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CASE REPORT

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Intravitreal clindamycin in the treatment of ocular toxoplasmosis: a report of two cases

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ABSTRACT

We present a report of two patients with active ocular toxoplasmosis treated with intravitreal clindamycin. The location of the retinochoroiditis close to the optic disc validated the injection of 1 mg clindamycin, even though the visual acuity was not diminished. After 7 days, inflammatory lesions and vitritis regressed significantly. Moreover, no side effects occurred.

KEY WORDS: *Toxoplasma gondii*, clindamycin, intravitreal injection, toxoplasmic retinochoroiditis.

INTRODUCTION

The etiological agent of ocular toxoplasmosis is the protozoan *Toxoplasma gondii.* This obligate intracellular parasite is the most common causative organism of infectious posterior uveitis both in adults and children worldwide [1, 2]. During *T. gondii* infection, which is usually clinically silent, the protozoan forms cysts in various body tissues including the retina [1]. Ocular symptoms may appear already at the stage of primary infection or during reactivation, when non-invasive bradyzoites are released from intraretinal cysts and transform into tachyzoites, i.e. the invasive form in the life cycle of *T. gondii*. During tachyzoite replication, necrotizing retinitis occurs, and in the course of recurrent retinitis a characteristic satellite lesion develops near the pre-existing retinochoroidal scar [1, 3]. The diagnosis is based on the typical clinical findings and serological tests (detection of IgM/IgG antibodies against *T. gondii*). If the inflammation is non-specific, for example in immunosuppressed individuals, the level of antibodies can be additionally measured or the protozoan DNA can be detected in the aqueous humor sampled from the anterior chamber or the vitreous body [3]. In immunocompetent individuals, retinitis is self-limiting and normally does not require treatment. However, if the focus of inflammation is centered in the macula, involves large vessels or the optic disc, or is located within a distance of up to two disc diameters from the optic nerve disc, the condition needs treatment [3-5]. Aside from the standard triple drug therapy (pyrimethamine, sulfadiazine and glucocorticosteroids), other therapeutic options include clindamycin, trimethoprim-sulfamethoxazole combination, spiramycin, azithromycin, atovaquone, dapsone, sulfadoxine, minocycline, trimetrexate or lincomycin [3, 6]. An alternative modality to oral therapy of many weeks' duration is the local administration of clindamycin at 1 mg by intravitreal injection [7-12]. The treatment results in achieving a high drug concentration in the vitreous body and retina, thus minimizing the risk of adverse effects associated with systemic therapy, such as nausea, vomiting, rash, bone marrow suppression, Stevens-Johnson syndrome or pseudomembranous enteritis [3].

CASE REPORTS

To conduct the treatment of active ocular toxoplasmosis, a consent was obtained from the Bioethics Committee at Poznan University of Medical Sciences for the intravitreal administration of clindamycin.

The injections were administered in the operating room under aseptic conditions. To prepare for the procedures, the eyes were anaesthetized with proxymetacaine eye drops (0.5%) administered into the conjunctival sac, followed by the application of povidone-iodine to the skin (10%) and the conjunctival sac (5%). Following these preparatory steps an intravitreal injection of 0.1 ml of clindamycin solution (containing 1 mg of the antibiotic) was administered, using a 30G needle, in the inferotemporal quadrant at a distance of 3.5 mm from the corneal limbus. After each procedure, the perception of light was checked.

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Patient 1

In 2018, a 24-year-old woman presented to the University Outpatient Clinic with the symptom of seeing halos around lights in the left eye (LE), persisting for 5 days. Her visual acuity in both eyes was 1.0. The intraocular pressure was within the normal range. The examination of the right eye revealed no abnormalities. The anterior segment of the left eye was normal as well. The left fundus examination revealed a yellow focal inflammatory lesion in the retina, located along the course of a blood vessel between the optic nerve disc and a heavily pigmented scar with a moderate inflammation in the vitreous body. Optical coherence tomography (OCT) visualized thickening and distortion of inner retinal layers within the affected area (Figure 1A). A serological examination detected IgG antibodies to *T. gondii* in the blood serum. The patient was prescribed oral clindamycin at a dose of 300 mg three times a day. However, as there was no clinical improvement after 2 weeks of therapy, and the focus of inflammation was located on the border of the optic disc, systemic therapy was discontinued, and clindamycin at a dose of 1 mg was administered by intravitreal injection. After the procedure, topical antibiotic prophylaxis (levofloxacin 5 times a day) was given. A follow-up examination performed a week after the injection showed regression of the focus of inflammation, reduction in retinal thickness and resolution of inflammation in the vitreous body (Figure 1B). No adverse effects were noted. Throughout the two-year follow-up, during which the patient was pregnant, there was no reactivation of the inflammation.

