JAMA Ophthalmology Clinical Challenge

A Man With Kaleidoscope Vision

Anuoluwapo Sopeyin, MD; Carl Wilkins, MD; Meghan Berkenstock, MD

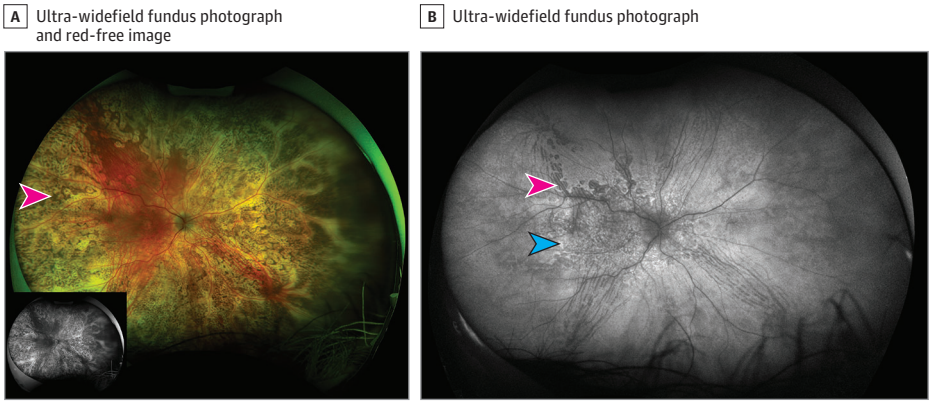

Figure 1. A, Ultra-widefield fundus photograph of the right eye showing pigmentary abnormalities (arrowhead) within and peripheral to the macula. This finding was similar in both eyes. A red-free image is depicted in the bottom left corner of the panel. B, Ultra-widefield fundus autofluorescence image of the right eye showing hypoautofluorescent (pink arrowhead) and hyperautofluorescent patches (blue arrowhead) within and peripheral to the macula. This finding was similar in both eyes.

A 63-year-old man with no ocular history and a history of stage 3 cutaneous melanoma of the scalp and chronic lymphocytic leukemia was referred for kaleidoscope vision. He received nivolumab (anti–programmed cell death 1 checkpoint inhibitor) 9 months prior, obinutuzumab (B-cell lymphoma 2 inhibitor) 3 months later, and 5-mg oral prednisone daily. On presentation, nivolumab and obinutuzumab treatment was complete.

His visual acuity was 20/125 OD and 20/50 OS. Ophthalmoscopy revealed bilateral panuveitis with diffuse pigmentary abnormalities. Fluorescein angiography showed diffuse retinal pigment epithelium loss and late staining of the retinal lesions. He received 60 mg of oral prednisone daily for 2 weeks with a planned 10-week taper. However, prednisone was discontinued due to positive Lyme disease exposure 6 weeks later. At this time, the active anterior and vitreous cells had resolved.

However, 2 weeks later, visual acuity decreased to count fingers in his right eye and hand motions in the left eye. The anterior and vitreous chambers had grade +0.5 pigmented cells. The ophthalmoscopic examination showed a leopard-spot pattern (**Figure 1**), and optical coherence tomography showed substantial retinal pigment epithelium and outer retinal layer loss. Repeat testing for *Treponema pallidum*, Lyme disease, and HIV was negative. Results of magnetic resonance imaging of the brain and orbit were negative for leukemic infiltration.

WHAT WOULD YOU DO NEXT?

A. Immunomodulatory therapy with another course of oral steroids

B. Pars plana vitrectomy for vitreous biopsy with or without chorioretinal biopsy for flow cytometry to assess for leukemic cells

C. Intravitreal steroid injection

D. Observation

CME Quiz at jamacmelookup.com

Diagnosis

Immune checkpoint inhibitor–induced panuveitis of both eyes

What to Do Next

C. Intravitreal steroid injection

Discussion

The patient was referred for simultaneous panuveitis 6 months after receiving immune checkpoint inhibitor therapy. After the initial consultation, he started an oral steroid, which was stopped due to positive Lyme disease exposure. Despite negative Lyme disease serology results, immunomodulatory therapy was deferred due to his oncologic history. As such, option 1 would not be the best course of action. Given the patient's oncologic history, there was a concern for a neoplastic masquerade syndrome. The utility of a pars plana vitreous biopsy with or without a chorioretinal biopsy to sample the subretinal lesions identified on optical coherence tomography (**Figure 2**) was discussed but ultimately deferred due to the likeli-

© 2023 American Medical Association. All rights reserved.

