Optic nerve changes in ocular toxoplasmosis

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Abstract

Purpose To determine the prevalence and features of the different types of involvement of the optic nerve in ocular toxoplasmosis.

Methods Retrospective cross-sectional study. All patients with active ocular toxoplasmosis, consulting in the Uveitis Section of the Ophthalmology Department were selected. The involvement of the optic nerve was classified in the following categories:

juxtapapillary retinochoroiditis, pure papillitis, neuroretinitis, distant lesion, and mixed lesion.

Results The prevalence of involvement of the optic nerve found was 5.3%. The optic nerve involvement with the presence of a concurrent active distant lesion, occurred in 22 eyes (43.1%). A juxtapapillary lesion was found in 18 eyes (35.3%). Eight eyes (15.7%) presented lesions characterised as mixed. Isolated papillitis occurred in 3 eyes (5.9%). Forty-seven lesions (95.9%) were unilateral and two (4.1%) were bilateral. Twenty-eight eyes (54.9%) had pre-existing lesions and 23 (45%) were primary lesions. Visual acuity improved in 35 eyes (71.4%) and remained unchanged in 14 eyes (28.5%).

Conclusion The involvement of the optic nerve most frequently found in ocular toxoplasmosis was optic nerve oedema with a concurrent distant active lesion. The second type of lesion most often found was juxtapapillary retinochoroiditis. Involvement was monocular in most cases and the visual prognosis was favourable.

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Introduction

Uveitis is a worldwide prevalent disease, affecting people at productive age and it is a

major cause of blindness.¹ Ocular toxoplasmosis, in turn, is one of the most frequent aetiologies of posterior uveitis.² In the State of Rio Grande do Sul, Brazil, it assumes considerable proportions, becoming a public health problem of extreme relevance.³

Ocular involvement in toxoplasmosis may result from acquired infection after birth or from the congenital form of the disease.^{4–8} The diagnosis is basically clinical, complemented by serologic tests in order to obtain evidence of previous exposure to the parasite.⁹

The involvement of the optic nerve in ocular toxoplasmosis was already described by several authors at the beginning of last century, and more recently new studies on this subject have appeared. *Toxoplasma gondii* may cause a lesion in the optic disc because of contiguousness;^{10,11} by direct involvement^{11–17} or even become involved when a retinochoroiditis lesion is located far from the optic nerve.^{8,9}

The contiguous form was described by Jensen many years ago¹⁸ as a specific entity in four cases of juxtapapillary choroiditis, later considered as probably due to tuberculous aetiology. In 1952, Wilder recognised *T. gondii* histopathologically in necrotic retinochoroidal lesion in adult patients.^{19–21} Lesions had granulomatous character and marked necrosis in many instances led to a pathologic diagnosis of tuberculosis. So, currently it is accepted that most cases of Jensen's choroiditis are of toxoplasmic aetiology. This type of lesion consists of a typical area of retinochoroiditis in contact with a swollen optic disc and accompanied by a typical sectorial deficit in the visual field.

The direct involvement of the optic nerve by *T. gondii* was demonstrated histopathologically by the presence of different forms of the parasite inside it.²² At ophthalmoscopic observation, this involvement may be subdivided into pure anterior neuritis or papillitis and neuroretinitis.¹¹ In pure papillitis the parasite affects the optic disc directly, causing a swollen

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papilla with sheathing of the peripapillary veins and there may be no concurrent active retinochoroiditis lesion.⁸ However, in the majority of these cases a peripheral scar lesion and vitreitis is always present over the optic disc.^{13,17}

Neuroretinitis is characterised usually by a swollen optic nerve accompanied of papillo-macular or serous macular detachment of the retina associated to hard exudates in the macula distributed in a star shape.^{14,16,23,24}

We have observed another form of involvement of the optic disc due to toxoplasmosis that would be caused secondarily by an active distant retinal lesion.⁹ In these cases there is an active focal necrotising retinochoroiditis lesion located at variable distances from the optic disc that presents changes that resembles papillitis.⁸ There are no detailed studies about this type of optic nerve involvement in the literature.

