Outbreak of Acquired Ocular Toxoplasmosis Involving 248 Patients

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Objective: To describe the demographic profile and clinical and laboratory findings of 248 patients with acquired retinitis caused by systemic infection with toxoplasmosis in a presumed outbreak of the disease.

Design: Retrospective observational case series.

Results: Most patients (209) were residents of one city in Southern India. A total of 35 patients had a prodrome of fever, and 242 patients had unilateral retinitis without associated old retinochoroidal scars. All had laboratory evidence of acquired systemic infection with Toxoplasma gondii, and all favorably responded to anti-toxoplasma therapy. Toxoplasma IgM and IgG antibodies were detected, suggesting recently acquired systemic disease. Complications seen were macular scars in 50 eyes (25.1%); epiretinal membranes, 23 eyes (11.5%); cataract, 5 eyes (2.5%); posterior vitreous detachment, 12 eyes (6%); and retinal detachment, 12 eyes (6%). One recurrence has been seen. The suspected source of infection is municipal drinking water.

Conclusion: Large numbers of residents of any age in a population are at risk of acquiring ocular disease during an outbreak of toxoplasmosis, which can go unnoticed, and can cause significant ocular morbidity.


Toxoplasma gondii is a coccidian parasite of worldwide distribution that infects a wide range of birds and animals but does not appear to cause disease in them. Their normal hosts are cats and other members of the family Felidae. It can cause severe life-threatening or destructive cerebral and ocular disease in newborns, and it is an important cause of ocular disease in both immunocompetent and immunosuppressed individuals.

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RESULTS

In 2003 at Aravind Eye Hospital in Coimbatore, Tamil Nadu, India, a total of 35 cases of ocular toxoplasmosis were seen. In 2004, only 12 cases of ocular toxoplas-
mosis were seen in the first half of the year. These patients had a characteristic retinitis adjacent to an old scar or showed presence of a scar in the other eye, with serologic evidence suggestive of recurrent ocular toxoplasmosis (IgG positive only). In August 2004, we saw a marked rise in the number of cases of active retinitis without evidence of chorioretinal scars, with serological evidence compatible with that of acquired acute toxoplasmosis (IgM positive). The striking aspect in this case series was the sheer number of patients who reported to our hospital: 28 in September, 56 in October, 51 in November, 43 in December 2004, and then 24 in January, 15 in February, 8 in March, 10 in April, 12 in May, and 1 to 2 cases per month until July 2005 (Figure 1 and Figure 2). Demographic data showed that most patients were residents of the city of Coimbatore and its suburbs, in Tamil Nadu, South India. A total of 248 patients were seen from August 2004 to July 2005.

From 2004 to 2005, 248 patients (254 eyes) presented with clinical and/or serological evidence of acquired T gondii retinitis. Patients aged between 12 and 73 years (Figure 3) were seen, with male preponderance (64.9%). One patient had tested positive for human immunodeficiency virus, and 1 was pregnant. Most (209 patients; 84.27%) were residents of the city of Coimbatore and its suburbs in Tamil Nadu, India; 237 patients (95.56%) used municipal drinking water for drinking/consumption purposes. Most patients (242; 97.58%) were not vegetarian (chicken and lamb were the most common meats consumed), and only 5 patients (2%) had household pets (cat). A prodrome of fever was seen in 35 patients (14.11%), with onset ranging from 7 to 180 days preceding the ocular symptoms.

Ophthalmic symptoms consisting of defective vision in 240 patients (96.77%) and floaters in 71 patients (28.62%) were present, with onset 1 to 210 days (mean, 24.2 days) before the first hospital visit. Right and left eyes were almost equally affected (123 right and 131 left). Six patients (2.41%) had bilateral involvement. Anterior chamber inflammation was seen in 174 eyes (68.50%), and 3 of those had granulomatous keratic precipitates. Intraocular pressure was measured by applanation tonometry in 199 eyes, and was elevated in 18 eyes (9%; range, 22-44 mm Hg).

Unifocal retinitis was seen in 230 eyes (90.55%). The location of retinitis was categorized in zones as described by Holland et al.11 In 171 eyes (67.32%), it was located in zone I (3000 µm from the fovea or 1500 µm from the optic nerve head margin); in 75 eyes (29.52%), zone II (from zone 1 to anterior borders of the vortex veins); and in 8 eyes (3.14%), zone III (anterior from zone 2 to the ora serrata). All lesions were active, raised, yellow patches with irregular ill-defined borders (Figure 4). Lesions in zones I and II were predominantly 1 to 2 disc diameter (DD) in size, and lesions in zone III were larger. Vitritis was seen in 228 eyes (89.76%). All lesions healed with scar formation with early retinal pigment atrophy and later pigment clumping. Multifocal retinitis was seen in 24 eyes (9.44%). Vasculitis was a feature in 89 eyes (35.03%), involving arterioles in most patients. Focal plaquelike yellow deposits on branches of the arteriolar tree known as Kyrieles-type periarteritis were seen in 42 eyes (47.19% of those with vasculitis). The periarteritis was seen in vessels that were coursing through the retina, both proximal and distal to the lesion, and also in vessels that were adjacent to the lesion (Figure 5). Disc edema due to peripapillary retinitis was seen in 17 eyes.
Figure 6. Fundus photograph of toxoplasma neuroretinitis. Active juxtapapillary retinitis and hard exudates are seen around the macula (macular star).

