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CASE REPORT

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Eye toxoplasmosis complicated by choroidal neovascularization effectively treated with the anti-vascular endothelial growth factor aflibercept

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ABSTRACT

The aim of the study was to present a case of choroidal neovascularization (CNV) secondary to post-inflammatory scar caused by ocular toxoplasma, effectively treated with one intravitreal injection of anti-vascular endothelial growth factor therapy (anti-VEGF), aflibercept.

Case report: A case of a 44 year-old woman with choroidal neovascularization secondary to a post-inflammatory scar caused by ocular toxoplasma is described. The diagnosis was made on the basis of medical history, fundus examination (VOLK Digital Wide Field), fluorescein angiography (CARL ZEISS Visucam Lite Fundus Camera), and optical coherence tomography (NIDEK RS-3000 OCT and REVO NX OCT OPTOPOL). Treatment with intravitreal injection, anti-VEGF (aflibercept), was applied.

After aflibercept treatment the following results were obtained: partial constriction of choroidal neovascularization, choroidal neovascularization borders became clearer, particularly from the top, nose, and temples. Visual acuity improved after one intravitreal injection of the anti-vascular endothelial growth factor therapy aflibercept. Subjective eye symptoms improved.

Optical coherent tomography of an eye the second day after intravitreous injection of aflibercept presented resorption of subretinal fluid with reduction of retinal thickness and characteristic increase in reflexibility of choroidal neovascularization.

Conclusions: The reported case confirms that secondary CNV to the post-inflammatory scar is a rare complication of toxoplasmosis retinitis and choroiditis and should be considered in the diagnosis. OCT and fluorescein angiography play an important role in the diagnosis of choroidal neovascularization secondary to a post-inflammatory scar caused by ocular toxoplasmosis. Intravitreal anti-VEGF injection therapy is an available, effective, and safe method of choroidal neovascularization secondary to the post-inflammatory scar caused by ocular toxoplasma. Treatment with intravitreal anti-VEGF injection improves retinal anatomy and visual function.

KEY WORDS: eye toxoplasmosis, post-inflammatory scar, active choroidal neovascularization, anti-vascular endothelial growth factor, intravitreal injection, optical coherence tomography.

INTRODUCTION

Toxoplasmosis is caused by the intracellular protozoa *Toxoplasma gondii*, for which a cat is the final host. Indirect hosts may be mammals (sheep, cattle, pigs, horses, dogs, mice), birds, or people [1, 2]. The human eye may be infected with *Toxoplasma gondii* by: consumption of oocysts residing on unwashed (or washed in non-boiled water) vegetables and fruit; oocysts located in raw milk or on dirty hands; consumption of tissue bradyzoites (an inactive form of protozoa presents in skeletal muscles, eyes, brain) present among others in raw, undercooked or dry meat [1, 2].

Transplacental infection of the fetus during active toxoplasmosis infection in pregnancy [1, 2].

Blood transfusion, during organ transplantation, as well as during work with biological materials in a laboratory [1, 2].

Toxoplasmosis is rarely recognized, because of the asymptomatic course. About 20% of toxoplasmosis patients report influenza-like symptoms, enlargement of lymphatic glands, bone and joint pain, influenza-like symptoms [1, 2]. Toxoplasma retinitis and choroiditis proceeds as single, fluffy-yellow inflammatory locus at the retina and choroidea, located predominantly in the back pole. Frequently, an eye

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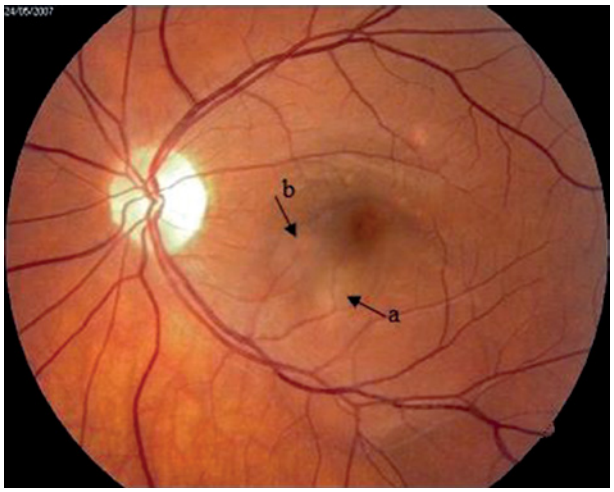

