INFLAMMATORY SKIN DISEASES (OTHER THAN ATOPIC DERMATITIS & PSORIASIS)

IMMUNOLOGICAL AND GENETIC PROFILES OF DRUG-INDUCED PARADOXICAL PSORIASIS

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Background: Immunomodulation with biologics targeting pathogenic molecules are highly effective in the treatment of various immune-mediated inflammatory diseases, such as psoriasis, hidradenitis suppurativa (HS) and rheumatoid arthritis (RA). However, they may be responsible for unexpected paradoxical psoriasiform reactions. The mechanisms underlying the induction of these events is not clear, even though a genetic susceptibility could be hypothesized to be involved.

Objective: To investigate the immunological and genetic profiles of four patients developing paradoxical psoriasiform reactions, after treatment with anti-TNF-α or anti-CD80/CD86 therapy initiation (Adalimumab for n=3 HS; Abatacept for n=1 RA).

Materials and Method: The characteristics of the inflammatory reactions were investigated by immunohistochemistry. Blood and skin-derived T cells from the four patients were analysed by multiparametric cytometry and compared to those isolated from canonical psoriasis. In parallel, 44 Single-Nucleotide Polymorphisms (SNPs) associated to psoriasis-related risk loci were analysed by a NGS approach.

Results: All patients showed erythematosus and/or pustular lesions on palmo-plantar region, lower limbs and scalp. Both peripheral and skin-infiltrating T cells were enriched in IFN-γ- and IL-17-releasing CD4+ and CD8+ T cells, although IFN-γ levels were lower if compared to T cells isolated from canonical psoriasis. A high number of infiltrating CD15+ neutrophils releasing IL-17, as well as CD11c+ or BDCA2+ dendritic cells was also present. IFN-β in the epidermal compartment of paradoxical reactions was higher than that observed in canonical psoriatic lesions. Interestingly, allelic variants in HLA-C, CDSN, CCHCR1 and NFKBIZ genes were present in all patients affected by paradoxical psoriasis, whereas SNPs in ERAP1 gene were present in HS patients, but not in RA.

Conclusions: Paradoxical psoriasiform reactions show immunological features common to early phases of psoriasis, characterized by cellular and molecular players of innate immunity. All patients with paradoxical reactions have SNPs in psoriasis-related genes involved in cytokine pathways, antigen presentation and keratinocyte differentiation.