

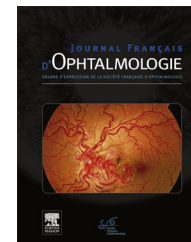


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LETTER TO THE EDITOR

Simultaneous retinal pigment epithelium tear and lamellar macular hole evolving to a full-thickness macular hole after intravitreal injection

Déchirure simultanée de l'épithélium pigmentaire rétinien et trou maculaire lamellaire évoluant en trou maculaire complet après traitement intravitréen

Introduction

Retinal pigment epithelium (RPE) tear is an uncommon complication of neovascular age-related macular degeneration (nAMD) with an increasing risk in cases with pigment epithelium detachment (PED) and may appear spontaneously or after intravitreal therapy (IVT). Other uncommon complications of IVT related to nAMD are lamellar macular hole (LMH) and full-thickness macular hole (FTMH). Here, we present a patient with nAMD that developed a RPE tear associated with LMH that evolved into a FTMH two months later after IVT with ranibizumab (Lucentis®). Long-term follow-up was registered.

Case report

A 86-year-old woman presenting bilateral nAMD, had six IVT with ranibizumab in her right eye (RE) and ten in her left eye (OS) on a "pro re nata" (PRN) regimen. Visual acuity (VA) was 20/200 in her RE and 20/100 in her OS. Spectral-domain optical coherence tomography (SD-OCT; Cirrus HD OCT®, Carl Zeiss, USA) showed a PED with cystoid macular edema and subretinal fluid (Fig. 1A) in OS, so a new IVT with ranibizumab was indicated. Four weeks after treatment, the patient reported central scotoma related with VA impairment (20/400). SD-OCT showed a RPE tear and LMH (Fig. 2B). Well-delimited denuded area of RPE was observed and ultra-wide field autofluorescence (Optomap®) showed hypo-autofluorescence of the same area (Fig. 2A and B). IVT was stopped and two months later, the LMH had evolved into a FTMH (Fig. 1C). Despite the presence of fibrotic changes in the lesion (Fig. 1D) and association with retinochoroidal anastomosis (Fig. 3A), after five years, the patient maintained the same visual acuity.

Discussion

RPE tear in nAMD may occur spontaneously or during treatment, either under antiangiogenic IVT or after

photodynamic therapy [1]. It is an uncommon complication with a non-greater prevalence in patients treated with anti-VEGF than in those in which it occurred spontaneously [2]. RPE tear is most commonly observed in patients with previous PED and has been directly correlated with its size [2,3]. The exact pathogenesis of the RPE tear is not well known: RPE degenerative events by the AMD itself and the mechanisms of contraction and involution of the newly formed vessel complex that take place after intravitreal anti-VEGF injection are considered the main involved factors [1–3]. Thus, the visual prognosis varies according to the affected area, being worse if it affects the foveal region due to the evolution towards fibrosis and atrophy.

On the other hand, several pathogenic mechanisms have been involved in the formation of MH in AMD [4–8]:

- formation of an epiretinal membrane (ERM) by exudative changes arising from the neovascular complex [4];
- changes on the vitreoretinal interface in patients treated with IVT [5], due to the vitreous incarceration at the puncture point or by vitreous structural changes with syneresis, formation of partial vitreous detachment and vitreomacular traction after injection;
- contraction of the neovascular membrane with tangential traction of the retina from the subretinal side [6,7];
- tractional mechanisms do not appear to be found in all patients with MH [5].

Other factors such as cortex contraction, retinal cystic degeneration and macular ischemia may be involved in patients with MH in vitrectomized eyes [8]. Also, previous PED in treated nAMD eyes can also predispose to MH formation [5]; a rapid resolution of macular edema and PED reduction could trigger changes in the structure of the retina that favour the development of a MH after IVT [6].

Neovascular complex progression would also be the cause of progression from LMH to FTMH, after stopping treatment. Regarding this, we consider that a more aggressive proactive regimen rather than the PRN would have been more appropriate. Both, disease progression and an inappropriate IVT regimen, may have favoured the appearance of complications.

