Cytokine analysis in hidradenitis suppurativa supports therapeutic approaches

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Hidradenitis suppurativa (HS) is a recurrent inflammatory skin disease characterized by painful, deep-seated, inflamed lesions in the inverse skin areas of the body with a prevalence of about 1%. Patients with HS have a significantly impaired quality of life, including social withdrawal, and because medical treatment options for HS are limited and their efficacy moderate, these patients also experience a great unmet need.2

The pathogenesis of HS is largely unknown and is probably multifactorial. An immunological basis was considered conceivable, because there is a known association between HS and other immune-mediated diseases and improvement is observed with immunosuppressive therapy such as antitumour necrosis factor (TNF)-α biologics, oral corticosteroids and ciclosporin.2 In this issue of the BJD, Genevieve Kelly and colleagues report on the cytokine expression in lesional and nonlesional skin of HS.3 They show that the expression of the inflammatory cytokines interleukin (IL)-17, IL-1β and TNF-α is enhanced in the lesional skin of patients with HS, and that IL-17 and IL-1β mRNA are also enhanced in clinically normal perilesional skin. Van der Zee et al.4 had already shown that the cytokines IL-1β, TNF-α and IL-17 were elevated in HS compared with perilesional and normal skin. Kelly et al.3 expanded the experiments by digesting HS biopsies and preparing cell suspensions. They used intracellular cytokine staining and flow cytometry and identified classic CD4+ T cells as the source of IL-17, and CD11c+ CD1a- CD14+ inflammatory dermal dendritic cells as the source of IL-1β in HS lesions. Activated caspase-1, required for the activation of pro-IL-1β and IL-18, was detected in HS skin together with enhanced expression of NLRP3 (NOD-like receptor family, pyrin domain containing 3) and proinflammatory IL-18. They inhibited caspase-1 activity by a fluorochrome inhibitor of caspases, and show that IL-1β and IL-18 production are decreased, suggesting that the caspase-1 pathway mediates IL-1β and IL-18 expression in HS. Based on the abnormal cytokine expression detected in perilesional and uninvolved skin, it is proposed that subclinical inflammation is present in HS skin prior to the formation of active lesions. Collectively the results indicate that IL-17 and the caspase-1-associated cytokines IL-1β and IL-18 are important in the pathogenesis of HS. Their investigations for the first time convincingly demonstrate activation of the NLRP3 inflammasome in HS.

What is the importance of this study? The current situation in the field of research in HS is comparable with the landscape in psoriasis a decade ago. Since then several new therapeutic targets for psoriasis have been identified leading to at least five commercially available biologics (three anti-TNF, one anti-IL-12/23 and one anti-IL-17) and two biosimilars and a huge pipeline of candidate compounds.5 The improvement obtained in psoriasis, and the reduction in the unmet need of patients with psoriasis, is based mainly on meticulous investigations into the immunopathogenesis of the disease. The studies included careful dissection of the inflammatory process in lesional, perilesional and nonlesional psoriasis skin as Kelly et al.5 now apply for HS. Such studies are crucial for the discovery of novel therapeutic targets and pathways in HS. IL-1β and IL-17 and their respective receptors are now recognized therapeutic targets in HS. A phase II clinical trial targeting IL-17 is currently underway (ClinicalTrials.gov identifier: NCT02421172). The NLRP3 inflammasome might well be the next therapeutic target in HS, as several specific inhibitors are available. Identification of the exogenous and endogenous triggers of NLRP3 and perhaps other inflammasomes is a promising challenge in HS.

Conflicts of interest
None declared.

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