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Clinical features of ocular toxoplasmosis in an immigrant population in the Barcelona area: Study of 22 patients

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A B S T R A C T

Purpose: To report the epidemiological, clinical and prognostic features of ocular toxoplasmosis in an immigrant population in the Barcelona area.
Methods: A retrospective non-comparative observational study was conducted on a case series of 22 immigrant patients diagnosed with ocular toxoplasmosis by ophthalmoscopic and serological findings. Demographic, clinical and laboratory data were analysed under baseline conditions. The minimum follow-up was 6 months.
Results: Bilateral involvement was observed in five of the 22 patients (22.7%), a total of 27 eyes being affected by active lesions and old scars. Atypical presentations, including multiple or large necrotizing lesions, were observed in 5 eyes (25%). In 15 eyes (75%) the retinal lesions were associated with intraocular inflammation. Vitreoretinal complications were observed in eight eyes (29.6%), with 22.7% of them requiring vitreous surgery.
Conclusions: In immigrant patients from our area in Barcelona, ocular toxoplasmosis has specific clinical and prognostic features, including high rates of atypical presentations, frequent intraocular inflammation, and vitreoretinal complications, requiring surgery in most of the cases.

Características clínicas de toxoplasmosis ocular en población inmigrante del área de Barcelona: estudio de 22 pacientes

Palabras clave:
Toxoplasmosis
Retinocoroiditis
Inmigrantes

R E S U M E N

Propósito: Describir las características epidemiológicas, clínicas y pronósticas de la toxoplasmosis ocular en un grupo de población inmigrante de nuestra área.
Método: Para ello se realizó un estudio descriptivo retrospectivo no-comparativo de 22 pacientes inmigrantes diagnosticados de toxoplasmosis ocular mediante oftalmoscopía y serología. Se evaluaron datos demográficos, clínicos y de laboratorio basalmente. Los pacientes fueron seguidos por un período mínimo de 6 meses.

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Resultados: Cinco de los 22 pacientes (22,7%) tenían afectación bilateral, presentando lesiones activas y/o cicatriciales un total de 27 ojos. En cinco ojos (25%) se evidenciaron lesiones atípicas retinianas en forma de múltiples focos de retinitis o áreas extensas de necrosis. En quince ojos (75%) las lesiones retinianas se acompañaron de signos inflamatorios intraoculares. En ocho ojos (29,6%) aparecieron complicaciones vítreo-retinianas precisando de cirugía de vitrectomía cinco de ellos (22,7%).

Conclusiones: La toxoplasmosis ocular en pacientes inmigrantes de nuestra área tiene unas características clínicas y pronósticas específicas que incluyen el presentar unas tasas elevadas de formas atípicas, acompañarse frecuentemente de inflamación intraocular y tener asociadas complicaciones vítreo-retinianas que requieren en la mayoría de los casos cirugía de vitrectomía.

Introduction

Ocular toxoplasmosis is the most frequent cause of infectious posterior uveitis in our environment. Epidemiological studies on the infection demonstrate a varying prevalence in different geographical regions. Accordingly, while seroprevalence in developed countries like the United States is of 22.5%[1] in South America, and particularly in the South of Brazil, it can reach 98%.[2] In Spain, the prevalence rate is not determined with precision and ranges between 25% and 45% according to different studies.[3] Specifically, in Catalonia it reaches 28.6%.[4] Similarly, the proportion of individuals infected by Toxoplasma gondii (T. gondii) who develop ocular involvement also varies between geographic areas: while in some developed countries it has been estimated at 2%,[1] in Southern Brazil it reaches 17.7%.[5] In what concerns Africa, even though there are no published studies, the ocular toxoplasmosis rate is also high.[1]

As in recent years Spain has received an increasing amount of immigrants, we have made a descriptive study on the characteristics of ocular toxoplasmosis in this population group in the area of Barcelona in order to analyze the clinical patterns and prognostic factors in this sub-group of patients.

