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Review

SERUM CXCL9 AND CXCL10 AS EMERGING BIOMARKERS IN OCULAR TOXOPLASMOSIS : BRIDGING INFLAMMATION AND DIAGNOSTIC PRECISION

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ABSTRACT

Introduction: Globally, ocular toxoplasmosis (OT) is the most frequent etiology of posterior uveitis and is associated with potentially vision-threatening ocular inflammation. Chemokines produced in response to interferon-gamma (IFN-γ), notably CXCL9 and CXCL10, play a critical role in directing T lymphocytes and monocytes to sites of infection. This changes the balance between controlling the parasites and causing damage to the retina through the immune system. Currently, the literature examining CXCL9 and CXCL10 within the context of OT remains sparse, underscoring a distinct necessity for more comprehensive exploration.

Methods: This review integrates recent empirical evidence concerning the functions of CXCL9 and CXCL10 in ocular toxoplasmosis, utilizing articles from PubMed, MEDLINE, and ScienceDirect published from 2015 to 2025. The review encompasses human clinical trials and experimental models that examined the concentrations of chemokines in blood, ocular fluids, or retinal tissues.

Results: There were 7 studies in total, of which 6 involved humans and 1 involved animals. Most of the studies used serum samples. Across study types, CXCL9 and CXCL10 were consistently elevated during the acute phase of T. gondii infection compared to chronic or latent stages. Increased chemokine levels closely paralleled IFN-γ activity and were associated with enhanced recruitment of $CD4^+$ and $CD8^+$ T lymphocytes, reflecting active inflammatory responses. Combined assessment of CXCL9 and CXCL10 improved the identification of active infection and showed potential for distinguishing disease severity.

Conclusion: In conclusion, CXCL9 and CXCL10 represent promising immunological biomarkers of disease activity in ocular toxoplasmosis and warrant further evaluation for clinical application.

Keywords: Toxoplasma gondii, Ocular Toxoplasma, CXCL9, CXCL10, Chemokines, Immune Response

Introduction

Ocular toxoplasmosis (OT) stands as the main cause of posterior uveitis, stemming from the infection with Toxoplasma gondii (T. gondii), an essential intracellular protozoan. The life cycle of Toxoplasma gondii is quite complicated, predominantly depending on cats for hosting, with humans serving as additional hosts. Humans and other animals often receive T. gondii primarily via the ingestion of food or water that is compromised by oocysts.[1,2] Toxoplasma gondii infection is widespread, with an estimated 500 million people infected globally. The Centers for Disease Control and Prevention (CDC) disclosed findings in 2018 which indicate that roughly 11% of people aged 6 and up in the United States may have exhibited traits that point to a history of infection. In a corresponding manner, the National Health and Nutrition Examination Survey (NHANES) obtained during the years 2011 through 2014 noted a seroprevalence ratio around 11%. Despite the lack of extensive prevalence data in Indonesia, some reports suggest a relatively high seroprevalence ranging from 43% to 88% in certain regions. A retrospective study by Sofia et al. reported 38 cases of OT at Dr. Saiful Anwar General Hospital in Malang between 2013 and 2015.[1–4]

