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TOXOPLASMA GONDII-SPECIFIC T CELL CLONES ISOLATED FROM THE VITREOUS FLUID OF PATIENTS WITH RECURRENT OCULAR TOXOPLASMOSIS

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Purpose Recurrent ocular toxoplasmosis is a major cause of blindness throughout the world. However, the pathogenetic mechanisms of reactivation of latent Toxoplasma gondii (T. gondii) infections are still unknown. An important question is whether the recurrent focal inflammatory responses in the retina are primarily directed against the parasite itself or whether autoimmune mechanisms play a role in the reactivations.
Methods We designed a study to isolate and characterise the intraocular T cells involved in the recurrent inflammations. We tested a panel of T cell lines and T cell clones (TLCs) that have been derived from the vitreous of 7 patients with active recurrent ocular toxoplasmosis.
Results While no reactivity was found against retinal antigens, all T cell lines and 52 TLCs generated responded significantly to *T. gondii*. The T. gondii-specific TLCs had the $CD4^+$ phenotype, were generally HLA-DR restricted and displayed a heterogeneous T cell receptor usage.
Conclusions Our findings suggest that the intraocular cellular immune response in recurrent ocular toxoplasmosis is predominantly *T. gondii*-specific. These observations are relevant not only to a further understanding of protective immunity and immunopathology but also may have implications for the design of effective vaccines.

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OCULAR TOXOPLASMOSIS AFTER THE FOURTH DECADE.

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Purpose. Toxoplasma retinochoroiditis remain the most prevalent form of infectious posterior uveitis in immunocompetent young adults but is uncommon after the age of 50. This entity is often misdiagnosed due to the older age of patients at presentation. We reviewed ten recent cases with positive laboratory tests for intraocular samples and analysed the clinical features of these unusual forms of ocular toxoplasmosis.
Patients. Ten patients, with age ranged between 50 and 87 years old (m = 65), were included in this study during the period february 92-october 94. All presented a severe unilateral uveitis with active retinochoroiditis. Serum titers of antitoxoplasmic IgG were positive for all these patients. The clinical evaluation of the patient noted : 1) the history of the uveitis 2) the time between clinical onset of the disease and anterior chamber paracentesis 3) the uveitis grade 4) the existence of a retinochoroidal scar 5) the size of the active retinochoroiditis lesion 6) the presence of a posterior vitreous detachment and 7) the received treatment.
Methods. After topical anesthesia, an anterior paracentesis was performed by taking 0.15 to 0.30 ml of aqueous humor. At the same time, a serological test was achieved. Samples were immediately processed at the Parasitology laboratory of CHRU de Lille. The PCR procedure used chemoluminescence probing of the B1 gene of Toxoplama gondii. The segment used for the amplification corresponded to nucleotides 694 to 887. The procedure allowed the detection of 0.1 T. gondii per sample. Analysis for specific antibodies included IgG, IgM and IgA isotypes (Enzygnost Toxoplasmosis IgG, Behring, Germany / ISAgA-M, bioMérieux, France / ISAgA-A, CHRU de Lille, France).
Results. In our series the rate of patients with positive PCR for intraocular samples was 60 %. Intraocular IgG synthesis, IgA or IgM detection allowed us to obtain a positive diagnosis in the 10 cases. For all samples, two or more of the techniques were positive. Our clinical examination showed some particular features : the long time between clinical onset and ocular paracentesis, the severity of intraocular inflammation, the big size of the retinochoroiditis lesion and the presence of a posterior vitreous detachment.
Conclusions. Confirmation of the toxoplasma origin was obtained in all the ten uveitis cases by combination of PCR and serological tests. Local conditions favorizing the diffusion of parasitic material may explain the high rate of positive result for PCR. This series shows some clinical features that may encompass this often misdiagnosed form of ocular toxoplasmosis.

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Association of IgG and IgE antibodies detection for the diagnosis of Toxocariosis

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Purpose : Clinical examination is poorly informative for the diagnosis of ocular and visceral toxocariosis. Various serological tests are available, but none of them provide definitive confirmation of the diagnosis. We propose to evaluate specific IgG and IgE and to correlate these data with clinical presentation and evolution of patients with long lasting follow up.
Methods : Serum from 11 patients suffering visceral or ocular toxocariosis, based on epidemiological, clinical and therapeute consideration, were collected and stored frozen. Serum from normal individuals or patients suffering other infectious diseases were collected in the same conditions.
Serodiagnosis was performed by immunoenzymatic way using antigen from Toxocara canis larvae stage to determine specific IgG and IgE levels. Data were expressed as toxocara units obtained by correction of the valve of optic density of the sample go with a calculated index factor.
Results : When data from IgG and IgE assays were plugged on the same graph, we observed that all the eleven greatly probable toxocariosis were confirmed by IgG and IgE data over cut-off valves. None of the others patients presented a positive combined serological test.
Conclusion : We suggest that diagnosis of toxocariosis could be greatly enhanced by the concomittent determination of IgG and IgE anti-toxocara canis antibodies. A positive IgG only, is in favour of an infection in the past while a positivity of both IgG and IgE is in favour of a in progress infection. Experiments are actually performed to evaluate the usefullness of such analysis on aqueous humor samples during ocular toxocariosis.

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THE ROLE OF IMMUNOLOGICALLY CROSS-REACTIVE ANTIGENS IN THE DEVELOPMENT OF OCULAR ONCHOCERCIASIS

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Purpose: Our primary objective is the study of mechanisms involved in the development of posterior segmemt pathology in onchocerciasis. Based on the observation of immunological cross-reactivity we suggest that structural similarities between a host ocular antigen and an antigen of *Onchocerca volvulus* may have a role in the initiation of autoimmune reactivity.
Methods: The cross-reactive antigens, designated Ov39 and hr44, derived from*O. volvulus* and human retina respectively, have been cloned and their primary structures compared. For the characterisation of the cross-reactivity, monoclonal antibodies to these antigens have been prepared and T cell lines established. The recombinant antigens have also been used to study the potential to induce disease in the Lewis rat.
Results: Primary structure analysis showed limited sequence identities, confined to small peptides, between the antigens Ov39 and hr44 and Ov39 and visual rhodopsin. A monoclonal antibody raised to Ov39 is cross-reactive with hr44 and gave evidence for a shared conformational epitope. Hr44 and Ov39 also share T cell cross-reactivity. Hr44 is a neurospecific, membrane associated class I antigen and localises in those tissues affected by ocular onchocerciasis. Like some other self-antigens, hr44 induces ocular disease in the Lewis rat, however, the histopathology appears to differ from all the other autoimmune uveitis models.
Conclusions: These findings suggest a potential mechanism for an autoimmune etiology of uveitis in ocular onchocerciasis.
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