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CASE REPORT

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Sea-fan retinal neovascularization associated with rickettsial retinitis: a case report

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Abstract

Background Rickettsial disease has been commonly associated with retinitis, retinal vasculitis, and optic nerve involvement, but the development of retinal neovascularization has been very rarely reported. We herein describe a case of rickettsial retinitis complicated with the development of sea-fan retinal neovascularization documented with multimodal imaging, including fundus photography, SS-OCT, fluorescein angiography, and SS-OCT angiography.

Case presentation A 26-year-old female with a history of fever one week earlier presented with sudden decreased vision in the left eye. Best-corrected visual acuity (BCVA) was 20/2000 and the patient was diagnosed with rickettsial retinitis along the superotemporal retinal vascular arcade associated with serous retinal detachment and retinal hard exudates. The indirect immunofluorescence test was positive for *Rickettsia conorii*, and the patient was treated with oral doxycycline (200 mg/day) and oral prednisone (0.75 mg/kg/day, with gradual tapering). Four weeks after presentation, the retinal infiltrate and associated serous retinal detachment had resolved, but retinal hard exudates had increased. A large sea-fan preretinal fibrovascular neovascularization became apparent along the superotemporal retinal vascular arcade, but there was no associated retinal ischemia on fluorescein angiography. The patient received an adjunctive single intravitreal injection of 1.25 bevacizumab. Sequential follow-up examinations showed shrinking of sea-fan retinal neovascularization, a complete resolution of retinal hard exudates, and the development of a self-limited vitreous hemorrhage. On last follow-up, 30 months after intravitreal bevacizumab injection, BCVA was 20/25.

Conclusion Patients with rickettsial retinitis may develop a sea-fan retinal neovascularization, with subsequent vitreous hemorrhage, putatively through inflammatory mechanisms. Multimodal imaging including OCT, fluorescein angiography, and OCT-angiography, is highly useful for accurate diagnosis and reliable monitoring of the evolution of retinitis, retinal neovascularization, and other retinal changes. The use of a combination therapy with oral doxycycline and corticosteroids and intravitreal anti-VEGF can improve outcomes.

Keywords Retinitis, Rickettsiosis, Optical coherence tomography, Optical coherence tomography angiography, Sea-fan retinal neovascularization, Vascular endothelial growth factor inhibitors

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Background

Asymptomatic or symptomatic ocular involvement is common in patients with rickettsial disease and mainly includes mild vitritis, superficial retinitis, retinal vasculitis, and optic neuropathy [1–3]. Retinal neovascularization is an unusual finding in that setting and has been scarcely reported in the literature [2, 4]. We herein present a case of rickettsial retinitis complicated with the development of sea-fan retinal neovascularization documented with multimodal imaging, including fundus photography, swept-source optical coherence tomography (SS-OCT), fundus fluorescein angiography, and SS-OCT angiography (SS-OCTA).

Case presentation

A 26-year-old female with a history of fever one week earlier presented with sudden decreased vision in the left eye (LE). BCVA was 20/20 in the right eye (RE) and 20/2000 in the LE, with no relative afferent pupillary defect. Results of slit-lamp and fundus examination of the RE were unremarkable, and there was 1+vitreous cells in the LE. Intraocular pressure was 14 mmHg bilaterally. Fundus examination of the LE showed a superficial white retinal lesion identified along the distribution of the superotemporal retinal vascular arcade with associated retinal hemorrhages, retinal edema, serous retinal detachment (SRD), and retinal hard exudates arranged in a macular stellate pattern (Fig. 1A). There also were abnormal retinal telangiectatic vascular changes overlying and surrounding the area of retinitis (Fig. 1A). Fundus autofluorescence of the LE showed a large superotemporal hypoautofluorescent area extending beyond the white retinal lesion and associated retinal hemorrhages seen clinically. There also were hyperautofluorescent streaks, corresponding to retinal hard exudates (Fig. 1B). SS-OCT (DRI OCT Triton plus; Topcon, Tokyo, Japan) showed increased inner retinal reflectivity and thickening with posterior shadowing at the white retinal lesion (Fig. 1C). There were associated multiple hyperreflective dots corresponding to the hard exudates and a macular serous retinal detachment with subretinal hyperreflective material (Fig. 1, C and D). Fluorescein angiography of the LE showed early hypofluorescence and late staining of the white retinal lesion, with associated marked adjacent leakage from the retinal vascular telangiectatic abnormalities (Fig. 1, E and F). There were no associated areas of retinal capillary non-perfusion. SS-OCTA of the LE showed a dark area of no flow signal due to blockage in the superficial and especially the deep capillary plexus from the white retinal lesion and surrounding edema with adjacent retinal vascular telangiectatic changes.

