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CASE REPORT: REACTIVATION OF CONGENITAL OCULAR TOXOPLASMOSIS IN AN IMMUNOCOMPETENT PATIENT AFTER RECEIVING MEASLES

Vesna Cheleva Markovska[1,2], Stefan Pandilov[1], Zoran Jovanov[3]
[1]University Clinic for Eye Diseases Skopje, [2]Faculty of Medicine,
Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia,
[3]Public Health Institution General Hospital, Gevgelija, Republic of North Macedonia

Abstract

A case of recurrent ocular toxoplasmosis, presented through diagnostic imaging techniques and laboratory tests.

To show the course and development of the clinical picture of ocular toxoplasmosis in a 19-year-old girl with good visual acuity in both eyes, which was accidentally detected during a routine ophthalmological examination for a driver's license.

At the University Clinic for Eye Diseases in Skopje, several imaging diagnostic methods have been performed, such as: fundus photography, aurofluorescence, optical coherence tomography (OCT) and fundus fluorescence angiography (FFA).

Imaging techniques, along with laboratory tests for specific anti-toxoplasmosis IgG and IgM antibodies, have helped to diagnose this not-so-common entity-ocular toxoplasmosis.

The development of the disease was followed by a clinical picture, certain diagnostic methods in a period of seven years. Three recurrences of the parasitosis occurred during that period.

The third attack of toxoplasmosis was associated with the occurrence of measles in an otherwise healthy young woman, a possible trigger for reactivation of the disease.

Regular laboratory tests of anti-toxoplasma IgG and IgM antibody titers were performed with the help of ELISA at PHI UC for infectious diseases and febrile conditions in Skopje, during the entire process of monitoring.

The lesion described by the diagnostic modalities corresponded to the data obtained from the literature and together with the elevated values of anti-toxoplasma IgG and IgM antibodies confirmed the diagnosis of congenital ocular toxoplasmosis.

Keywords: toxoplasmosis, ocular toxoplasmosis, therapy, laboratory tests, FFA, OCT.

Introduction

Ocular toxoplasmosis is a parasitic, zoonotic disease caused by the protozoa Toxoplasma gondii. This organism is an obligate intracellular parasite, widespread throughout the world, especially in the tropics, and affects a large number of warm-blooded vertebrates, including humans.

Toxoplasma gondii was first described in the literature in 1908. Its definite host is the cat, but it is also found in parts without cats. In the early twentieth century, Nicolle and Manceaux identified toxoplasmosis in rodents in North Africa, and a few years later Splendere repeated the same in a rabbit in Brazil [1].

In 1913, Carini in Italy described a case of toxoplasma infestation in a dog [2], later a similar parasites were found in sections of retinal tissue taken at the autopsy of a baby who had died of congenital toxoplasmosis [1].

Infection can occur congenitally, through the placenta, when the mother becomes infected with the parasite for the first time during pregnancy, or acquired through ingestion into cat feces oocysts or bradyzoites of the parasite in poorly cooked, infected meat, or water.

Once ingested, the parasite travels through the bloodstream to multiple organs and enters their cells [3]. The immune status of the major immuno-privileged areas of the body (brain, eye, and placenta) strikes

a delicate balance between parasite invasion and host resistance. The local progression of the disease depends on it [4,5].

It is important to note that most people infected with this parasite will not develop the disease because of the protection of their own immune system. Several studies have shown that 20% of the population in North America are seropositive for this parasite, and even 60-80% in France and Brazil [3,6].

However, during pregnancy, infection can lead to fetal death, congenital malformation, and in the third trimester of pregnancy to moderate infection of the brain tissue and retina of the fetus.

Until recently, ocular toxoplasmosis in adults was thought to be only a recurrence of congenital infection. However, recent findings suggest that it is more often due to postnatal infection. Most commonly, congenital ocular toxoplasmosis is a bilateral disease, while acquired ocular disease occurs more often unilaterally.

It should also be noted that toxoplasmosis is one of the most common causes of uveitis in the human population, and in some parts of the world, such as Brazil, is the leading cause of uveitis [7,8].