Figure 1. The eye toxoplasmosis (a female patient, year 2007). There are visible larger (a) and smaller (b) yellowish inflammatory focuses

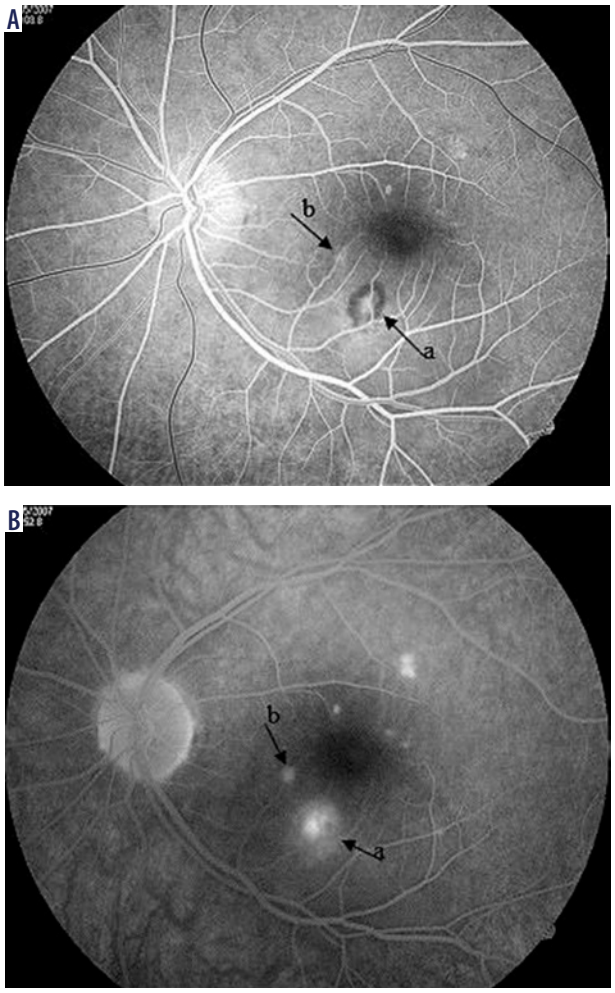

Figure 2. Fluorescein angiography of the eye toxoplasmosis in a female patient (year 2007). **A**) Early stage of fluorescein angiography showing hypofluorescent inflammatory focuses, transformed in visible, subsequently stepwise growing and spilled hyperfluorescence (leak of dye) in angiography from inflammatory focus (a – larger focus, b – smaller focus), **B**) late stage of fluorescein angiography

inflammatory locus is accompanied by an inflammatory reaction in the anterior chamber and vitreous body chamber. Eye toxoplasmosis has a chronic recurrent-remissive nature. In the case of toxoplasma recurrence, the fresh inflammatory focus is located in the area of the old stained post-inflammatory scar. In the case of hypoimmunity patients (e.g. HIV) multiple inflammatory focuses form independently from old scar, possibly affect both eyes and have a rapid course [1, 2]. After resolution of toxoplasma eye inflammation (after about 2-6 weeks) there is an atrophic oval scar with the pigmented periphery, compromising vision [2].

AIM

The paper aims to present a case of choroidal neovascularization secondary to post-inflammatory scar caused by ocular toxoplasma, treated by intravitreous injection of a VEGF inhibitor (aflibercept).

CASE PRESENTATION

A 44-year-old woman, with complaints of deterioration of left eye vision caused by a dark stain in the central visual area, was readmitted to the Ophthalmic Department of the Provincial Hospital in Białystok in September 2018.

