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Viral Meningoencephalitis and Bilateral Blurry Vision

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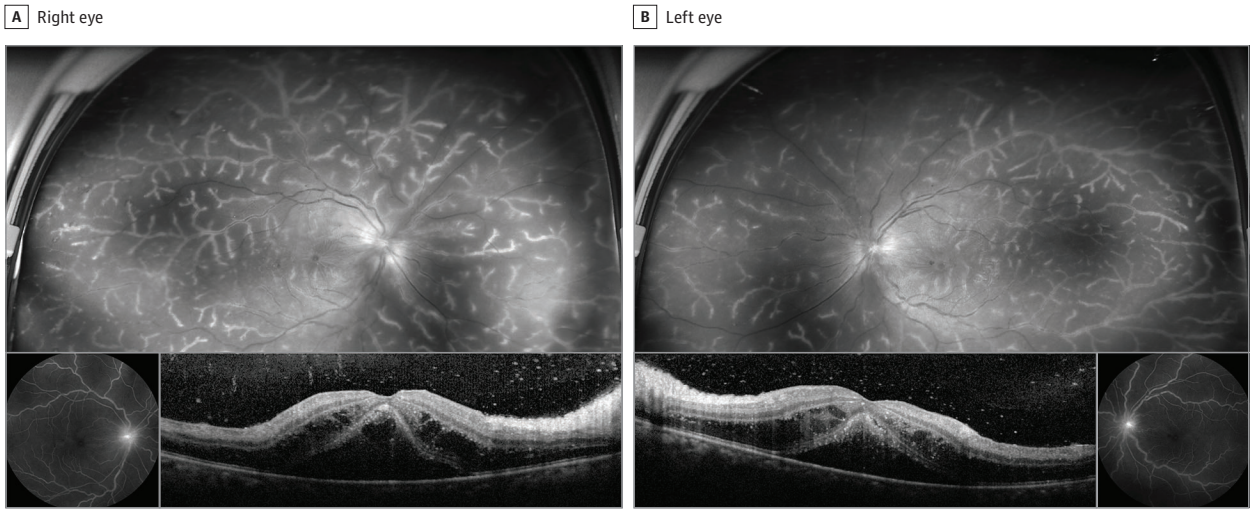

Figure 1. Red-free scanning laser ophthalmoscopy images revealing extensive retinal vascular sheathing (inset: macular edema seen on optical coherence tomography; fluorescein angiogram revealed late dye leakage).

A previously healthy 20-year-old Asian woman was hospitalized in the neurology department after experiencing fever, malaise, headache, nausea, vomiting, and neck stiffness for 2 weeks. Computed tomography scan results revealed meningoencephalitis. Her systemic inflammatory markers were elevated, including a left-shifted leukocytosis with a white blood cell count of 19 610 μL (normal values, 3500-9500 μL), a monocyte count of 900 × 10^3 μL (normal values, 100-600 × 10^3 μL), and normal C-reactive protein level. Cerebrospinal fluid studies were suggestive of viral meningoencephalitis, including elevated protein levels (0.074 g/dL; normal values, 0.015-0.045 g/dL) and increased leucocyte (93 × 10^6/L; normal values, 0-8 × 10^6/L). Cytological examination showed an increase in lymphocytes. Intracranial pressure was elevated (>320 mm H_2O), and the glucose level was 2.08 mmol/L (normal values, 2.5-4.5 mmol/L).

On day 2 of hospitalization, the patient experienced blurred vision in both eyes. Her visual acuity was 20/500 in both eyes. Both eyes had normal pupillary responses, color vision, and intraocular pressures. The results of an anterior chamber examination were unremarkable. The results of scanning laser ophthalmoscopy of both eyes revealed substantial inflammation, including marked disc edema, retinal vein dilation and tortuosity, extensive retinal vascular sheathing (**Figure 1**). Optical coherence tomography showed vitritis and cystoid macular edema in both eyes. Fluorescein angiogram revealed tortuous dilatation of retinal venous vessels with fluorescence leakage, while the optic disc exhibited hyperfluorescence.

WHAT WOULD YOU DO NEXT?