Laboratory work-up including complete blood count, chemistry panel, serological testing for syphilis, toxoplasmosis and bartonellosis, C-reactive protein, erythrocyte sedimentation rate, tuberculin skin test, Quantiferon, and chest X-ray were performed, all of which were within normal limits or negative. The indirect immunofluorescence test was positive for *Rickettsia conorii* with a titer of IgM 1/160 and negative IgG titer. The patient was treated with doxycycline (200 mg/day) and oral prednisone (0.75 mg/kg/day, with gradual tapering).

Four weeks after initial presentation, whilst the patient was still receiving treatment, BCVA of the LE had slightly improved to 20/1000. Fundus examination and SS-OCT showed resolution of the retinal infiltrate and associated serous retinal detachment and a marked increase in retinal hard exudates, seen as multiple intraretinal hyperreflective dots with associated outer retinal layers alterations on SS-OCT (Fig. 2, A and B). A large sea-fan preretinal neovascularization became apparent along the superotemporal retinal vascular arcade (Fig. 2A). Horizontal SS-OCT scan through the healed retinitis and sea-fan fibrovascular lesion showed retinal thickening and inner layer hyperreflectivity with posterior shadowing, along with focal vitreoretinal adhesion (Fig. 2C). Fluorescein angiography showed early hyperfluorescence and late dye leakage from the sea-fan neovascularization, without associated areas of retinal capillary non-perfusion (Fig. 2, D and E). En face OCTA of the superficial retinal plexus showed a well-defined large preretinal filamentous vascular complex corresponding to the sea-fan neovascular area (Fig. 2, F and G). A B-scan OCTA showed a superficial flat flow signal complex consistent with preretinal neovascularization (Fig. 2H). The patient was maintained on treatment with doxycycline and tapering corticosteroids and received one dose of 1.25 mg intravitreal bevacizumab in the left eye. On re-evaluation two weeks later, BCVA of the LE was 20/100, and the retinal neovascularization was shrunk.

The total duration of systemic treatment with doxycycline and gradually tapered corticosteroids was 45 days.

On re-evaluation 16 months after the intravitreal injection, examination showed mild vitreous and preretinal hemorrhages. The hard exudates and sea-fan neovascular lesion had regressed, and there was residual fibrosis at the area of regressed neovascularization (Fig. 3A, B). There was incomplete posterior vitreous detachment better seen on SS-OCT (Fig. 3B) without clinically evident retinal break or retinal vascular abnormalities. Fluorescein angiography showed no features of active neovascularization or retinal ischemia (Fig. 3C, D). OCTA showed no flow signal at the area of the regressed retinal new vessels (Fig. 3E, F). After a further observation period of six months, the vitreous and preretinal hemorrhages had spontaneously cleared, and retinal hard exudates had completely resolved. The fibrotic lesion at the area of sea-fan neovascularization remained unchanged (Fig. 3G). Final BCVA of the LE was measured at 20/25.

