



Disappearance of Drusen after Intravitreal Anti-VEGF Injections for Submacular Hemorrhage (SMH) Secondary to Neovascular Macular Degeneration (n-AMD)

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Purpose

Neovascular age-related macular degeneration (N-AMD) is the most common cause of legal blindness in the western world.¹ Intravitreal pan anti-VEGF agents, bevacizumab (Avastin) and ranibizumab (Lucentis) are currently the most effective treatment for N-AMD.²⁻⁴ Patients are treated with monthly injections, at least initially, although less frequent injections may be appropriate after three to four loading injections in some patients. Both bevacizumab and ranibizumab appear to have equal efficacy.⁴

Although excluded from the pivotal trial that led to the FDA approval of ranibizumab, predominantly hemorrhagic N-AMD lesions seem to respond well to anti-VEGF monotherapy.⁵⁻⁶

The purpose of this communication is to report rapid regression of soft drusen in three eyes with hemorrhagic N-AMD treated with intravitreal anti-VEGF injections.

Methods

We performed a retrospective chart review of three eyes of three patients (age 63,85 and 70 years, F=2, M=1) presenting with acute central scotoma of ≤ 7 days secondary to SMH from n-AMD. Inclusion criteria: availability of color fundus photos obtained ≤ 2 year prior to the onset of SMH, presence of multiple, large (soft) drusen on those photographs, clear media and follow up until resolution of SMH. Exclusion criteria: symptoms ≥ 7 days, treatment other than anti-VEGF injections, pre-existing subretinal fibrosis or GA and non-AMD SMH.

After initial work up including IVFA and OCT, monthly injections of bevacizumab 1.25 mg/0.05mL were initiated until complete resolution of SMH, and less frequently thereafter. Fundus photos obtained after resolution of SMH were compared side-by-side with those prior to onset of SMH for change in soft drusen, and other findings.

Results. Case 1

A 63-year-old female presented with central distortion and decreased vision OD (20/50) for one week secondary to hemorrhagic AMD (Figure 1A and B). Fundus photos 19 months earlier showed extensive drusen (Figure 2). Hemorrhage resolved after 4 monthly avastin injections (1.25 mg/0.05mL). Fundus photos 4 months after presentation showed marked reduction of drusen (Figure 3). Fellow eye did not show significant change in drusen. (Figure 4, and Figure 5). After 33 months follow-up (26 avastin injections), her VA was 20/30.

Financial Disclosures: None

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Figure 1A Color Photo, Presentation

