

reported in individuals who eat crocodile meat, but crocodiles can be infected by pentastomids.<sup>6</sup> We therefore recognize the possibility that the infection occurred after the consumption of crocodile meat contaminated with pentastomid eggs. This meat could also have been contaminated via infected snake meat on a market stall.

No serological test currently exists, and in most cases, the final diagnosis is still made on the basis of morphological criteria or histopathology.<sup>2,3,5</sup> PCR tests targeting the parasite's 18S rRNA gene and mitochondrial cytochrome oxidase subunit genes are reliable diagnostic methods with restricted availability to high-resource laboratories, rendering these methods often difficult to access in rural endemic regions.<sup>4</sup>

Ocular pentastomiasis is a rare infection. Ophthalmologists should consider the diagnosis in patients coming from endemic countries. Our case suggests that crocodile meat could be a source of infection. Higher awareness for this rare but sometimes heavily symptomatic disease seems warranted.

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1. Drabick JJ. Pentastomiasis. *Rev Infect Dis*. 1987;9(6):1087-1094. doi:10.1093/clinids/9.6.1087

2. Vanhecke C, Le-Gall P, Le Breton M, Malvy D. Human pentastomiasis in Sub-Saharan Africa. *Med Mal Infect*. 2016;46(6):269-275. doi:10.1016/j.medmal.2016.02.006

3. Sulyok M, Rózsa L, Bodó I, Tappe D, Hardi R. Ocular pentastomiasis in the Democratic Republic of the Congo. *PLoS Negl Trop Dis*. 2014;8(7):e3041. doi:10.1371/journal.pntd.0003041

4. Tappe D, Sulyok M, Riu T, et al. Coinfections in visceral pentastomiasis, Democratic Republic of the Congo. *Emerg Infect Dis*. 2016;22(8):1333-1339. doi:10.3201/eid2208.151895

5. Tappe D, Büttner DW. Diagnosis of human visceral pentastomiasis. *PLoS Negl Trop Dis*. 2009;3(2):e320. doi:10.1371/journal.pntd.0000320

6. Ladds PW, Sims LD. Diseases of young captive crocodiles in Papua New Guinea. *Aust Vet J*. 1990;67(9):323-330. doi:10.1111/j.1751-0813.1990.tb07815.x

## Association of Occlusive Retinal Vasculitis With Intravitreal Faricimab

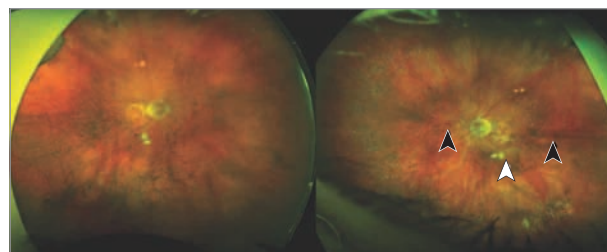
**Report of a Case** | A 96-year-old woman with neovascular age-related macular degeneration (nAMD) presented with a 2-week history of bilateral eye pain and reduced vision 18 days fol-

lowing bilateral intravitreal faricimab injections. Before initiating faricimab, she had received 15 ranibizumab injections and then 38 aflibercept injections in the right eye, and 21 aflibercept injections in the left eye over 8 years. At her last bilateral faricimab injections, visual acuity (VA) was 20/120 OD and 1/36 OS. She had no history of intraocular inflammation (IOI), systemic autoimmune disease, or medications associated with retinal vasculitis. Presenting VA was 20/160 OD and counting fingers OS, with intraocular pressure of 31 mmHg OU, keratic precipitates, and bilateral anterior and posterior vitreous cells. Attenuation of retinal arterioles and veins was associated with 2 blot hemorrhages and pallor of the inferotemporal retina without emboli in the left eye (Figure 1A).

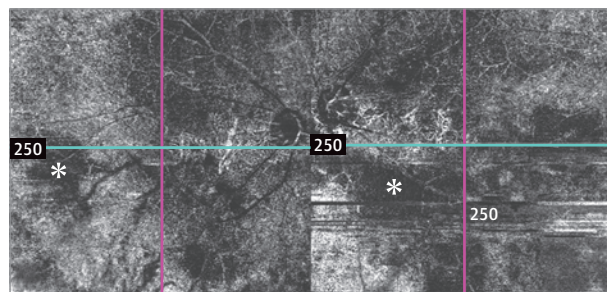
Optical coherence tomography angiography had choriocapillaris flow voids, more marked in the left eye (Figure 1B). Ultra-widefield fundus fluorescein angiogram (UWF-FFA) demonstrated peripheral retinal venous, arteriolar, and capillary nonperfusion and hyperfluorescent leakage of retinal veins, arteries, and optic discs, with veins more involved than arteries and the left eye more affected than the right (Figure 2). Results for chest radiography, syphilis serology, QuantiFERON gold, rheumatoid factor, angiotensin-converting enzyme, antinuclear antibody, and antineutrophilic cytoplasmic antibody were unremarkable. With only mild inflammation, nei-