The ocular structure is defined as an immune-privileged system, exhibiting tolerance mechanisms that suppress immune responses and alleviate inflammation triggered by T. gondii. This parasite cannot directly infect ocular tissues, and several theories explain its invasion, including the "Trojan Horse" mechanism, in which infected dendritic cells (DCs) and macrophages facilitate the translocation of the parasite into ocular tissues.[5] Cell-mediated immunity constitutes the major host defense against T gondii, with interferon-gamma (IFN-γ) playing a crucial role in controlling parasite proliferation and limiting infection. Cytokines, particularly IFN-γ and Transforming Growth Factor-beta (TGF-β), regulate the infection process within retinal pigment epithelial (RPE) cells and provide protective effects. Immunity against T. gondii largely depends on IFN-γ production by $CD4^+$ and $CD8^+$ T lymphocytes, with IFN-γ promoting defense by inducing chemokines such as chemokine (C-X-C motif) ligand (CXCL), which recruit T cells to infected sites. In acute T. gondii infection, circulating concentrations of the chemokines CXCL9 and CXCL10 are markedly higher than in the chronic phase, independent of ocular manifestations, as previous studies have reported that the chemokine CXCL11, another CXCR3 ligand did not differ significantly between individuals with T. gondii infection and control subjects. Certain circulating cytokines and chemokines including CXCL1, CXCL2, CXCL5, CXCL6, CXCL8, CXCL13, CXCL16, CX3CL1, CCL2, CCL1, CCL3, CCL8, CCL13, CCL15, CCL25, CCL17, CCL19, CCL21, CCL20, CCL22, CCL23, CCL24, and CCL27 have shown no significant differences and therefore are not considered potential biomarkers for predicting ocular toxoplasmosis.[5–8]

Chemokines such as CXCL9 and CXCL10 guide immune cells into the eye, playing a crucial role in controlling T. gondii proliferation; however, this process may also contribute to the development of OT, as infected lymphocytes can likewise enter the ocular environment. This delicate balance of immune responses can both contain the parasite and simultaneously trigger ocular infection.[5] The exact pathogenesis of T. gondii infection leading to OT remains incompletely understood. Even though cytokines like IFN-γ and ILs have been studied in relation to OT, many chemokines' precise activities remain unknown. A deeper understanding of cytokine regulation within chemokine-mediated cellular immune responses could enhance our comprehension of OT pathophysiology. In order to enhance diagnosis and treatment methods, this literature review attempts to investigate the function of chemokines in the immunological response to OT infection.

Infection Process of Toxoplasma gondii in the Retina

In most instances, T. gondii persists in a latent state within the host without provoking a detectable immune response. Following entry into the human body, the parasite undergoes rapid differentiation into tachyzoites within the small intestine, subsequently invading nucleated cells and initiating an inflammatory cascade that results in immune-mediated tissue injury.[9] Once host cells lyse, tachyzoites enter the bloodstream and lymphatic system, where they can be detected within leukocytes or as free parasites in patients with active or chronic toxoplasmosis. Toxoplasma gondii may reach the retina via two vascular routes: the retinal and choroidal blood vessels.

The parasite gains access to the neural retina by penetrating the choroidal endothelium and breaching the outer blood–retinal barrier. Infected leukocytes promote disruption of the barrier by activating focal adhesion kinase signaling and modulating epithelial tight junction proteins via CXCL8 activity.[5] Smith et al.[5] demonstrated in adult retinal pigment epithelial (ARPE-19) cells that tachyzoite infection compromises cellular integrity, resulting in loss of barrier function. Three potential routes for T. gondii to cross the retina have been identified: (i) the “Trojan horse” mechanism, (ii) direct invasion of free parasites via the endothelium, and (iii) entry through retinal endothelium. In the Trojan horse mechanism, $CD11^+$ DCs and monocytes play a key role by becoming infected and undergoing phenotypic changes that enhance their migratory capacity. The production and release of γ-aminobutyric acid (GABA) by DCs triggers a hypermigratory phenotype that facilitates the spread of parasites by activating GABA-A receptors. Additionally, these DCs show higher expression of Chemokine Receptor 7 (CCR7), which is linked to improved chemotactic mobility and is not seen in uninfected cells.[7,10]

In the paracellular route through the endothelium, leukocytes migrate slowly within retinal blood vessels due to the relatively wide diameter of these vessels. Adhesion of endothelial molecules and chemokines facilitate interactions between leukocytes and retinal endothelial cells. Following T. gondii exposure, retinal endothelial cells exhibit elevated expression of intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and CXCL10, a response mediated by tachyzoite-derived micronemal protein 2 (MIC2). Lysis of infected leukocytes within retinal vessels may release tachyzoites directly onto the endothelium.[5,10,11]