The objective of this study was to determine the total prevalence and the different types of involvement of the optic nerve in ocular toxoplasmosis, as well as to study several accompanying clinical parameters.

Materials and methods

The present retrospective cross-sectional study was performed in the Uveitis Section of the Ophthalmology Department at Hospital de Clínicas de Porto Alegre.

All patients attended in our Uveitis Section (926 records) who presented active ocular toxoplasmosis in the 1987–2001 period were reviewed. Patients who were immunocompromised and those who had a previous optic nerve lesion by causes other than toxoplasmosis were excluded. Patients with atrophic optic nerve caused by toxoplasmosis were also excluded because this alteration is considered a sequelae and in this study we wanted to evaluate the evolution of active lesions.

To be included in the study, the patient had to present alterations of the optic nerve in the form of swollen disc or papillitis concomitantly with the presence of an active ocular lesion caused by *T. gondii*.

The diagnosis of ocular toxoplasmosis was based on the presence of typical retinochoroiditis lesions and IgM- and/or IgG-specific antibodies for toxoplasmosis. The methods used for serology were indirect immunofluorescence reactions (IFI), ELFA (enzyme-linked fluorescent assay) and MEIA (microparticle enzyme immunoassay) for IgM and IgG. Serological tests were also performed to detect other infectious diseases such as syphilis, rubella, herpes, cytomegalovirus, and tuberculosis. Fundoscopy was performed under mydriasis, with direct and indirect ophthalmoscope, and fundoscopic biomicroscopy with 78 diopter lens.

Angiography and retinography were also performed in all patients for documentation.

All patients were treated with the usual therapeutic scheme used in our Department.²⁵ (Sulphadiazine 500 mg 2 cp four time/day, pyrimethamine 25 mg 1 cp two time/day, Folinic acid 7.5 mg every day and oral corticosteroids – prednisone 1 mg/kg/day).

The files were analysed using a protocol containing the following data: patient identification, date of initial exam, eye affected, laterality, type of optic nerve lesion according to classification described elsewhere and initial and final visual acuity. The presence of pre-existing retinochoroiditis scars in the affected eye was also studied. The visual acuity was measured with Snellen chart at 6 m (better optical correction). The final visual acuity was measured when the lesion was considered cured (1–3 months).

The optic nerve involvement was classified as follows:

- (1) *Juxtapapillary retinochoroiditis*: retinochoroidal lesion contiguous to the swollen optic disc (Figure 1).
- (2) *Pure Papillitis*: swollen optic disc and sheathing of the peripapillary veins in the presence of a healed toxoplasmic retinochoroiditis lesion (Figure 2).
- (3) *Neuroretinitis*: swollen optic disc, papillo-macular or serous macular detachment of the retina with hard exudates at the macula.
- (4) *Distant lesion*: swollen optic disc in the presence of a distant active lesion (Figure 3).
- (5) *Mixed lesion*: presence of more than one type of involvement previously described concurrently (Figure 4).

Statistical analysis of the data was performed by SPSS program version 10. The χ^2 Pearson statistical test and

Figure 1 Retinography of a patient with superior juxtapapillary lesion and swollen disc.

Figure 2 Fluorescent angiography showing swollen disc (hyperfluorescence) with a superior retinochoroiditis scar.

Figure 3 Photograph showing temporal white lesion with concomitant swollen disc.

t-Student's test were also applied. The level of significance considered was 0.05.

The present study was approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre.

Results

Of the 926 patients, 49 patients (51 eyes) had involvement of the optic nerve with a total prevalence of 5.03%. The mean age of the patients with changes in the optic disc was 27 years and 4 months (with a variation of 6–65 years) (Table 1). The optic nerve involvement concomitantly with a distant lesion occurred in 22 eyes

Figure 4 Mixed lesion with a retinal white exsudate superior to swollen optic disc and a macular star (a juxtapapillary lesion mixed with a neuroretinitis).

