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Active Ocular Toxoplasmosis in Patients Diagnosed and Treated at General Hospital Zadar

Aktivna okularna toksoplazmoza pacijenata dijagnosticiranih i liječenih u Općoj bolnici Zadar

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Abstract

Toxoplasma gondii is responsible for the 20-60% of all the cases of chorioretinitis. Causes of permanently reduced vision (found in about 25% of the patients) include macular active lesions and macular oedema, optic nerve involvement, vascular occlusion, retinal detachment, and late secondary choroidal neovascularization. A retrospective, non-consecutive chart review was performed on 11 patients with active ocular toxoplasmosis. At examination, all patients had central active lesions on retina. Preexisting chorioretinal scars were found in seven patients (63.6%). Eight patients (72.7%) had vitritis, while three patients (27,3%) had iridocyclitis. Six patients (54.6%) had macular inflammatory lesions, four (36,37%) of them had active lesions out of vascular arcades, and one (9.1%) had active lesions inside vascular arcades, while macula was not affected. The mean value of visual acuity at first visit of the patients was 0,5. The mean value of visual acuity was 0.9 after the healing process. All the patients were treated with oral antibiotics. Seven patients also received oral corticosteriods, and seven of them were also treated with pyrimethamine. All patients with signs of iridocyclitis were also treated with topical corticosteroids. Although toxoplasmosis chorioretinitis is usually a self-limited infection and generally resolves spontaneously, unrecognised cases can result in severe visual impairments.

Sažetak

Toxoplasma gondii je uzročnik 20-60 % svih slučajeva korioretinitisa. Uzroci trajno smanjenog vida (slučaj kod otprilike 25% pacijenata) uključuju aktivne lezije u makuli, makularni edem, lezije optičkog živca, vaskularne okluzije, ablacije mrežnice i kasne koroidalne neovaskularizacije. Prilikom pregleda, svi su pacijenti imali aktivne lezije na mrežnici. Raniji korioretinalni ožiljci pronađeni su u sedam pacijenata (63,6%). Osam pacijenata je imalo vitritis (72,7%), dok su tri pacijenta imala iridociklitis (27,3%). Šest pacijenata (54,6 %) imalo je upalne lezije u makuli, četvero (36,37%) je imalo aktivne lezije izvan krvožilnih arkada, a jedan (9,1%) je imao aktivne lezije unutar krvožilnih arkada, dok makula nije bila zahvaćena. Srednja vrijednost vidne oštrine prilikom prvog pregleda bila je 0,5. Poslije izlječenja srednja vrijednost vidne oštrine bila je 0,9. Svi pacijenti liječeni su peroralnim antibioticima. Sedam pacijenata je, također, primilo peroralne kortikosteroide, a sedam pirimetamin. Svi pacijenti s iridociklitisom su, također, primili topičke kortikosteroide. Iako je korioretinitis uzrokovan toksoplazmozom uobičajeno samolimitirajuća bolest koja se može spontano izliječiti, nedijagnosticirani slučajevi mogu rezultirati ozbiljnim oštećenjima vida.

Introduction

Ocular toxoplasmosis is caused by the protozoan parasite Toxoplasma gondii and it infects humans and warm-blooded animals. Toxoplasmosis prevalence varies worldwide which depends on climate, eating habits and hygiene, but the incidence is higher in tropical areas and decreases with increasing latitude [1-5].

It is responsible for the 20-60% of all the cases of chorioretinitis. This disease has predilection spot for the posterior pole. The infection is usually unilateral and the lesions can be isolated, multiple or satellite to a pigmented retinal scar. The infection begins in the superficial layers of retina and then affects the retinal pigment epithelium and choroid. Characteristic of retinitis is focal necrotizing retinitis resulting in atrophic scars. Retinitis can be accompanied with choroiditis, vasculitis, haemorrhage, vitritis and anterior uveitis [6].

The complications can be vision-threatening such as choroidal neovascularisation, glaucoma, optic nerve atrophy, rhegmatogenous and exudative retinal detachment, retinal vessel occlusion, epiretinal membrane formation and cataract. Rhegmatogenous retinal detachments, for example, have been related to the severity of inflammation [7]. Prolonged infections, intense inflammation, and complications can occasionally result with phthisis or enucleation[8-9]. It is progressive and reccurent disease and patients have to be monitored after the healing process to avoid late complications.

