Published in final edited form as:

Retina. 2018 September ; 38(9): e74–e75. doi:10.1097/IAE.0000000000002261.

Reversal of retinal vascular leakage and arrest of progressive retinal non-perfusion with monthly anti-vascular endothelial growth factor therapy for proliferative diabetic retinopathy

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Summary Statement

We report a case of proliferative diabetic retinopathy (PDR) with severe, vision-threatening retinal non-perfusion (RNP) in which anti-vascular endothelial growth factor (VEGF) therapy resulted not only PDR reversal but also in arrest of RNP and resolution of retinal vascular leakage which had previously preceded vascular dropout and progressive RNP in the same patient.

Keywords

diabetic retinopathy; retinal non-perfusion; anti-vascular endothelial growth factor (VEGF)

A 59-year-old male with type 2 diabetes mellitus (HbA1c 6.8–7.2% during the clinical course described herein) with non-proliferative diabetic retinopathy (DR) without diabetic macular edema (DME) underwent fluorescein angiography (FA) revealing retinal non-perfusion (RNP) and leakage along the retinal vessels (Fig. 1A). Subsequent FA (Fig. 1B) revealed neovascularization (NV) and persistent vascular leakage (Fig. 1B, yellow circles), with new areas of RNP due to dropout (Fig. 1B, red circles) of retinal vessels that had previously shown leakage (Fig. 1A, red circles). After pan-retinal photocoagulation (PRP) and loss to follow-up, repeat FA six months later revealed persistent but improved NV and retinal vascular leakage (Fig. 1C) with increased RNP due to further dropout (Fig. 1C, yellow circles) of previously leaking vessels (Fig. 1B, yellow circles). PRP, monthly intravitreal anti-vascular endothelial growth factor (VEGF) injection (ranibizumab 0.3mg), or combination therapy were offered, and the patient chose anti-VEGF therapy. FA one year later revealed regressed NV, resolved retinal vascular leakage, and no further progression of RNP (Fig. 1D).

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Relevant Financial Disclosures/Proprietary Interests: MPG has served as a paid consultant for advisory boards for Genentech (San Francisco, CA) and Regeneron (Tarrytown, NY). RVPC serves as a paid advisor for Allergan (Irvine, CA). SK serves as a paid consultant for Genentech (San Francisco, CA), Regeneron (Tarrytown, NY), and Optos (Dunfermline, UK).

Presentations at prior meetings: none

Studies have demonstrated a reduction in DR severity scores with anti-VEGF therapy for PDR¹ or DME.^{2–3} Although RNP can cause irreversible vision loss, it is not incorporated in these DR scoring systems. Retinal vascular leakage is also not included in these scoring systems.^{1–3} In this patient, angiographic retinal vascular leakage preceded vascular dropout and progressive RNP. Anti-VEGF therapy reversed the vascular leakage and arrested RNP progression. This case is consistent with a prior report of RNP slowing during anti-VEGF therapy for DME.⁴ Anti-VEGF therapy may have a role for preserving retinal vasculature in cases with vision-threatening, progressive RNP; and angiographic vascular leakage may be a useful imaging marker for vasculopathy amenable to such therapy. It is also possible that additional PRP sufficient to reduce VEGF drive and regress the NV may have similarly reduced vascular leakage and RNP progression. Additionally, there is controversy regarding the potential for anti-VEGF therapy to promote retinal reperfusion.⁵ In this case, areas of less hypofluorescence noted after anti-VEGF therapy were evaluated with optical coherence tomography-angiography and did not reveal reperfusion. A limitation of this retrospective report includes variability in the exposure and timings of FA images, although all images shown range from 3 minutes 41 seconds to 4 minutes 18 seconds. Further studies are necessary.

Acknowledgments

Grants and Funding: Unrestricted departmental grant from Research to Prevent Blindness (MPG, SK, RVPC); National Institutes of Health P30 EY001792 Core Grant for Vision Research (RVPC); Research to Prevent Blindness Physician-Scientist Award (SK).

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Figure 1.

(A) Fluorescein angiogram (FA) of the left eye demonstrates non-proliferative diabetic retinopathy with areas of retinal non-perfusion (RNP) and marked leakage along retinal vessels (red circles). (B) Subsequent FA shows development of neovascularization (NV) of the disc and elsewhere, along with continued retinal vascular leakage and increased RNP due to dropout of vessels (red circles) that previously had shown leakage (A, red circles). (C) Pan-retinal photocoagulation (PRP) was performed and FA six months later shows improved but persistent NV and retinal vascular leakage, with further increased RNP due to dropout (yellow circles) of vessels that had shown leakage prior to FA (B, yellow circles). (D) After one year of monthly anti-vascular endothelial growth factor therapy in that eye, NV is regressed and retinal vascular leakage is resolved. There is no interval progression of RNP.