Studies have indicated that retinal endothelial cells are more vulnerable to T. gondii infection than other endothelial cell types in relation to the endothelial cell infection route. Toxoplasma gondii is capable of invading all nucleated cells, the retinal vascular endothelium serves as a plausible site of infection. Tachyzoites have been demonstrated to have a high binding affinity for the molecular phenotype of the human retinal endothelium, which facilitates their attachment and possible invasion. Smith et al.[5] also detected elevated transcript levels encoding ICAM-1 and various enzymes, suggesting the expression of surface proteoglycans that facilitate parasite adhesion. Moreover, tachyzoites possess the capacity to retain their infectivity and survive extracellularly for extended periods while retaining the ability to bond with retinal endothelial cells.[5] The retina can be reached by T. gondii through direct penetration of tachyzoites throughout the retinal vascular endothelium. The migration is facilitated through specific molecular interactions, in which intercellular adhesion molecule-1 (ICAM-1) on endothelial cells binds with micronemal protein 2 (MIC2) expressed on the surface of tachyzoites. Upon entering the retinal circulation, tachyzoites secrete MIC2 at their apical end, which subsequently forms a hexameric complex with the MIC2-associated protein (M2AP) to specifically bind ICAM-1 on host cell membranes. The release of rhoptry proteins (ROPs) further cooperates with MIC2, enabling endothelial cell invasion and the establishment of a parasitophorous vacuole (PV) (Figure 1).[12]

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Figure 1. Migration of Toxoplasma gondii to reach retina as target organ. Toxoplasma gondii, enter the body and differentiate into tachyzoites in the small intestine. CD11⁺ dendritic cells and CD11⁺ monocytes facilitate the translocation of these tachyzoites to the central nervous system and the retina by traversing the blood-brain and blood-retina barriers, as denoted by the presence of plus signs. Following the entry of tachyzoites into the retina through the circulatory system, MIC2 is rapidly secreted from the apical end of the parasite and subsequently assembles into a hexameric MIC2-M2AP complex together with MIC2-associated protein (M2AP), which steers its activity towards the intercellular adhesion molecule ICAM-1 found on the host cell. Next, rhoptry proteins (ROPs) are released and interact with MIC2 to facilitate the parasite's entry into retinal endothelial cells, forming a parasitophorous vacuole (PV). Subsequent to this process, dense granule proteins (GRAs) are released to alter the structure of the parasitophorous vacuole (PV), thereby facilitating the parasite's uptake of vital nutrients necessary for its survival and reproductive processes.

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Immune Regulation in Ocular Toxoplasmosis

Toxoplasma gondii infection triggers an immune response in the host to limit parasite replication. In the acute phase, parasites entering the bloodstream provoke inflammation and recruit polymorphonuclear cells, monocytes, and dendritic cells. Tachyzoites spread to the eye through systemic circulation and subsequently infect the retina, predominantly affecting Muller glial cells and astrocytes. Muller cells and astrocytes are essential for preserving retinal homeostasis and providing neural support. Muller cells span from the outer limiting membrane (OLM) to the inner limiting membrane (ILM), whereas astrocytes are located in the nerve fiber layer (NFL) and ganglion cell layer (GCL). Astrocytes secrete prostaglandin (PGE), nitric oxide (NO), arachidonic acid (AA), and endothelial-stabilizing substances that mitigate inflammatory damage to neurons. Bradyzoites form cysts in the inner retinal layers, capable of infecting Muller cells, astrocytes, and neurons.[12,13] In light of pro-inflammatory catalysts, including leukocytes, platelets, and plasma proteins, Muller cells excrete a vast selection of inflammatory mediators, among them TNF-α, several interleukins, interferons, and ICAM-1. Overexpression of TNF-α and MCP-1 by Muller cells directly contributes to cytotoxicity, leading to further retinal damage. T. gondii retinal infection promotes VEGF synthesis in retinal pigment epithelial (RPE) cells via activation of ALK4 and HIF-1 signaling pathways. Following retinal injury, Muller cells secrete elevated levels of VEGF, disrupting the blood–retina barrier (BRB) and facilitating parasite migration. VEGF released by activated astrocytes exacerbates the advancement of the disease by enhancing vascular permeability, promoting angiogenesis, and causing cytotoxic harm that undermines the integrity of both neuronal and glial populations.[12]

