INTRAVITREAL AFLIBERCEPT IN THE TREATMENT OF POLYPOIDAL CHOROIDAL VASCULOPATHY ASSOCIATED WITH MORNING GLORY SYNDROME

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Purpose: To describe an unusual case of polypoidal choroidal vasculopathy secondary to morning glory syndrome successfully treated with three aflibercept intravitreal injections.

Methods: Case report.

Results: A 68-year-old white man presented with a 2-month history of diminished vision of his left eye. Fundus examination showed a morning glory syndrome disk anomaly with some perimacular subretinal hemorrhages and lipid depositions. Fundus autofluorescence, fluorescein and green indocyanine angiography, spectral domain optical coherence tomography, and optical coherence tomography angiography were performed and confirmed the presence of a juxtapapillary polypoidal choroidal vasculopathy with intraretinal and subretinal fluid. Patient underwent 3 monthly intravitreal injections of aflibercept and at 4-month follow-up visit, multimodal imaging findings did not show any kind of neovascular lesion activity.

Conclusion: Polypoidal choroidal vasculopathy can occur in morning glory syndrome and it can be successfully treated with anti–vascular endothelial growth factor intravitreal injections of aflibercept.

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Morning glory syndrome (MGS) is a rare and often unilateral congenital anomaly of the optic disk named by Kindler[1] in 1970 for its similarity to the tropical flower.

It is characterized by the presence of an increase of optical disk size with poorly defined wedges, with a central funnel-shaped excavation filled with glial tissue. The number of retinal blood vessels is increased and they arise from the periphery of the disk with a straight course. An abnormal communication between subretinal and subarachnoid space has been reported by Cennamo et al,[2] and the association with the development of retinal detachment has been clearly identified with this syndrome.[3]

Morning glory syndrome can be even associated with cataract, strabismus, nystagmus, optic nerve drusen, and choroidal neovascularization (CNV) represents a rare cause of visual loss. In this article, we aimed to present the clinical and therapeutic outcomes of the first case of unilateral polypoidal choroidal vasculopathy (PCV) secondary to MGS treated with aflibercept intravitreal injections.

None of the authors has any financial/conflicting interests to disclose.

Written informed consent has been provided by the patient to have the case details and any accompanying images published.

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Case Report

A 68-year-old white man was referred to our retina service at Cagliari Eye Clinic, complaining of worsening vision in the left eye

over the past 2 months and reporting a history of functional amblyopia in the same eye. Best-corrected visual acuity was 20/25 in the right eye and 20/320 in the left eye.

Anterior segment slit-lamp examination was unremarkable in both eyes with no signs of anterior chamber and vitreous inflammation. Fundus examination under mydriasis was normal in the right eye, and the left eye revealed an enlarged, pallid optic disk with fibroglial tissue in its center and radial retinal vessels arising from the periphery suggestive of MGS, with a juxtapapillary yellowish-gray area surrounded by small subretinal hemorrhages and perimacular lipid depositions (Figure 1A). Fundus autofluorescence (FAF) performed with the Heidelberg Spectralis HRA +OCT device (Heidelberg Engineering, Heidelberg, Germany) showed a peripapillary hypoautofluorescent halo with an adjacent area of hyperautofluorescence and a slight hypoautofluorescence in macular area due to the pigment epithelium damage (Figure 1B).

Both fluorescein angiography and indocyanine green angiography disclosed the existence of peripapillary choroidal neovascular network with some aneurysmatic dilatations suggestive for a PCV (Figure 1, C and D). Horizontal oriented spectral domain optical coherence tomography scan (Spectralis OCT; Heidelberg Engineering) confirmed the presence of a PCV with the characteristic steep pigment epithelial detachment, intraretinal hyporeflective cysts, and subretinal fluid (Figure 1E). Optical coherence tomography angiography acquired using Angiovue System (RTVue-100; Optovue Inc, Fremont, CA) was able to detect blood flowing through the neovascular complex beneath the pigment epithelial detachment by a 6 × 6 angio disk scan in choroidal plexus (Figure 1F). Neither facial abnormalities nor any other neurologic disorder were found; therefore, cranial magnetic resonance imaging was not requested.

We discussed, with the patient, all the available treatment strategies and by mutual agreement, we opted for an "off-label" aflibercept use. Once a written consent was obtained, 3 monthly doses of intravitreal aflibercept injections (2 mg/0.05 mL) at 4-week intervals were administered. There was no complication related to the injections and after 4 months, best-corrected visual acuity in left eye increased to 20/125 (+20 Early Treatment Diabetic Retinopathy Study letters). Fundus examination showed a resolution of the peripapillary subretinal hemorrhages and an important decrease of lipid depositions, whereas FAF showed an increased hyperautofluorescence in correspondence of the neovascular lesion (Figure 2A). Fluorescein angiography demonstrated the leakage reduction and indocyanine green angiography allowed us to confirm the shrinking of the neovascular network (Figure 2, B and C).