Subjects, material and method

A retrospective, observational and descriptive study of immigrant population affected by ocular toxoplasmosis who visited the Ophthalmology Service of the Clinic and Provincial Hospital of Barcelona between January 2000 and November 2008. The study included only the cases with confirmed clinical and/or serologic diagnostic and with a minimum follow-up period of 6 months. The clinical diagnostic of typical ocular toxoplasmosis was based on the criteria set by Holland et al[6] which are defined by the presence of a focal retinal lesion having a white-creamish appearance, occasionally accompanied by one or several retinal-choroidal hyperpigmented scars in the same eye. The serological criteria for the acute phase of the infection included the presence of IgM antibodies (index above 1.20 of determination of the presence of antibodies by means of immunoanalysis), while the chronic stage was defined by the elevation of IgG antibodies (over 14.2μU/ml) without positivity for IgM. The inclusion criteria were fulfilled by 22 patients. These clinical records were checked and the following data were obtained at baseline: sex, age and nationality, relevant systemic and ophthalmological history, affected eye, bilaterality, possible previous toxoplasmosis episodes and immunological condition.

All patients took a complete ophthalmological checkup comprising the determination of the bet corrected visual acuity (BCVA) with Snellen optotypes, slit lamp evaluation, applanation tonometry and ocular fundus examination with biomicroscopy and non-contact lens as well as indirect ophthalmoscopy.

The morphology of the active lesion was classified as focal retinitis adjacent to scar (recurring toxoplasmosis) and single or multiple focus points without adjacent scar (primary toxoplasmosis).[7] The congenital forms were defined as those exhibiting a large macular atrophic scar with pigmented edges. As regards the location of the lesions, they were divided in macular posterior for those located between the vascular arcs and the equator, and peripheral lesions. The presence or absence of associated inflammatory signs in eye fundus such as vitreitis was also recorded (scale: +,++,+++) and vasculitis as well as scar lesions in ocular fundus and their location (macular or peripheral). The baseline data input also recorded the presence of cells in the anterior chamber and variations in the intra-ocular pressure (IOP).

All the patients with an active ocular toxoplasmosis outbreak were treated with anti-parasite medication, of choice sulphametoxazol-trimetoprim (Septrin oral forte®, 800/160mg /12 hours during 4-6 weeks), adding oral corticoids at a dose of 1mg/kg/day 48 hours after having started the antibiotic treatment for the patients who exhibited active macular lesions, optic nerve involvement and moderate or severe intraocular inflammation. The cases that exhibited inflammation in anterior chamber also were prescribed prednisolone acetate and cyclopentholate. Those exhibiting ocular hypertension were also given topical hypotensor treatment (timolole maleate every 12 hours).

Finally, we recorded the cases that during follow-up had exhibited ocular recurrence of the infection, and the morphological characteristics were studied (focus adjacent to previous scar, focus not adjacent to scar, other forms) and their location (macular, posterior or peripheral). The vitreoretinal complications which arose during the evolution and the need of surgery were also recorded.

Results

The demographic data of this series comprise 22 patients, 10 male (45.4%) and 12 female (54.5%), who engaged in a follow-up averaging 12.4 months (range 6- 56 months). Most of the patients were of Latin origin (77.3%), and five of African origin (22.7%) (fig. 1). The mean age at diagnostic was of 29.8 years (range from 11 to 50 years) and the standard deviation was 9.9 years. One patient had a history of systemic toxoplasmosis. Three patients (13.6%) had a previous diagnostic of at least 1 outbreak of ocular toxoplasmosis. Two patients exhibited immunodepression (9.1%), in one case due to chronic use of systemic corticoids for dermatomiositis, and in the other case secondary to infection by the human immune defficiency virus (HIV). Five of the 22 patients (22.7%) had bilateral involvement, and therefore 27 eyes exhibited active and/or cicatricial lesions. Active lesions were determined in 20 eyes (74%). Serologies were performed for T. gondii in all patients, and only 1 patient gave positive for IgM (4.5%) while all patients (100%) gave positive for IgG (table 1).