Case report

A 19-year-old girl underwent a routine ophthalmological examination, for a driver's license, in an ophthalmological clinic in 2014.

During the examination of the posterior segment of the eye, the ophthalmologist noticed oval lesions on the fundus of both eyes, which is why he referred her to the University Clinic for Eye Diseases in Skopje for further examination and treatment. At the first examination at our clinic, the patient's best-corrected visual acuity (BCVA) was 1.0 without correction, according to the Snellen Optotype, on both sides.

Intraocular pressure in both eyes was within the normal range (18mmHg) determined by indentation tonometry.

In order to perform a detailed clinical examination, the patient's pupils were artificially dilated with Sol.Tropicamide 1%. Biomicroscopic examination of the anterior segment of the eyes was normal. On fundoscopic examination of the right eye, small oval pale-cream-colored lesions were observed near the upper-temporal arcade. Similar changes, with pigmented center, were present in the macular region of the left eye.

OCT scan of the posterior segment of the eye, autofluorescence, fundus photography and fundus fluorescence angiography were performed to document the condition.

During autofluorescence, destruction of RPE was observed at the sites of the present lesions, shown as hypo-hyperautofluorescence changes (Figure 1).

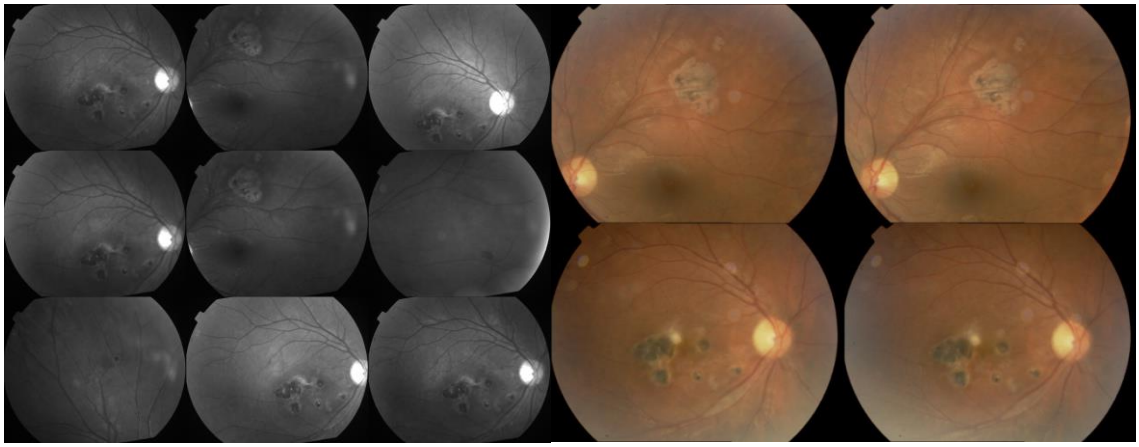

Figure 1. Autofluorescence and fundus photography. The left image shows autofluorescence of the lesions on both eyes, respectively, and the right image shows the same lesions with fundus photography.

The angiogram of the right eye showed three clearly demarcated hyperfluorescence zones, near to the upper-temporal venous blood vessel, which remained with the same intensity in the late stages of imaging.

On the left angiogram, multiple hypofluorescence zones were obtained in the macular region, lined with clear hyperfluorescence rings, suggesting activity on that part of the lesion (Figure 2).

In this way, a clinical diagnosis for congenital ocular toxoplasmosis was made.