Macrophage activation by IFN-γ and $CD8^+$ T cell–mediated cytotoxicity are central to controlling T. gondii infection. During the early phase, $CD8^+$ T cells promote IFN-γ release, while rhoptry proteins (ROPs) of the parasite activate STAT signaling, inducing the production of IFN-γ and IL-12. Effective regulation of both acute and chronic T. gondii infection relies on a coordinated immune response involving dendritic cells (DCs), T cells, NK cells, macrophages, and key cytokines including IL-12 and IFN-γ. IL-12 activates $CD4^+$ T cells to produce IFN-γ, inducing inducible nitric oxide synthase (iNOS) and nitric oxide (NO) generation, leading to cytotoxic degradation of parasitophorous vacuoles.[12] During infection, IFN-γ, TNF-α, CTLA-4, CD80/CD86, and other inflammatory mediators interact with epithelial cells, dendritic cells, and macrophages to stimulate indoleamine 2,3-dioxygenase (IDO). While IDO suppresses parasite proliferation, metabolites generated through the kynurenine pathway inhibit $CD8^+$ T cells, NK cells, DCs, macrophage function, and promote Th2 cells and Treg differentiation, along with TGF-β production.[12] $CD4^+$ T lymphocytes undergo differentiation into distinct effector subsets Th1, Th2, Th17, and Treg, each with distinct roles in immune defense. Th1 cells secrete IFN-γ, which is critical for protection against intracellular pathogens, whereas Th2 cells release IL-4, IL-5, and IL-10 to mediate protection against extracellular parasites. Th17 cells are known to produce cytokines such as IL-17, IL-21, and IL-22, which are frequently linked to the pathogenesis of autoimmune disorders, while Treg cells maintain immune tolerance. The balance between pro-inflammatory cytokines (IL-1β, IL-12, IL-18, TNF-α, IFN-γ) and anti-inflammatory cytokines (IL-4, IL-10, TGF-β) determines the body's immunity to toxoplasmosis. IL-10, an immunomodulatory cytokine, inhibits Th1 differentiation and mitigates excessive inflammation. IL-10 deficiency leads to elevated levels of IL-12 and IFN-γ, highlighting its function in attenuating inflammation and constraining excessive pro-inflammatory reactions.[14–16]

The Role of Chemokines in the Immune Response in Ocular Toxoplasmosis

Chemokines are chemotactic polypeptides that play a critical role in the regulation of leukocyte activation and migration. The cysteine residues are categorized into distinct groups based on their positioning in the amino-terminal region. The C-X-C (α) family of chemokines predominantly facilitates the recruitment and activation of neutrophils, while also attracting other leukocyte subsets. Conversely, C-C or beta chemokines, such as MCP-1, predominantly recruit monocytes, macrophages, and T lymphocytes. Chemokines bind to glycosaminoglycans on endothelial surfaces or within the extracellular matrix and interact with chemokine receptors, promoting receptor engagement and directed cell movement.[16,17]

Chemokines, classified primarily into the CC and CXC subfamilies, are produced by a wide range of immune and non-immune cells, including leukocytes, endothelial and epithelial cells, macrophages, fibroblasts, and stromal cells. IL-1, IL-17, and TNF are pro-inflammatory cytokines that can trigger their tightly controlled expression. Notably, certain CC chemokines are synthesized by T lymphocytes, highlighting their role as a molecular link between adaptive immunity and the recruitment of inflammatory leukocyte populations.[14,15]