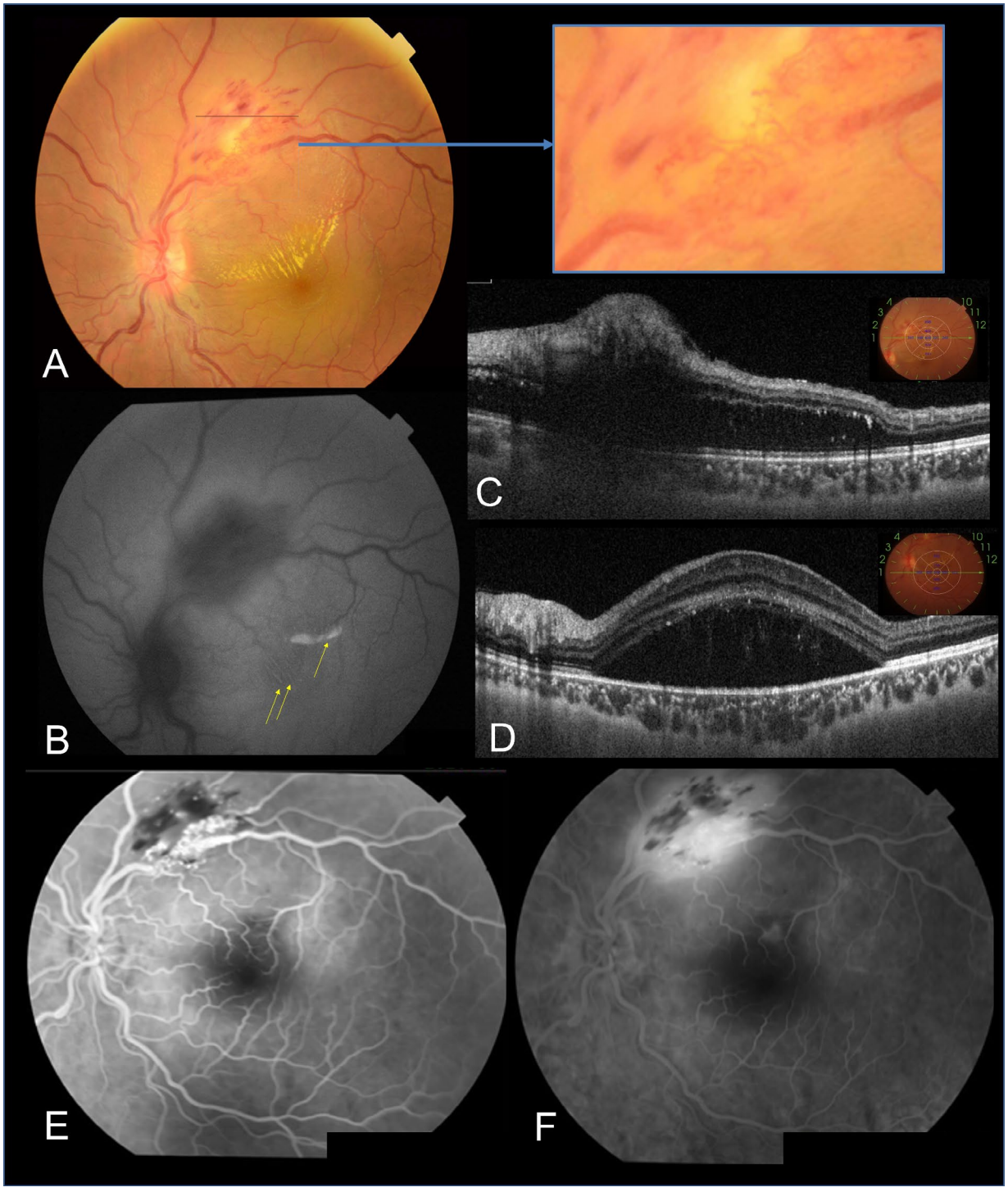

Fig. 1 Multimodal imaging of the left eye at initial presentation. (**A**) Fundus photograph shows a white retinal lesion identified along the superotemporal retinal vascular arcade associated with retinal hemorrhages and overlying and surrounding abnormal retinal telangiectatic vascular changes better visible in the magnified rectangle. Also note the presence of retinal hard exudates arranged in a macular stellate pattern and serous retinal detachment. (**B**) Fundus autofluorescence shows a localized area of hypoautofluorescence larger than the area of retinitis seen clinically and hyperautofluorescent streaks corresponding to retinal hard exudates (arrows). (**C**) Horizontal SS-OCT scan through the white retinal lesion shows increased inner retinal reflectivity, retinal thickening, posterior shadowing, disorganization of the retinal layers, and hyperreflective dots corresponding to retinal hard exudates. (**D**) Horizontal macular SS-OCT scan shows a prominent serous retinal detachment and hyperreflective dots corresponding to hard exudates. (**E**, **F**) Fluorescein angiography shows early hypofluorescence and late staining of the white retinal lesion with adjacent retinal vascular leakage, and a masking effect by retinal hemorrhages