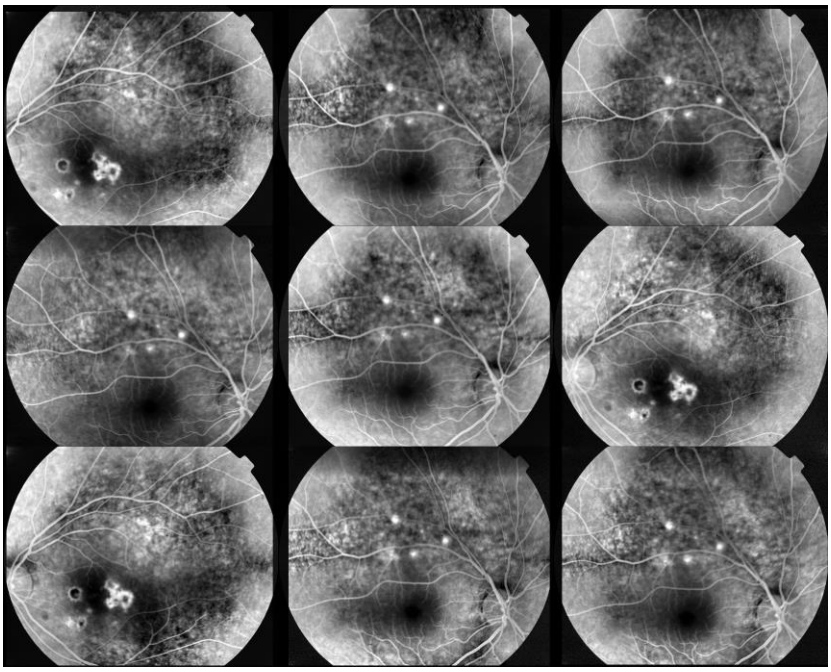

Figure 2. Fundus fluorescent angiography (2014). Images 2,3,4,5,8 and 9 show the course of an angiogram of the right eye, Images 1,6 and 7 show the course of an angiogram of the left eye.

In order to accurately confirm the finding, as well as the activity of the process, laboratory examinations were performed, as well as a native radiograph of the head.

The radiograph was orderly, while the ELISA (enzyme-linked immunosorbent assay) of the anti-toxoplasmic IgG antibody in serum showed a titer higher than the reference limit <1.11, and the anti-toxoplasmic IgM antibody was within the normal range.

Non-involvement of the foveal region, papillae, and negative IgM antibodies were the reason for monitoring the patient without concomitant antiparasitic therapy.

After a year and a half (in 2015) from the initial examination, we repeated the FFA. On the right angiogram, near the upper temporal arcade, two clearly limited hyperfluorescences were still present without changes in the late stages of imaging.

Above these lesions, not clearly defined, ring-shaped discontinuous hyperfluorescence (with a hypofluorescence center) was obtained. Limited hyperfluorescence was observed on the papilla of the optic nerve, which expanded over time.

On the left angiogram, confluence of some of the lesions was noticed perimacularly, with central hypofluorescence, lined with a hyperfluorescence ring (Figure 3).

Due to the progression of the FFA finding, and elevated titer (ELISA) for anti-toxoplasma IgG and IgM antibodies, suggesting activity of the process (along with involvement of the papillary region of the right eye), triple therapy (pyrimethamine, sulphadia and prednisolone) was prescribed in consultation with an infectologist.

The patient was monitored regularly in the following period.

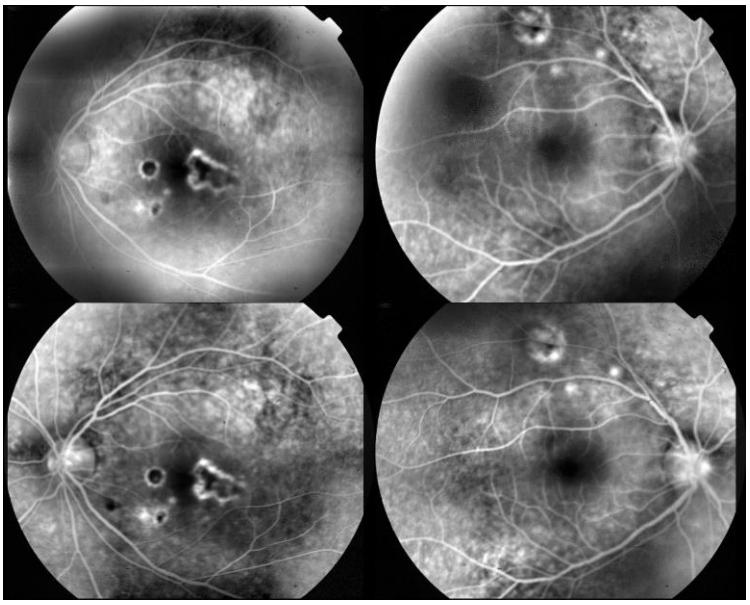

Figure 3. Fundus fluorescent angiography (2015). The right images show the early and late stage of angiogram of the right eye and the left images show the angiogram of the other eye.