Ocular toxoplasmosis can be a consequence of congenital or acquired infection. For a long time, ocular toxoplasmosis was considered to be a result of recurrence of the congenital infection[10]. However, recent researches support the theory that acquired infections might be a more important cause of ocular diseases than congenital ones [11-13]. The age of first onset of ocular symptoms is one of the clinical characteristics that is expected to be helpful in making a distinction between prenatal and postnatal Toxoplasma gondii infection. A study from French authors showed that ocular lesions in congenitally infected children occur mainly before the age of 5 years and almost always before the age of 10 years [14].

The aim of this study is to report clinical features of patients who were diagnosed, treated and had control check ups at least 6 months after an episode of active ocular toxmoplasmosis at General Hospital Zadar.

Methods

The retrospective analysis (retrospective chart review) of medical records of patients diagnosed with active ocular toxoplasmosis at the Department of Opthalmology of the General Hospital Zadar was conducted. All participants were diagnosed with ocular toxoplasmosis and treated in the period between January 2010 and January 2018.

The inclusion criteria were proven diagnosis of ocular toxoplasmosis and a minimum six months follow-up. The patients with acquired immunodeficiency syndrome (AIDS) were excluded.

The diagnosis was based on the presence of active creamy-white focal necrotizing retinitis, with or without preexisting chorioretinal scars. The diagnosis was supported by serologic tests.

We performed serologic tests, including serum IgG and IgM antibodies against Toxoplasma gondii using enzyme-linked immunosorbent assay-ELISA.

All patients underwent ophtalmological examination, including best-corrected Snellen visual acuity, slit-lamp examination, Goldmann tonometry and indirect ophthalmoscopy.

The presence of anterior chamber and vitreous inflammation was studied according to the SUN Working Group Grading system for anterior chamber cells and vitreous haze.

Demographic information, clinical features, systemic or topical treatments and treatment outcomes were recorded.

After obtaining necessary data, statistical analysis was conducted. SPSS for WINDOWS (version 13.0 SPSS Inc. Chicago, Illinos, USA) and Microsoft Excell (version of Office 2007, Microsoft Corporation, Redmont, WA, USA) were used. Nominal variables are represented as absolute (number) and relative (percentage) frequency.

Results

This retrospective chart review included 11 patients diagnosed with active ocular toxoplasmosis (Figure 1). The demographic and general characteristics of the participants in the study are summarized in the Table 1.

Figure 1. Fundus of a Patient with Ocular Toxoplasmosis at the Initial Examination

Slika 1. *Fotografija fundusa bolesnika s očnom toksoplazmozom pri prvom pregledu*