Patient 2

In 2019, a 19-year-old man presented to the ophthalmology emergency department with floaters in the field of vision of the right eye (RE). The ophthalmological examination revealed full visual acuity in both eyes, intraocular pressure within the normal range, and no pathologies in the anterior segment of the RE/LE. There were no abnormalities in the fundus examination of the LE, but a yellow focal inflammatory lesion with blurred margins was identified at the fundus of the RE. The lesion was located along the course of the artery, at a distance of one disc diameter from the optic disc (Figure 2A). In addition, a moderate inflammatory reaction was observed in the vitreous body above the lesion. Also, the OCT examination showed an increased thickness of the retina with distortion of all retinal layers, and thickening of the choroid within the inflammatory lesion (Figure 2A). An IgG-positive result was obtained in a serum assay for *T. gondii* antibodies. Despite the patient having full visual acuity, an intravitreal injection of clindamycin (1 mg /0.1 ml) was administered because of the location of retinitis. The patient did not receive any systemic antiprotozoal treatment. Only topical antibiotic prophylaxis was prescribed after the procedure. A follow-up examination performed 7 days later showed a significant reduction both in retinal and choroidal thickness (Figure 2B), and isolated inflammatory cells in the vitreous body. One month after the administration of the drug, a retinal scar with clearly defined borders was already seen, with hyperreflectivity observed on OCT images. In addition, the reverse shadowing effect was indicative of the loss of retinal pigment epithelial cells (Figure 2C). During the 6-month follow-up, there was no recurrence of the inflammation, and no adverse effects of the therapy were observed.

DISCUSSION

Systemic therapy of toxoplasmosis is indicated in immunosuppressed patients, in cases of congenital toxoplasmosis and primary infection in pregnant women [13]. In cases of reactivated retinitis, intravitreal clindamycin therapy seems to be superior to standard treatment, providing an option which prevents potential adverse effects induced by orally administered drugs. Clindamycin is also administered via intravitreal injection in the treatment of individuals with allergy to sulfonamides, and patients who have not achieved adequate response to systemic therapy [3, 7, 14]. Intravitreal injections of clindamycin have also been reported in women with recurrent retinitis during pregnancy. In such cases, local administration of the drug reduces its adverse effect on the fetus [8, 15]. Although there is no clear evidence that pregnancy is

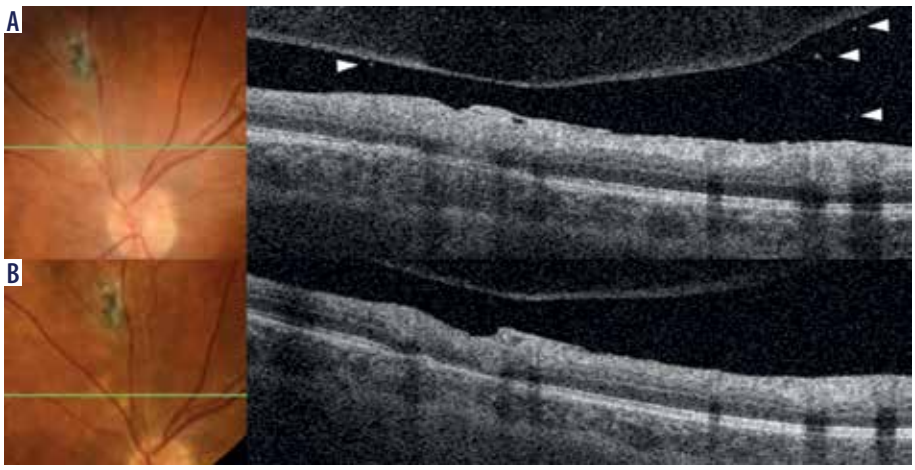

Figure 1. Retinitis caused by *Toxoplasma gondii* in Patient 1: **A**) The fundus photograph shows an active inflammatory focus in the retina and a heavily pigmented post-inflammatory scar. The OCT image reveals thickening and distortion of inner retinal layers within the area of active inflammation, with coexisting inflammatory reaction in the vitreous body (arrowheads). **B**) Regression of focal inflammatory lesion and reduced retinal thickness 7 days after intravitreal administration of clindamycin