The mean BCVA at diagnostic time was 0.43 (range 0.01-1), and the BCVA obtained in the last visit after anti-parasitic treatment had a mean value of 0.59 (range 0.03-1). The cases

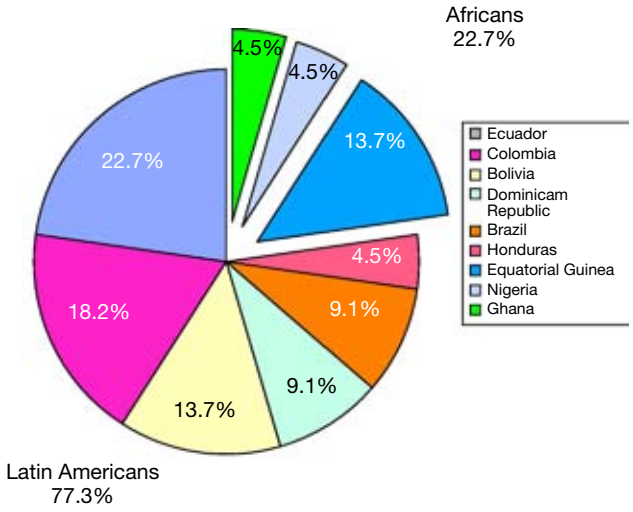

Figure 1 – Chart showing the distribution of the study patients per country of origin, and groups by ethnic origin.

exhibiting macular involvement (9 eyes, 33.3%) either due to active lesion or previous chorioretinal scar, exhibited a mean BCVA of 0.11 (range 0.01-0.6) which improved with treatment to reach 0.25 (range 0.03-0.75).

Only 2 of our patients had no active lesion at diagnostic time (9%). Of the 20 eyes that exhibited an active focus, three had them in the macula (15%), 8 were posterior (40%) and in the remaining 9 the focus was peripheral (45%). Thirteen cases (65%) exhibited the typical form of the disease, consisting in the presence of an active focus adjacent to a previous

Table 1 – Epidemiological data, bilaterality, previous toxoplasmosis history, immunological condition and serological findings of the patients in our series.

	Nationality	Sex	Age	Affected eye	Bilaterality	Previous outbreaks	Immunodepression	Serologies
1	Ecuador	M	26	LE	Yes	No	No	IgM–, IgG+
2	Dominican Republic	M	26	RE	No	No	No	IgM–, IgG+
3	Colombia	M	43	LE	No	No	No	IgM–, IgG+
4	Colombia	M	25	LE	Yes	No	No	IgM+, IgG+
5	Brazil	F	20	LE	No	No	No	IgM–, IgG+
6	Ecuador	F	26	LE	Yes	Yes, 12 months	No	IgM–, IgG+
7	Bolivia	M	38	RE	No	No	No	IgM–, IgG+
8	Equatorial Guinea	F	48	RE	No	No	Chronic GCC	IgM–, IgG+
9	Ecuador	F	50	RE	No	No	No	IgM–, IgG+
10	Bolivia	M	22	LE	Yes	No	No	IgM–, IgG+
11	Dominican Republic	F	17	RE	Yes	No	No	IgM–, IgG+
12	Bolivia	M	25	LE	No	No	No	IgM–, IgG+
13	Brazil	F	26	LE	No	No	No	IgM–, IgG+
14	Equatorial Guinea	M	40	RE	No	No	HIV+	IgM–, IgG+
15	Nigeria	F	25	LE	No	No	No	IgM–, IgG+
16	Equatorial Guinea	F	11	RE	No	Yes, 2 months	No	IgM–, IgG+
17	Ecuador	M	23	LE	No	No	No	IgM–, IgG+
18	Ghana	M	28	RE	No	No	No	IgM–, IgG+
19	Honduras	F	32	LE	No	No	No	IgM–, IgG+
20	Ecuador	F	38	LE	No	No	No	IgM–, IgG+
21	Colombia	F	38	LE	No	Yes, 60 months	No	IgM–, IgG+
22	Colombia	F	29	LE	No	No	No	IgM–, IgG+

M: male; F: female; RE: right eye; LE: left eye.