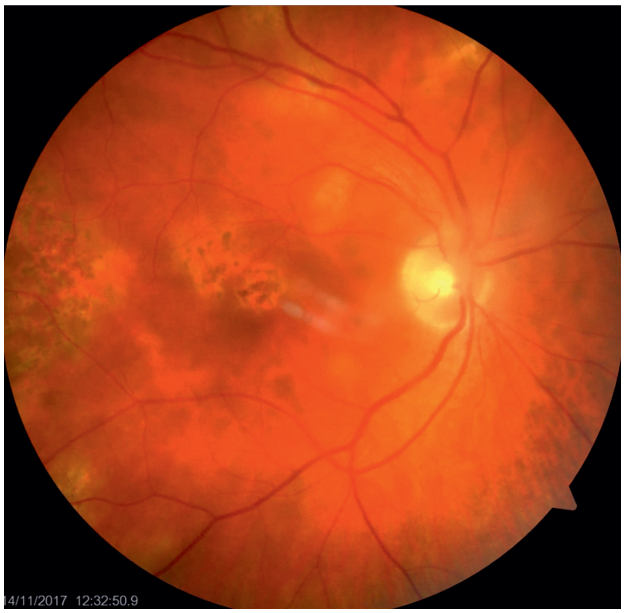

Table 1. Clinical Features of Patients with Active Ocular Toxoplasmosis

Tablica 1. *Kliničke karakteristike bolesnika s aktivnom očnom toksoplazmozom*

Case No[1]	Age	Gender	Clinical manifestation	First VA[2]	Control VA[2]	Previous recorded episodes	No[1] of recurrences	Corticosteroid th[3]	Pyrimethamine	Antibiotic th[3]
1	32	Female	Active chorioretinitis, vitritis, chorioretinal scars	1	1	yes	3	yes	yes	yes
2	61	Female	Active chorioretinitis, vitritis, iridocyclitis	0,25	0,75	no	0	yes	yes	yes
3	49	Female	Active chorioretinitis, iridocyclitis	1	1	no	0	yes	no	yes
4	27	Female	Active chorioretinitis, vitritis, chorioretinal scars	1	1	no	0	yes	no	yes
5	52	Female	Active chorioretinitis, vitritis	0,5	1	no	0	yes	yes	yes
6	47	Male	Active chorioretinitis, vitritis, chorioretinal scars	0,75	1	yes	4	no	yes	yes
7	61	Female	Active chorioretinitis, chorioretinal scars	0,75	0,75	no	0	no	no	yes
8	15	Female	Active chorioretinitis, vitritis, iridocyclitis	0,01	1	no	0	yes	yes	yes
9	65	Male	Active chorioretinitis, chorioretinal scars	0,33	0,33	no	0	no	yes	yes
10	45	Female	Active chorioretinitis, vitritis, chorioretinal scars	0,5	1	yes	3	no	yes	yes
11	16	Male	Active chorioretinitis, vitritis, chorioretinal scars	0,05	1	yes	2	yes	no	yes

[1]No - number, [2]VA – visual acuity, [3]Th – therapy

All of them were diagnosed, treated and had control check ups at least 6 months after an episode of chorioretinitis at General Hospital Zadar.

Eight patients were female, and three patients were male.

The age range of patients was 15 to 65 years and the mean age of the patients was 42.73.

The mean value of visual acuity at first patients' visit was 0,5 with the range from 0.05 to 1. After the healing process, the mean value of visual acuity was equal or better in all patients. The mean value of visual acuity after the healing process was 0.9 with the range from 0.33 to 1.

At examination, all patients had active lesions on retina. The preexisting chorioretinal scars were found in seven patients (63.64%). Eight patients (72.73%) had vitritis, while three patients (27.27%) had iridocyclitis. Six patients (54.55%) had macular inflammatory lesions, four (36.37%) of them had active lesions out of vascular arcades, and one (9.09%) was diagnosed with active lesions inside vascular arcades, while macula was not affected.

All the patients had positive serum anti-toxoplasma IgG antibodies, but negative IgM antibodies. Complete blood cell counts and erythrocyte sedimentation rate, c-reactive protein, liver and kidney functions tests were within normal range in all patients.

All patients had unilateral involvements.

The patients had no extraocular involvements.

Recurrent ocular toxoplasmosis is defined as an active focal retinal lesion in the presence of old chorioretinals scar. The preexisting chorioretinal scars were found in seven patients which means that the recurrence was present in 63.6% of patients. In seven patients, this was the first diagnosed episode of ocular toxoplasmosis. Four patients had previous episodes of toxoplasmosis chorioretinitis. One patient had two previous episodes, two of them had three and one of them had four previous episodes. Since four patients had previous episodes of toxoplasmosis chorioretinitis, three of them had previous subclinical episode.

All patients were treated with oral antibiotics, azithromycin (250 mg per day) or sulfamethoxazole/trimethoprim (800/160 mg twice daily).

Seven patients were treated with oral corticosteriods prednisolone (0.5 mg – 1 mg/kg/day depending on the severity of the inflammation).

Seven patients were treated with pyrimethamine 200 mg orally, once on the first day, followed by 50 mg orally

per day and then for a period of 4 weeks. The treatment was combined with sulfadiazine. Sulfadiazine was administered at a dosage level of 2 g orally as a loading dose, followed by 1 g orally every 6 hours.

