Case Reports in Ophthalmology

Case Rep Ophthalmol 2023;14:267–273
DOI: 10.1159/000530876
Received: October 31, 2022
Accepted: April 24, 2023
Published online: July 3, 2023

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**Case Report**

# Ocular Syphilis with Retinal and Disc Neovascularization Treated with Bevacizumab: A Case Report

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**Keywords**
Ocular syphilis · Retinal neovascularization · Intravitreal bevacizumab · Vascular dilation · Case report

**Abstract**
We report the findings observed in a young woman with ocular syphilis complicated with retinal and disc neovascularization successfully treated with intravitreal bevacizumab. Fluorescein angiography revealed in both eyes intense hyperfluorescence at the level of the disc, multifocal venous wall staining, multifocal paravenous leakage, multiple peripheral saccular venular dilations, diffuse retinal and macular edema, and retinal and disc neovascularization. There was no evidence of retinal ischemia in both eyes. After antibiotic and corticosteroid treatment, the neovascularization persisted in both eyes. Three consecutive doses of intravitreal bevacizumab were administered, with total regression of the retinal and disc neovascularization. Disc and retinal neovascularization along with nonocclusive retinal vasculitis may be a form of presentation of ocular syphilis. Combination of specific treatment, oral corticosteroids, and intravitreal bevacizumab may be useful for treating this clinical manifestation.

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## Introduction

Syphilis is a sexually transmitted infectious disease caused by *Treponema pallidum*, a spirochete [1]. Since the introduction of the antiretroviral therapy against human immunodeficiency virus at the beginning of this century, its incidence has been increasing significantly

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[2]. It can involve any part of the body. Uveitis is the most common ocular manifestation of this infection [3]. While retinal and/or disc neovascularization can occur as complications of different etiologies of infectious and noninfectious posterior uveitis [4–6], there is scarce information about them occurring in ocular syphilis [2, 7].

In this report, we describe a case of a young female with ocular syphilis whose presenting signs include retinal and disc neovascularization as well as its management. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000530876).

## Case Report

A 21-year-old female patient was admitted to the ophthalmology eye emergency room at Hospital Alemán with complaints of floaters ("red spots") in her left eye, which began the previous day. She denied any other associated visual symptoms.

At ocular examination, best corrected visual acuity was 20/20 and 20/40 in her right (OD) and left (OS) eyes, respectively. Slit lamp examination of the anterior segment was unremarkable in both eyes (OU). The intraocular pressure was 13 mm Hg in OU.

Fundus examination revealed disc swelling, dilated retinal veins, multiple peripheral venular saccular dilations, scattered cotton wool spots, retinal and disc neovascularization in OU. In OD, the vitreous was clear, while a vitreous hemorrhage was observed in OS (Fig. 1). Fluorescein angiography revealed in both eyes intense hyperfluorescence at the level of the disc, multifocal venous wall staining, multifocal paravenous leakage, multiple peripheral saccular venular dilations, diffuse retinal and macular edema, and retinal and disc neovascularization. In addition, posterior pole venular and arteriolar saccular dilations were also present in OD (Fig. 2). There was no evidence of retinal ischemia in OU.

Considering a presumptive diagnosis of retinal vasculitis, a complete blood count, liver function test, blood urea nitrogen, creatinine, fasting blood glucose level, erythrocyte sedimentation rate, C reactive protein, venereal disease research laboratory (VDRL), fluorescent treponemal antibody absorption test (FTA ABS), PPD, HIV, brain magnetic resonance imaging with and without gadolinium, and spinal tap with measurement of the opening pressure were ordered. Laboratory results revealed a positive FTA ABS and a VDRL titer of 1:512. VDRL was negative in the cerebrospinal fluid. She was treated with 4 million units of intravenous penicillin G every 4 h for 2 weeks. Meprednisone was also added, at an initial dose of 1 mg/kg/day for 3 weeks, with a gradual tapering until its discontinuation 2 months later. Two weeks after the end of the antibiotic treatment course, BCVA in OD was 20/20, and in OS, it improved to 20/20. Fundus examination revealed persistence of the retinal and disc neovascularization. Therefore, monthly dose of 1.25 mg/0.05 mL of intravitreal bevacizumab was administered for 3 months. Fluorescein angiography after the third dose revealed a dramatic reduction of retinal and disc neovascularization, with disappearance of retinal vasculitis, although a mild retinal edema and papillitis persisted in both eyes (Fig. 3). At 1 year of follow-up, bilateral BCVA remained in 20/20. Fundus examination did not reveal abnormalities.