Table 2 – Clinical characteristics of acute and cicatricial lesions, associated inflammatory signals and repercussion on visual acuity at diagnostic time and at end of follow-up of the patients in our series.

	AVDX	VA post-TT	Location of active lesion	Characteristics of active lesion	Inflammation	Cicatricial lesions	Location of cicatricial lesions	Aspect
1	1/0.03	1/0.1	Peripheral	Single site with adjacent scar	Vitreitis+/Vasculitis	Yes	RE and LE peripheral	Acquired
2	0.01	0.2	Macular	Single site with adjacent scar	Anterior uveitis/ Vitreitis+++	Yes	RE macular and posterior	Acquired
3	0.1	0.75	Posterior	Single site with adjacent scar	Anterior uveitis	Yes	LE macular and posterior	Acquired
4	0.01/0.7	0.3/0.8	Peripheral	Multiple foci without adjacent scar	Anterior uveitis/ Vitreitis+/Vasculitis	Yes	RE macular and LE peripheral	Congenital
5	0.03	0.4	Posterior	Single site without adjacent scar	No	No	No	Acquired
6	0.1/1	0.1/1	Posterior	Single site with adjacent scar	No	Yes	RE macular	Congenital
7	0.2	0.9	Peripheral	ARN	Anterior uveitis /exudative RD	No	No	Acquired
8	1	1	Posterior	Single site with adjacent scar	No	Yes	RE posterior	Acquired
9	0.01	0.1	Peripheral	Two foci with adjacent scar	Anterior uveitis /OHT	Yes	RE macular and peripheral	Congenital
10	1/0.01	1/0.4	Peripheral	Single site with adjacent scar	Vitreitis+++/ exudative RD	Yes	RE peripheral/LE peripheral	Acquired
11	1/0.05	1/0.1	No	No	No	Yes	RE posterior and LE macular	Congenital
12	0.3	0.7	Posterior	Single site without adjacent scar	Anterior uveitis /OHT/Vitreitis++	No	No	Acquired
13	0.6	0.6	Macular	Single site with adjacent scar	No	Yes	LE posterior	Acquired
14	0.2	0.4	Posterior	ARN	Vasculitis	No	No	Acquired
15	0.9	1	Posterior	Single site with adjacent scar	Vasculitis	Yes	LE posterior	Acquired
16	0.05	0.05	No	No	No	Yes	RE macular and posterior	Congenital
17	0.9	0.9	Peripheral	Single site with adjacent scar	Vasculitis	Yes	LE peripheral	Acquired
18	0.05	0.03	Macular	Two foci with adjacent scar	Vasculitis	Yes	RE macular	Congenital
19	0.5	1	Posterior	Single site with adjacent scar	Anterior uveitis /Vitreitis++	Yes	LE posterior	Acquired
20	0.4	0.2	Peripheral	Single site with adjacent scar	Anterior uveitis /OHT/Vitreitis++	Yes	LE peripheral	Acquired
21	0.6	0.95	Peripheral	Single site with adjacent scar	Vitreitis+	Yes	LE peripheral	Acquired
22	0.9	1	Peripheral	Single site with adjacent scar	No	No	LE peripheral	Acquired

VA: visual acuity; RD: retina detachment; DX: diagnostic; ARN: acute retinal necrosis; TT: treatment.

Table 3 – Recurring outbreaks registered during the follow-up period of our series and characterization thereof.