The migration and extravasation of immune cells across blood vessels to the site of infection represent essential processes for an effective host defense. These events are primarily regulated by chemokines and matrix metalloproteinases. In response to microbial encounters in extravascular tissues, macrophages, dendritic cells, and other immune cells release cytokines such as TNF and IL-1. These cytokines upregulate E-selectin on vascular endothelial cells, while mast cell–derived histamine stimulates P-selectin expression. The combined effects lead to vasodilation and reduced hemodynamic shear, driving leukocytes closer to the vessel wall in a process known as margination. E- and P-selectins expressed on endothelial cells interact with their ligands on leukocyte microvilli through low-affinity, rapidly reversible bonds, generating a rolling motion along the endothelium. Subsequently, endothelial chemokines bind to receptors on leukocytes, inducing conformational changes in integrins that strengthen adhesion and enable firm leukocyte attachment at the infection site. Chemokines expressed on the endothelial cells at the site of infection bind to leukocyte receptors, resulting in stronger binding between leukocyte integrins and the endothelial surface.[18]

T cells, especially $CD4^+$ and $CD8^+$ cells, are involved in the cross-talk between chemokines and immunological responses in the eye during ocular toxoplasmosis (TO), which is primarily mediated by IFN-γ.

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Figure 2. Leukocyte recruitment into tissues involves a multistep interaction with the vascular endothelium. At sites of infection or tissue injury, cytokines are produced, leading to the activation of endothelial cells. These activated cells express chemokines that bind to receptors on leukocytes, enhancing integrin affinity and strengthening leukocyte adhesion. The process begins with selectin-mediated leukocyte rolling along the endothelium, followed by chemokine-induced integrin activation. This results in firm integrin-mediated adhesion of leukocytes to the endothelial surface. The leukocytes then transmigrate across the endothelial barrier and continue migrating through the tissue to the area of infection or damage, guided by chemotactic cues.

Table 1. Research Related to Chemokine Regulation in Toxoplasma gondii Infection Over the Past 10 Years

Researcher Name and Year	Research Title	Research Design	Sample Type	Sample Size	Result
Ochiai E *et al.* 2015[21]	*CXCL9 Is Important for Recruiting Immune T Cells into the Brain and Inducing an Accumulation of the T Cells to the Areas of Tachyzoite Proliferation to Prevent Reactivation of Chronic Cerebral Infection with Toxoplasma gondii*	*Cross sectional*	Serum	Mice with acute *T. gondii* infection = 4 mice Mice with chronic *T. gondii* infection = 4 mice	There was a significant increase in CXCL9, CXCL10, IFN-γ, and CCL5 on day 5 after infection.
de Araújo *et al.* 2017[22]	*Early serum biomarker networks in infants with distinct retinochoroidal lesion status of congenital toxoplasmosis*	*Cross sectional*	Serum	Infants with positive IgM *T. gondii* = 108 infants Healthy infants = 26 infants	There was an increase in chemokine production mediated by CXCL8, CXCL9, CXCL10, and CXCL5, IL4, IL5, IL10 compared to controls.
de Faria Junior *et al.* 2018[23]	*CCR5 chemokine receptor gene polymorphisms in ocular toxoplasmosis*	*Cross sectional*	Serum	Patients with positive IgG *T. gondii* and TO = 160 patients Patients with positive IgG *T. gondii* without TO = 160 patients Healthy patients = 160 patients	No differences in CCR5 alleles and genotypes (homozygous and heterozygous) were found between individuals with TO and controls. However, patients with CCR5/CCR5 AA or AG genotypes had a higher risk of developing TO (4% higher).
de Araújo *et al.*, 2020[19]	*Putative biomarkers for early diagnosis and prognosis of congenital ocular toxoplasmosis*	*Cross sectional*	Serum	Infants with congenital *T. gondii* infection = 108 infants Healthy infants = 26 infants	There is an increase (CXCL9, CXCL10, $CD4^+$, T cells, and IFN-γ) that can be used as biological markers for congenital TO in infected and uninfected infants. Simultaneous testing of CXCL9 and CXCL10 improves the accuracy of biological markers for congenital TO.