During her first hospitalization (in 2007) she was diagnosed with toxoplasma inflammation (recognized by typical retinal clinical findings and IgM antibodies present in blood serum) of the retina and choroidea of the left eye (according to patient records): at admission Vol = 0.5 cc-0.5 Dsph = 1.0; after discharge from hospital Vol = 1.0 s.c., frontal part of the left eye was normal. On the eyeground of the left eye (Figure 1) a flat, pale, clear-cut pink disc of the second nerve was visible. Blood vessels of the retina had normal shape and caliber. The retinal macula was swollen and below the pit were visible different-sized yellowish inflammatory focuses. Fluorescein angiography (Figure 2) showed hypofluorescent inflammatory focuses, transformed in visible, subsequently stepwise growing, and spilled hyperfluorescence. After efficient pyrimethamine and spiramycin treatment, the woman was discharged from the hospital. Between 2007 and 2018 when the patient was under ophthalmic control, there were no noted relapses of toxoplasmosis.

At admission to the Ophthalmological Department of the Provincial Hospital in Białystok in September 2018: Vol = 0.016 cc-1.25 Dsph = 0.1; and at discharge from hospital: Vol = 0.1 cc-1.25 Dsph = 0.25. Hospital admission, the frontal part of the left eye was normal and on the eyeground of the left eye (Figure 3) a flat, pale, clear cut a pink disc of the second nerve was visible. Blood vessels of the retina had normal shape and caliber. In the retinal macula below the pit, there was an old post-inflammatory scar (Figure 3B) with adjacent CNV fibromatous about 1.5 DD with marked but blurred borders (Figure 3, a). In the direction of the nose from after inflammatory scar with accompanying adjacent CNV (Figure 3, a) there was a visible singular retinal hemorrhage (Figure 3, d). In the direction of the temple, there were observed fenestrated defects in retinal pigment epithelium (RPE) (Figure 3, c).

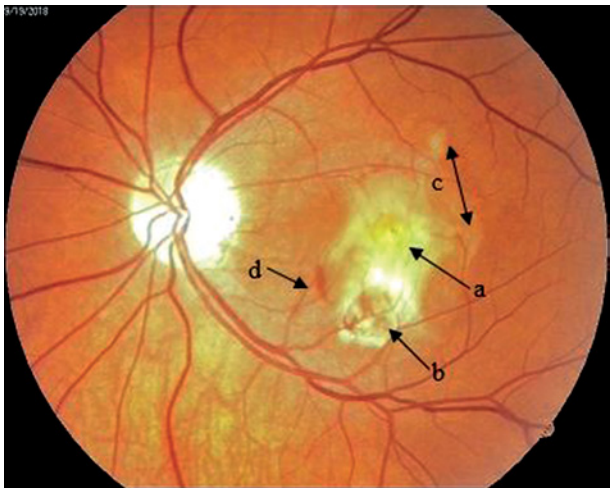

Figure 3. The fundus of the eye of a female patient with toxoplasmosis (September 2018) before aflibercept treatment. Choroidal neovascularization (a); after inflammatory scar (b); fenestrated defects in retinal pigment epithelium (c); retinal hemorrhage (d)

Optical coherent tomography (OCT) of retinal macula of the left eye before intravitreal injection of aflibercept (Figure 4) demonstrated an area of increased reflectiveness under the pit, corresponding to choroidal neovascularization (Figure 4, a) with accompanying fluid space under the neurosensory retina (Figure 4, b); around the retina, photoreceptor atrophy is visible (Figure 4, c); with low reflectiveness. Retinal thickness (Figure 4, d).

Fluorescein angiography (Figure 5) at early stages shows about 2 dd area of hypofluorescence at the back pole of the left eye with the clear border that is covered by a hyperfluorescent area (CNV) (Figure 5A) in subsequent stages of angiography; an old post-inflammatory scar adheres to the bottom of the hyperfluorescent area (Figure 5B); in the nasal direction from the hyperfluorescence area a small focus of hypofluorescence caused by blood blocking fluorescein passage is visible (Figure 5D).