Vitreoretinal surgery for FTMH was not indicated in our case due to the subretinal fibrosis and RPE tear which is the main reason for a poor prognosis and the lack of VA improvement besides the surgery.

Conclusion

RPE tear and MH are uncommon complications in patients with nAMD under antiangiogenic IVT, and can occur in

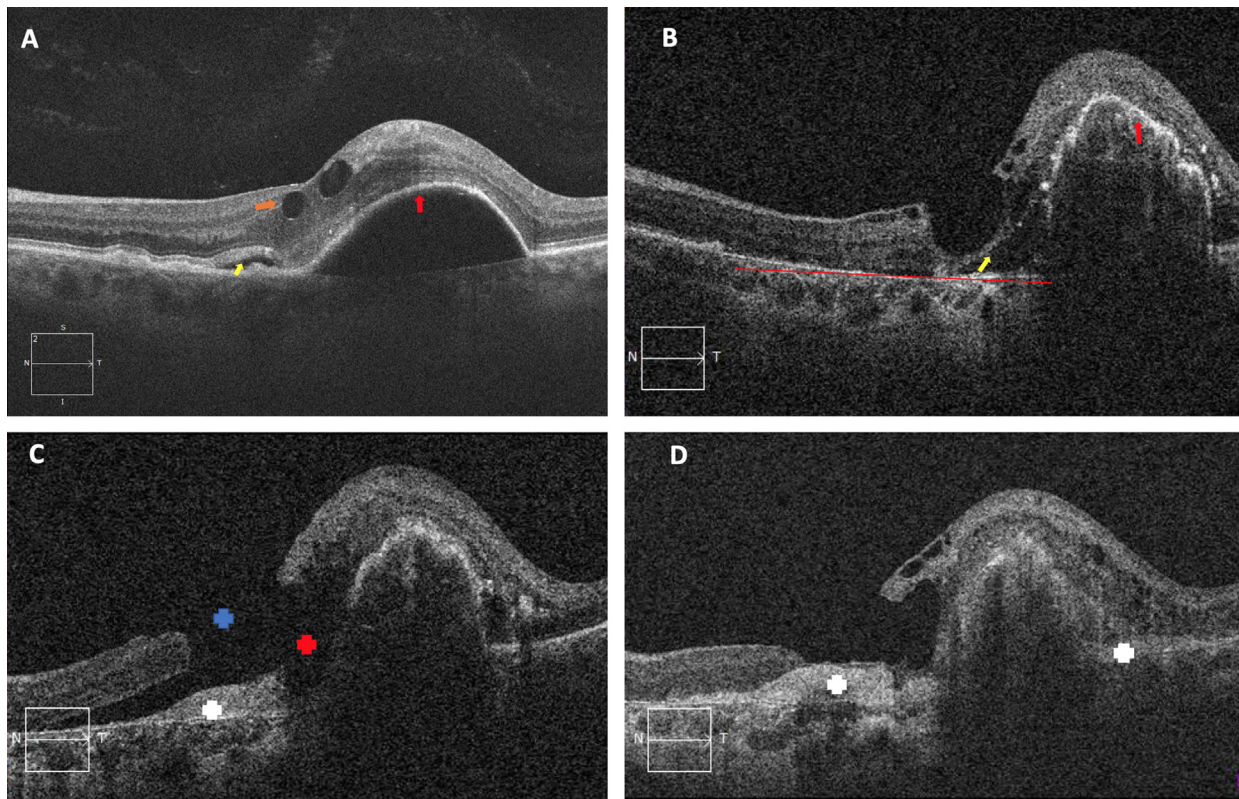


Figure 1. Spectral-domain optical coherence tomography of the OS. A. Prior to the last IVT there was no anomalies of the vitreoretinal interface. Intraretinal cysts (orange arrow), subretinal fluid (yellow arrow) and subfoveal PED (red arrow) are observed. B. After the tenth injection of ranibizumab, LMH with subretinal fluid (yellow arrow), a retracted RPE (red arrow), a denuded area of RPE (red line) and secondary choroidal hyperreflectivity were observed. C. Two months later, a FTMH (blue cross), with RPE tear (red cross) and subretinal hyperreflectivity (white cross) by fibrosis were present. D. After a five-year long-term follow-up, an enlargement of RPE and subretinal hyperreflective area (white crosses) due to increased fibrosis were seen.