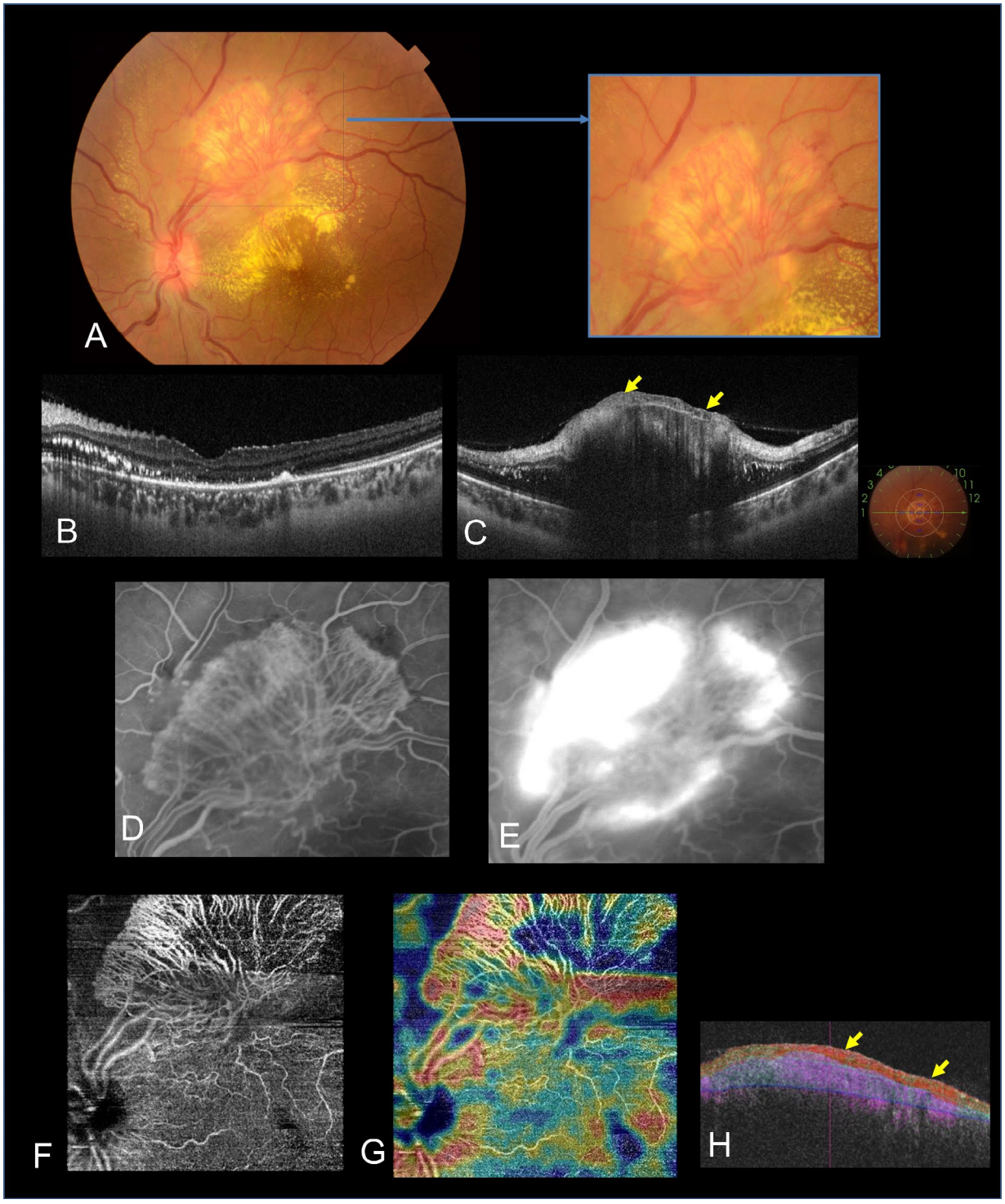

Fig. 2 Multimodal imaging of the left eye four weeks after initial presentation. (**A**) Fundus photograph shows the increase of hard exudates and resolution of serous retinal detachment. A large sea-fan preretinal fibrovascular lesion becomes evident along the superotemporal retinal vascular arcade and is better visible in the magnified rectangle. (**B**) Macular SS-OCT confirms the resolution of serous retinal detachment and shows the presence of numerous hyperreflective intraretinal dots corresponding to increased retinal exudates and outer retinal layer alterations. (**C**) Horizontal SS-OCT scan through the healed area of retinitis and sea-fan fibrovascular lesion shows retinal thickening and inner layer hyperreflectivity with posterior shadowing, along with focal vitreoretinal adhesion (arrows). (**D**, **E**) Magnified fluorescein angiography shows early hyperfluorescence and late profuse leakage from the sea-fan neovascular complex. (**F**, **G**) En face SS-OCT angiography of the superficial retinal plexus shows a well-defined preretinal filamentous vascular complex corresponding to the sea-fan neovascular area. (**H**) B-scan SS-OCTA shows a superficial flat flow signal complex (arrows) under the posterior hyaloid thickening seen on SS-OCT, consistent with preretinal neovascularization