The spectral domain optical coherence tomography revealed a complete resolution of subretinal fluid and disappearance of intraretinal cysts (Figure 2D) and OCTA picked up the variation in the neovascular flow pattern showing a decreasing of capillaries and persisting of the larger trunks (Figure 2E). Currently, at the 10-month follow-up visit, the clinical picture remains stable with no signs of recurrence.

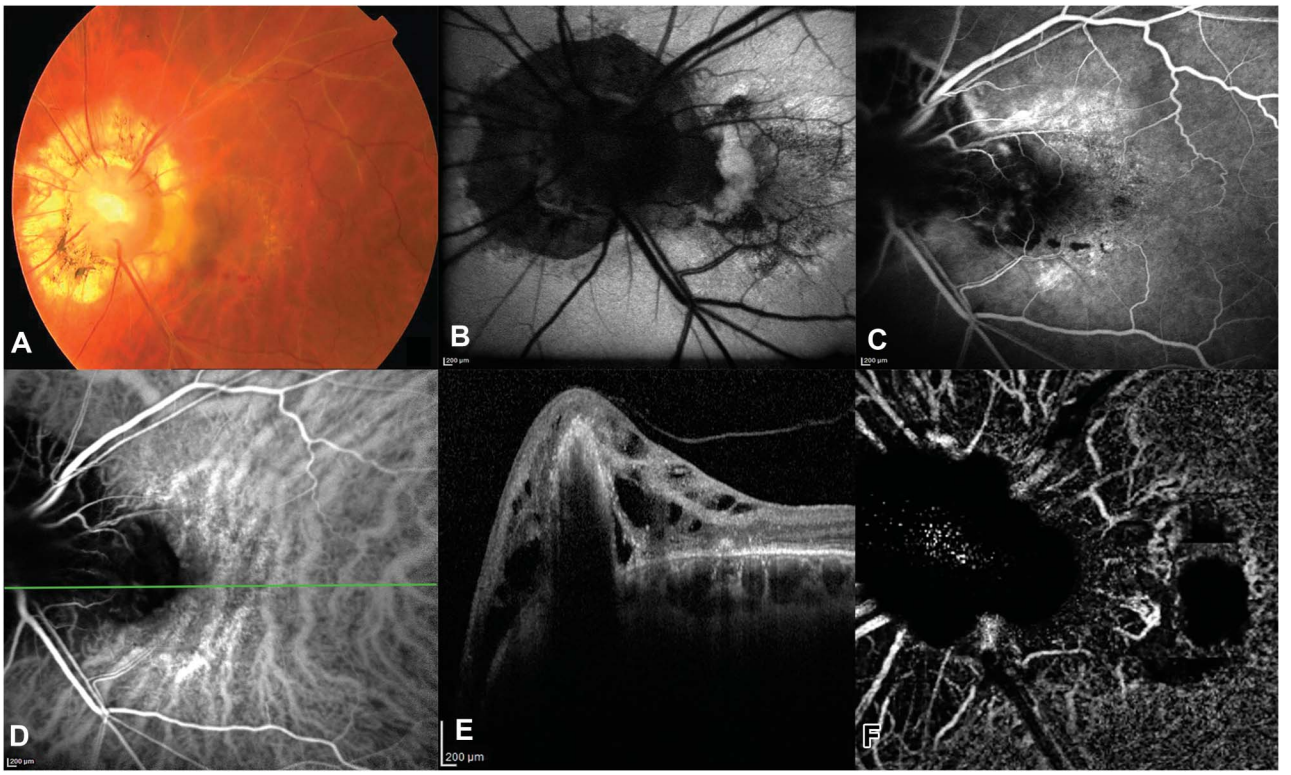

Fig. 1. Baseline evaluation of the left eye. **A.** Fundus photograph showing a morning glory syndrome with juxtapapillary yellowish-gray area surrounded by small subretinal hemorrhages and perimacular lipid depositions. **B.** Fundus autofluorescence disclosing a peripapillary hypoautofluorescent halo corresponding to the pigment epithelium atrophy, with an adjacent area of hyperautofluorescence and a slight hypoautofluorescence in macular area due to pigment epithelium damage. **C** and **D.** Intermediate phase of both fluorescein angiography and indocyanine green angiography revealing a peripapillary neovascular complex with some aneurysmatic dilatation suggestive of a polypoidal choroidal vasculopathy. **E.** Spectral domain optical coherence tomography horizontal line scan showing a pigment epithelial detachment with subretinal fluid and intraretinal cysts in the peripapillary area. **F.** Optical coherence tomography angiography confirming the juxtapapillary choroidal neovascularization beneath the pigment epithelial detachment.

