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Elevated serum level of type-2 cytokine and low IL-17 in first episode psychosis and schizophrenia in relapse

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ABSTRACT

Schizophrenia is chronic and debilitating mental disorder. In broad spectrum of possible causes or contributing factors, immune system and cytokines were investigated in the onset and development of schizophrenia. The aim of our study was to analyze the serum concentrations of type-1 cytokines: TNF-α, IFN-γ, type-2 cytokines: IL-4, IL-10, type-17 cytokine: IL-17 and regulatory cytokines: TGF-β, IL-27, IL-6, in drug-naive patients with First Episode Psychosis – FEP ($n = 88$) and Schizophrenia in relapse – SC in relapse patients ($n = 45$), comparing to healthy controls ($n = 36$). Also, we attempted to determine potential correlation between cytokine levels and/or cytokine ratios with clinical parameters, such as severity of illness, positive, negative and general psychopathology. Our results showed decreased levels of IL-17 ($p = 0.018$), demonstrating that type-17 response is blunted in psychotic episode. Increased levels of IL-4 ($p = 0.033$) showed that type-2 response is overweight in psychotic episode. Also, levels of IL-4 in serum of SC in relapse patients were higher than controls ($p < 0.0005$) and patient with FEP ($p = 0.003$). This alteration was accompanied with increase in production of TGF-β in psychotic patients ($p = 0.009$) and also in FEP ($p < 0.0005$) and SC in relapse ($p < 0.0005$). Analysis showed that TGF-β can be a valuable marker for psychosis. The presence of enhanced anti-inflammatory/immunosuppressive activity in schizophrenia may be an attempt to counteract or limit ongoing pro-inflammatory processes and downregulating chronic inflammation. Finally we have documented decreased levels of IL-17 and IL-17/TGF-β ratio in these types of psychotic patients, suggesting the new aspects of schizophrenia pathophysiology.

1. Introduction

Schizophrenia is chronic and debilitating mental disorder, with onset of full-blown disease in late adolescence or early adulthood (Freedman, 2003). Clinical symptomatology of schizophrenia is diverse: delusions, hallucinations, thought disorders and behavioral and emotional changes, with progressive cognitive declining and deterioration of personality (Sadock et al., 2009). In broad spectrum of possible causes or contributing factors, immune system was investigated in the onset and development of schizophrenia (Yolken and Torrey, 1995; Haack et al., 1999; Cazzullo et al., 2003; Keshavan et al., 2011). There have been numerous attempts to find a connection between schizophrenia and immune response (reviewed by Müller and Schwarz, 2010). Several studies have indicated the interrelationship between cytokine levels and pathology of schizophrenia (Kronfol and Remick, 2000; Cazzullo et al., 2001).

The principal cells that modulate immune response are T helper (Th) lymphocytes, which orchestrate the function of other immune cells by cytokine production. In addition, macrophages, natural killer cells (NK cells), natural killer T cells (NKT cells) and dendritic cells (DCs) can also produce cytokines. Regarding this fact, the immune response can be named type-1, type-2 or type-17 and hallmark criteria for this categorization are specific cytokine profiles. Type-1 immune response is followed by secretion of mainly interferon-gamma (IFN-γ) and interleukin-2 (IL-2), while during type-2, interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-9 (IL-9) and interleukin-13 (IL-13) are mostly secreted cytokines (Fort et al., 2001). The hallmark of type-17 immune response is interleukin-17 (IL-17), a potent mediator of

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