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Choroidal Neovascularization Associated with Punctate Inner Choroidopathy: Combination of Intravitreal Anti-VEGF and Systemic Immunosuppressive Therapy

Bettina Hohberger Michael Rudolph Antonio Bergua

Department of Ophthalmology and Eye Hospital, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, Germany

Key Words

Punctate inner choroidopathy · Choroidal neovascularization · Intravitreal anti-VEGF therapy · Choroiditis

Abstract

Purpose: Choroidal neovascularization (CNV) associated with punctate inner choroidopathy (PIC) is a rare clinical entity, yet still a challenge for medical treatment. A case of a young myopic woman developing CNV secondary to unilateral PIC is presented. Clinical morphology, diagnostic procedure and follow-up are reported. ***Case Report:*** A 29-year-old woman presented with multiple yellowish dots at the posterior pole. No other signs of inflammation could be seen. Angiography with fluorescein yielded hyperfluorescent signals in the affected areas with a diffuse leak, and SD-OCT showed a slightly elevated retinal pigment epithelial layer, consistent with the diagnosis of PIC. Additionally a classic CNV was observed. ***Results:*** Anti-inflammatory therapy with local prednisolone acetate eye drops in combination with intravitreal injection of anti-vascular endothelial growth factor (VEGF, bevacizumab) yielded an increased best-corrected visual acuity. As CNV reappeared, systemic medication with prednisone and azathioprine in combination with two further intravitreal injections of anti-VEGF stabilized CNV and increased visual acuity again. ***Conclusion:*** Combined therapy of immunosuppression with intravitreal anti-VEGF injections can be considered as therapeutic strategy in the management of recurrent CNV associated with PIC.

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Prof. Dr. med. Antonio Bergua
Department of Ophthalmology and Eye Hospital
Friedrich-Alexander-University Erlangen-Nuremberg
Schwabachanlage 6, DE–91054 Erlangen (Germany)
E-Mail antonio.bergua@uk-erlangen.de

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Introduction

Punctate inner choroidopathy (PIC) [1], an idiopathic primary choriocapillaritis, affects especially young myopic women [2]. Multiple yellowish white dots (100–300 μm) can aggregate in the inner choroid or retinal pigment epithelial layer, resulting in exudative retinal detachment [1, 3]. Choroidal neovascularization (CNV) secondary to PIC is the most vision-impairing complication next to subretinal fibrosis [2, 4]. Due to CNV maculopathy, reduced visual acuity, loss of central visual field and photopsia occur [1]. Clinical diagnosis is based on funduscopy, angiography with fluorescein (FA) or indocyanine green (ICGA) and spectral-domain optical coherence tomography (SD-OCT). Additionally autofluorescence images can provide further information due to autofluorescent spots in active and hypofluorescent spots in scar regions [5].

We report about a young myopic woman with unilateral CNV associated with PIC. The clinical features, diagnostic procedure and follow-up are presented.

Case Report

A 29-year-old woman was referred to our Department of Ophthalmology with impaired visual acuity, photopsia and a central scotoma at her right eye (RE) for 2 weeks. Neither operation nor laser surgery was done before, and no additional ocular or systemic diseases were known. Best corrected visual acuity (BCVA) was 0.3 (RE, –8.50 sph) and 1.0 at the left eye (LE, –6.50 sph). Intraocular pressure was normal. Funduscopy of RE showed 'vitreoretinal glitter' (*Glitzerbeete*) at the inferior part of the retina and multiple yellowish dots at the posterior pole without other signs of inflammation (fig. 1a), being hyperfluorescent (early phase) with a diffuse leak (late phase) in FA (fig. 2a). SD-OCT showed a slightly elevated retinal pigment epithelial layer (fig. 1b). Blood chemistry and count (except decreased basophil granulocytes) as well as immunoglobulins (IgM and IgG) for *Borrelia burgdorferi*, *Treponema pallidum* (TPHA) were normal. Starting with an anti-inflammatory therapy (prednisolone acetate eye drops) in our policlinic resulted in a discrete improvement of BCVA (0.5 RE) after already 4 days until 0.8 BCVA after 2 months. As paracentral scotoma occurred at that point of follow-up, further FA revealed a classic CNV. ICGA showed a hypofluorescent signal (fig. 2b). Because of this CNV, an intravitreal injection of anti-vascular endothelial growth factor (VEGF, bevacizumab, 1 mg/0.05 ml) was administered, stabilizing BCVA at 0.8–1.0 in the following months. Local antiglaucomatous drops were added as intraocular pressure increased (30 mm Hg). Three months after the first anti-VEGF injection, the patient was referred again because of spreading of central scotoma (RE: BCVA 0.8). FA revealed a new activity of the classic CNV. Now a systemic anti-inflammatory therapy with prednisone (120 mg) and azathioprine (2 mg/kg body weight/day) was started. Two more intravitreal injections of bevacizumab (1 mg/0.05 ml, BCVA at injection 2: 0.5; BCVA at injection 3: 0.8; RE) were administered. Under this therapy, BCVA was stabilized at 0.8 (RE) for 5 months. Afterwards BCVA decreased again (0.2) with recurrence of CNV and increased spreading in the central part of the fovea. On the patient's demand, no further intravitreal injection of anti-VEGF was done, but local and systemic therapy were continued. BCVA stabilized at 0.5 under azathioprine and tapered prednisone medication without CNV activity in SD-OCT.