(43.1%). The involvement of the optic disc by a juxtapapillary lesion occurred in 18 eyes (35.3%). Eight eyes (15.7%) presented more than one type of lesion concurrently, being characterised as mixed. Of these eight eyes, six eyes (75%) presented a distant lesion associated with neuroretinitis and two (25%) presented with juxtapapillary lesion and neuroretinitis. The pure papillitis occurred in three eyes (5.9%) (Graph 1). No cases of isolated neuroretinitis were found.

Forty-seven had (95.9%) unilateral lesions and two (4.1%) had bilateral (Table 1).

Twenty-eight eyes (54.9%) had pre-existing lesions and 23 (45%) were primary lesions (Table 1).

After treatment the visual acuity improved in 35 eyes (71.4%), and remained unchanged in 14 eyes (28.5%) (Graph 2). Patients with mixed lesions had the best visual prognosis because 75% of them improved visual acuity. The percentage of improved visual acuity was 66.6, 63.63, and 61.1% in papillitis, distant lesions, and juxtapapillary lesions, respectively.

Discussion

Ocular toxoplasmosis is very frequent in Rio Grande do Sul, and it is the main cause of uveitis in our Department.³ After many years of observations, we could verify a wide variety of clinical presentations of this disease.²⁶ Concomitantly, we have had opportunity to observe and treat a considerable number of patients presenting with optic nerve alterations. Although the prevalence found in our study seems not to be very high (5.3%) this type of involvement represents concern for

Table 1 Involvement of optic nerve in patients with ocular toxoplasmosis

	Type of lesion	Eye	Age	Laterality	Pre-existing lesions	Initial VA	Final VA
1	Mixed	RE	38	U	—	HM	0.5
2	Juxtapapillary	LE	34	U	+	CF	0.8
3	Juxtapapillary	RE	34	U	+	0.8	1
4	Distant	LE	61	U	—	0.5	0.5
5	Distant	LE	27	U	+	CF	CF
6	Mixed	LE	20	U	—	0.1	1
7	Juxtapapillary	RE	26	U	+	0.1	1
8	Distant	RE	21	U	—	CF	CF
9	Juxtapapillary	RE	24	U	—	0.33	1
10	Distant	LE	26	U	+	0.33	0.5
11	Mixed	LE	43	U	+	0.1	1
12	Juxtapapillary	RE	65	U	—	0.5	1
13	Distant	RE	19	U	+	CF	CF
14	Distant	LE	16	U	—	0.4	0.5
15	Mixed	LE	27	U	—	0.1	0.33
16	Distant	RE	26	U	+	0.1	0.5
17	Distant	LE	17	U	+	HM	0.1
18	Distant	LE	41	U	+	0.2	0.2
19	Distant	RE	36	U	+	0.2	1
20	Juxtapapillary	LE	32	U	+	0.33	0.6
21	Juxtapapillary	LE	38	U	+	0.1	0.6
22	Juxtapapillary	LE	29	U	—	1	1
23	Mixed	RE	13	U	—	CF	1
24	Mixed	RE	14	U	—	0.7	1
25	Juxtapapillary	LE	34	U	—	1	1
26	Papillitis	RE	17	B	+	1	1
	Papillitis	LE			—	0.1	0.2
27	Distant	LE	29	U	+	0.7	1
28	Distant	RE	26	U	+	0.2	1
29	Distant	LE	25	U	—	0.1	0.5
30	Distant	RE	11	U	+	0.2	0.5
31	Juxtapapillary	RE	44	U	+	0.1	1
32	Distant	LE	13	U	+	0.1	0.6
33	Distant	LE	30	U	—	0.1	0.3
34	Distant	LE	20	U	—	0.2	1
35	Juxtapapillary	RE	39	U	+	0.6	1
36 ^a	Distant	RE	6	B	+	—	0.3
	Distant	LE			+	—	0.1
37	Juxtapapillary	RE	20	U	+	CF	0.1
38	Distant	LE	24	U	—	0.8	1
39	Juxtapapillary	RE	22	U	+	0.1	0.1
40	Mixed	LE	15	U	—	CF	0.2
41	Juxtapapillary	LE	32	U	+	0.2	0.2
42	Juxtapapillary	RE	11	U	+	0.1	0.1
43	Papillitis	RE	25	U	—	HM	0.2
44	Juxtapapillary	LE	36	U	+	0.5	0.9
45	Juxtapapillary	LE	64	U	—	1	1
46	Mixed	LE	14	U	—	1	1
47	Juxtapapillary	RE	21	U	—	0.8	0.8
48	Distant	LE	18	U	—	0.33	1
49	Distant	LE	7	U	+	0.4	0.6

RE = right eye; LE = left eye; U = unilateral; B = bilateral; CF = count fingers; HM = hand's movements; — = primary lesion; + = Pre-existing lesion; VA = visual acuity.