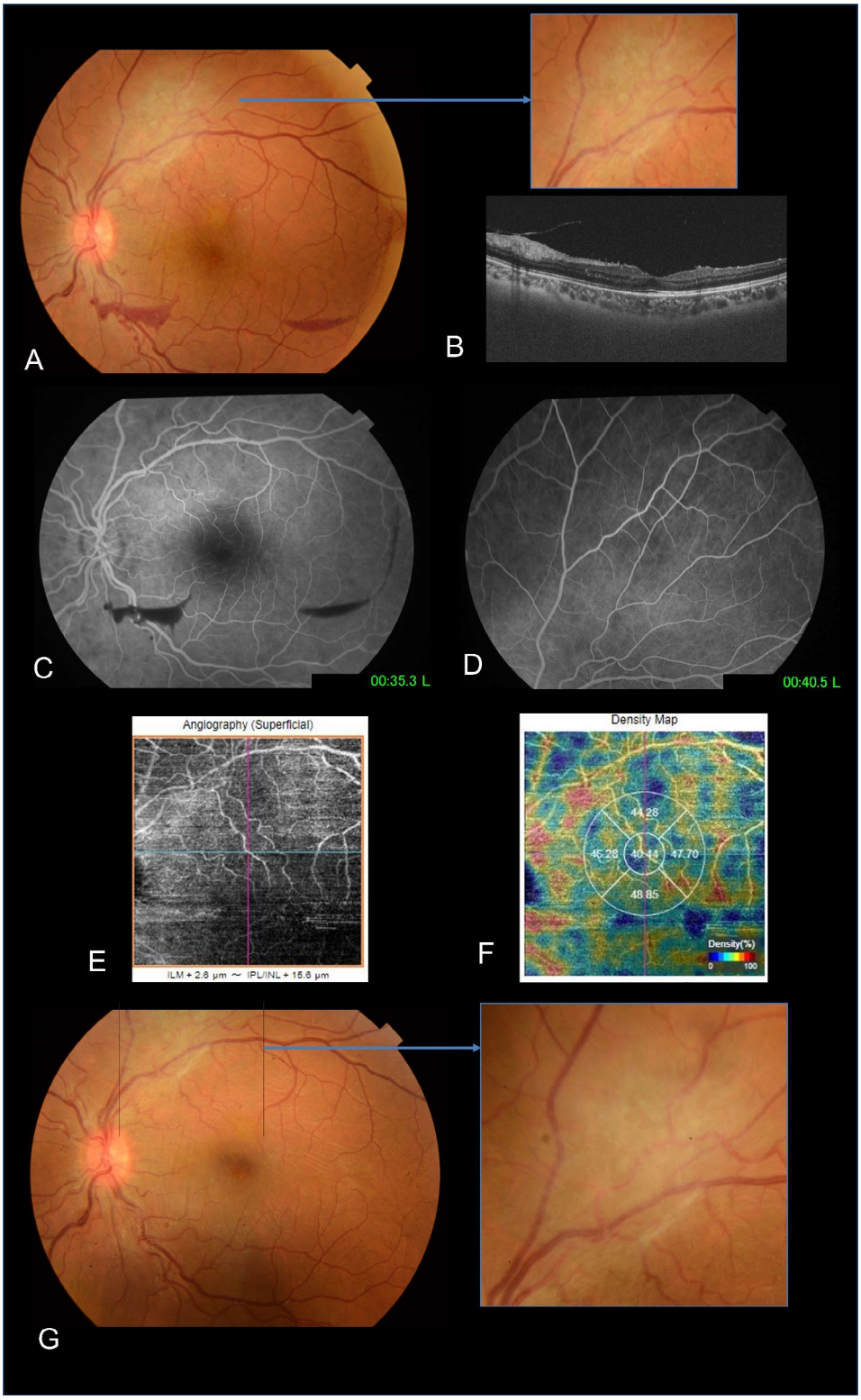

Fig. 3 Multimodal imaging of the left eye after sixteen months. (**A**) Fundus photograph shows a near complete resolution of retinal hard exudates and regression of active sea-fan neovascularization, with a residual fibrotic lesion better visible in the magnified rectangle. Note the presence of persistent small preretinal hemorrhages inferiorly. (**B**) Macular SS-OCT scan shows a near complete restoration of retinal structures with partially detached posterior hyaloid. (**C**, **D**) Fluorescein angiography shows no active retinal neovascularization or capillary non perfusion areas. (**E**, **F**) SS-OCTA confirms the full regression of the preretinal neovascular network. (**G**) Fundus photograph after a further observation period of six months from (**A**) shows a complete regression of retinal hard exudates and resorption of preretinal hemorrhages