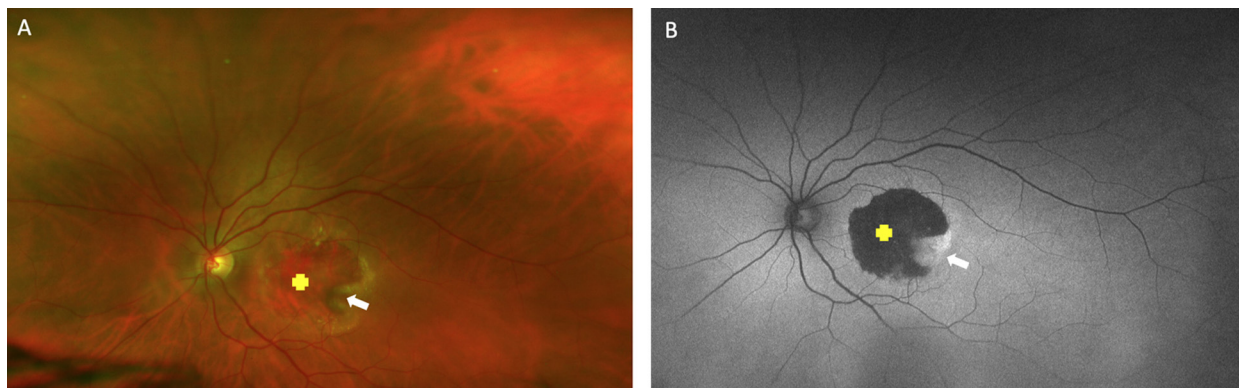


Figure 2. Ultra widefield images of the OS. A. Denuded area of macular RPE (yellow cross) and rolled RPE (white arrow) were observed in color image. B. Macular hypo-autofluorescence area, due to the absence of RPE (yellow cross), with hyper-autofluorescence in the temporal side of lesion, by retracted and rolled RPE (white arrow), were seen.

both, treated and non-treated patients. Diagnostic suspicion is crucial in patients who have experienced important visual acuity impairment, especially in the presence of previous vitreoretinal interface anomalies, PED and

cystoid macular edema under anti-VEGF IVT. It would be interesting a further assessment for the incidence of both complications in a PRN versus proactive treatment regimen.

