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Specific antibody levels in the aqueous humor and serum of two distinct populations of patients with ocular toxoplasmosis

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Abstract

The population of Erechim, Southern Brazil, is characterized by a high incidence of ocular toxoplasmosis, which is presumed to be of acquired origin. We wished to compare the local specific humoral immune response of individuals from this region with that of Swiss patients suffering from the same disease. Paired samples of aqueous humor and serum were withdrawn from 27 Brazilian and 50 Swiss patients presenting consecutively with active ocular toxoplasmosis. The total and specific levels of IgG in each of these were determined. The populations did not differ with respect either to age or sex. The serum levels of total IgG in Brazilian (10.8 g/l) and Swiss patients (11.1 g/l) were similar ($p = 0.499$), but the aqueous humor ones were higher in the former group (95 vs. 20 mg/l; $p = 0.0001$). The systemic and local levels of specific IgG were likewise higher in Brazilian patients [206 i.u. vs. 72 i.u. ($p = 0.001$) and 14 i.u. vs. 4 i.u. ($p = 0.005$), respectively] and the number of individuals without detectable levels of local specific IgG was correspondingly lower (11% vs. 54%; $p = 0.0005$). The Goldmann–Witmer coefficient (an index of local specific antibody production) did not differ between Brazilian and Swiss patients (2.1 vs. 0.08, respectively; $p = 0.107$). Our findings are indicative of a more pronounced uveovascular barrier breakdown in Brazilians than in Swiss patients with active ocular toxoplasmosis. That the systemic and local specific immune response is weaker in Swiss than in Brazilian patients has not been hitherto documented. This finding may reflect differences in the immunological handling of the infection.

Keywords: Ocular toxoplasmosis; Local immune response; Antibody coefficient; Host-specific factors; Population-based studies

Introduction

Ocular toxoplasmosis may account for more than 30% of posterior uveitis cases in western populations (McCannel et al., 1996), and in 95% of these instances the disease has been ascribed a congenital origin

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(Akstein et al., 1982; Hohlfeld et al., 1989; Holland, 2003; Koppe et al., 1986; Perkins, 1973). Up to 80% of congenitally infected individuals manifest signs of ocular recurrence (in association with pre-existing retinal scars) by the age of 20 years (Holland, 2004; McAuley et al., 1994; Wilson et al., 1980).

Acquired ocular toxoplasmosis is a rare condition in Europe and North America (Akstein et al., 1982), but more prevalent in Southern Brazil (incidence:18%), where it seems to be endemic (Glasner et al., 1992). Southern Brazilians have thus been assumed, although not proven, to have a distinct immunologic background. In contrast to toxoplasmosis of congenital origin, the acquired condition has been reported to be typically manifested as a unilateral disease, with a single, active lesion frequently occurring in the absence of pre-existing scars (Montoya and Remington, 1996). However, a few years ago, two prospective studies, involving, respectively, 49 and 154 immunocompetent, non-Brazilian individuals with acquired ocular or neurological toxoplasmosis, revealed one-half of the patients to develop ocular recurrences within 3 years of the initial presentation (Bosch-Driessen and Rothova, 1999; Couvreur and Thulliez, 1996). Hence, the acquired condition can be reactivated (Bosch-Driessen and Rothova, 1999). Moreover, it probably occurs more frequently outside Brazil than was previously supposed (Gilbert et al., 1999). Human (Suzuki et al., 1996) and animal studies (Brown et al., 1995; Gazzinelli et al., 1994) have yielded some evidence of a population-specific background to ocular involvement in toxoplasmosis, but the data are inconclusive (Holland, 2004; Meenken et al., 1995; Nussenblatt et al., 1989). We therefore compared the specific antibody levels in paired samples of aqueous humor and serum derived from a Brazilian population and a European group of patients with active ocular toxoplasmosis. We wished to ascertain whether differences in local or systemic specific antibody levels existed between the two populations.

Materials and methods

In this prospective study, paired samples of aqueous humor and serum were withdrawn in parallel from two collectives of consecutive HIV-negative, immunocompetent patients presenting with active ocular toxoplasmosis at the Departments of Ophthalmology in the Inselspital, Bern, Switzerland ($n = 57$) and in the Clinica Silveira, Erechim, Brazil ($n = 34$). None of the patients had undergone either local or systemic treatment for the disease when the samples were withdrawn. Informed consent was obtained for the analyses, which were approved by the local Ethical Committees in São Paulo and Bern; in the latter case, as part of a routine diagnostic procedure. The Brazilian samples were stored locally at −20 °C and then shipped together on dry ice to Bern, where paired samples were analyzed in parallel. Paired Swiss samples were likewise analyzed in parallel, but within 24 h of collection. Information respecting the age of patients, their history of symptoms, the site of ocular inflammation (which was not quantified) and clinical findings relating to the diagnosis of active ocular toxoplasmosis was documented. Patients with other ocular infections were excluded from the study. The diagnosis of ocular toxoplasmosis was confirmed at a later stage in all patients.

Patients from Erechim

Thirty-four consecutive patients from Erechim, Brazil, presenting with a varying clinical picture, which was nevertheless consistent with active ocular toxoplasmosis, were assigned to this group by two experienced ophthalmologists (A.C. Sobottka Ventura and C. Silveira). Anti-*Toxoplasma* IgG was present within the serum of all patients; anti-*Toxoplasma* IgM was not mandatory for inclusion in this group. Seven patients were subsequently excluded owing either to the lack of informed consent for anterior chamber puncture (two cases) or to an insufficient volume of aqueous humor (five cases). Of the remaining 27 patients, eight manifested no pre-existing scars. According to established criteria, this finding is consistent with a primary ocular disease condition (Bosch-Driessen et al., 2002). The other 19 patients exhibited chorioretinal scars at the time of presentation. This finding is indicative of a recurrent ocular disease condition.

Patients from Bern

Fifty-seven consecutive Caucasian patients from Bern, Switzerland, presenting with a typical clinical picture of recurrent ocular toxoplasmosis, were assigned to this group by a single ophthalmologist (J.G. Garweg). None of these individuals had a history of fever or lymphadenopathy within the 6 months prior to presentation. In all cases, the serological analysis yielded a picture that was compatible with chronic infection, i.e., anti-*Toxoplasma* IgG antibodies were present whereas specific IgM antibodies lay below a detectable level. Nevertheless, seven cases were subsequently excluded, owing either to duplicated inclusion on two separate occasions with consecutive recurrences (four cases), or to the identification of an immunocompromising disease (three cases). A congenital etiology was confirmed at birth in five cases. In the other 45 individuals, the disease origin remained undetermined, although the presence of pre-existing scars was consistent with a recurrent ocular condition.