Anamnesis and clinical pictures (Figures 3, 4, and 5) diagnosed the choroidal neovascularization secondary to the post-inflammatory scar caused by ocular toxoplasmosis. A fresh, fluffy, yellow chorioretinitis inflammatory focus was not observed, so recurrent eye toxoplasmosis was excluded and antiparasitic therapy was not applied. It was decided to treat CNV secondary to post-inflammatory scar by anti-VEGF (aflibercept 2 mg [0.05 ml]) injection. After intravitreous injection of the VEGF inhibitor (aflibercept), clinical improvement of the patient was observed. Figure 6 shows on the first day after intravitreous injection of aflibercept, a visible partial constriction of choroidal neovascularization (Figure 6a). CNV borders became clearer, particularly from the top, nose, and temple (Figure 6a).

The OCT of the eyeground on the second day after intravitreous injection of aflibercept (Figure 7) presented total resorption of subretinal fluid with reduction of retinal thickness and characteristic increase in reflexibility of choroidal neovascularization (increase in the fibrous component of the neovascular membrane).

The patient was recommended constant ophthalmological care. The patient was instructed to visit the Ophthalmology Clinic in the event of deteriorating eyesight or disturbing symptoms to continue the treatment. From 2018, the patient did not need a follow-up visit. As part of checking the effects of treatment with an intravitreal injection, a follow-up visit was planned on April 27, 2021. During the visit, the patient did not report any deterioration of vision. According to the patient, the vision has been stable since 2018. During the visit,

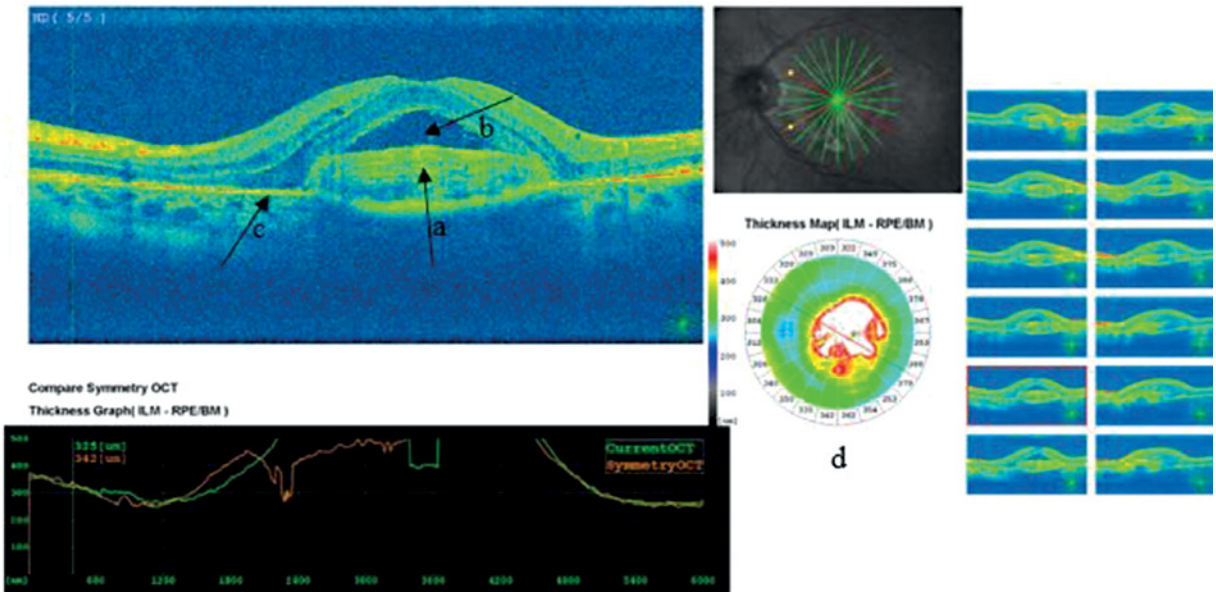

Figure 4. OCT of the left eye retinal macula of the female patient with toxoplasmosis before intravitreal injection of aflibercept. Area of increased reflexibility corresponding to choroidal neovascularization (a), fluid space with low reflexibility under the neurosensory retina (b); retinal photoreceptors atrophy (c), retinal thickness (d)