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Marino *et al.* 2020[18]	*Circulating inflammatory mediators as biomarkers of ocular toxoplasmosis in acute and in chronic infection.*	*Cross sectional*	Plasma	*T. gondii* seropositive: 29 patients Healthy patients: 21 patients	During the acute phase of infection, higher levels of CXCL9 and CXCL10 were found compared to the chronic phase, without comparing manifestations in the eyes. In acute TO patients, higher levels of IL-2, TNF, and IL-10 were also found compared to chronic TO patients.
Denis J, *et al.*, 2022[24]	*Dynamic Immune Profile in French Toxoplasmosis Patient*	*Cross sectional*	Serum	IgM *T. gondii* positive = 33 patients IgG *T. gondii* positive = 29 patients Healthy patients = 39 patients	There was an increase in cytokines (IFN-γ, IL-12p70, CSF2, CXCL9, CCL-2, IFN-β, IL-4, IL-5, IL-10, IL-6, and IL-15) indicating a significant increase in regulation only in acute phase patients. In patients with chronic infection, cytokine levels return to pre-infection levels, so the uninfected group and the chronic group are not statistically different. [38]
Mariam N, Al-Qaisi AQ. 2023[25]	*Assessing the Potentiality of Using CXCL9 as A Predictive Biomarker for Acute and Chronic Toxoplasmosis, and Study the Correlation Between CXCL9, Toxoplasmosis and Thyroid Disorder in These Cases*	*Cross sectional*	Serum	Pregnant women who experienced miscarriage with *T. gondii* infection = 67 pregnant women Healthy pregnant women = 20 pregnant women	An increase in CXCL9 levels was observed in pregnant women with *T. gondii* infection (271.93 ±62.58) compared to pregnant women without infection (166.33 ±32.83).

During the acute phase of infection, T cell–attracting chemokines such as CXCL9, CXCL10, and CCL5 are markedly upregulated in an IFN-γ–dependent manner. The expression of several chemokine and receptor genes, such as CCL5, CCL2, CXCR3, CXCL9, CXCL10, and CXCL11, is stimulated when astrocytes or microglia get infected (Figure 2).[8,17]

Tachyzoites settle in astrocytes and microglia in the eye, causing leukocyte migration to the site of infection and tissue damage, activating host immune defenses aimed at suppressing parasite replication. Infected microglia produce pro-inflammatory cytokines that exacerbate blood-retinal barrier (BRB) dysfunction. Microglia and astrocytes upregulate CXCR3 expression and release chemokines such as CXCL9, CXCL10, and CXCL11, facilitating the recruitment of T lymphocytes and myeloid cells, including granulocytes and monocytes, into infected retinal tissues. Matrix metalloproteinases (MMP-8 and MMP-10) and Tissue Inhibitor of Metalloproteinase (TIMP-1) also contribute to regulating lymphocyte accumulation and entry to prevent cyst reactivation. Latent reactivation may occur when integrin (VCAM-1), IFN-γ, $CD3^+$, $CD4^+$, $CD8^+$, or iNOS expression is reduced. Lower levels of CXCL9 and CXCL10 during T. gondii infection reactivation impair T cell entry.[17,18] Research by Marino et al. (2020) on serum samples from 29 patients with acute toxoplasmosis (with or without ocular manifestations) and 21 healthy controls found differences in chemokine profiles between acute and chronic toxoplasmosis. In the acute phase, CXCL9, CXCL10, and CXCL11 levels, including CXCR3 ligands, were higher than in the chronic phase, regardless of ocular involvement. IL-2, IL-10, and TNF levels were also higher in acute conditions, with IL-6 and IL-4 being elevated regardless of ocular lesions.[8] Araujo et al. (2020) found that CXCL9 expression in the retina significantly increased in experimental TO, indicating its potential as a biomarker for diagnosing toxoplasmosis in infants. Elevated CXCL9 levels in serum and aqueous humor of TO patients suggest a role for chemokines in mediating inflammation in the parasite's microenvironment.[19] Norose et al. (2011) demonstrated that T. gondii infection triggers CXCL10 expression in an IFN-γ–dependent manner, with this chemokine being prominently detected in infected tissues during the acute stage of disease. This finding supports previous research demonstrating that CXCL10 functions as a key chemotactic mediator, guiding $CXCR3^+$ Th1 effector cells to infected tissues.[20]