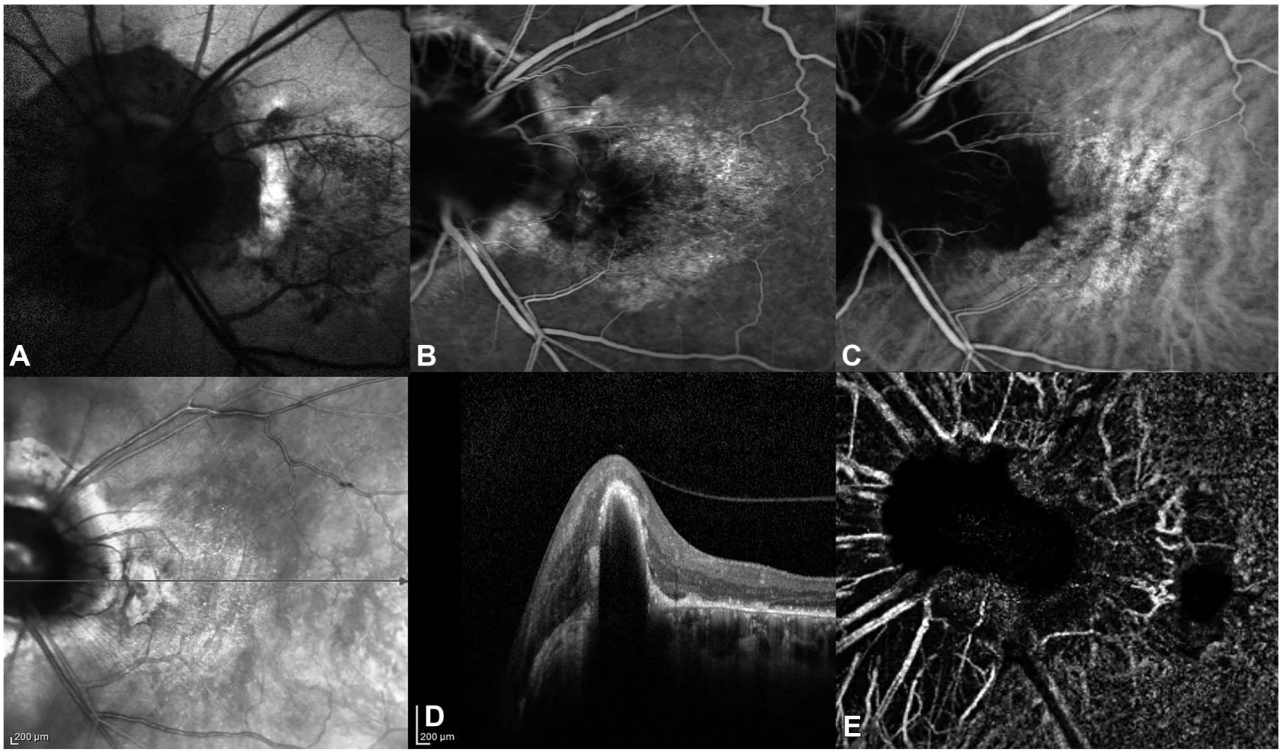

Fig. 2. Posttreatment evaluation of the left eye. **A.** Fundus autofluorescence showing an increase of the hyperautofluorescence in correspondence of the neovascular lesion. **B** and **C.** Intermediate phase of both fluorescein angiography and indocyanine green angiography detecting a reduction of the neovascular lesion leakage. **D.** Spectral domain optical coherence tomography horizontal line scan revealing a complete resolution of intraretinal and subretinal fluid. **E.** Optical coherence tomography angiography disclosing a decrease of tiny branching vessels associated with persisting of larger trunks.

Discussion

Previous studies have suggested that MGS may result from a mesenchymal abnormality with poor development of the lamina cribrosa and faulty closure of the posterior sclera.[4,5]

Systemic associations including cranial anomalies with skull base midline defects can be present but our patient did not show any abnormality in clinical examination. Among ocular complications, serous retinal detachment can develop in up to 30% of patients, whereas CNV is very rare and there is no established treatment regimen yet.

Mechanical and hemodynamic changes at the border of the optic disk, characteristic of this syndrome, may predispose to the development of the CNV.

Mauget-Faÿsse et al[6] proposed a relationship between localized retinal pigment epithelium dysfunction and choroidal perfusion anomalies occurring at the edge of staphyloma in patients with tilted disk syndrome complicated using PCV. In our patient, the vascular abnormality is located just at the border of retinal pigment epithelium atrophy, confirming a common pathologic mechanism.

Anti-VEGF therapy is nowadays approved for the treatment of CNV in age-related maculopathy and myopia and for macular edema associated with vascular occlusion or diabetes mellitus. Few cases of CNV secondary to MGS are reported in the literature,[7–9] and two of them analyze the clinical outcomes of ranibizumab (Cennamo et al; Ozkaya et al).[8,9] Our patient shows the efficacy of aflibercept injections even if there is only a slightly improvement of the final visual acuity due to the related amblyopia. To the best of our knowledge, this is the first report to show that a PCV can occur in MGS and that it can be successfully treated with intravitreal injections of aflibercept.

Key words: aflibercept, morning glory syndrome, polypoidal choroidal vasculopathy.

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