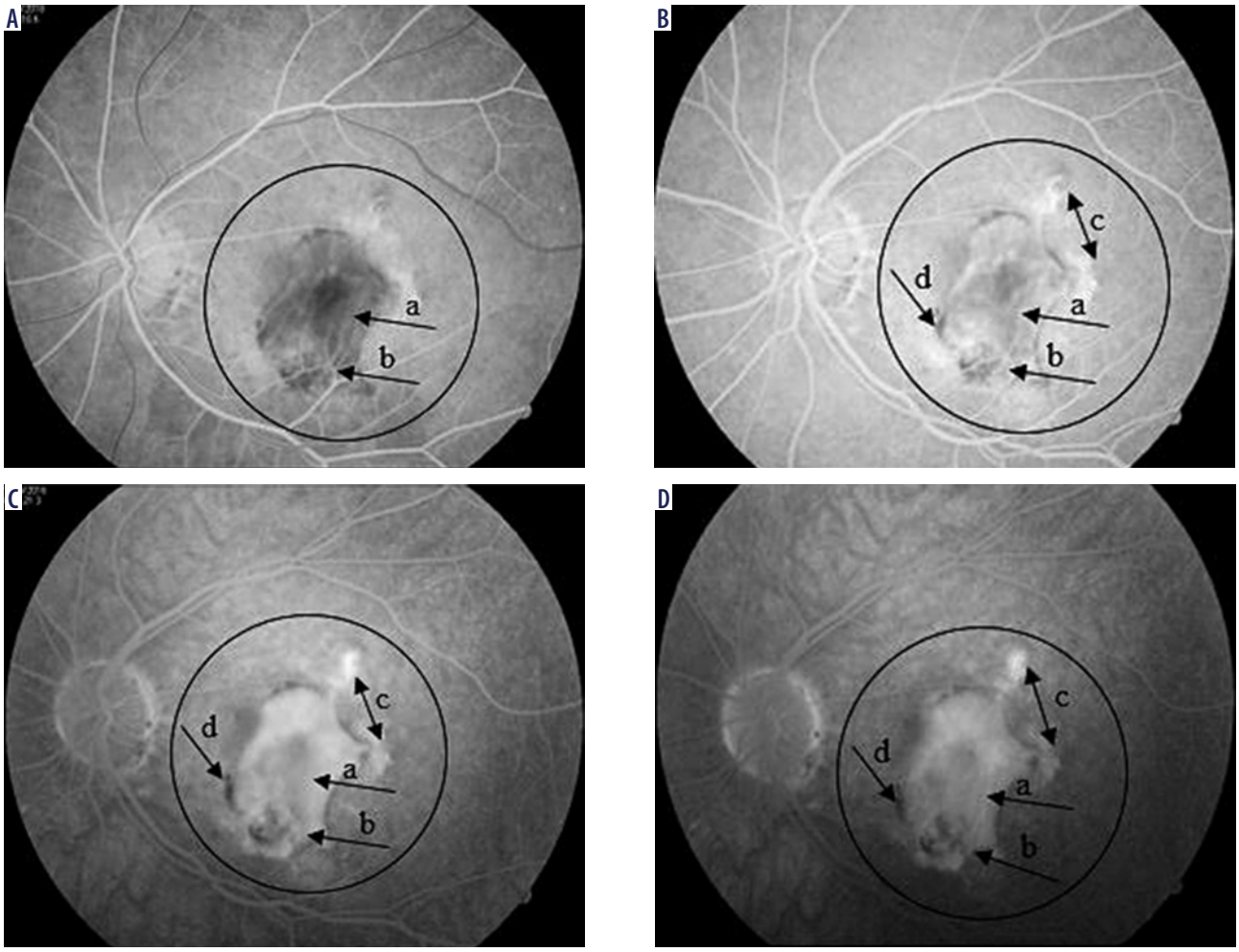

Figure 5. Fluorescein angiography of the female patient with choroidal neovascularization secondary to a post-inflammatory scar caused by ocular toxoplasma before treatment. **A**) 10 second, arterial phase of angiography; **B**) 18 seconds, venous phase of angiography; **C**) 1 minute 21 seconds, late recirculation phase of angiography; **D**) 5 minutes 5 seconds, late recirculation phase of angiography. Choroidal neovascularization (a); post-inflammatory scar (b); retinal pigment epithelial window defect (c); retinal hemorrhage (d)

the vision was stable: Vol = 0.1 cc-1.25 Dsph = 0.25, the macular OCT was performed: inactive secondary post-inflammatory neovascular membrane (Figure 8), the fundus – inactive post-inflammatory neovascular scar. The clinical picture was considered stable. The next visit was planned for 6 months. In the event of deterioration of vision or disturbing symptoms, report before the planned check-up visit.