## Discussion

Ocular syphilis has a wide range of clinical manifestations. It may be unilateral or bilateral, and it can involve anterior, intermediate, or posterior segments [8]. Different case series have shown disparate predominant types of syphilitic uveitis [1, 9, 10]. Barile and Flynn


**Fig. 1. a** Color fundus photography of the right eye shows a clear vitreous with optic disc neovascularization, posterior pole cotton wool spots, and a hyperemic disc. **b** Color fundus photography of the left eye shows a vitreous hemorrhage, with a hyperemic disc.

reported in a series of 24 patients that granulomatous iridocyclitis was present in 46% of cases [9]. Amaratunge et al. [1], in their series of 143 patients, have shown that 55.2% of the cases were of posterior uveitis and 25.2% were of panuveitis.

Posterior segment involvement of ocular syphilis englobes a great variety of manifestations such as superficial retinal precipitates, exudative retinal detachment, acute syphilitic placoid posterior chorioretinopathy, papillitis, vasculitis, neuroretinitis, chorioretinitis, and retinitis [3, 11]. Villanueva et al. [10], in a retrospective case series of 20 patients with syphilitic posterior segment involvement, have shown that 10% of the patients had retinal vasculitis. Furtado et al. [12] found retinal vasculitis in 25% of their syphilitic patients. In ocular syphilis, occlusive retinal vasculitis occurs unfrequently, with a range of reported percentages between 0 and 25% of the patients [12, 13]. In the present case, retinal ischemia was not observed.

To our knowledge, there are few reports on retinal and disc neovascularization occurring in ocular syphilis [2, 7]. Trechot et al. [2] described a case of ocular syphilis which developed optic disc neovascularization, with neither retinal vasculitis nor retinal ischemia. In this case, neovascularization was successfully treated with antibiotic therapy, steroids, and intravitreal bevacizumab. Recently, Miura et al. [7] described a case of ocular syphilis complicated with optic disc neovascularization associated to peripheral retinal ischemia. The patient required intravitreal bevacizumab followed by a panretinal laser photocoagulation to fully control this complication. In the present case, retinal vasculitis was observed, which was complicated with optic disc and retinal neovascularization without detection of retinal ischemia.

Retinal neovascularization can occur rarely in uveitis (less than 1% of the cases) either in the presence or absence of retinal ischemia [6]. Inflammation without ischemia can lead to neovascularization. At a molecular level, IL-1β and TNF-α can promote angiogenesis and endothelial proliferation. IL-6 and IL-8 are also associated to neovascularization development [6]. These facts are related with the rationale for the use of steroids and immunosuppressive treatment in inflammatory retinal neovascularization associated to nonischemic retina [6].