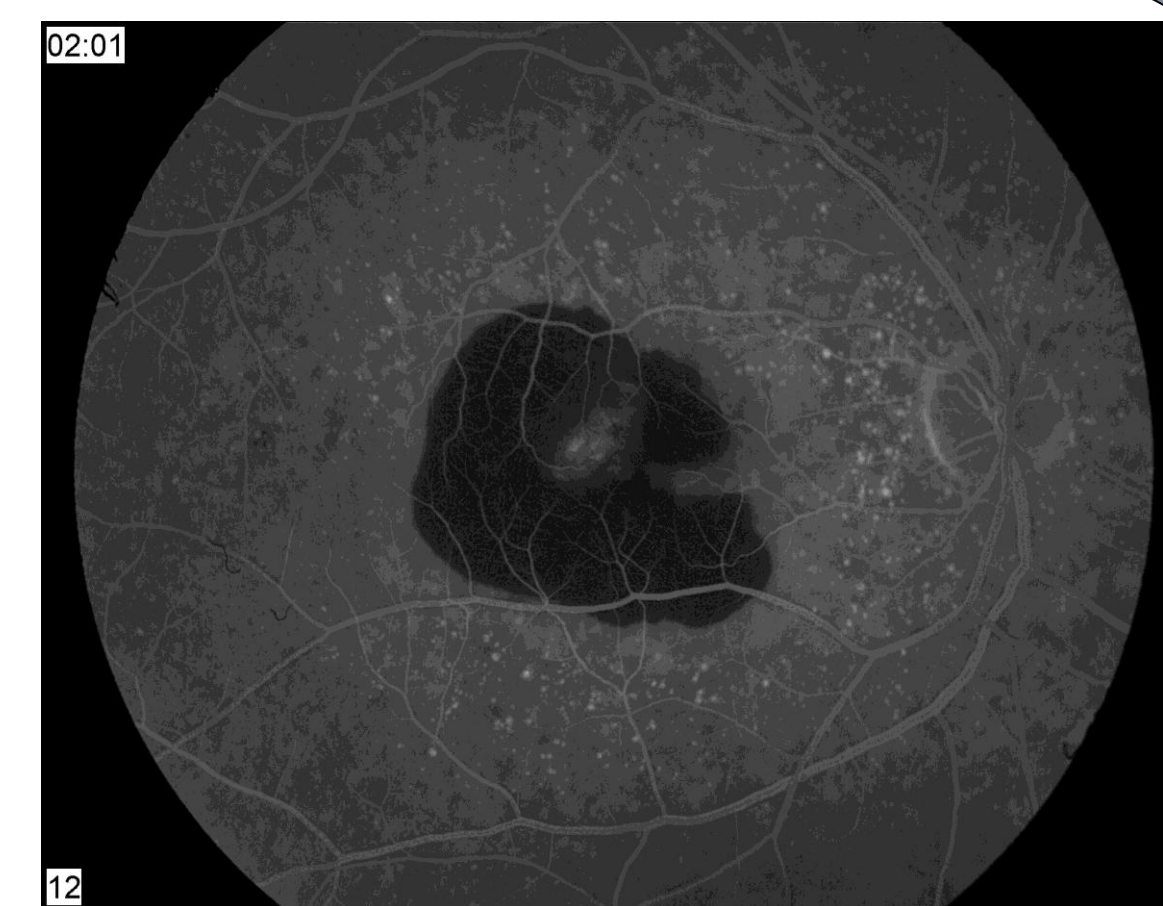


Figure 1B FA, Presentation



Figure 2 Color Photo, 19 months prior to SMH



Figure 3 Color Photo, 4 months after onset of SMH



Figure 4 Color Photo, Fellow Eye 19 months prior to SMH in OD



Figure 5 Color Photo, Fellow Eye 4 months after onset of SMH in OD

Case 2

An 85-year-old female presented with 4-day history of loss of vision OD (HM) secondary to a large hemorrhagic AMD (Figure 6 and 7). Color fundus photo 2 months prior to SMH showed extensive soft and calcific drusen (Figure 8). Fundus photos 5 months later (s/p avastin X 4) showed resolution of subfoveal hemorrhage and marked reduction in drusen (Figure 9). RPE hypopigmentation and further reduction of drusen was noted 7 month after the onset of SMH. (Figure 10). Her final VA was 20/50 (9 avastin injections) 10 months after the onset of SMH when she was lost to follow-up.