Discussion

CNV is a common complication in PIC disease. Rates of 69–75% were reported in the literature [5], yet treatment is still a challenge. Only few cases have been published reporting the use of local or systemic anti-inflammatory medications (e.g. corticosteroids, immunomodulators), argon laser photocoagulation, photodynamic therapy (PDT), retinal surgery of CNV or intravitreal anti-VEGF injections.

Systemic corticosteroids were applied successfully in the treatment of juxtafoveal (BCVA increase 1/10–6.7/10 [6]) and subfoveal CNV (average BCVA increase 6/18–6/12 [7]). The frequency of recurrent PIC can be reduced by immunomodulators like mycophenolate mofetil [8]. Laser photocoagulation is discussed controversially because of an increased risk of generating CNV, scare growth and the potential of reaching foveal structures [9]. Alternatively, PDT was shown to increase BCVA and stabilize CNV [10]. An increase in BCVA was also observed for the combination of PDT with systemic corticosteroids (mean: 8.6 letters, follow-up 12 months, number of PDT: 2 [11]) or with intravitreal triamcinolone (BCVA 0.52–0.20, follow-up 12 months [12]). Submacular surgery can be considered for subfoveal CNV, yet a 66.7% recurrence of CNV was reported [13]. No studies are available for surgical treatment of extrafoveal CNV at this moment. A further option in medical treatment offers the off-label application of anti-VEGF injections. Either bevacizumab (1.25 mg/0.05 ml [14]) or ranibizumab (0.5 mg/0.1 ml [15]) resulted in an improved BCVA (mean: 64–85 ETDRS letters, follow-up 87.2 weeks [15]).

In our patient, after resolution of the acute PIC inflammation, resulting in a rapid increase of BCVA from 0.3 to 0.8, a classic CNV decreased BCVA due to macula involvement. An intravitreal anti-VEGF injection (bevacizumab) was given, and BCVA increased up to 1.0. After 3 months, a recurrence of CNV occurred, systemic immunosuppression was intensified (prednisone and azathioprine), and two additionally bevacizumab injections were applied. BCVA increased again up to 0.8. A further recurrence of CNV after 5 months (BCVA 0.2) was treated without anti-VEGF injection (considering the patient's desire), but with continuation of local and systemic immunosuppression, resulting in a lasting improvement of BCVA (0.5) and stabilizing CNV in SD-OCT. It is not a matter of course that a combined therapy, as in the presented case, does always lead to this good visual outcome. Whether a combination of distinct therapeutic options, a single medical treatment or a simple 'wait and see' regime is the best therapy for PIC remains open, as PIC can also show a spontaneous resolution.

Conclusion

Combined therapy of immunosuppression with intravitreal anti-VEGF injections should be considered as therapeutic strategy in the management of recurrent CNV associated with PIC.

Statement of Ethics

The patient has consented to the submission of the case report for submission to this journal.

Disclosure Statement

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, participation in speakers' bureaus, membership, employment, consultancies, stock ownership, or other equity interest, and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this paper.