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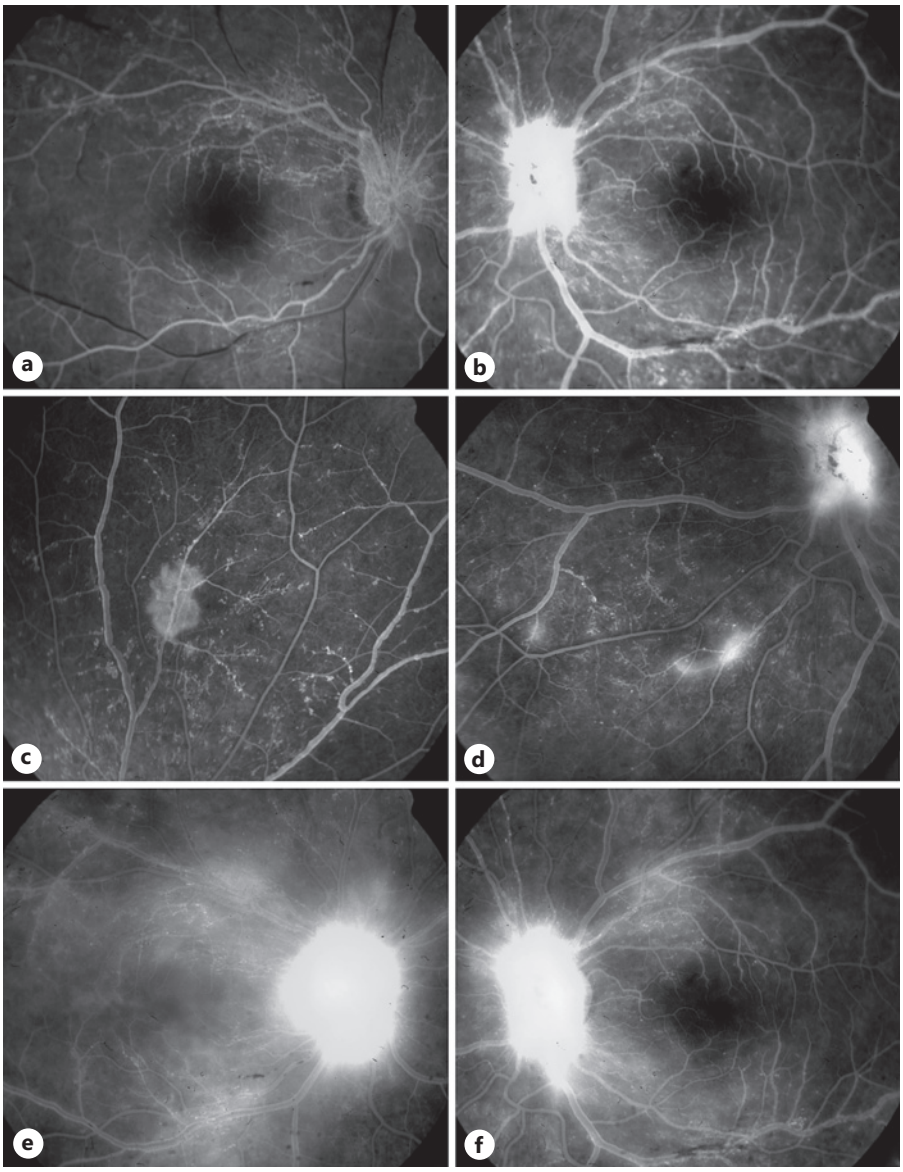


**Fig. 2.** Fluorescein angiography of both eyes at presentation. In the arteriovenous frames, disc (**a**, **b**) and retinal (**c**, **d**) neovascularization can be seen. In (**a**, **b**) and (**c**, **d**), numerous saccular venular dilations can be observed. In (**a**), arteriolar saccular dilations can also be seen. In the late frames (**e**, **f**), a strong leakage of the disc neovascularization can be appreciated, along with staining of the vessel walls and segmental paravascular leakage.

Recently, the *Treponema pallidum* antigen TpF1 was shown to induce angiogenesis through the activation of the IL-8 pathway [14]. Interestingly, in the case described by Trechot et al. [2], the specific antibiotic treatment along with steroid therapy and intravitreal bevacizumab was successful in achieving a complete regression of the disc neovascularization. Likewise, in the present case, antibiotic therapy along with high-dose steroid treatment and intravitreal bevacizumab was enough to treat successfully retinal neovascularization. Paroli et al. [15] have shown elevated levels of VEGF in the aqueous humor of eyes with quiescent uveitis. Therefore, in case of persistent retinal neovascularization after anti-inflammatory treatment, anti-VEGF therapy has its rationale. Mansour et al. [5], in a multicenter retrospective study, have