N°	T (months)	Localization of lesion	Characteristics of recurring lesion
3	5, 21, 48	Peripheral x3	Single site not adjacent to previous scar, reactivation of previous focus, single site not adjacent to previous scar
1	13	Macular	Single site adjacent to previous scar
1	12	Macular	Juxtafoveal choroiditis
1	3	Peripheral	Single site not adjacent to previous scar
1	9	Macular	Single site not adjacent to previous scar

N°: number; T: time.

chorioretinal scar. Two eyes (10%) exhibited a single active site without adjacent scar. Finally, 3 eyes (15%) had multiple active focal points at diagnostic time and in 2 (10%) a large retinal necrosis focus was determined. One of the latter cases was the HIV patient. Consequently, up to 25% of the eyes exhibited atypical forms of the disease.

A total of 15 eyes (75%) exhibited inflammatory signs in the initial outbreak, of which 8 (40%) evidenced cells in the anterior chamber, 8 (40%) exhibited vitreitis and 8 (40%) exhibited inflammation in the posterior pole in the form of peri-lesional retinal vasculitis (30%) and exudative retinal detachment (10%). In only 3 cases (15%) intraocular hypertension was determined.

In 21 eyes (77.7%) chorioretinal cicatricial lesions were observed due to previous ocular involvement caused by T. gondii. Most of these lesions were extra-macular, 9 were located peripherally (42.8%) and 8 were posterior (38.1%), while macular location was observed in 8 eyes (38.1%).

According to the funduscopic appearance of the lesions and the patient history, the patients were divided in 2 groups: those with probable congenital origin due to toxoplasma, totaling 6 (27.2%), and those with acquired toxoplasmosis (72.7%) (table 2). The majority of patients (81.8%) exhibited clinical characteristics compatible with recurring forms of the disease, while only 4 patients (18.18%) exhibited primary ocular toxoplasmosis lesions (table 2).

Overall, 5 patients exhibited one or more recurring lesions (22.7%) during their evolution. The mean of recurring episodes was of 1.4 (range from 1 to 3), with a mean of only one episode. The lesions recurred in a mean time of 15.8 months (standard deviation 15.3, range from 3 to 48 months) as from the first diagnosed onset. The lesions were peripherally located in 4 cases (57.1%) and in the macula in 3 (42.8%). Only 2 cases exhibited a reactivation of the previous focus (28.5%), while in the remainder a new focus arose (71.4%) (table 3).

Vitreoretinal complications were found in 8 eyes (29.6%). Considering the cases that exhibited complications, persistent vitreous opacity was observed in 3 eyes (37.5%), vitreous hemorrhage in 2 (25%), peripheral retinal tears in 1 (12.5%), regmatogenous retina detachment (RD) in 1 (12.5%), exudative RD in 2 (25%), epiretinal macular membrane (EMM) in 3 (37.5%), neuroretinitis in 2 (25%) and retinal neovascularization in 1 (12.5%). Five patients (22.7%) needed vitreoretinal surgery with pars plana vitrectomy (PPV). This procedure was indicated due to EMM in patients 3 and 16, due to vitreous hemorrhage and neovascularization secondary to ischemializing vasculitis in patients 1 and 10, and due to persistent vitreous opacity and regmatogenous RD (confirmed in surgery) in patient 2. Patient 10 was intervened with pars plana vitrectomy and silicone oil injection which was removed in a second surgery, who associated lensectomy due to secondary cataracts. Finally, an intra-ocular lens was implanted in sulcus (table 4).

Discussion

This study analyzed the clinical records of 22 patients of Latin American and African origin with the objective of observing

Table 4 – Presence of vitreoretinal complications, and necessity of surgery and surgical technique applied to the patients of our series.

Patient	Complications	Surgery
1	HV, vasculitis ischemia, NV LE	PPV, endolaser, posterior hyaloids peeling
2	Inferior tears, RD, opacity vitreous RE	PPV, endolaser, cryotherapy
3	ERM, cataract, vitreous opacity LE	PPV, peeling ERM, FACO+IOL
5	Neuroretinitis LE	No
7	RD exudative RE	No
10	HV, exudative RD. Vitreous opacity, ERM LE	PPV+SO, PPV+lensectomy+ SO extraction, implant 2nd IOL to sulcus
14	Neuroretinitis RE	No
16	ERM RE	PPV, ERM peeling