Bactrim DS, for the first week, which was then tapered by 10 mg every week for a maximum of 5 weeks. One pregnant woman was treated with 3 million U of oral spiramycin 3 times per day, and one patient who developed dry mouth and dry throat after using Bactrim DS was treated with 300 mg of clindamycin orally 3 times per day. One patient received 500 mg of azithromycin orally once per day.

Most patients were followed up (194; 78.22%), while 54 patients (21.77%), of whom 1 patient had bilateral ocular disease, were lost to follow-up. Improvement in visual acuity of at least 1 Snellen line was seen in 141 eyes (70.8%); in 46 eyes (23.1%), visual acuity remained the same, while 11 eyes (5.52%) worsened.

Complications seen were scars in zone 1, with resultant decrease in visual acuity occurring in 50 eyes (25.1%), epiretinal membrane in 23 eyes (11.5%), cataract in 5 eyes (2.5%), juxtapapillary and juxtafoveal lesions causing retinal folds in the macula in 3 eyes (1.5%) (Figure 7), posterior vitreous detachment in 12 eyes (6%), retinal detachment in 6 eyes (3%), persistent vitritis in 3 eyes (1.5%), and branch retinal vein occlusion in 1 eye (0.5%). One recurrence was seen in a 46-year-old woman 13 months after initial presentation; the recurrent retinitis was 2 DD away and nasal to the first healed scar. Both lesions were 2 DD inferior to the optic disc (Figure 5).

(6.69%) (Figure 6), and 3 of those patients had associated hard exudates in the macula, suggesting neuroretinitislike presentation. One patient who presented with severe panuveitis and was diagnosed with endogenous endophthalmitis had a core vitrectomy during which active retinitis was detected. Fundus fluorescein angiography typically showed blockage of fluorescence in early phases and staining of the lesion and leakage of the dye in the later phases.

All 198 patients had IgM antibodies against T gondii in their serum samples as well as high levels of toxoplasma IgG antibodies. Levels of IgG against T gondii were 200 IU/mL or higher in 90.18% and higher than 500 IU/mL in 50.4% of cases. Serology was repeated for only 10 patients 2 to 3 months following their first visit and demonstrated a fall in IgG titers in all 10 patients (Table).

Most patients were treated with a combination of 160 mg of trimethoprim and 800 mg of sulphamethoxazole (Bactrim DS, Roche, Basel, Switzerland) twice daily for a minimum of 5 weeks. Patients with vision-threatening retinitis (in zone 1) were also treated with 40 mg of oral prednisolone daily, 2 days after beginning therapy with

Retinochoroidal lesions can occur in acquired toxoplasmosis, either sporadically or in the context of an epidemic of acute toxoplasmosis. Whether toxoplasmic chorioretinitis is congenital or postnatally acquired is difficult to determine. The diagnosis of acute systemic toxoplasmosis is usually based on clinical features combined with an increase of specific IgG antibodies in the blood during a 3-week period. The presence of IgM antibodies is also a sign of recently acquired infection. If chorioretinitis develops subsequently, it is presumed to be acquired.12

We have described ocular involvement due to toxoplasmosis in 248 patients who had active retinochoroiditis and with no preexisting scars in either eye. Only
1 patient was immunodeficient (positive for human immunodeficiency virus); all other patients were immune competent.

