

# Intravitreal aflibercept for ruptured retinal arterial macroaneurysm

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## Dear Editor,

Retinal arterial macroaneurysm (RAM), which usually occurs within the first three orders of arterial bifurcation, is acquired fusiform or saccular dilatations of retinal arterioles<sup>[1-2]</sup>. Aging, the female gender, and systemic vascular pathology are common risk factors<sup>[3]</sup>.

RAM usually resolves spontaneously without any ocular complication. However, a ruptured RAM may be associated with hemorrhagic and/or exudative complications, such as chronic macular edema<sup>[4]</sup>. Bleeding from a ruptured RAM may result in a subretinal, intraretinal, preretinal, or vitreous hemorrhage. Exudation from a RAM usually is seen in a circinate pattern surrounding the aneurysm. Although treatment for RAMs is required in patients with sight-threatening macular involvement, there is no well-established option.

In recent studies, the promising results of intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents, such as bevacizumab and ranibizumab, for symptomatic RAM with macular hemorrhage or secondary macular edema have been demonstrated<sup>[5-8]</sup>. This case report describes the experience with a patient experiencing a ruptured RAM with sub-internal limiting membrane (ILM) preretinal hemorrhage who was treated with intravitreal aflibercept injection.

The 74-year-old woman had a history of visual loss in her right eye of 3 weeks' duration. Her medical history revealed that she had poorly regulated blood pressure. Her best-corrected visual acuity (BCVA) was hand motion in the right eye and 20/200 in the left eye. A slit-lamp examination revealed senile nuclear cataracts in both eyes. Intraocular pressures were normal. Funduscopy showed a significant preretinal macular hemorrhage in the right eye, a retinal pigment epithelium irregularity in the

left eye, and generalized attenuation of the arteries and mild tortuosity in both eyes (Figure 1A). Spectral domain optical coherence tomography (SD-OCT) demonstrated an inner-layer hyper reflectivity with a subsequent outer-layer shadowing consistent with the dense preretinal hemorrhage (Figure 1B). Fluorescein angiography (FA) was postponed due to a large amount of hemorrhaging.

With the diagnosis of a possible ruptured RAM, the patient underwent three intravitreal aflibercept injections four weeks apart. Additionally, her blood pressure was regulated. Four weeks after the first aflibercept injection, a fundus examination showed the presence of a RAM located at the end of a second arterial bifurcation in the superior-temporal arcades (Figure 1C, 1E and 1G). Furthermore, a retinal hemorrhage was located in the superficial retina between the ILM and the retinal nerve fibre layer in our patient (Figure 1D, 1F). SD-OCT scans and an FA were performed, and both confirmed the presence of RAM, and no leakage was reported (Figures 1H, 2A and 2B). SD-OCT showed gradual improvement of sub-ILM hemorrhage and associated retinal edema. BCVA was improved to 20/50 in the right eye. Five months later, her clinical findings were still stable.

In the majority of RAMs, spontaneous resolution occurs with thrombosis and fibrosis<sup>[4]</sup>. Intervention for treatment depends on the clinical findings and associated complications of the disease. Laser photocoagulation, vitreoretinal surgery, pulsed neodymium:yttrium aluminum garnet laser (Nd:YAG) membranotomy, pneumatic displacement or submacular surgery are current treatment options for complicated RAMs<sup>[4,8-9]</sup>.

Recently, intravitreal injection of anti-VEGF agents (bevacizumab and ranibizumab) were used in the treatment of RAMs<sup>[10-14]</sup>. In this case, following the aflibercept injections, the macular edema and macular hemorrhage were regressed, and visual acuity was improved and stabilized during the follow up. The therapy was well tolerated without any adverse events. To the best of our knowledge, this is the first report about intravitreal aflibercept injection for RAM.