SO: silicone oil; RD: retina detachment; HV: hemovitreous; IOL: intra-ocular lens; ERM: epiretinal membrane; NV: neovascularization; PPV: pars plana vitrectomy.

possible clinical patterns characteristic of these population groups. In the sample, most of the patients were young (mean age 29.8 years), of whom 76.1% were of Latin American origin, without differences in what concerns sex and with only two cases (patient 8 and 14) with immunodepression. The distribution of toxoplasmic retinochoroiditis episodes in relation to the age of patients is similar to that observed in other studies like the Bosch-Driessen et al[7] study in which the mean age was of 31.1 years. In our series, 5 patients (18.5%) exhibited bilateral lesions, and 3 of these had an ophthalmoscopic appearance of congenital infection. Previous studies have described large variations in bilateral ocular involvement due to toxoplasmosis, ranging from 22% to 40%, with greater frequency in congenital infections.[7,8]

It is interesting to note that in our series 11 out of 27 eyes, a high percentage of 40.7%, exhibited visual acuity below 0.1 at diagnostic time. The causes of low visual acuity were: presumably congenital macular scars in 5 patients, vitreous opacity in 4, neuroretinitis in one, and ischemic vasculitis in one. In a previous study with European patients, only 19% of the eyes had legal blindness.[7]

The majority of patients (65%) exhibited typical toxoplasmosis lesions, i.e., the presence of an active focus with chorioretinal scars in the same eye[6,9] which indicates that the majority of our cases would be a recurrence of the disease. This hypothesis is supported by the serological findings (only 1 case positive for IgM). Most series describe a higher prevalence of recurring injuries.[7] Two eyes (10%) exhibited a single active site without adjacent scar, 25% of eyes had multiple active foci at diagnostic time and in 2 (10%) a large retinal necrosis area was determined, one of them being the HIV patient, which means that up to 25% of the eyes exhibited non-typical forms of the disease.

The recurrence rate in the follow-up period of our patients was of 22.7%, similar to that of European patients in a previous study[10] which gave a rate of 21% in the first year and 27% in the second one. The recurrence risk of the disease is greater in the first year after an active episode of chorioretinitis, as stated by some authors.[11] For this reason the majority of our patients stay in follow-up for this period of time (12.4 months).

Up to 36.3% of eyes exhibited some vitreoretinal complication, the most frequent being vitreous opacity and formation of epiretinal membrane, as also described in the study of Bosch-Driessen et al[7] with 5 eyes requiring vitreoretinal surgery, representing 22.7% of the entire sample. In general, complications arose in patients with severe ocular inflammation. In addition, 75% exhibited ocular inflammatory signals in active phase. Said signals suggest a severity of the infection in this group of patients, matching the results obtained by Dodds et al[12] who found a greater prevalence and severity of associated inflammatory signals in the subgroup of South American patients compared to European ones.

Consequently, in our population ocular toxoplasmosis has specific clinical characteristics with a higher rate of visual sequels. This could be due to a number of concurring individual factors (genetic and immunologic) as well as environmental factors (higher prevalence of toxoplasma infection) and factors inherent to the parasite (the literature describes several serotypes of the parasite with different aggressiveness and geographic distribution). Specifically, in our series the high rate of patients with legal blindness could be due to the higher prevalence of congenital toxoplasmosis in their countries because, after treating the 6 eyes which exhibited visual acuity values of 0.1 or less, it was observed that five had macular scars of probable congenital origin.

Despite the limitations of the retrospective nature of our study and the relatively small sample size, it is possible to observer clinical and evolutionary characteristics specific to the immigrant population of our area affected by ocular toxoplasmosis. It is difficult to compare our results with those of other clinical series of patients because, in general, said series do not analyze the origin of the patients. A prospective study with determination of the T. gondii serotypes and inflammatory mediators in active outbreaks would allow for a deeper research of the pathogenesis and expression of the infection at the ocular level in different population groups.

Conflict of interest

The authors declare they have no conflict of interest.

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