The Role of Chemokines in Retinal Infection by Toxoplasma gondii

After T. gondii infects a cell, pro-inflammatory cytokines such as TNF-α, IFN-γ, and others attach to DCs, macrophages, and epithelial cells. In the Trojan horse mechanism, $CD11^+$ and $CD11^+$ monocytes are primarily responsible for the infection. Dendritic cells invaded by tachyzoites show upregulation of Chemokine Receptor 7 (CCR7) movement.[7,10]

The establishment of T. gondii infection is supported by a microenvironment enriched with activated immune cells and a variety of soluble inflammatory mediators, such as chemokines, cytokines, and additional cellular components. During OT, the crosstalk between chemokines and ocular immune responses involves $CD4^+$ and $CD8^+$ T cells, with IFN-γ acting as the central mediator.

Elevated levels of T cell chemoattractants, particularly CCL5, CXCL9, and CXCL10, are detected during latent infection and are IFN-γ-dependent. Infection of astrocytes or microglia by T. gondii induces the expression of CXCL9, CXCL10, CCL5, and CCL2.[8,17] Astrocytes and microglia contribute to the orchestration of immune responses through the release of CXCL9 and CXCL10, key ligands for the CXCR3 receptor, facilitating the migration of T cells and myeloid cells (monocytes and granulocytes) into infected cells. During the acute infection phase, levels of CXCL9 and CXCL10 are higher compared to the chronic phase, although ocular manifestation differences are not specifically compared. During reactivated T. gondii infection, reduced levels of CXCL9 and CXCL10 correlate with decreased T cell infiltration into infected tissue.[17,18]

Previous studies have shown that CXCL9 performs well in distinguishing neonates infected with T. gondii. CXCL9 improves the accuracy of biological markers for diagnosing toxoplasmosis in congenitally infected infants. Chemokine levels are considerably higher in the aqueous humor of individuals with OT than in that of controls. It has been noted that in experimental models of OT, CXCL9 expression in the retina is markedly increased. [19]

CXCL10, one of the chemokines elevated during T. gondii infection, is triggered by IFN-γ and found in parasitized tissues during the acute phase. This supports evidence that T. gondii triggers CXCL10 production, which regulates effector T cell trafficking and function. CXCL10 is essential for recruiting activated Th1 cells that express its receptor, CXCR3, during immune responses to diverse pathogens.[20] (Table 1)

Conclusion

Ocular toxoplasmosis (OT) serves as the leading cause of posterior uveitis. The underlying pathophysiological mechanisms of ocular toxoplasmosis are not yet fully understood. This literature review summarizes and describes several studies related to the cellular immune response mediated by chemokines. Various groups of studies have explored the role of chemokines in the pathophysiology of OT. Most of the studies are cross-sectional in nature, showing correlations between different cytokines and chemokines with OT. Among the many cytokines involved, CXCL9 and CXCL10 play significant roles. These chemokines are crucial for recruiting $CD4^+$, $CD8^+$, and other immune T cells to the area of tachyzoite proliferation to prevent further pathogen growth. The expression of CXCL9 and CXCL10 is highly dependent on IFN-γ produced by infected cells. Therefore, understanding the function and production of CXCL9 and CXCL10 is important in predicting the occurrence of OT.

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