- **A.** Administer systemic corticosteroids
- **B.** Evaluate for systemic infectious disease
- **C.** Initiate immunomodulatory therapy with intravenous immunoglobulin
- **D.** Intravitreal injection with anti–vascular endothelial growth factor

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Diagnosis

Frosted branch angiitis

What to Do Next

B. Evaluate for systemic infectious disease

Discussion

Administering systemic corticosteroids (choice A) would not be the preferred answer because corticosteroids could suppress the immune response, potentially worsening an undiagnosed infectious process. Initiating immunomodulatory therapy with intravenous immunoglobulin (choice C) was not recommended as the next step because intravenous immunoglobulin is typically used for autoimmune or inflammatory conditions rather than primary infectious diseases. Performing an intravitreal injection with anti–vascular endothelial growth factor (choice D) would not be the next recommended step because there was not proof that the cystoid macular edema was vascular endothelial growth factor driven vs inflammation driven.

This patient was diagnosed with bilateral frosted branch angiitis (FBA). FBA may be idiopathic or associated with infections, inflammation, or tumors.[1] Prior to initiating intraocular or systemic corticosteroid treatment, it is important to exclude infectious diseases. Bacterial cultures of the patient's cerebrospinal fluid were negative. However, next-generation sequencing of the cerebrospinal fluid indicated Epstein-Barr virus infection. Therefore, the patient was diagnosed with FBA combined with viral meningoencephalitis and treated with ganciclovir and corticosteroids.

The term *frosted branch angiitis* was first reported by Ito et al[2] in 1976 and named after its distinctive retinal appearance. FBA is a rare retinal vasculitis characterized by lymphoplasmacytic infiltration of the perivascular space.[1,2] The co-occurrence of viral meningoencephalitis and FBA is uncommon. FBA predominantly affects young, healthy individuals, with a higher prevalence in female individuals (61%) compared with male individuals (39%). The age at onset has a bimodal distribution, peaking in childhood and between ages 25 and 30 years. Favorable prognoses have been observed in patients undergoing systemic corticosteroid therapy.[3] Common conditions associated with FBA include cytomegalovirus retinitis, HIV retinitis, and toxoplasma chorioretinitis.[4,5] However, several systemic diseases may be associated with FBA, including graft vs host disease, systemic lupus erythematosus, Crohn disease, large cell lymphoma, and acute lymphoblastic leukemia.[6-8] The prognosis of FBA is variable,[9] and may be complicated by macular scarring, retinal neovascularization, or epiretinal membranes. Clinicians, including infectious disease specialists and ophthalmologists, should be aware of the vision-threatening potential of FBA and try to provide timely diagnosis and treatment, potentially reducing the risk of poor ocular outcomes.

Patients with FBA may experience a sudden decrease in visual acuity. Severe cases may result in light perception, although some patients maintain 20/20 visual acuity in both eyes.[1] Fluorescein angiogram may be important to diagnosis FBA, as it can reveal extensive perivascular fluorescein leakage. High-dose corticosteroids have been associated with resolution of retinal abnormalities and improvement of visual acuity in idiopathic FBA. Cases associated with systemic disease typically will need treatment of the primary disease along with corticosteroids for the retina. Some patients may experience relapse if the primary disease recurs.[4] The extensive vasculitis and sensitivity to short-term corticosteroid treatment suggest that FBA might be a specific vascular reaction triggered by various stimuli, potentially mediated by immune complexes.[10]

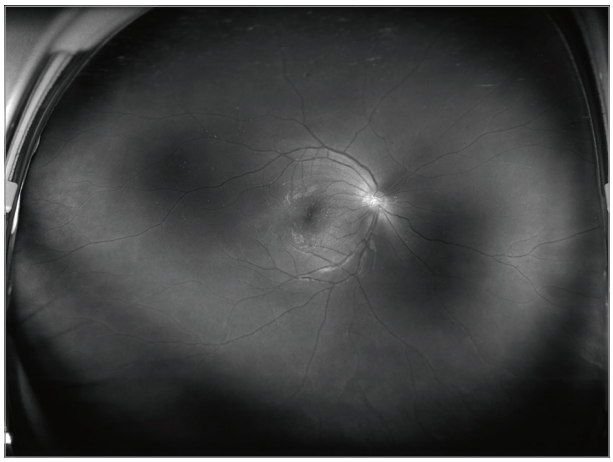

Figure 2. Four weeks later, frosted branch angiitis disappeared.

Patient Outcome

The patient received high-dose systemic corticosteroid therapy and ganciclovir. Four weeks later, the FBA and macular edema had disappeared (**Figure 2**). Seven weeks later, the patient's visual acuity improved to 20/40 in both eyes. Continued vision loss is likely due to delayed functional recovery compared with structural recovery.

ARTICLE INFORMATION

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