Figure 6 Color Photo, Presentation

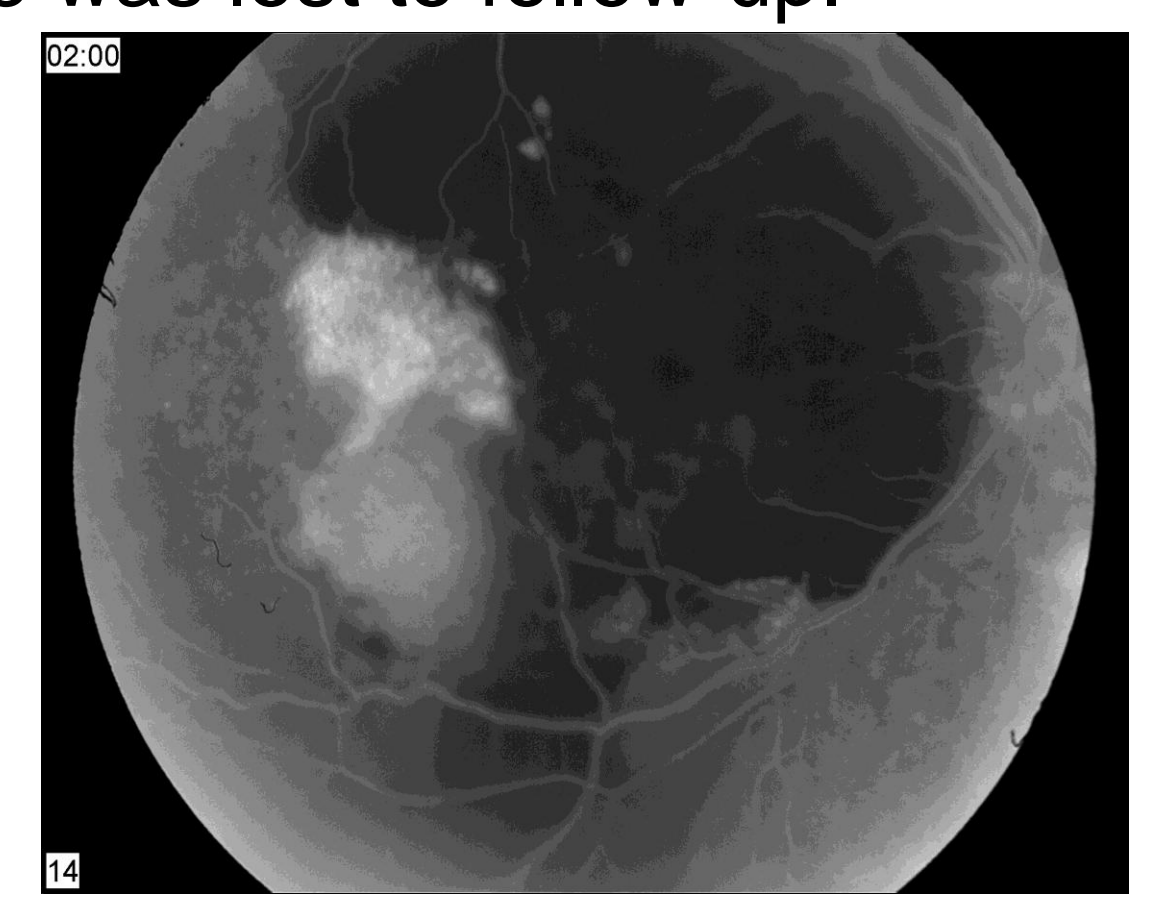


Figure 7 FA, Presentation

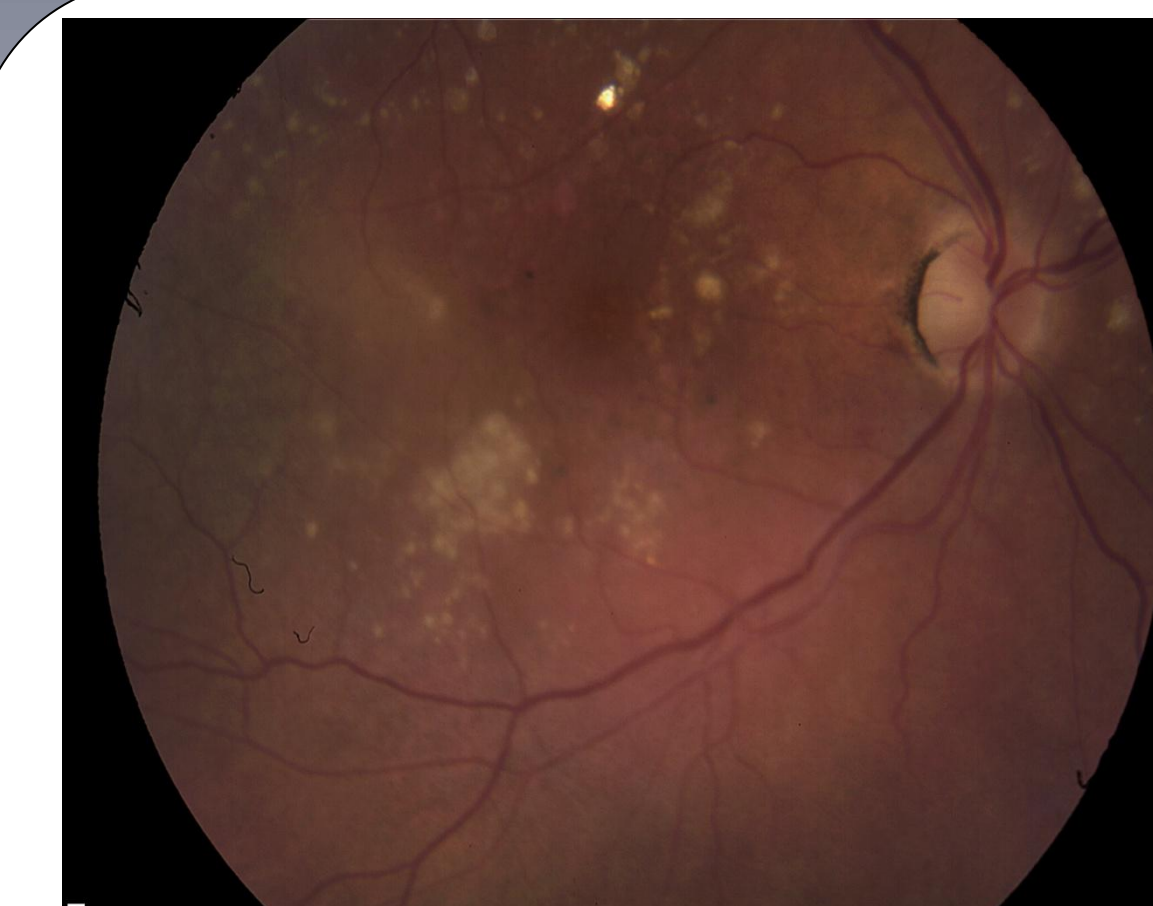


Figure 8, 2 months prior to SMH



Figure 9, 5 months after SMH



Figure 10, 7 months after SMH (20/50)

Case 3

A 70-year-old male presented with a 4-day history of sudden loss of central vision OS (HM) secondary to a large SMH (Figure 11, 12). He was previously treated with 6 intravitreal avastin injections in that eye for N-AMD, but had not received any treatment for 56 months prior to the onset of SMH. Fundus photo six months prior to SMH showed significant soft drusen and noncentral GA. (Figure 13). Four months later (s/p avastin X 4), fundus photo showed significant reduction in drusen, central GA and a subretinal scar superior to fovea (VA CF)(Figure 14).