**Figure 1. Ultra-Widefield Color Fundus Photography and Optical Coherence Tomography Angiography of Faricimab-Associated Occlusive Retinal Vasculitis**

**A** Left inferotemporal retinal pallor and blot hemorrhages

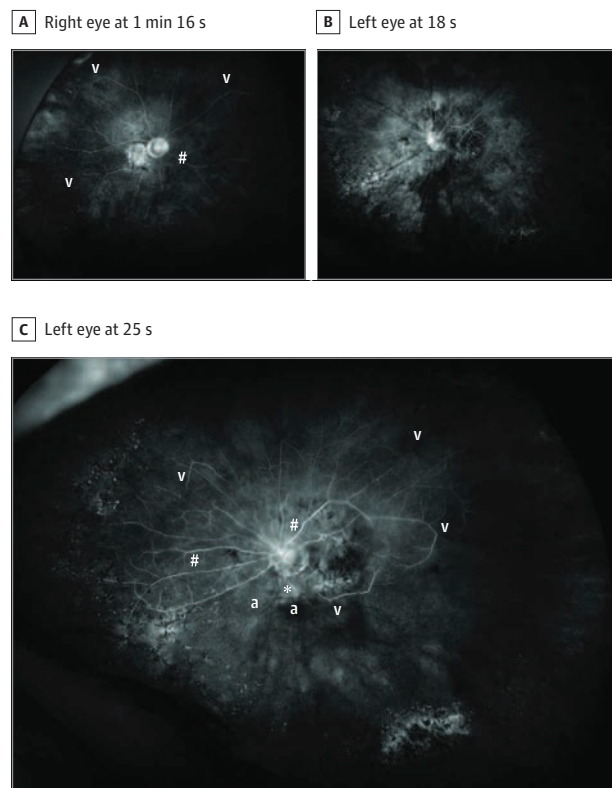


**B** Patchy choriocapillaris flow voids



A, Eighteen days following bilateral intravitreal faricimab, the patient presented with bilateral panuveitis, attenuation of retinal arteries and veins, and left inferotemporal retinal pallor (white arrowhead) and blot hemorrhages (black arrowheads) (Optos California). There was geographic atrophy at both maculae associated with age-related macular degeneration. B, Optical coherence tomography (OCT) angiography (12 × 12-mm scans of the outer retina to choriocapillaris layer; Cirrus high-definition OCT, 500/5000; Carl Zeiss Meditec) demonstrates patchy choriocapillaris flow voids (white asterisks), more pronounced in the left eye.

**Figure 2. Ultra-Widefield Fundus Fluorescein Angiography of Faricimab-Associated Occlusive Retinal Vasculitis**



Ultra-widefield fundus fluorescein angiography (Optos California) of the right eye at 1 minute 16 seconds (A), left eye at 18 seconds (B), and left eye at 25 seconds (C). There was retinal arteriolar (a) occlusion in the left eye inferior to the optic disc and more extensive bilateral retinal venous occlusion (v). This was associated with widespread peripheral capillary nonperfusion, worse in the left than right eye, and hyperfluorescent leakage of the retinal veins (#), arteries (asterisk), and both optic discs.

ther anterior nor vitreous taps for bacterial, fungal, or viral polymerase chain reaction analyses were performed.

This bilateral occlusive vasculitis associated with bilateral intravitreal faricimab injections was treated with a 7-week tapering course of oral corticosteroids, initially 75 mg, and topical dexamethasone 4 times daily and brinzolamide twice daily. After 7 weeks, VA remained 20/160 OD and counting fingers OS with no signs of IOI or exudation. A suspected adverse event was reported to Roche.

