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Toxoplasma chorioretinitis: Role of host genetics and cytokines in determining tissue damage and disease severity

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Objective: To study the role of host genetics and cytokine responses to ocular tissue damage post-virulent *T. gondii* (RH) infection.

Background: Toxoplasmosis is generally self-limiting in healthy adults but it may cause toxoplasmic retinochoroiditis in cases of congenital infection leading to blindness. The importance of host genetics in determining disease severity in ocular toxoplasmosis has been shown in different inbred mouse strains using low-virulence *Toxoplasma* strain.

Material & Methods: In this study, we studied intraocular immune response and tissue alterations in the genetically resistant BALB/c and susceptible MF1 mice infected with a virulent type-I RH *T. gondii* strain by intravitreal route.

Results: We observed a significant up-regulation of IFN- γ and TNF- α to >2200 pg/ml and >300 pg/ml respectively in the blood of both BALB/c and MF1mice during the early stages of post intraocular infection (p<0.01) but the levels dropped sharply to normal during the late stages of the infection on day 26. The cytokine levels detected were higher in the MF1 mice compared with the BALB/c mice and relatively higher levels were observed in the aqueous humor (AqH) than in the blood of both groups of mice. The TGF- β 1 level in the blood and AqH of BALB/c mice remained low throughout the infection period compared with MF1 mice which showed gradual increase to 50 pg/ml in the blood and AqH during the early stages of infection which then further increased 2-fold to 132 pg/ml on day 11 (p<0.01) and remained high till the last day of observation on day 26 except that the TGF- β 1 level in AqH dropped sharply to normal level.

Conclusions: Our results support that TGF- $\beta1$ down-regulates the effector functions of anti-Toxoplasma cellular immunity during acute infection. We document that a mild Th1 pro-inflammatory response in BALB/c mice with high IFN- γ and TNF- α and, low TGF- $\beta1$ levels during the early stages of infection may have contributed to an effective cellular immune response leading to lower morbidity, mortality and less ocular tissue damage. However in the MF1 mice, a significantly high TGF- $\beta1$ level in the blood and in the AqH during the acute infection may have adversely interfered with an effective cellular immune response leading to an increased mortality and extensive ocular tissue damage with parasite tachyzoites observed in the pigment epithelium layers.

Biography

Jamshaid Iqbal is an Associate Professor and Director, Faculty of Medicine, Kuwait University, Consultant, Mubarak Al-Kabir Teaching Hospital, Kuwait. His main research work is to Study of Tropical & Parasitic infections in Kuwait with specific focus on immuno- and molecular diagnosis.

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