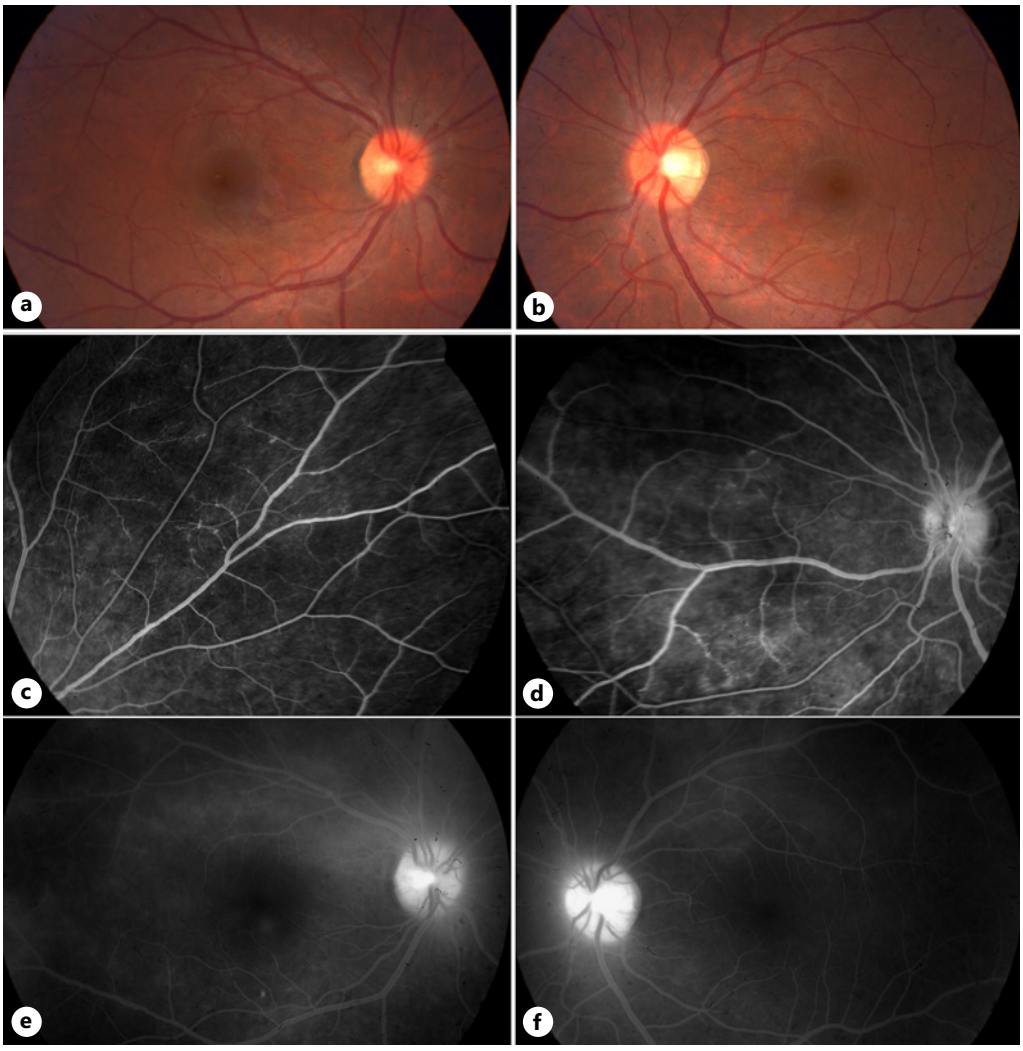


**Fig. 3.** **a**, **b** Color fundus photographs of both eyes. The bilateral disappearance of the discal neovascularization and the saccular dilations. **c**, **d** Arteriovenous frames of the fluorescein angiogram. The disappearance of the retinal neovascularization. There is also a significant regression of the saccular dilations. **e**, **f** Late frames of fluorescein angiography at the posterior pole reveal the disappearance of disc neovascularization, with persistence of papillitis and a mild diffuse macular edema in both eyes. There is also a complete disappearance of the saccular dilations.