**Discussion** | Faricimab, a bispecific immunoglobulin G-derived monoclonal angiopoietin 2 and vascular endothelial growth factor A antibody, approved and commercially available in the US since 2022 for nAMD and diabetic macular edema (DME) and since 2023 for retinal vascular occlusion (RVO), has IOI as an uncommon complication.<sup>1</sup>

Reported rates of IOI (excluding endophthalmitis) were 13 of 664 cases in nAMD (2.0%), 17 of 1262 in DME (1.3%), and 9 of 641 in RVO (1.4%),<sup>1</sup> numerically higher than the aflibercept groups. Reported rates of IOI among other intravitreal agents include brolocizumab 4.6%,<sup>2</sup> pegcetacoplan 2.1%-3.8%,<sup>3</sup>

aflibercept 0% to 0.16%,<sup>4</sup> bevacizumab 0.081% to 0.10%,<sup>4</sup> and ranibizumab 0.005% to 0.02%.<sup>4</sup> In February 2024, investigators published 3 cases of acute severe IOI within 1 month at a single institution following injection of faricimab (2 different lot numbers at 3 locations).<sup>5</sup>

Retinal vasculitis is a sight-threatening variant of IOI, hypothesized to occur through a type III/IV delayed hypersensitivity reaction. Although there were no cases of reported retinal vasculitis in the faricimab phase 3 clinical trials, in November 2023, Genentech issued a letter<sup>6</sup> on post-marketing safety of faricimab. As of August 2023, they estimated an incidence of 0.17 per 10 000 injections for vasculitis with or without occlusion and 0.06 per 10 000 injections for occlusive vasculitis, equivalent to 26 and 9 patients, respectively, of 1.5 million vials distributed worldwide.<sup>6</sup> Despite these reports, to our knowledge, no cases of occlusive retinal vasculitis associated with faricimab have been published in a peer-reviewed journal. In the present case, faricimab was thought to be the most likely cause for the occlusive retinal vasculitis in these cases, given the time course of onset, the bilateral panuveitic presentation, and absence of other causes, such as prior uveitis or accountable medications.

Retinal vasculitis, with or without occlusion, has also been described following intravitreal brolocizumab or pegcetacoplan injections. The clinical presentation, progress, and outcomes of retinal vasculitis among various intravitreal therapies may differ as the pathogenesis may differ. Most brolocizumab-related vasculitis occurred within the first 6 months of initiation.<sup>2</sup> Occlusive retinal vasculitis following intravitreal brolocizumab was associated with substantial permanent visual loss in 5 of 23 eyes.<sup>2</sup> Although no cases were reported in the OAKS/DERBY trials for pegcetacoplan, at least 13 postmarketing cases of retinal vasculitis were reported, all after the first injection.<sup>3</sup>

Occlusive retinal vasculitis should be recognized as a possible adverse event associated with intravitreal faricimab and support prompt evaluation of patients who experience persistent discomfort or blurred vision following intravitreal injection to exclude IOI or infection. UWF-FFA may be helpful in evaluating such cases prior to the initiation of corticosteroids, which may assist in visual recovery. Large databases would be needed to determine the precise frequency of these relatively rare inflammatory events. The bilateral involvement in this case emphasizes that risks of bilateral concurrent administration of intravitreal injections need to be balanced against potential advantages of greater convenience and treatment compliance.

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- Genetech. VABYSMO (faricimab-svoa) safety information. Accessed March 15, 2024. <https://www.vabysmo-hcp.com/safety.html>
- Monés J, Srivastava SK, Jaffe GJ, et al. Risk of inflammation, retinal vasculitis, and retinal occlusion-related events with brodalumab: post hoc review of HAWK and HARRIER. *Ophthalmology*. 2021;128(7):1050-1059. doi:[10.1016/j.ophtha.2020.11.011](https://doi.org/10.1016/j.ophtha.2020.11.011)
- Witkin AJ, Jaffe GJ, Srivastava SK, Davis JL, Kim JE. Retinal vasculitis after intravitreal pegcetacoplan: report from the ASRS Research and Safety in Therapeutics (REST) Committee. *J Vitreoretin Dis*. 2023;8(1):9-20. doi:[10.1177/24741264231220224](https://doi.org/10.1177/24741264231220224)
- Daïen V, Nguyen V, Essex RW, Morlet N, Barthelmes D, Gillies MC. Fight Retinal Blindness! Study Group. Incidence and outcomes of infectious and noninfectious endophthalmitis after intravitreal injections for age-related macular degeneration. *Ophthalmology*. 2018;125(1):66-74. doi:[10.1016/j.ophtha.2017.07.005](https://doi.org/10.1016/j.ophtha.2017.07.005)
- Thangamathesvaran L, Kong J, Bressler SB, et al. Severe intraocular inflammation following intravitreal faricimab. *JAMA Ophthalmol*. Published online February 29, 2024; doi:[10.1001/jamaophthalmol.2024.0530](https://doi.org/10.1001/jamaophthalmol.2024.0530)
- Genentech. VABYSMO (faricimab-svoa): new warnings and precautions: retinal vasculitis and/or retinal vascular occlusion. Accessed January 14, 2024. [https://www.gene.com/download/pdf/Vabysmo\\_DHCP\\_Important\\_Drug\\_Warning\\_2023-11-03.pdf](https://www.gene.com/download/pdf/Vabysmo_DHCP_Important_Drug_Warning_2023-11-03.pdf)

