auditory disturbances, exudative retinal detachments, choroidal thickening, and the multifocal areas of pinpoint leakage on fluorescein angiography with pooling of the fluorescein dye in the subretinal space. Several features, however, are atypical for VKH and raise the suspicion for an alternative etiology. These include Caucasian ethnicity, absence of vitritis, and absence of optic disc hyperemia.[13] While these features are not incompatible with a diagnosis of VKH, they should prompt careful consideration of other diagnostic possibilities, including leukemia and lymphoma, which can present similarly.[14–19] The initial response to high dose systemic corticosteroid in this case, followed by a refractory and worsening course despite continued high dose systemic corticosteroid and immunosuppression, should alert the clinician that this is likely a masquerade syndrome, and further work-up, including systemic imaging to consider malignancy, should be strongly considered. A unique aspect of this case is the absence of other inflammatory signs reported in other cases, such as vitritis, retinitis, intraretinal or subretinal infiltration, or vitreous hemorrhage, suggesting that systemic lymphoma can present with exudative retinal detachments as the only ocular manifestation.[3–9,11]

A few mechanisms may explain the ocular manifestations observed in this case. First, it is possible that hematogenous spread of lymphoma cells led to infiltration of the choroid with subsequent dysfunction of the retinal pigment epithelium and accumulation of fluid in the subretinal space, leading to exudative retinal detachments. Thickening of the choroid on OCT may support this hypothesis. Second, CNS involvement as well as eye involvement may represent a paraneoplastic response that resolved following treatment of the primary malignancy. Support for this mechanism is the demonstration of inflammatory cells and absence of malignant cells in the brain specimen obtained by biopsy, though it is possible lymphoma cells were missed given the inherent sample limitation of brain biopsies. Third, CNS involvement may be due to primarily intravascular lymphomatous involvement, in which the lymphoma cells proliferate within the lumen of blood vessels. While we cannot state with certainty which of these mechanisms is ultimately responsible for the eye involvement, the neurology and oncology services believe intravascular lymphoma is most likely given the previous transient ischemic attack-like symptoms at presentation as well as the CNS hemorrhages. In this rare subset of patients, the VKH-like inflammatory response appears to mimic robust T-cell mediated inflammation. Future studies may provide insight into the mechanism of disease.

4. Conclusions

Systemic malignancy can affect various ocular structures, and it is an important consideration in the evaluation of patients with unexplained ocular findings. As demonstrated in this case, eye involvement may precede systemic involvement, and a multidisciplinary approach is necessary for prompt diagnosis. Masquerade syndromes should be considered when the constellation of findings is atypical for known inflammatory disorders, and systemic imaging should be considered early in the course of disease when malignancy is suspected.

Patient consent

As the images included in this manuscript are entirely anonymized and do not allow for identification of the patient whose clinical course is described, formal patient consent is not required per Elsevier policy.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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