DISCUSSION

Choroidal neovascularization depends on the proliferation of blood vessels from the choroidea through the Bruch membrane and retinal pigment epithelium under the neurosensory retina [3]. Secondary CNV on the post-inflammatory scar is a rare complication of toxoplasmosis retinitis and choroiditis. CNV significantly impairs patient vision leading eventually to loss of vision [3].

Korol *et al.* [4] presented results of one-year observation of 15 eyes with secondary CNV in the course of toxoplasmosis treated with an intravitreous injection of aflibercept (Eylea). After aflibercept treatment, every patient presented an im-

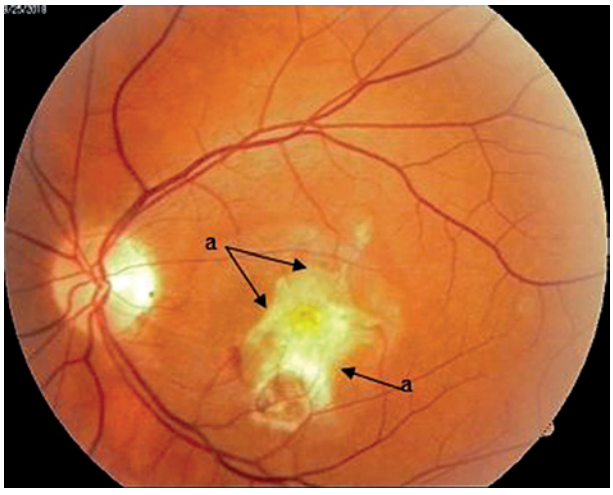

Figure 6. Figure 6. The fundus of the eye toxoplasmosis patient on the first day after intravitreous injection of aflibercept. Partial constriction of the neovascular membrane and more distinct borders of CNV particularly from the top, nose, and temple (a)

