THE ROLE OF CYTOKINE PROFILE IN THE PATHOGENESIS OF CHRONIC BRUCELLOSIS: A REVIEW

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Annotation: Brucellosis is a zoonotic infection that can progress to a chronic form, characterized by persistent inflammation and immune dysregulation. Cytokines, as key mediators of immune response, play a significant role in the transition from acute to chronic disease. This review focuses on the alterations in cytokine profiles during chronic brucellosis and their impact on pathogen persistence, immune evasion, and chronic inflammation. Particular emphasis is placed on the balance between pro- and anti-inflammatory cytokines and the dysfunction of Th1/Th2/Th17 immune responses.

Keywords: Brucellosis, chronic infection, cytokines, immune response, inflammation, Th1/Th2/Th17

Introduction. Brucellosis remains a significant public health concern in endemic regions. While acute brucellosis can be treated effectively with antibiotics, a notable proportion of patients progress to a chronic form, characterized by persistent symptoms, immune dysregulation, and pathogen persistence in host tissues [1].

The transition to chronicity is largely influenced by the host immune response, particularly cytokines, which orchestrate the interplay between pathogen clearance and tissue damage [2].

Cytokine Response in Acute and Chronic Brucellosis.

In acute brucellosis, cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6) play a central role in initiating the inflammatory response. These cytokines activate macrophages and dendritic cells, promoting intracellular killing of Brucella spp. [3]. However, in chronic brucellosis, persistent elevation of these cytokines may lead to tissue damage and chronic inflammation, contributing to symptoms like arthralgia and fatigue [4]. Skendros et al. Reported increased serum levels of IL-6 and TNF-α in patients with chronic brucellosis, suggesting ongoing inflammation despite antibiotic therapy [4].

- Th1/Th2 Imbalance

Th1 cytokines (e.g., IFN-γ, IL-12) are essential for activating macrophages to clear intracellular Brucella. In contrast, Th2 cytokines (e.g., IL-4, IL-10) inhibit this process by promoting antibody responses and suppressing cell-mediated immunity [5]. Chronic brucellosis is often associated with a shift towards Th2 dominance, which impairs bacterial clearance and allows for the establishment of persistent infection [6]. Zhan and Cheers demonstrated that mice deficient in IFN-γ or IL-12 had delayed clearance of Brucella, highlighting the role of Th1 immunity in controlling the infection [5].

- Role of IL-10 and TGF-β

Anti-inflammatory cytokines such as interleukin-10 (IL-10) and transforming growth factor-beta (TGF-β) are often elevated in chronic brucellosis. These

cytokines suppress the activation of macrophages and cytotoxic T cells, facilitating Brucella survival in host cells [7]. Eskandari et al. Found elevated IL-10 and TGF-β levels in chronic brucellosis patients, which correlated with disease duration and symptom severity [7].

- Emerging role of IL-17 and Th17 Cells

Recent studies have highlighted the involvement of Th17 cells and IL-17 in brucellosis. While IL-17 promotes neutrophil recruitment and inflammation, its role in intracellular bacterial infections remains controversial.

In chronic brucellosis, dysregulation of IL-17 may contribute to tissue damage and autoimmune-like manifestations, especially in joints and bones [8]. Dey et al. Reported that excessive IL-17 production may be linked to osteomyelitis and arthritis in chronic brucellosis patients [8].

Cytokine-based diagnostic and therapeutic approaches. Given the pivotal role of cytokines in chronic brucellosis, cytokine profiling may serve as a diagnostic marker and guide therapeutic interventions. Elevated IL-6, IL-10, and TNF-α levels have been proposed as biomarkers of disease chronicity [4, 7]. Therapeutic modulation of the cytokine response using anti-inflammatory agents, cytokine antagonists, or immunomodulators may enhance treatment outcomes in refractory cases [6]. Research by Skendros et al. Suggests that targeting TNF-α or boosting IFN-γ responses could improve pathogen clearance and reduce chronic symptoms [4].

Conclusion. Cytokines play a central role in the pathogenesis of chronic brucellosis, modulating the balance between host defense and immune evasion. A shift from Th1 to Th2/Th17 responses, along with elevated anti-inflammatory cytokines, contributes to persistent infection and chronic inflammation. Understanding cytokine dynamics opens avenues for biomarker development and immunomodulatory therapies aimed at preventing or reversing chronic disease.

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