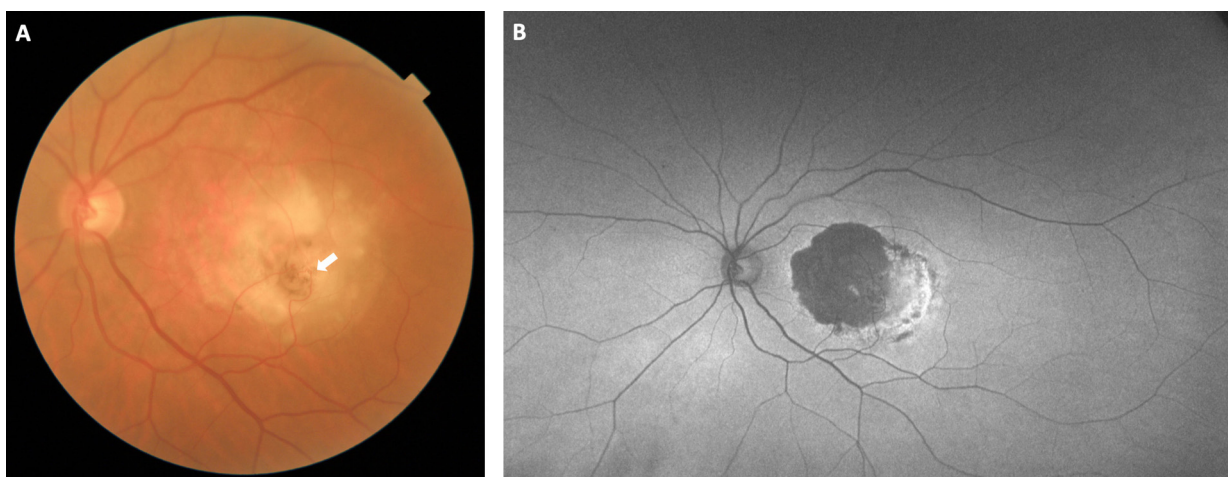


Figure 3. Color Retinography and Ultra-widefield Autofluorescence image of an OS five-year follow-up. A. Macular fibrosis with central hyperpigmentation and retinochoroidal anastomosis (white arrow) were observed in color retinography. B. Lesion enlargement and increased hyper-autofluorescence area were due to the progression of macular degeneration.

Informed consent

The patient has consented to the publication of the case.
The article has not been presented at congresses.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Casalino G, Sivagnanavel V, Dowlut S, Keane PA, Chakravarthy U. Spontaneous retinal pigment epithelial tear in type 2 choroidal neovascularization: repair mechanism following anti-VEGF therapy. *Int J Retina Vitreous* 2019;5:4, <http://dx.doi.org/10.1186/s40942-019-0155-1>.
- [2] Invernizzi A, Nguyen V, Arnold J, Young S, Barthelmes D, Gillies MC. Early and late retinal pigment epithelium tears after anti-vascular endothelial growth factor therapy for neovascular age-related macular degeneration. *Ophthalmology* 2018;125:237–44, <http://dx.doi.org/10.1016/j.ophtha.2017.08.039>.
- [3] Monés J, Biarnés M, Badal J. Bimonthly half-dose ranibizumab in large pigment epithelial detachment and retinal angiomatous proliferation with high risk of retinal pigment epithelium tear: a case report. *Clin Ophthalmol* 2013;7:1089–92, <http://dx.doi.org/10.2147/OPHTH.S45155>.
- [4] Oshima Y, Apte RS, Nakao S. Full thickness macular hole case after intravitreal aflibercept treatment. *BMC Ophthalmol* 2015;15:30, <http://dx.doi.org/10.1186/s12886-015-0021-3>.
- [5] Kabanarou SA, Xirou T, Mangouritsas G, Garnavou-Xirou C, Boutouri E, Gkizis I, et al. Full-thickness macular hole formation following anti-VEGF injections for neovascular age-related macular degeneration. *Clin Interv Aging* 2017;12:911–5, <http://dx.doi.org/10.2147/CIA.S135364>.
- [6] Hirata A, Hayashi K, Murata KL. Removal of choroidal neovascular membrane in a case of macular hole after anti-VEGF therapy for age-related macular degeneration. *Am J Ophthalmol Case Rep* 2017;19:14–7, <http://dx.doi.org/10.1016/j.ajoc.2017.12.003>.
- [7] Mukherjee C, Mitra A, Kumar A, Elsherbiny S, Lip PL. Macular hole formation after intravitreal ranibizumab injection in wet age-related macular degeneration. *Open Ophthalmol J* 2015;9:177–80, <http://dx.doi.org/10.2174/1874364101509010177>.
- [8] Ranjan R, Manayath GJ, Avadhani U, Narendran V. Rapid macular hole formation and closure in a vitrectomized eye following rhegmatogenous retinal detachment repair. *Oman J Ophthalmol* 2018;11:71–4, http://dx.doi.org/10.4103/ojo.OJO_35_2017.

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