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Frosted Branch Angiitis Secondary to Granulomatosis with Polyangiitis

Dear Editor,

Granulomatosis with polyangiitis (GPA, formerly known as Wegener's granulomatosis) is a systemic inflammatory disease in which the histopathologic features often include necrosis, granuloma formation, and vasculitis of small-to-medium-sized vessels [1]. Ophthalmologic manifestations occur in up to 58% of patients with GPA [1]. Previous reports revealed that the most common ophthalmic involvement was orbital disease, followed by scleritis, episcleritis, and corneal and nasolacrimal abnormalities [1,2]. On the other hand, GPA with retinal and choroidal involvement is known to be rare [1,2].

Frosted branch angiitis (FBA), also considered a relatively rare condition, is a retinal perivasculitis with severe retinal vessel sheathing resembling the frosted branches of a tree [3,4]. Kleiner [5] proposed that the entity can be divided into primary idiopathic and secondary FBA. The known causes of secondary FBA are viral infections, sarcoidosis, multiple sclerosis, toxoplasmosis, syphilis, Behcet's disease, lymphoma, and leukemia [4,5]. In this report, we present a rare case of FBA secondary to GPA.

A 70-year-old female with acute kidney injury of unknown cause presented with sudden visual loss in her left eye. She had emergent hemodialysis and underwent a kidney biopsy to determine the cause of the acute kidney injury. Antineutrophil cytoplasmic antibodies were detected on serologic testing, and the renal biopsy revealed granulomatous inflammation with giant cells (Fig. 1A) and fibrinoid necrosis (Fig. 1B), consistent with GPA. Her best-corrected visual acuity was 20 / 30 in the right eye and finger count 30 cm in the left eye. Her intraocular pressures were 8 mmHg in the right eye and 12 mmHg in the left eye. Slit lamp examination showed mild anterior chamber inflammation in the left eye. However, there was no vitreous haziness in either eye. Interestingly, the degree of retinal and