## COMMENT & RESPONSE

### Limitations of Assessing Barriers in Diabetic Retinopathy Screening

**To the Editor** It was with great interest that we read the article by Ravindranath et al,<sup>1</sup> which found that factors, such as food and housing insecurity, mental health, and practitioner concordance, hinder diabetic retinopathy screening. However, several limitations not necessarily completely addressed by the authors should be considered when interpreting the study's conclusions.

First, this study included participants from May 1, 2018, to July 1, 2022. During this period, the association of COVID-19 disease with patients visiting eye care practitioners should be considered in more detail. A previous study<sup>2</sup> showed that fear of SARS-CoV-2 exposure was associated with patients missing ophthalmic care appointments, suggesting this confounding factor should be considered. Could the authors<sup>1</sup> pursue sensitivity analyses wherein participants enrolled after the COVID-19 outbreak to consider the potential effect of the pandemic on the results?

Second, the authors defined patients with type 2 diabetes (T2D) as those who use diabetes drugs or with codes for T2D complications. We wonder why the authors<sup>1</sup> did not use *International Classification of Diseases Ninth Revision* or *Tenth Revision* T2D diagnosis codes to include patients instead of the SNOMED codes listed in eTable 1, which seem to be incomplete with many codes missing?

Third, self-report surveys may involve recall or nonresponse bias due to unwillingness or inability to participate. Could the authors<sup>1</sup> opine on the degree to which the All of Us Research Program's self-registration<sup>3</sup> attracted individuals with a positive health attitude may have influenced the outcomes? Specifically, participants who completed surveys may not have had severe diabetic retinopathy, contributing to selection bias.<sup>4</sup>

Furthermore, the study<sup>1</sup> highlights a significant link between practitioner concordance and delayed eye care, influenced by factors including race, ethnicity, religion, and language. Further analysis will identify the key factors on concordance to overcome the overall health care barriers. We look forward to the authors' reply.

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- Ravindranath R, Bernstein IA, Fernandez KS, Ludwig CA, Wang SY. Social determinants of health and perceived barriers to care in diabetic retinopathy screening. *JAMA Ophthalmol*. 2023;141(12):1161-1171. doi:[10.1001/jamaophthalmol.2023.5287](https://doi.org/10.1001/jamaophthalmol.2023.5287)
- Lindeke-Myers A, Zhao PYC, Meyer BI, et al. Patient perceptions of SARS-CoV-2 exposure risk and association with continuity of ophthalmic care. *JAMA Ophthalmol*. 2021;139(5):508-515. doi:[10.1001/jamaophthalmol.2021.0114](https://doi.org/10.1001/jamaophthalmol.2021.0114)
- Denny JC, Rutter JL, Goldstein DB, et al. All of Us Research Program Investigators. The "All of Us" research program. *N Engl J Med*. 2019;381(7):668-676. doi:[10.1056/NEJMs1809937](https://doi.org/10.1056/NEJMs1809937)
- Bradley ER, Delaffon V. Diabetic retinopathy screening in persons with mental illness: a literature review. *BMJ Open Ophthalmol*. 2020;5(1):e000437. doi:[10.1136/bmjophth-2020-000437](https://doi.org/10.1136/bmjophth-2020-000437)

**In Reply** We appreciate Yang and colleagues' interest in our study<sup>1</sup> on the impact of social determinants of health on eye care in patients with type 2 diabetes in the All of US national cohort. We agree with the many thoughtful points raised and we are pleased to offer some additional analyses and clarifications.

Yang et al raise excellent points about the globally disruptive nature of the SARS-CoV-2 pandemic. In the US, the initial responses to the pandemic varied by location with some areas issuing stay-at-home orders encouraging the population to stay at home except for essential activities, while other areas did not enact such policies.<sup>2</sup> Analyses have shown that the pandemic was associated with profound decreases in eye care utilization.<sup>3</sup> The impact of the COVID-19 pandemic on receipt of eye care services is likely to be complex, varying over different phases of the pandemic, by geographical location, and by patient subpopulations. We agree that these effects deserve dedicated comprehensive analyses, which we hope to pursue in the future. For this particular analysis of eye care