The mechanism of anti-VEGF medication in the treatment of RAMs is not fully understood<sup>[4]</sup>. The inhibition of VEGF resulted from the reduced vascular permeability and central macular thickness, which also leads to visual acuity gain and clearance of the various retinal hemorrhages<sup>[7,15]</sup>. VEGF causes vasodilation by stimulating endothelial production of nitric

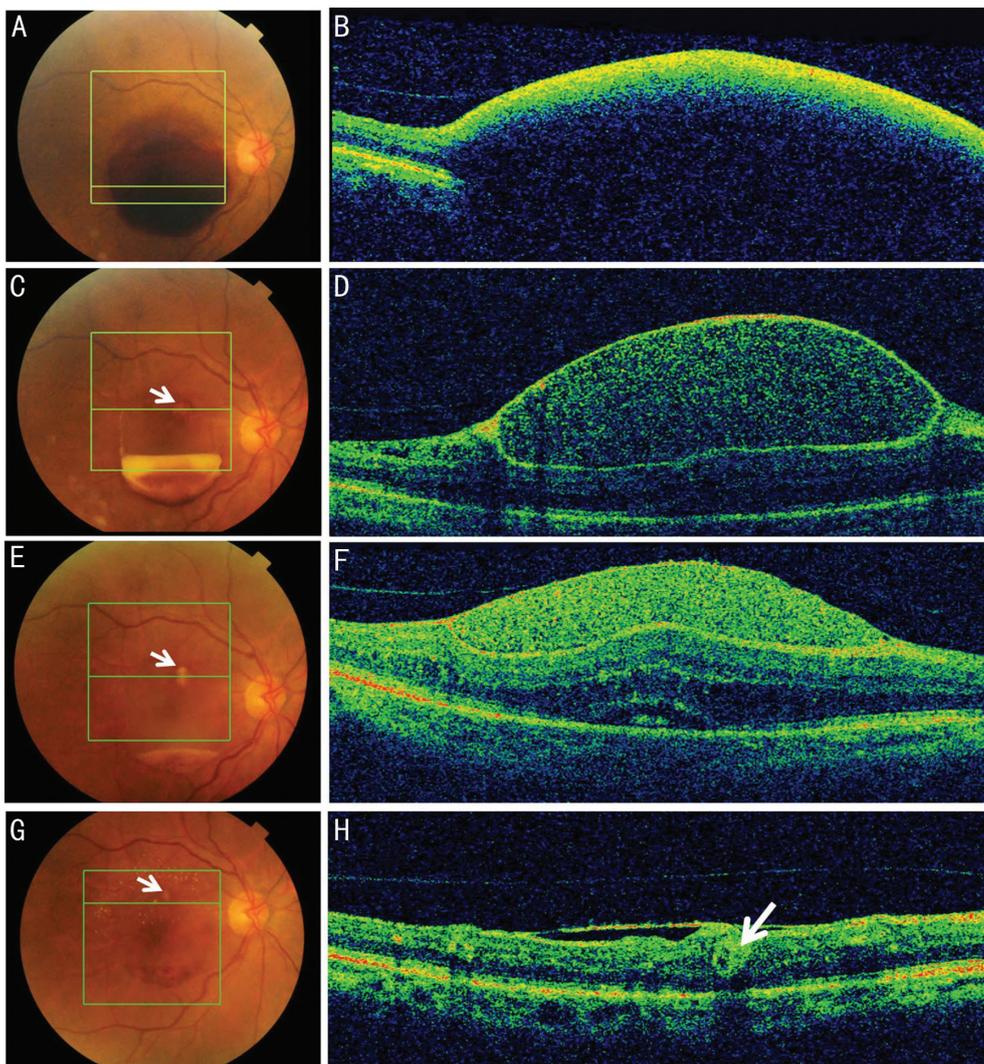


Figure 1 Color fundus picture showing preretinal hemorrhage and SD-OCT scans reveal the initial retinal inner-layer hyper reflectivity and outer-layer shadowing (A, B), four weeks after the first intravitreal aflibercept injection; the RAM was located at the end of the second arterial bifurcation in the superior-temporal arcades (white arrows), and the SD-OCT demonstrated that the hemorrhage was between the internal limiting membrane and the retinal nerve fibre layer (C, D), four weeks after the second injection (E, F), and four weeks after the third injection (G, H).