The clinical presentation of our patients differs from those of patients with toxoplasmic chorioretinitis that occurs as a late sequela of infection that occurs in utero. Congenital disease tends to be bilateral, while acute acquired toxoplasmosis tends to be unilateral, single, and variable in size.8 Those with recrudescent congenital disease are relatively young, and have bilateral disease, old scars, and involvement of the macula.13 Acute acquired systemic toxoplasmosis in 80% to 90% of adults and children is an asymptomatic, self-limiting disease that goes unnoticed.14 Not all patients with postnatally acquired toxoplasmosis will develop ocular disease, as evidenced by a study from a Pacific island in which 90% of the adult population had been infected with *T gondii*; no adult had ocular toxoplasmosis.15 Those affected with visual symptoms later may visit the ophthalmologist weeks to months after the systemic illness.7 Most of our patients (n = 242; 97.58%) had unilateral disease, while only 6 (2.42%) had bilateral disease. Most patients presented with solitary, discrete, active focus of retinochoroiditis with no preexisting scars, consistent with acquired ocular toxoplasmosis.8-10,12,16 The mean age of 40.47 years in our patients is higher than those with recurrent congenital disease in whom toxoplasmic retinochoroiditis occurs more frequently in the second and third decades of life.17 However, the mean age of our patients is lower than that reported in 2 other case series of acquired ocular toxoplasmosis reported by Remington and Montoya7 (mean, 50.2 years) and by Burnett et al (mean, 54 years).18 In our series, serum was positive for *T gondii* IgM antibodies in all 198 cases for whom the tests were done. It was noticeably absent in patients with features of recurrent ocular toxoplasmosis seen in the previous 18 months. We do not consider the acute titer that we observed to be secondary to exacerbation of chronic latent infection in these patients because such cases are associated with absence of IgM antibodies.7 Most of our patients had high IgG levels (more than 500 IU/mL; 50.4%). Such high IgG levels were seen in patients with primary ocular toxoplasmosis, as reported by Ongkosuwito et al.19 Pathognomonic for recent infection is a seroconversion or an increase of toxoplasma IgG antibodies from a low to a high titer during a 3-week period.12 In general, IgG antibodies appear 1 to 2 weeks after infection, peak at 1 to 2 months, and then fall at variable rates.2 We have not seen patients while affected by acute systemic toxoplasmosis, only after the onset of ocular symptoms a mean of 37 days later; hence, we do not have baseline IgG titers. But we have shown a demonstrable fall in IgG titers in 10 patients on follow-up, suggesting a recent previous acute phase of the systemic disease.

Response to treatment in all of our patients has been excellent, though patients with large retinitis needed pro-

<table>
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<th>Patient No./Age, y</th>
<th>IgM</th>
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<th>Repeated IgM</th>
<th>Repeated IgG</th>
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<td>0.6</td>
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</table>

*Repeated enzyme-linked immunosorbent assay (ELISA) shows a fall in IgG titers in all 10 patients.*
longed antimicrobial treatment beyond the 5 weeks of routine therapy. Visual acuity worsened from baseline values in only 11 eyes (5.52%). Except for 1 patient who experienced dry mouth and throat, there were no complications seen with Bactrim DS therapy.20

Recent estimates show the city’s population at 1.5 million, predominantly Hindu, with a sizeable Muslim and Christian population.

A noticeable feature was that 209 patients (84.27%) were residents of a city and its suburbs, implying the source of infection to be common to everyone infected. Unfortunately, we have not been able to pinpoint the source of infection, as we have not seen similar cases of retinitis after the latter half of 2005. Documented modes of transmission in acquired toxoplasmosis are exposure to oocysts shed by cats in their feces, consumption of inadequately cooked infected meat, particularly pork or lamb, leukocyte transmission, and possibly, consumption of raw milk.2,21 Other well-documented modes of transmission are aerozilation of oocysts and oocysts in municipal drinking water.8,22 Most of our patients used municipal drinking water for drinking/consumption purposes, indicating municipal drinking water as the most probable source of infection. Small rivers and streams from the hills in the west and north of Coimbatore city contribute to its large reservoirs, the source of its municipal drinking water.

The fact that those affected with visual symptoms came to the hospital in high numbers (as opposed to earlier statistics) between the months of September 2004 and July 2005, 14.1% with a history of prodromal symptoms of patients with primary and recurrent ocular toxoplasmosis for evidence of recent infection. The purpose of this article is to alert all concerned that an outbreak like this could take any population by surprise, can involve all age groups and sexes, and that ocular toxoplasmosis in Southern Brazil.

The purpose of this article is to alert all concerned that an outbreak like this could take any population by surprise, can involve all age groups and sexes, and that ocular involvement can occur without any significant evidence of systemic disease. We do not know the number of women of childbearing age in the general population who may have been infected. If a big population is affected, there could be significant ocular and systemic morbidity as well as enormous stress on the public health system.

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REFERENCES


COMMENTS AND OPINIONS

Pitfall of Nonfasting Venous Blood Samples

I read with interest the article by Jeganathan and colleagues. Participants are overdiagnosed with lipid disorders and diabetes mellitus. First, the authors use nonfasting venous blood to evaluate the lipid profile. Nonfasting blood can be used to measure total cholesterol and high-density lipoprotein cholesterol levels, while triglyceride and low-density lipoprotein cholesterol levels require a 9- to 12-hour fasting state. Second, the authors defined persons with diabetes as those with only casual glucose levels of 200 mg/dL or higher but fail to recognize symptoms of hyperglycemia (polyuria, polydipsia, and unexplained weight loss), which are mandatory, as described in the standard diagnostic criteria of diabetes in the Table.

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