Figure 11 Color Photo, Presentation

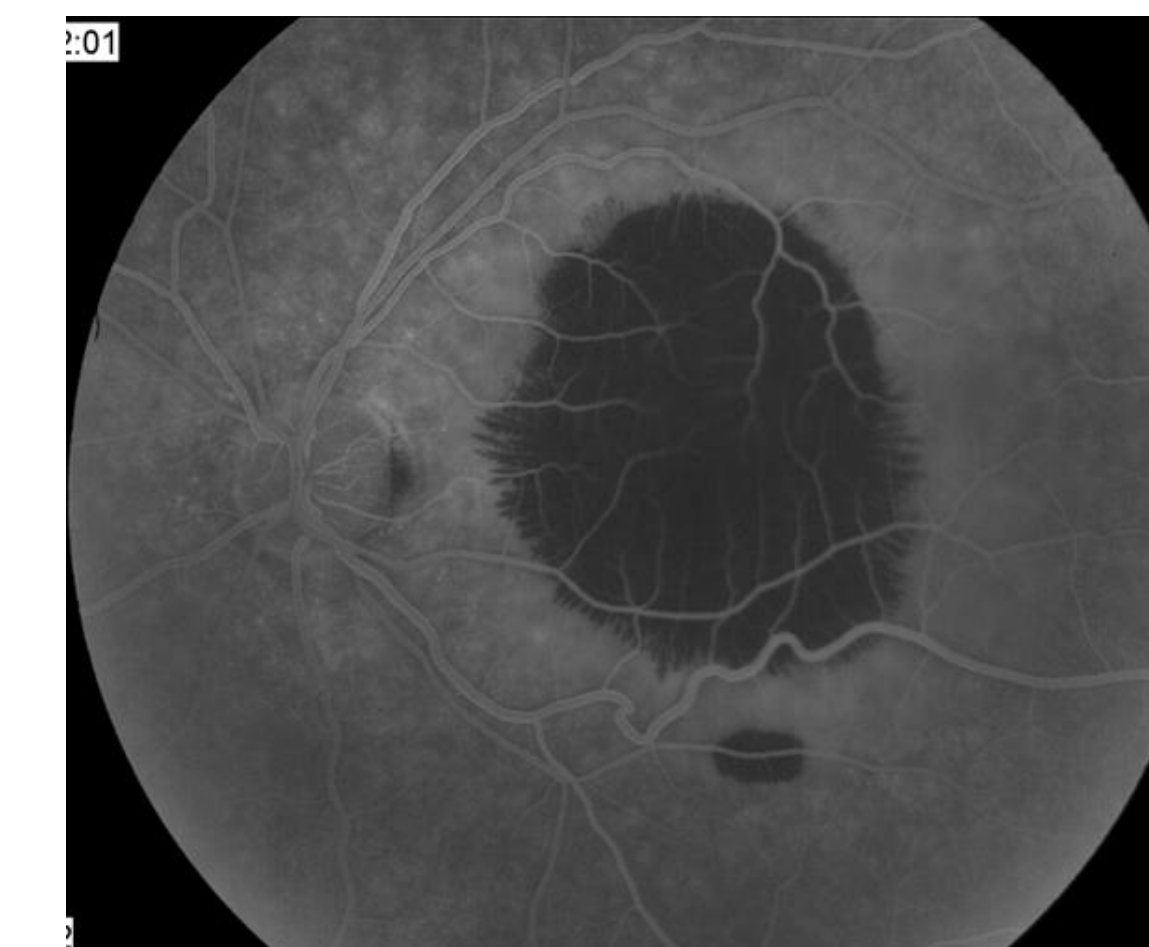


Figure 12, FA, Presentation



Figure 13, 6 months prior to SMH



Figure 14, 4 months after SMH

Discussion

Soft drusen may regress spontaneously, but it is usually accompanied by RPE atrophy and visual impairment.^{7,8} Drusen disappearance with improvement in vision has been reported after laser photocoagulation,⁹ macular hole surgery,¹⁰ retinal detachment surgery,¹¹ and anti-VEGF therapy for drusenoid PED.¹²

The rapid regression of drusen in our patients suggests a causal relationship between resolution of SMH and drusen disappearance. The mechanism of drusen disappearance after laser photocoagulation has been postulated to be stimulation of macrophages and/or proliferation of RPE cells that phagocytose drusen material. Autologous platelet concentrate and mechanical stimulation of RPE may explain drusen disappearance after macular hole surgery. Subretinal fluid may "wash out" drusen material in a case of drusen disappearance after RD surgery. A combination of these factors may have played a role in drusen disappearance in our patients.

Bibliography

- Congdon N, O'Colmain B, Klaver CC, et al. Causes and prevalence of visual impairment among adults in the United States. Arch Ophthalmol 2004;122:477-85.
- Rosenfeld PJ, Brown DM, Heier JS, et al. Ranibizumab for neovascular age-related macular degeneration. N Engl J Med 2006;355(14):1419-31.
- Brown DM, Kaiser PK, Michels M, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med 2006;355:1432-44.
- CATT Research Group, Martin DF, Maguire MG, et al. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. N Engl J Med 2011; 364:1897-908
- Stifter E, Michels S, Prager F, Georgopoulos M, Polak K, Hirn C, et al. Intravitreal bevacizumab therapy for neovascular age-related macular degeneration with large submacular hemorrhage. Am J Ophthalmol 2007;144:886-892.
- Chang MA, Do DV, Bressler SB, Cassard SD, Gower EW, Bressler NM. Prospective one-year study of ranibizumab for predominantly hemorrhagic choroidal neovascular lesions in age-related macular degeneration. Retina 2010;30:1171-1176.
- Bressler NM, Munoz B, Maguire MG, et al. Five-year incidence and disappearance of drusen and retinal pigment epithelial abnormalities. Waterman study. Arch Ophthalmol 1995;113:301-8.
- Cukras C, Agron E, Klein ML, et al; Age-Related Eye Disease Study Research Group. Natural history of drusenoid pigment epithelial detachment in age-related macular degeneration: Age-Related Eye Disease Study Report No. 28. Ophthalmology. 2010;117:489-99.
- Complications of Age-Related Macular Degeneration Prevention Trial Research Group. Laser treatment in patients with bilateral large drusen: the complications of age-related macular degeneration prevention trial. Ophthalmology 2006; 113:1974-1986.
- Holz FG, Staudt S. Disappearance of soft drusen following macular hole surgery. Retina.2001; 21:184-6.
- Margolis R, Ober MD, Freund KB. Disappearance of drusen after rhegmatogenous retinal detachment. Retinal Cases & Brief Reports 2010; 4:254-256.
- Gallego-Pinazo R, Marina A, Suelves-Cogollo, et al. Intravitreal ranibizumab for symptomatic drusenoid pigment epithelial detachment without choroidal neovascularization in age-related macular degeneration. Clin Ophthalmol. 2011;5:161-5.