Four years after the first examination, in 2018, there were signs of acute inflammation in the vitreous with a lot of inflammatory cells and haze of vitreous (2 +) - vitritis, accompanied by a decrease in visual acuity of the right eye (0.8 sine corectionem) according to the Snellen optotype.

Examination of the left eye also showed signs of active inflammation of the posterior pole, with haze of the vitreous of (0.5+), but without a decrease in visual acuity.

A new angiogram was made. Clear fluorescence results were not obtained on the right eye due to vitreous opacity.

However, on the left angiogram, progression of the lesion to the macular region was noted, with hyperfluorescence zones, which remained unchanged during imaging and a masking effect of accumulated pigment epithelium in the central part of the lesions remained.

In addition to the upper-temporal arcade, in the early stages of filming, the initial hyperfluorescence was vaguely limited, which expanded in the late stages of filming. The titer of anti-toxoplasma IgG and IgM antibodies was increased again and in consultation with an infectologist, the triple therapy was repeated, as well as local corticosteroid therapy on the right eye due to the inflammatory process in the vitreous.

After 6 weeks, the patient's visual acuity improved and it was 1.0 sine corectionem in both eyes.

A few months later, the patient experienced a rapid decline in visual acuity in the left eye, 0.32 sine corectionem, fever with 39^0C body temperature and maculopapular rash on the body. At the University Clinic for Infectious Diseases and Febrile Conditions, the diagnosis of measles was made and ruled out possible HIV infection.

After the clinical picture of measles was withdrawn, posterior segment OCT (Figure 4) and FFA were done again. On the right's angiogram, near to the upper-temporal arcade, progression of the previously described lesion was noted (window effect with central hypofluorescence due to regrouping and atrophy of retinal pigment epithelium-RPE) lined with clear hyperfluorescence and no angiogram changes in the late phases of angiogram.

A zone of destruction is noted in the left macular region, with central hypofluorescence, accompanied by a pronounced hyperfluorescence ring, which remained clear even in the late stages of imaging. Smaller clearly demarcated hyperfluorescence zones were also present, as well as a masked effect due to atrophy and regrouping of the retinal pigment epithelium (Figure 5).

Due to the obtained activity shown by increasing the hyperfluorescence in the left macular region, its destruction as well as a significant decrease in the visual acuity of the left eye, the patient was prescribed the triple therapy again.

In the following period, a moderate improvement of the visual acuity of the left eye was achieved by 2 rows per Snellen (0,5 sine corectionem), the vision of the right eye remained unchanged during the overall acute attack (1,0 sine corectionem).

Destruction in the morphology of the macular region, fibrosis, thickening of the inner limiting membrane, regrouping and hypertrophy of the retinal pigment epithelium.

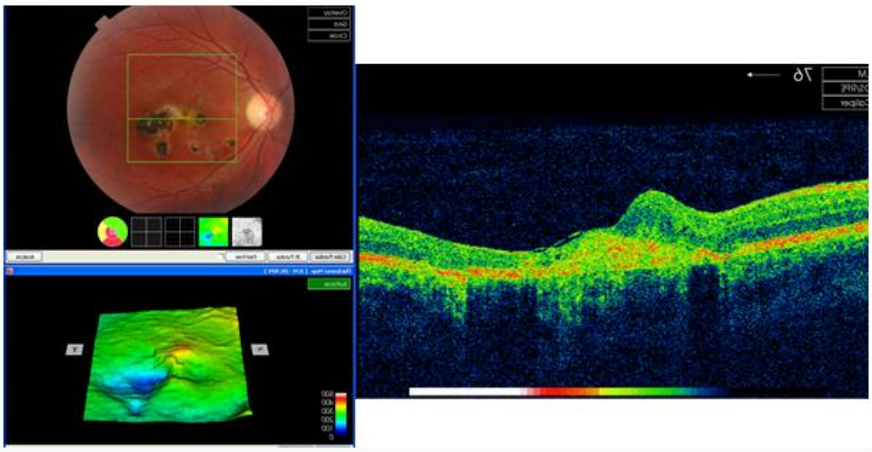

Figure 4. OCT finding of the macular region of the left eye.

