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Immune Disregulation in Inflammatory Skin Diseases with Comorbid Metabolic Disorders

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Abstract : Skin barrier dysfunction induces multiple inflammatory skin diseases. Epidemiological studies clearly support the link between most dermatological pathologies, immune disorders and metabolic disorders. Among them most common are psoriasis (PS) and Atopic dermatitis (AD). Psoriasis is a chronic immune-mediated inflammatory skin disease that affects 1.5 to 3.0% of the world's population. Comorbid metabolic disorders play an important role in the progression of PS and AD, as well. It is well known that PS, AD and overweight/obesity are associated with common pathophysiological mechanisms of mild chronic inflammation. The goal of the study was to study the immune disturbances in patients with PS, AD and comorbid metabolic disorders. To study the prevalence of comorbidity of PS and AD (data from 1406 patient's histories of diseases) were analyzed. The severity of the disease is assessed using the PASI index (Psoriasis Area and Severity Index). 59 patients with psoriasis of different localizations of lesions and severity, as well as with different body mass index (BMI), were examined. The determination of the concentration of pro-inflammatory cytokines (IL-6, IL-8, IFNγ, IL-17, L-18 and TNFa) and chemokines (RANTES, IP-10, MCP-1 and Eotaxin) in sera and supernatants of 48h-cultivated peripheral blood mononuclear cell (PBMC) of psoriasis patients and healthy volunteers (36 adults) have been carried out by multiplex assay (Luminex Corporation, USA). It has been demonstrated that 42% of PS patients had comorbidity with different types of atopies. The most common was bronchial asthma and allergic rhinitis. At the same time, the prevalence of AD in PS patients was determined in 8.7% of patients. It has been shown that serum levels of all studied cytokines (IL-6, IL-8, IFNγ, IL-17, L-18 and TNF□) in most of the studied patients were higher in PS patients than in those with AD and healthy controls ($p<0.05$). An in vitro synthesis of the IL-6 and IFNγ by PBMC demonstrated similar results to those determined in blood sera. There was a high correlation between BMI, immune mediators and the concentrations of adipokines and chemokines ($p<0.05$). The concentrations of Leptin and Resistin in obese psoriatic patients were greater by 28.6% and 17%, respectively, compared to non-obese psoriatic patients. In obese patients with psoriasis the serum levels of adiponectin were decreased up to 1.3-fold. The mean serum RANTES, IP-10, MCP-1, EOTAXIN levels in obese psoriatic patients were decreased by up to 13.1%, 21.9%, 40.4% and 28.2%, respectively. Similar results have been demonstrated in AD patients with comorbid overweight and obesity. Thus, the study demonstrated the important role of cytokines and chemokines dysregulation in inflammatory skin diseases, especially in patients with comorbid obesity and overweight. Metabolic disorders promote the severity of PS and AD, highly increase immune dysregulation, and synthesis of adipokines, which correlates with the production of proinflammatory immune mediators in comorbid obesity and overweight.

Keywords : psoriasis, atopic dermatitis, pro-inflammatory cytokines, chemokines, comorbid obesity
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