Discussion and conclusions

This is an unusual case of retinal neovascularization complicating a rickettsial retinitis documented longitudinally with multimodal imaging, including fundus photography, SS-OCT, fluorescein angiography, and SS-OCT angiography.

A search on pubmed was made using the following keywords: ("rickettsial disease" or "rickettsial infection" or "rickettsiosis") AND ("retinal neovascularization" or "retinitis" or "retinal vasculitis" or "ocular"). There is one published case of retinal neovascularization in a patient with resolving rickettsial retinitis documented with fluorescein angiography six months after initial presentation. No treatment other than doxycycline was given to the patient, and no vitreous hemorrhage occurred over a further follow-up of 6 months [2].

The occurrence of retinal neovascularization also has been recently described in a patient with ocular sarcoidosis and concomitant rickettsial infection, diagnosed based on a Weil-Felix test which has low sensitivity and specificity [4]. This patient was treated with local and systemic corticosteroids, doxycycline, and laser photocoagulation followed by oral methotrexate therapy which resulted in clinical resolution with recovery of visual acuity.

Our patient initially presented with a typical rickettsial unifocal inner retinitis, characterized by focal hyperreflectivity and thickening primarily involving the inner retinal layers on SS-OCT and by early hypofluorescence and late staining on fluorescein angiography. The white retinal lesion was associated with adjacent retinal hemorrhages, a prominent serous retinal detachment surrounded with retinal hard exudates with a partial star pattern, and intraretinal telangiectatic retinal vascular changes, mainly involving the superficial plexus. There was no evidence of associated retinal ischemia on fluorescein angiography. Treatment with doxycycline and oral corticosteroids in our patient was effective in inducing the resolution of the retinal lesion and serous retinal detachment, with however a transient paradoxical increase in retinal exudation. It is noteworthy that at the same time a large sea-fan prereretinal neovascular lesion became evident along the superotemporal arcade over the area of resolved retinitis. The patient received a supplemental single intravitreal bevacizumab injection to address the neovascular complex. Sequential follow-up examinations showed a gradual resolution of the sea-fan neovascular lesion, regression of retinal hard exudates, and the development of a self-limited mild vitreous hemorrhage, and a full visual recovery.

The marked tropism of rickettsial organisms for retinal vasculature has been previously evidenced by the frequent occurrence of retinal hemorrhages, retinal vasculitis, and vascular occlusive events, usually in the form of branch retinal arteriolar occlusion intimately related to a white retinal inflammatory lesion [2, 4–6]. Retinal/optic disc neovascularization is a rare early or late complication of uveitis involving the posterior segment that most commonly occurs in response to retinal ischemia demonstrated on fluorescein angiography or OCT angiography [7]. The growth of abnormal retinal vessels could be stimulated by the release from ischemic retina of pro-angiogenic molecules such as vascular endothelial growth factor (VEGF). Alternatively, neovascularization may occur in the absence of demonstrable retinal ischemia, probably through inflammatory mechanisms. Our findings are consistent with the latter hypothesis. Rickettsial infection of vascular endothelium stimulates cell signaling cascades leading to the secretion of a wide variety of cytokines, chemokines, and other molecules. Some of these inflammatory mediators were found to be involved in endothelial proliferation and pathologic angiogenesis, and this therefore might explain the development of preretinal neovascularization in our patient [8]. The development of vitreous and preretinal hemorrhages during follow-up might result from retinal neovascularization before its complete regression or from posterior vitreous detachment.

Besides medical treatment including anti-inflammatory drugs, peripheral scatter laser photocoagulation is usually recommended in those patients where ischemic retina is driving neovascularization [9]. Conversely, in those patients without ischemia, laser treatment appears less likely to help, and adequate medical therapy alone may induce the regression of retinal neovascularization to effectively prevent vitreous hemorrhage or promote its clearance [10]. Our data, consistent with results of previous reports, show that intravitreal anti-VEGF may be a useful therapeutic option for selected cases of therapy-refractory or aggressive uveitic retinal neovascularization [11, 12]. However, additional studies will be necessary to determine the role of anti-VEGF therapy as adjunctive treatment for patients with uveitis and retinal neovascularization.

