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Recent Advances in Ocular Toxoplasmosis

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Editorial
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Introduction

Ocular toxoplasmosis, the most intriguing parasite infection is a vision threatening infection of the eye. The recent advances in pathophysiology coupled with imaging and diagnostic methods on the diagnostic variants have advanced the treatment approach in leaps and bounds. This mini review article addresses all these domains.

Advances in Pathophysiology

''Trojan Horse phenomenon''[1] of ocular Toxoplasmosis[OT] is the most accepted hypothesis of parasite dissemination by which Toxoplasma takes advantage of the immune cell mobility using the dendritic cells using a parasite derived protein called GRA 5.Toxoplasma has the unique ability to modify the phenotype of infected monocyte/ macrophage and increases their mobility, marginalization and extravasation. Recent studies Song, et al. [2] have proven that inner blood retinal barrier is the preferred route than the outer blood retinal barrier.

The conversion of tachyzoites into bradyzoites, the key event involved in recurrence of OT is mediated by parasite derived proteins called ROP17, ROP35 and ROP38.In this phenomenon the transformation of parasitophorous vacuole into a cyst by modification of vacuole membrane, by adding parasite proteins and glycosylation. The transformed cells exhibit strongly modified microtubules and intermediate filaments network.

The diverse molecules involved in the unique immunosuppressive microenvironment of the posterior pole were recently identified. They provide a suitable niche for OT persistence and development. The central role of IL-17 is proven by strong IL-17 A expression on the Muller cells by immunoflorescence studies. It correlates to severe retinal lesions. The molecular basis of regional variation of the presentation between European, south American strains are identified by preferential expression of protective factors in a weaker way and paradoxical upregulation of IL-6 in addition to genetic polymorphisms [3]. The immune response to OT depends on the pivotal role of Interferon- gamma using the STAT-1/ STAT-2 pathway [4]. Molecular therapeutic targets to alleviate inflammation under the specific antitoxoplasmic drugs involved are IL-6, IL-23 are under research.

Newer Therapeutic Targets for Toxoplasmosis

The newer therapies involved in toxoplasmosis are subclassified into [a] Novel parasitic therapeutic targets [b]. Repurposing of promising compounds active against other pathogens.

The prominent ones are Dihydrotriazine, Naphthaquinones, Artmisones, Rolipram, Guanabenz, Tanshinone 2-A, Miltefosine, Tetraoxane. The mechanism of action, targets and invitro and in vivo activity are neatly elucidated by Konstantinovic N, et al. [5].

Novel Molecular Approach

In chronic toxoplasma infection adoptive transfer of immune CD8+ cells has shown to temporarily restrict the breakdown of cysts within 4 weeks of treatment. This transient protection does not help in long-term rescue of the exhausted T cells [central mechanism of recurrences] as the donor cells often rarely turn long-lived ones. This is applied as a prophylactic therapy of high –risk individuals [5]. Passive immunization strategies using specific recombinant anti-Toxoplasma antibodies against SAG1 antigens has shown

promising results by slowing parasite invasion in mouse models [5].

Novel Imaging Findings in Toxoplasma

The typical pattern of healing are elegantly documented using OCT, FAF, OCTA. They help to capture the variants like Peripheral Outer Retinal Toxoplasmosis [PORT]. Macular edema and Huge Outer Retinal Cyst [HORC] were elegantly described by Oyang Y, et al. as an intraretinal cyst with a membranous structure bordering the outer border of the cyst [6]. It proved that the edema is intraretinal rather than subretinal.

Novel Genetic Variants of Toxoplasmosis

Genetic mapping analysis has proven that there are only 3 variants 1, 2, 3 derived from 2 ancestral strains [A and E]. In the immunocompetent individuals the genetic type of the parasite has a substantial effect on the ocular manifestation such that type 1 has a severe disease, type 2 or 3 has mild or no disease. On the flip side in the immunocompromised individuals, the host parameters are of paramount importance on the disease severity with any genetic variant [7].

Novel Diagnostic Methods in Toxoplasmosis

The novel diagnostic methods in toxoplasmosis are neatly tabulated by Kalogeropoulos D, et al. [7]. Of late the dual targeted [B1, Rep 529] gene real time PCR has increased sensitivity without loss of specificity more so in immunosuppressed than in immunocompetent individuals. The novel 2 step protocol by Sugita S, et al. [8] is an eye-opener as in the first step it uses a qualitative multiplex PCR followed by a quantitatitaive real time PCR in the second step.

Immunophenotyping by 3 colour analysis flow cytometry helps to solve the enigma in challenging differentials like lymphomas. They distinguish lymphocytes from other leukocytes using the combination of fluorescence associated with CD45 per CP/ SSC and orthogonal light scatter. Polymerase Chain Reaction [PCR], Goldmann Witmer [GWC] Coeffecient, Western Blot [WB] are used in challenging scenarios.

The combined sensitivity and specificity of the 3 tests done together [PCR, GWS, WB]exceeds the sensitivity and specificity of each of the above tests done separately or in pairs. A novel interferon gamma release assay [9] similar to tuberculosis for toxoplasmosis has shown promising results with chronic toxoplasmosis with ocular involvement as well.

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