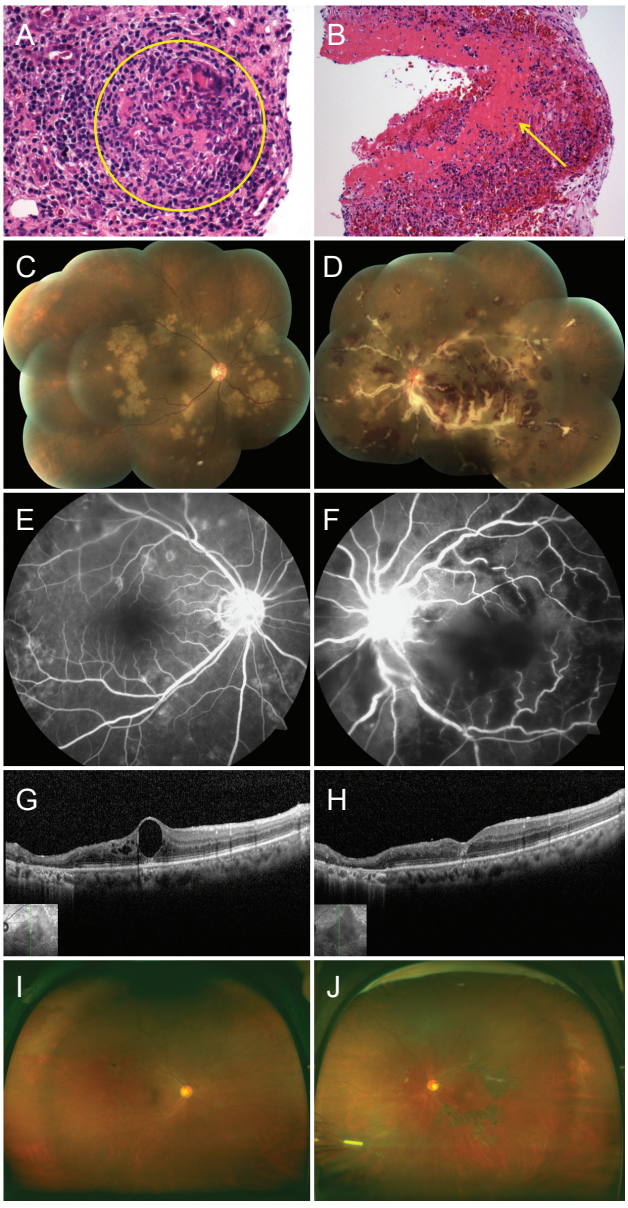

Fig. 1. Images of the patient (A-G) before treatment and (H-J) after treatment. (A,B) Hematoxylin and eosin staining revealed granulomatous inflammation with giant cells (×100, circle) and fibrinoid necrosis (×40, arrow) in the renal biopsy, consistent with granulomatosis with polyangiitis. (C,D) Fundus photographs showed multiple, patched, whitish lesions with retinal hemorrhage in the right eye and extensive perivascular sheathing with retinal hemorrhage in the left eye. (E,F) Fluorescein angiography revealed perivascular leakage with capillary non-perfusion. (G) Spectral-domain optical coherence tomography demonstrated macular edema in the left eye. (H) After two times of intravitreal dexamethasone implants, the macular edema improved and did not recur. (I,J) Retinal vasculitis, retinal hemorrhage, and exudation also decreased in both eyes.

choroidal involvements in both eyes was different. Fundus examination revealed multiple patched whitish lesions with few retinal hemorrhages in the right eye (Fig. 1C). Unlike the right eye, extensive perivascular sheathing with multiple retinal hemorrhages in the left eye was found (Fig. 1D). Fluorescein angiography revealed perivascular leakage with capillary non-perfusion (Fig. 1E, 1F). Optical coherence tomography demonstrated no macular edema in the right eye, but intraretinal fluid in the left eye (Fig. 1G). To exclude other causes of FBA, several tests were performed, including additional serologic testing and anterior chamber paracentesis with polymerase chain reaction for infectious causes, all of which were negative. The patient was diagnosed with secondary FBA associated with GPA and received a 3-day, high-dose, intravenous steroid (1 g/day; Methysol, Alvogen Korea, Seoul, Korea) followed by initiation of systemic cyclophosphamide (100 mg/day; Endoxan, Baxter Healthcare, Deerfield, IL, USA). After extensive treatment, her systemic and ophthalmic symptoms dramatically improved. Her kidney and other organ status improved, and the retinal vasculitis, hemorrhage and exudation resolved. However, the macular edema repeatedly recurred, and the patient twice received an intravitreal dexamethasone implant (Ozurdex; Allergan, Irvine, CA, USA). Six months later, her ophthalmic findings were improved; the macular edema was stable (Fig. 1H), and the retinal vasculitis, retinal hemorrhage, and exudation decreased in both eyes (Fig. 1I, 1J). The patient's best-corrected visual acuity improved to 20 / 25 in the right eye and 20 / 50 in the left eye.

In this case, we report a patient with acute-onset, painless, decreased vision, mild anterior chamber inflammation, extensive perivascular sheathing with retinal hemorrhage and recurrent macular edema. After excluding the known causes of FBA, we diagnosed FBA secondary to GPA.

Because FBA associated with GPA is extremely rare, there is no established treatment [3]. However, the mainstay of treatment for posterior segment involvement with GPA is systemic steroid and immunosuppressant therapy [3,4]. The patient in our case also showed a dramatic response to an intravitreal steroid implant in addition to a systemic steroid and immunosuppressants. Although the cause of FBA in the present case is unknown, the positive response to steroid treatment supports an immune-mediated mechanism.

To our knowledge, this is the first documented case of FBA associated with GPA treated with systemic steroids and an intravitreal dexamethasone implant. In conclusion, clinicians should recognize that GPA can cause vision-threatening retinal vasculitis, and extensive treatment with corticosteroids and immunosuppressants may help reduce the inflammatory response and improve visual acuity.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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