This case report has inherent limitations that hinder inference of causal relationships. Additional studies with larger number of patients are needed to further improve clinical knowledge about retinal neovascularization that may occur in patients with rickettsial disease.

In conclusion, patients with rickettsial retinitis may develop sea-fan retinal neovascularization, with subsequent vitreous hemorrhage, putatively through inflammatory mechanisms. Multimodal imaging including OCT, fluorescein angiography, and OCTA, is highly useful for accurate diagnosis and reliable monitoring of the evolution of retinitis, retinal neovascularization, and other retinal changes. The use of a combination therapy with oral doxycycline, corticosteroids, and intravitreal

anti-VEGF can be associated with good anatomical and visual outcomes.

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Author contributions
All authors contributed to the manuscript concept. NA, WN and MM collected data. IK and SBA drafted the manuscript. BJ and MK provided critical manuscript revisions and supervised the study. All authors read and approved the final manuscript.

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Data availability
The datasets used and analyzed in this case report are available from the corresponding author on reasonable request.

Declarations

Ethics approval
This case report was approved by local ethics committee (Faculty of Medicine, Monastir, Tunisia).

Consent for publication
Written informed consent was taken from the patient to publish this case report. Additionally, this report does not contain any personal information that could lead to the identification of the patient.

Competing interests
The authors declare no competing interests.

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References

1. Kawali A, Mahendradas P, Mohan A, Mallavarapu M, Shetty B. Epidemic Retinitis. Ocul Immunol Inflamm. 2019;27(4):571–7.
2. Khairallah M, Ladjimi A, Chakroun M, Messaoud R, Yahia SB, Zaouali S, et al. Posterior segment manifestations of Rickettsia conorii infection. Ophthalmol. mars 2004;111(3):529–34.
3. Kahloun R, Gargouri S, Abroug N, Sellami D, Ben Yahia S, Feki J, et al. Visual loss associated with rickettsial disease. Ocul Immunol Inflamm. oct 2014;22(5):373–8.
4. Mahendradas P, Acharya I, Mishra SB, Sanjay S, Kawali A, Shetty R et al. Bilateral retinal vasculitis due to presumed sarcoidosis with rickettsial retinitis. Eur J Ophthalmol. 13 nov 2023;11206721231212776.
5. Kahloun R, Mbarek S, Khairallah-Ksiaa I, Jelliti B, Yahia SB, Khairallah M. Branch retinal artery occlusion associated with posterior uveitis. J Ophthalmic Inflamm Infect. 21 janv 2013;3(1):16.
6. Ganekal S, Singnal K, Rajappa S, Hegde S. Ocular manifestation of rickettsial disease in South Indian population. Indian J Ophthalmol. mai 2021;69(5):1167–71.
7. Patel AK, Newcomb CW, Liesegang TL, Pujari SS, Suhler EB, Thorne JE, et al. Risk of retinal neovascularization in cases of Uveitis. Ophthalmol. mars 2016;123(3):646–54.
8. Helminiak L, Mishra S, Kim HK. Pathogenicity and virulence of Rickettsia. Virulence. déc 2022;13(1):1752–71.
9. Park SE, Mieler WF, Pulido JS. 2 peripheral scatter photocoagulation for neovascularization associated with pars planitis. Arch Ophthalmol Chic Ill 1960. oct 1995;113(10):1277–80.
10. Sanislo SR, Lowder CY, Kaiser PK, Gutman FA, Zegarra H, Dodds EM, et al. Corticosteroid therapy for optic disc neovascularization secondary to chronic uveitis. Am J Ophthalmol. déc 2000;130(6):724–31.
11. Kurup S, Lew J, Byrnes G, Yeh S, Nussenblatt R, Levy-Clarke G. Therapeutic efficacy of intravitreal bevacizumab on posterior uveitis complicated by neovascularization. Acta Ophthalmol (Copenh). mai 2009;87(3):349–52.
12. Mansour AM, Arevalo JF, Fardeau C, Hrisomalos EN, Chan WM, Lai TYY, et al. Three-year visual and anatomic results of administrating intravitreal bevacizumab in inflammatory ocular neovascularization. Can J Ophthalmol J Can Ophtalmol. juin 2012;47(3):269–74.

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