^aPatient with congenital toxoplasmosis, examined for the first time at the age of 3 months.

the clinician because of severity of the disease and the diagnostic difficulties with other types of neuritis.

The optic nerve involvement in the presence of an active distant retinochoroiditis was the most frequent

type of lesion found in our study. Some authors^{27,28} do not consider optic disc swelling caused by distant lesion as true papillitis but as a reactive oedema of the optic nerve due to a hypersensitivity reaction, and then the

Graph 1 Types of involvement of optic nerve.

alteration is then called secondary papillitis.²⁷ This study shows that they evolve favourably with treatment and usually do not leave any permanent change in the optic nerve (63.63% of patient had improve visual acuity after resolution of inflammation).

The second most numerous group was represented by a swollen optic disc with a juxtapapillary lesion. Although the clinical appearance is usually very serious, with a large amount of exudates, hemorrhage, optic nerve oedema and low visual acuity, this type of change responds rapidly to medication, reabsorbing the oedema and leaving a typical retinal pigmented lesion. A scar may not be apparent at the beginning of the disease and became evident later.¹⁷ In some cases, a glial reaction remains on the optic disc.

Eight eyes presented mixed lesions and all these cases neuroretinitis was present. In 1977, Gass²⁹ postulated the pathophysiological mechanisms of this entity. It is possible that papillitis and the macular star found, together with a distant toxoplasmic retinochoroiditis, occurs as a hypersensitivity reaction and not due to direct damage caused by the parasite to the optic nerve as described in isolated neuroretinitis.²⁹

Toxoplasmosis is an infrequent cause of pure papillitis. In our study, three eyes presented this manifestation (5.9%). The findings that suggest the direct injury of the optic nerve by the parasite are the presence of optic nerve inflammation, vitreitis, a healed toxoplasmic lesion, and the presence of toxoplasmic antibodies. Other causes of swollen optic disc, such as demyelination diseases, vasculitis of the optic disc, ischaemic optic neuropathy, increased intracranial pressure, sarcoidosis, systemic lupus erythematosus, toxocariasis, optic nerve tumor, and other infectious causes of retinitis must always be excluded.¹³

In the present study, 28 eyes already had a toxoplasmic lesion before the optic nerve become involved, suggesting recurrences of an old disease and in 23 eyes the lesion of the optic nerve was the first ocular manifestation of ocular infection by the parasite.

Graph 2 Initial and final visual acuity of the whole sample (IVA, initial visual acuity; FVA, final visual acuity).

There was a marked dominance of unilateral lesions in our sample. Only two patients presented a change in the optic nerve in both eyes. One of these patients had proven congenital toxoplasmosis and the other had probable of congenital infection, but we did not confirm the diagnosis.

Some patients of this study performed visual field testing, that was recorded using the Humphrey 24/2 FastPac Strategy but we did not evaluate this records because few patients was submitted to this examination. Stanford *et al*³⁰ suggest in their study that toxoplasmic retinochoroidal scars close to the optic disc are associated with absolute defects. In the other hand, lesions that are far from the disc are more likely to produce relative defects.

The involvement of the optic nerve in ocular toxoplasmosis may lead an inexperienced clinician to think that visual acuity may be severely and permanently affected. However, in most of the cases we initially observe a low visual acuity that after treatment and with the healing of the lesion, improves significantly. Concerning this point our findings are coincident with those in the literature.^{13,14,16,17,24,31} The final visual acuity depends basically on the location of the retinal lesion, and not on the involvement of the optic disc.

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