From the beginning of 2020, the patient does not have a control examination due to her moving to another country and COVID 19 pandemic.

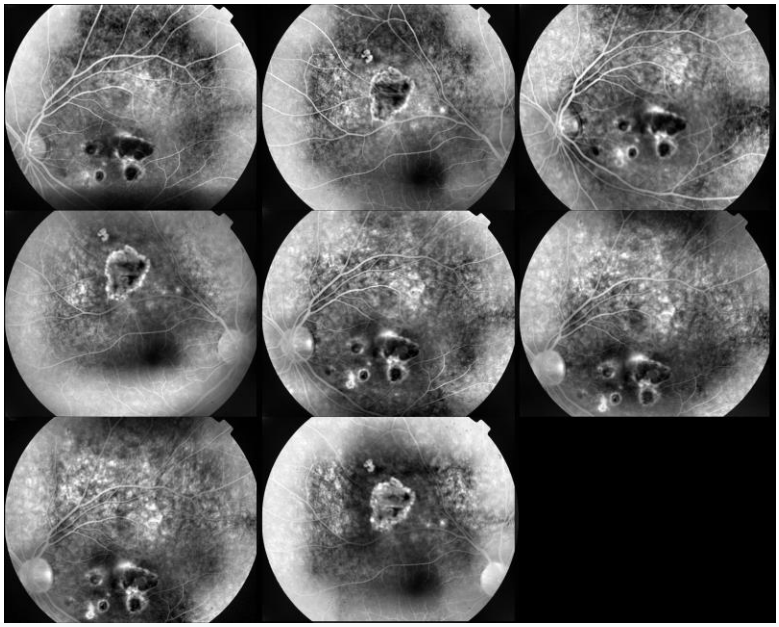

Figure 5. Fundus fluorescent angiography (2018). Images 2, 4 and 8 show the course of the angiogram of the right eye, images 1,3,5,6 and 7 of the left eye.

Discussion

The symptoms of ocular toxoplasmosis depend on the anatomical location of the pathological lesion. Decreased vision is seen when lesion is on macular or papillary region, as well as in opaque optic media: vitreous and anterior chamber.

If the lesion is on the periphery of the retina or in children who have not yet developed verbal skills, the changes will remain undetected [9].

The clinical presentation of this disease may be different. It is most commonly presented as retinochoroiditis, in the acute phase or as a pigmented inactive scar [10].

The active lesion presents as a creamy-pale coloration that limits the fibrous atrophic region. In addition, periphlebitis or arteritis (Kyrieleis) can be found near to the active process [11].

Vitritis is also a common manifestation of retinochoroiditis. That is an inflammatory cell infiltrate which lead to varying degrees of vitreous haze, resulting in the formation of an epiretinal membrane and vitreo-retinal traction syndrome.

Another presentation of ocular toxoplasmosis is anterior uveitis. It can be granulomatous or non-granulomatous, with varying degrees of inflammation, accompanied by the formation of posterior synechiae in severe cases. In immunocompromised patients, the inflammatory process may spread to the sclera, leading to scleritis [9,12].

Cases of papillitis, neuritis, or neuroretinitis have been reported in the literature, giving a differential diagnostic problem with other causes of these diseases [13]. Not very often, ocular toxoplasmosis may present as small multifocal whitish lesions in the outer layers of the retina as a result of the interaction of the parasite and the host's immune system. Such changes are known as Punctate outer retinal toxoplasmosis (PORT) [14].

Complications of ocular toxoplasmosis can be numerous. The inflammatory process in both the vitreous and the anterior chamber can lead to the formation of synechiae and obstruction of the trabecular meshwork, resulting in secondary glaucoma.