shown that in patients with uveitis for whom corticosteroids or immunosuppression failed to control disc or retinal neovascularization, the administration of only one injection of bevacizumab achieved complete regression in 63.6% of the eyes. In spite of the fact that the published data about the use of anti-VEGF therapy for disc or retinal neovascularization in patients with uveitis are scarce, the rationale of its administration is compelling, and the results are promising.

As far as we know, venous and arterial saccular dilations associated with ocular syphilis have not previously been reported in the literature. There is only one description about the presence of telangiectasia in a case report of ocular syphilis with posterior segment involvement with some signs of ischemia [16]. Usually, vascular dilations (i.e., macro and microaneurysms, telangiectasia) associated with uveitis occur in the ischemic retina [17]. IRVAN, an archetypical example, is a rare condition characterized by occlusive retinal arteritis, peripheral retinal ischemia, neuroretinitis, and multiple leaking aneurismal dilatations at retinal

arterial bifurcations and over the optic nerve head. Resolution of these vascular dilations was reported with the use of corticosteroids, laser photocoagulation of the ischemic retina, and even spontaneously [17, 18]. In the present case, no clinical evidence of retinal ischemia was found. There are several reports on retinal vascular dilations in uveitis without signs of retinal ischemia. Interestingly, microvascular dilations (parafoveal capillary telangiectasia) were observed in patients with Behcet disease without evident inflammatory ocular involvement. Moreover, in ocular sarcoidosis, an association of macroaneurysms and multifocal choroiditis was also reported [17]. The pathogenesis of these dilations is not clear. Ischemia and, frequently, inflammation occur with high levels of VEGF [19, 20]. In the present case, the saccular dilations resolved with a combination of antibiotic therapy, high doses of corticosteroids, and anti-VEGF treatment. Therefore, we may hypothesize that a mechanism triggered by inflammatory and angiogenic stimuli may have contributed to their development.

As a counterpart, the opportunity to perform an assessment with ultra-wide-field fluorescein angiography in the present case was not available. Therefore, it was not possible to detect ischemia in extreme periphery. However, the persistent long-term resolution of retinal neovascularization and vascular saccular dilations after 3 consecutive monthly injections of intravitreal bevacizumab without the need for laser photocoagulation supports the inflammatory origin of the angiogenic phenomena.

In conclusion, disc and retinal neovascularization associated to vascular saccular dilations, along with nonocclusive retinal vasculitis, may be a form of presentation of ocular syphilis. Combination of specific treatment, oral corticosteroids, and intravitreal bevacizumab may be useful for treating this clinical manifestation.

## Statement of Ethics

This case report was reviewed, and the need for approval was waived by the Institutional Review Board of Hospital Aleman de Buenos Aires. Written informed consent was obtained from the patients for publication of the details of their medical case and any accompanying images. Please note that patient identities will be treated confidentially.

## Conflict of Interest Statement

Lucia Comastri, Milagros Heredia, Diego Bar, and Guillermo Iribarren have no conflicts of interest to declare. Ariel Schlaen served as speaker for ABBVIE.

## Funding Sources

There was no funding or grant support.

## Author Contributions

Lucia Comastri and Ariel Schlaen drafted the manuscript. Milagros Heredia, Diego Bar, and Guillermo Iribarren contributed to acquisition of data of the clinical record and imaging. Lucia Comastri, Ariel Schlaen, Milagros Heredia, Diego Bar, and Guillermo Iribarren revised the draft critically and approved the final version.

## Data Availability Statement

Due to privacy and ethical concerns, neither the data nor the source of the data can be made available. All data that support the findings of this study are included in this article. Further inquiries can be directed to the corresponding author.

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