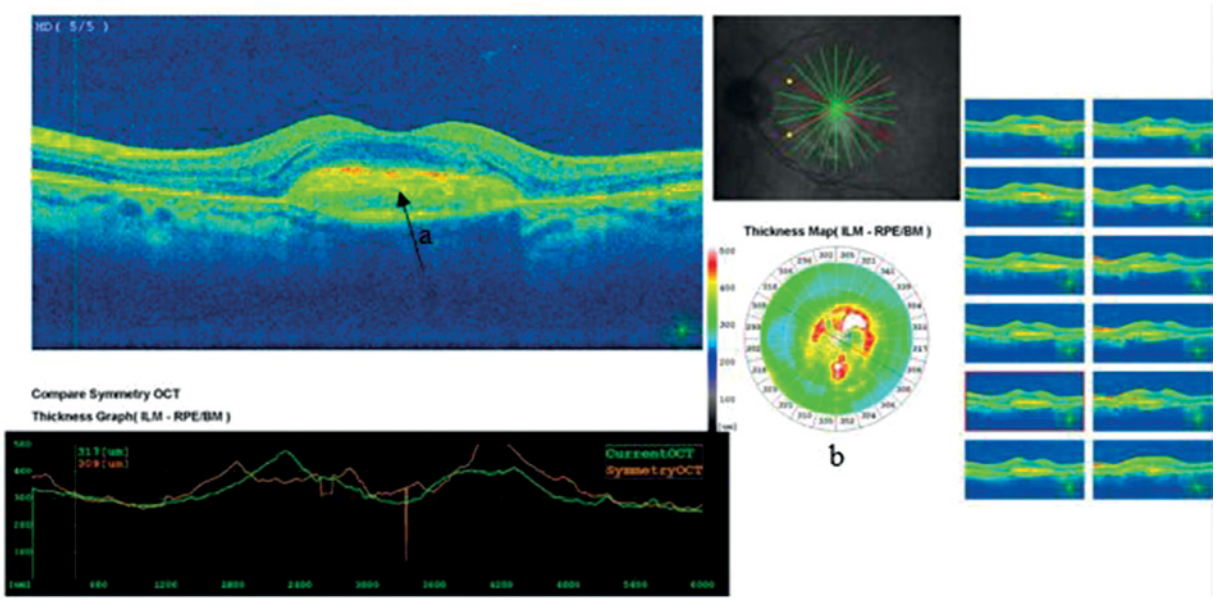

Figure 7. OCT of the left eye on the first day after intravitreous injection of aflibercept. **A**) Resorption of subretinal fluid and characteristic increase in reflexibility of choroidal neovascularization (increase in the fibrous component of the neovascular membrane); **B**) reduction of retinal thickness

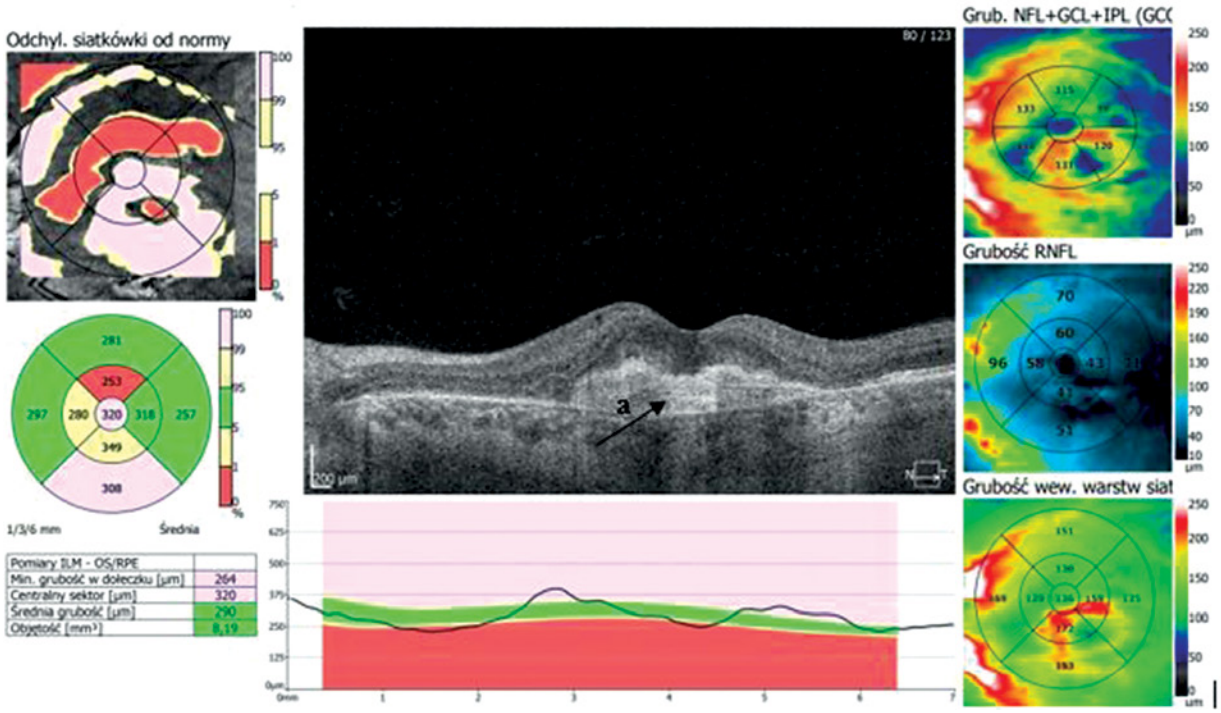

Figure 8. OCT of the left eye retinal macula. The female patient with inactive choroidal neovascularization secondary to a post-inflammatory scar caused by ocular toxoplasma (**A**) after intravitreal injection of aflibercept (31 months after the injection of aflibercept)