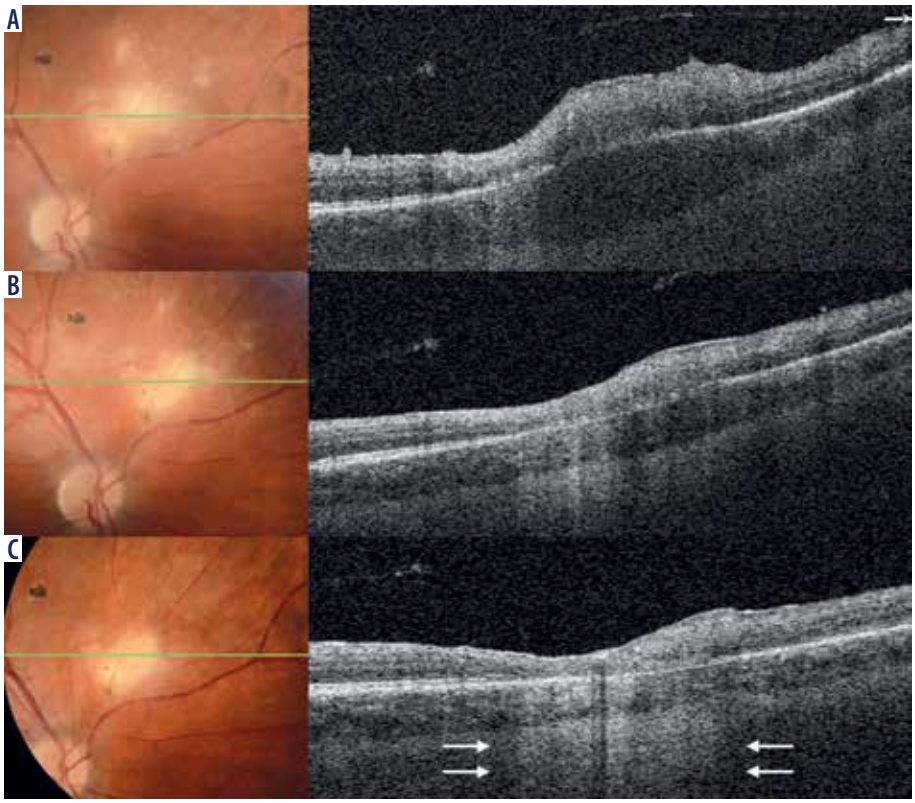

Figure 2. Retinitis caused by *Toxoplasma gondii* in Patient 2: **A**) The fundus photograph shows an active inflammatory focus with blurred margins and a pigmented retinal scar. A corresponding OCT image reveals increased retinal thickness with distortion of all retinal layers and choroidal thickening. A reduction in retinal and choroidal thickness was observed in subsequent evaluations, 7 days (**B**) and 1 month (**C**) after the intravitreal administration of clindamycin. The OCT image shows the reverse shadowing (arrows) caused by the loss of retinal pigment epithelial cells (**C**)

a factor causing reactivation of retinitis, a recurrence of ocular toxoplasmosis has been reported in pregnant women, even in each subsequent pregnancy of a particular patient [16, 17]. In our patient, we observed no recurrence of inflammation during pregnancy. However, if it had happened, intravitreal injections of clindamycin would have been a suitable alternative to standard therapy.

Two methods of intravitreal treatment of ocular toxoplasmosis have been reported in the literature: 1 mg of clindamycin as monotherapy [7, 14] or in combination with 400 μg of dexamethasone [8-11]. If clinical improvement was unsatisfactory after the injection, another one was administered. In prospective randomized studies, a single administration of clindamycin plus dexamethasone was sufficient to reduce retinal inflammation in 75% of patients. The remaining group needed 2-3 injections to achieve a desirable therapeutic effect. The authors also compared the efficacy of intravitreal therapy with standard triple drug therapy. The analysis of the findings showed both therapeutic options to be equally effective in the treatment of ocular toxoplasmosis. Moreover, drug administration via injection may be safer and more convenient for patients, with the added benefit of eliminating the need to perform follow-up blood tests [9, 10]. In our patients, we achieved a regression of the inflammation and a decrease in retinal thickness after one injection of clindamycin as monotherapy.

Importantly, patients receiving intravitreal injections should be informed about the potential risk of endophthalmitis or retinal detachment. However, based on the data on the prevalence of such complications in anti-VEGF therapy, it can be assumed that such situations are extremely rare [18, 19].

Administration of clindamycin directly into the eye, bypassing the blood-retinal barrier, results in high drug concentrations in the vitreous body. In 2017, Habot-Wilner *et al.* reported the results of their studies on the potential toxic retinal effects of clindamycin. The morphological and functional changes occurring in the retina after intravitreal administration of 1 mg of clindamycin were evaluated in an animal model, using the eyes of albino rabbits. Four weeks after the injection, the electroretinogram and visual-evoked potential assessment showed no ocular changes after drug administration compared to the control eye. In addition, the histopathological analysis found no retinal damage in the examined eye [20]. Therefore, a biodegradable intravitreal implant for the release of clindamycin [21-23] might provide an interesting therapeutic solution in the future. This route of drug administration would reduce the number of injections performed during the course of treatment.

CONCLUSIONS

The clinical cases presented in this paper indicate the therapeutic efficacy of intravitreal clindamycin in patients with active ocular toxoplasmosis. Since the treatment produces a high concentration of the drug in the vitreous body, it may be a beneficial option in patients where systemic therapy is to be avoided.

DISCLOSURE

The authors declare no conflict of interest.

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