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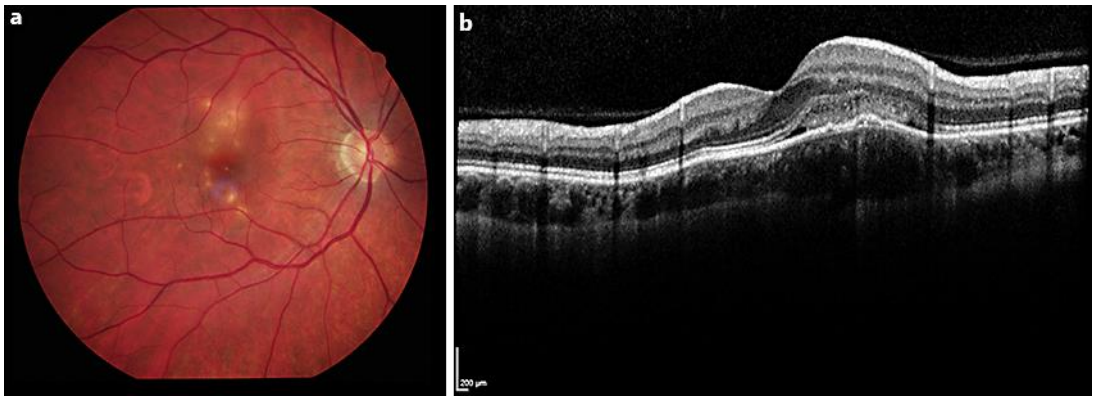

Fig. 1. Fundus photography and SD-OCT images of the right eye at the first visit (**a**, **b**). **a** Posterior pole with multiple yellowish dots. **b** SD-OCT image yielding a juxtafoveolar intraretinal edema as well as a slightly elevated retinal pigment epithelium.

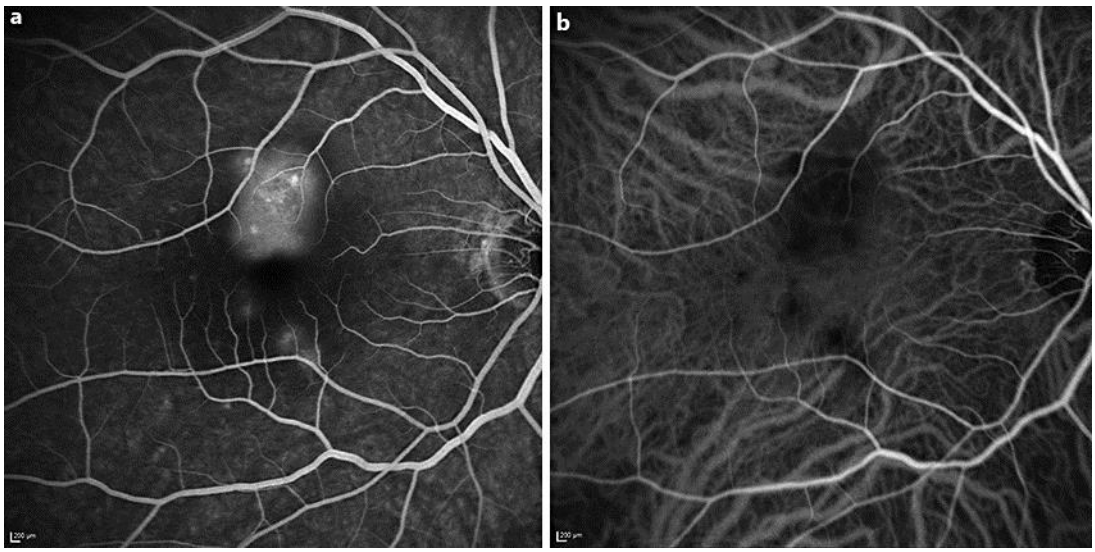

Fig. 2. Angiography with fluorescein (**a**) and indocyanine green (**b**) of the right eye. **a** Fluorescein angiography: circumscribed leakage increased in an area of the yellowish dots (late phase, 4:53 min). **b** Indocyanine green angiography: hypofluorescent signals corresponding to the hyperfluorescent angiographic ones (after 2:18 min).