All patients with signs of iridocyclitis were also prescribed topical corticosteroids.

None of the patients had any side effects of the drugs.

Discussion

Although toxoplasmosis is not newly discovered disease, there are still many issues related to it. There are many doubts on the factors influencing the epidemiology and pathophysiology of this disease that can even lead to blindness . We are only at the beginning of understanding the biology of this parasite and its mechanisms of invasion, virulence and interaction with the host's immune response.

Mean patients' age in our research was higher than in other similar researches [7, 15, 16]. The understanding of relationship between ocular toxoplasmosis and patient age is incomplete. The phenomena of age difference could be attributed to differences in lifestyle, such as eating habits and hygiene, but also to small sample size. The localization of active chorioretinitis in our patients was less frequent in the macula than in other studies. In our study, the macula was affected in approximately half of the patients, unlike in Japanese research in which the macula was affected in 74% of patients. Along with the application of an adeaquate treatment, this is a possible reason for good visual acuity after healing process in our patients [13]. In Turkish patients, preexisting chorioretinal scars were found in 83% of patients, while in Korean patients scars were found in 10% of patients, and in our and most other studies the incidence was somewhere beetwen. The reasons for the differences in severity of disease, recurrence and predilection spots for active lesions, could also be, besides different habits of population and different climate type, genotypic differences of infecting parasite. It is known that there are three main clonal lineages of Toxoplasma gondii named type I, II and III and they vary in their virulence [17]. Except these genotypes, other „atypical" genotypes were found worldwide. A high occurrence of ocular toxoplasmosis in Brasil is attributed to the higher prevalence of nonarchetypal Toxoplasma gondii strains [18]. Keats Shwab et al. suggest that the expansion of farming in the past 11,000 years established the domestic cat/mouse transmission cycle for Toxoplasma gondii, which has played a significant role in the selection of certain linages of Toxoplasma gondii. According to them, the domestic transmission cycle may have favoured the development of clonal populations dominated by genotypes that are less virulent. In contrast, within natural environments, such as the tropical Amazon rainforest, the sylvatic cycle seems to favour development of a diverse population supporting highly virulent Toxoplasma gondii genotypes [19]. It is believed that, except the parasite, a host also contributes to the development of this disease. The studies on the impact of host genes on infections are extremely important. Recent studies provide us the information on the contribution of the host's genetic factors on the development of this disease [20-22].

We did not notice any complications after the healing process, which may be due to antimicrobial drug therapy in all patients and timely treatment, especially in immediate complications. As far as the Korean study is concerned, 34.8% of the patients had complications after acute ocular toxoplasmosis. 26.1% of patients from this study did not receive any anti-Toxoplasma treatment [23]. Although toxoplasmosis causes 20 to 60% of all the cases of chorionetinitis, the effectiveness of treatment remains controversial. There is still no consensus regarding the choice of antiparasitic agents for treatment regimens. Furthermore, due to potential toxicity, the question is whether to treat all the patients, especially those who are immune-competent. Stanford et al. indicate the lack of evidence for the efficacy of treatment for acute toxoplasmic chorioretinitis [24]. They identified only three randomized controlled clinical trials, which were described as 'methodologically poor,' and none of which reported permanent visual outcome. Guaraldo et al. describe the side effects associated with the classic treatment of ocular toxoplasmosis. Out of 147 patients studied, 85% of them developed one or more side effects [25]. However, despite the unanswered questions, the survey among physicians showed that most ophthalmologists treat immune-competent patients with active chororietinitis while selecting a treatment depends on a clinical picture [26]. We treated all the patients with diagnosed active ocular toxoplasmosis and we had no therapeutic side effects. Due to the good outcome of the disease, unrecorded complications of the disease, as well as the side effects of the medications, we believe that the treatment is necessary. It should be adapted to a patient and depends on the severity of a clinical picture.

Conclusions

Although ocular toxoplasmosis is a self-limited disease, sometimes it can go unnoticed, especially if it does not reduce visual acuity, and in many cases it affects macula and seriously impairs visual acuity. Patients should have effective treatment and be monitored in order to avoid complications.

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Conflict of Interest

None to declare.

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