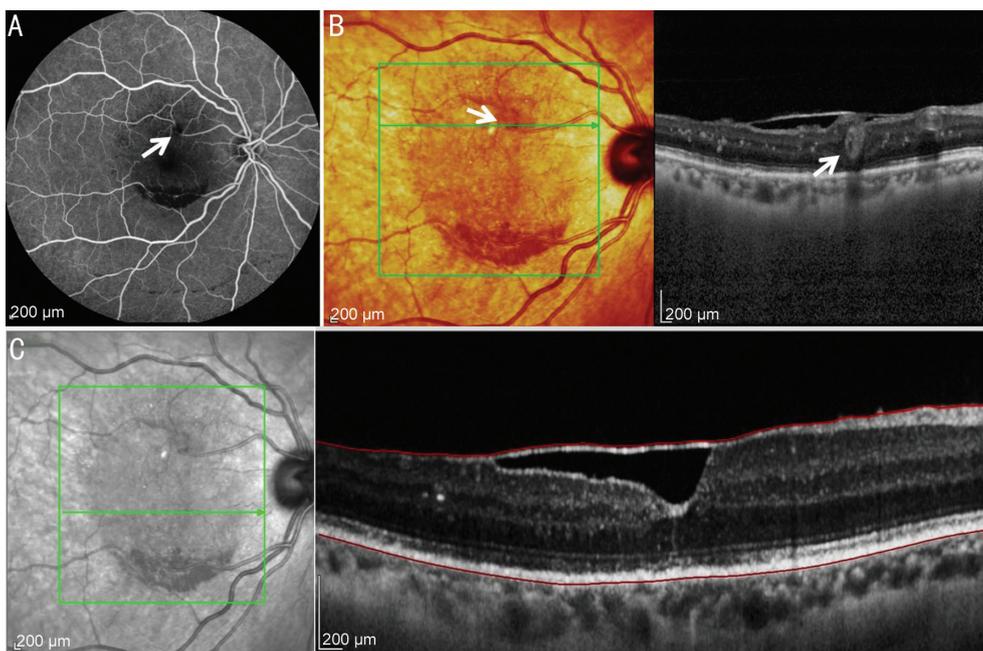


Figure 2 After three monthly aflibercept injections, FA of the right eye showed no leakage (A); the final SD-OCT shows the RAM (white arrows) and the fovea (B, C).

oxide, which is related to the activation of coagulation cascades. Anti-VEGF agents may reduce edema by reducing nitric oxide and causing vasoconstriction<sup>[7,15]</sup>. Additionally, inhibition of VEGF may alter the balance between coagulation and fibrinolysis, thus facilitating the clearing of retinal hemorrhage<sup>[7]</sup>.

There are a few reports about the anti-VEGF usage in RAM. Pichi *et al*<sup>[12]</sup> reported that intravitreal injection of bevacizumab is an effective therapy for complicated RAM, which leads to rapid improvement in central retinal thickness and BCVA. They performed with three monthly injections and observed 94% closure of the RAM after two injections (at six weeks) with 100% complete resolution of macular edema four weeks after the final bevacizumab injection. Cho *et al*<sup>[7]</sup> concluded that intravitreal bevacizumab injection fastens the resolution of the macular edema and hemorrhage by inducing vasoconstriction without any significant influence on final BCVA or central macular thickness. In accordance with bevacizumab studies, Erol *et al*<sup>[14]</sup> reported that intravitreal ranibizumab injection leads to rapid visual and anatomic rehabilitation in symptomatic RAMs.

Aflibercept is a potent anti-VEGF agent that acts like a “VEGF trap” and inhibits the activity of the VEGF subtypes (VEGF-A and VEGF-B) and placental growth factor. Accordingly, we preferred to use this potent anti-VEGF agent in our patient with a significant clinical benefit.

As a conclusion, intravitreal aflibercept injection may offer retina specialists a therapeutic option in cases with ruptured retinal arterial macroaneurysm.

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