provement of visual acuity. During 12 months of observation in 3 (20%) cases there was obtained an improvement of visual acuity amounting to 3 or more lines; 8 (53%) cases by ≥ 2 to < 3; 3 (20%) cases by ≥1 to < 2 lines. Visual acuity was unchanged only in one eye, which constituted 7% of their research group. Average central retinal thickness (CRT) diminished from 317 µm (range 239-528 µm) to 254 µm (range 192-362 µm) during 12 months observation. In 5 (33.33%) eyes one intravitreous injection of aflibercept was sufficient for vision stabilization and in 10 eyes (66.66%) for vision stabilization two intravitreous injections of aflibercept were necessary [4].

Ben Yahia *et al.* [5] presented two patients with CNV secondary to ocular toxoplasmosis which after singular intravitreal injection of anti-VEGF (bevacizumab) achieved an improve-

ment of visual acuity and retreatment of neovascular activity during 12 and 10 months observation was not required [5].

Shah and Shah [6] described a case of CNV secondary to toxoplasma chorioretinitis with a positive reply for a single intravitreal injection of anti-VEGF (ranibizumab – Lucentis). They observed improvement with best-corrected visual acuity from 20/80 to 20/30 and stabilization of the local state, without recurrence of CNV activity during 2 years of observation [6].

Martín García *et al*. [7] presented a case history of a 12-year-old male patient with choroidal neovascular membrane secondary to ocular toxoplasmosis, treated with systemic anti-toxoplasmosis drugs and two anti-VEGF (ranibizumab 0.5 mg) intravitreal injections at monthly intervals. Ocular examination showed a decreased visual acuity (VA) in his left eye and it was 0.05, and the fundus examination revealed a focus of chorioretinitis adjacent to a pigmented macular scar and a large subretinal hemorrhage. After systemic therapy with accompanying intravitreal injections of anti-VEGF (ranibizumab 0.5 mg) to the left eye, visual acuity improved and reached 0.4 and full disappearance of the hemorrhage, leaving a residual inactive pigmented scar. The patient remains stable after more than 5 months of close follow-up [7].

In the case of the complicated post-inflammatory scar on the background of toxoplasmosis, anti-VEGF (aflibercept) therapy was effective because improvement in retinal morphology was obtained. Total resorption of subretinal fluid occurred and retinal thickness decreased. Improvement of visual acuity occurred from Vol = 0.016 cc-1.25 Dsph = 0.1 to Vol = 0.1 cc-1.25 Dsph = 0.25. Following intravitreal injection of aflibercept, the patient reported an improvement in vision in the form of a reduction in the black spot in front of the left eye and "clearances" in the existing black spot. Stabilization of the local state without recurrence of secondary CNV activity. Retreatment of secondary CNV activity was not required. Observations suggest that a single dose of aflibercept in CNV secondary to toxoplasmosis may be sufficient.

In summary, it should be stated that CNV secondary to eye toxoplasmosis is a rare complication of eye toxoplasmosis. The presented case of the 44-year-old female patient with CNV secondary to eye toxoplasmosis confirms the crucial significance of use of OCT and fluorescein angiography in the diagnosis of choroidal neovascularization secondary to a post-inflammatory scar caused by ocular toxoplasmosis. OCT and fluorescein angiography permit the design of an effective treatment, which in this case depended on intravitreal anti-VEGF injection.

CONCLUSIONS

The reported case confirms that secondary CNV to the post-inflammatory scar is a rare complication of toxoplasmosis retinitis and choroiditis and should be considered in the diagnosis. OCT and fluorescein angiography play an important role in the diagnosis of choroidal neovascularization secondary to a post-inflammatory scar caused by ocular toxoplasmosis. Intravitreal anti-VEGF injection therapy is an available, effective, and safe method of choroidal neovascularization secondary to the post-inflammatory scar caused by ocular toxoplasma. Treatment with intravitreal anti-VEGF injection improves retinal anatomy and visual function.

DISCLOSURE

The authors declare no conflict of interest.

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