Downloaded from jamanetwork.com by Central South University user on 04/14/2025

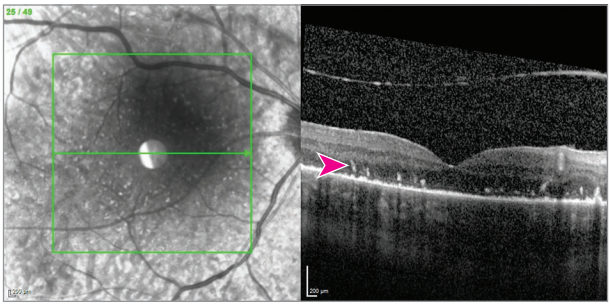

Figure 2. Spectral-domain optical coherence tomography of the right eye showing hyperreflective lesions (arrowhead) in the outer retina.

hood of low yield in the setting of a relatively quiet vitreous segment (option 2). It is difficult to fully exclude the likelihood that the cells were not leukemic metastases in the absence of a vitreous biopsy. However, given a sustained resolution of active anterior and vitreous segment cells after steroid treatment, a complete blood cell count not suggestive of leukocytosis, negative bone marrow biopsy a month after presentation, and a negative magnetic resonance imaging result of the brain and orbits, the likelihood of a neoplastic masquerade syndrome was thought to be low. Instead, the patient received an injection of dexamethasone into the vitreous cavity (option 3).

Immune checkpoint inhibitors have gained popularity in recent years due to their ability to circumvent the protective signals that prevent the immune system from sensing and destroying malignant cells. While they have led to a decrease in the morbidity and mortality rates of individuals with cancers,[1] their use has led to adverse reactions, including ocular sequelae like legal blindness, which presumably should be discussed with recipients of these treatments.

A 2019 study identified all cases of ocular adverse effects that were reported to the US Food and Drug Administration Adverse Events Reporting System database from 2003 to 2018.[2] They identified 131 adverse events ranging from uveitis, dry eye, ocular myasthenia, and eye inflammation. Nivolumab had the highest number of adverse events, accounting for 68 of 131 adverse events associated with immune checkpoint inhibitors.[2] Here, we show that nivolumab can present with bilateral diffuse panuveitis.

The precise mechanisms that mediate these events remain poorly understood. One study suggested that programmed cell death 1 inhibitors such as nivolumab produce pathologic autoantibodies that might be responsible for the high incidence of adverse effects with these drugs.[3] Cytotoxic T-lymphocyte antigen 4 inhibitors are known to have a dose-dependent incidence of adverse effects leaving room for dose titration.[4]

Patient Outcome

The patient's visual acuity continued to decline (hand motions in both eyes). He received an intravitreal dexamethasone implant injection without a significant decline in the disease progression. Systemic immune modulatory therapy was deferred due to the patient's poor response to local treatment.

ARTICLE INFORMATION

Author Affiliations: Wilmer Eye Institute, Johns Hopkins School of Medicine, Baltimore, Maryland.

Corresponding Author: Anuoluwapo Sopeyin, MD, Wilmer Eye Institute, Johns Hopkins School of Medicine, 600 N Wolfe St, Wilmer B29, Baltimore, MD 21287 (sopeyin@jhmi.edu).

Published Online: June 1, 2023. doi:10.1001/jamaophthalmol.2023.2063

Conflict of Interest Disclosures: Dr Wilkins reported personal fees from EyePoint Pharmaceuticals outside the submitted work. No other disclosures were reported.

Additional Contributions: We thank the patient for granting permission to publish this information.

REFERENCES

1. Webb ES, Liu P, Baleeiro R, Lemoine NR, Yuan M, Wang YH. Immune checkpoint inhibitors in cancer therapy. *J Biomed Res*. 2018;32(5):317-326. doi:10.7555/JBR.31.20160168

2. Fang T, Maberley DA, Etminan M. Ocular adverse events with immune checkpoint inhibitors. *J Curr Ophthalmol*. 2019;31(3):319-322. doi:10.1016/j.joco.2019.05.002

3. Inno A, Metro G, Bironzo P, et al. Pathogenesis, clinical manifestations and management of immune checkpoint inhibitors toxicity. *Tumori*. 2017;103(5):405-421. doi:10.5301/tj.5000625

4. Duong SL, Barbiero FJ, Nowak RJ, Baehring JM. Neurotoxicities associated with immune checkpoint inhibitor therapy. *J Neurooncol*. 2021;152(2):265-277. doi:10.1007/s11060-021-03695-w

© 2023 American Medical Association. All rights reserved.

Downloaded from jamanetwork.com by Central South University user on 04/14/2025