The inflammatory process also causes damage to the lens cristalina with subsequent uveal cataract. Vitritis, on the other hand, is associated with the formation of an epiretinal membrane and vitreous retinal traction. Vascular complications in the form of vasculitis, vascular occlusions, and the formation of a neovascular network are also concomitant sequelae of this disease [15,16,17].

Visual imaging techniques are very important in diagnosing this ocular parasitosis. As in our case, in modern ophthalmology for diagnosis are used: fundus photography, autofluorescence, fundus fluorescence angiography, optical coherence tomography of the posterior segment of the eye with or without angiography and ultrasonography.

Each of these tools has its own significance in the diagnostic process. Example: in distinguishing the lesion, its location, activity, depth, RPE changes, display of neovascularization, and possible vitreo-retinal traction [18].

However, clinical diagnosis alone may be insufficient due to differential diagnostic challenges. A number of other causes of uveitis give similar clinical manifestations, such as: toxocariasis, tuberculosis, syphilis, histoplasmosis, ocular lymphoma, endophthalmitis, multifocal choroiditis as well as acute retinal necrosis caused by the herpesviridae family [19].

In the case of differential diagnostic problems, the exact diagnosis is made with the help of laboratory tests. Today there are several direct and indirect methods of proving this parasite. In clinical practice are used: serological methods (Sabine-Feldman test, indirect fluorescence, direct agglutination test, ELISA, etc.), polymerase chain reaction, immunohistochemical identification of the parasite, inoculation of the parasite in animal models or in vitro cultivation [18,19].

However, serological methods are most often used in everyday clinical practice. A combination of imaging techniques and laboratory tests is a good way to diagnose ocular toxoplasmosis.

The treatment of the disease is still controversial. Most commonly in immunocompetent patients, spontaneous lesions resolve within one to two months [20].

Therefore, the assessment of treatment should be based on the age of the patient, his immune status, the characteristics of the lesion (its location and size), the presence of vitreous opacity, vasculitis, occlusion of blood vessels, the presence of macular edema or papillary edema [18].

Treatment usually lasts 4-6 weeks and includes two antimicrobials and a corticosteroid (topical and per os). Classical therapy, which is considered the first choice, is a combination of pyrimethamine, sulfadiazine, and the systemic corticosteroid-prednisone [21].

This treatment was first started in the 1950s and it is still used today, with certain side effects such as: thrombocytopenia, leukopenia and gastrointestinal and dermatological manifestations. Some authors suggest the inclusion of clindamycin in the treatment protocol, especially in patients who do not tolerate or are allergic to sulfa drugs. Spyramycin, atavaquone, azitromycin and cotrimoxazole are also mentioned as possible therapeutic drugs [22,23].

The course of this disease depends on the frequency of recurrences and the destruction of retinal tissue caused by them. Bosch-Driessen and colleagues in their study of 154 patients with ocular toxoplasmosis found that 79% had a recurrent episode over a 5-year period.

The same study found that the most active episodes occurred in the age group between 15 and 45 years, with a peak at the age of 25 years [10].

Decreased immunity for another reason, such as acquired immunodeficiency condition or congenital disease may be a trigger factor for parasite activation and recurrence [24]. It is important to note that immune suppression is not always necessary to reactivate the disease [23].

In our case, getting measles in an immunocompetent girl may have been the cause for reactivation of the parasite. In the literature we consulted during the follow-up and description of this case, we did not encounter any other work related to measles as a trigger factor for Toxoplasma gondii reactivation.

Conclusion

Through this paper we tried to present a case of retinochoroid caused by a parasitic disease - toxoplasmosis. Three recurrent episodes of parasitic reactivation were observed during follow-up of the patient over a period of several years.

The third, more severe attack, was followed by a significant drop in visual acuity in the left eye, probably due to a trigger mechanism caused by measles.

The specific clinical picture on both eyes and the laboratory tests for anti-toxoplasmosis IgG and IgM antibodies were consistent with the data we consulted from the literature, which helped to confirm the diagnosis of congenital toxoplasmosis.

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