Commentary 2

Although recognized more than 150 years ago, hidradenitis suppurativa (HS) is still a mysterious disease. Ever since inflammation of the apocrine glands was recognized as a secondary event in the pathogenesis of the disease, it has been speculated that comedonal and/or poral occlusion(s) and bacterial infection play a crucial role. Even though this concept has been questioned almost immediately, there is some consensus regarding the role of immunity and infection. Thus, even if I cannot provide an answer to the question posed by the editor, let me elaborate on the issues of skin immune response and infection in HS pathogenesis.

The involvement of immune response in HS remains controversial. Immunological investigations of patients with HS suggested no abnormalities of the immune system (1). By contrast, other authors showed increased peripheral suppressor T-cell activity (2), indicative of a cellular immune response. This is further supported by the presence of activated, HLA-DR-positive as well as Leu-8-positive immunoregulatory lymphocytes (3). These results indicate that the lymphocytic infiltrate is definitely the result of in vivo activation of lymphoid cells. Indeed, the significant fall of the T-helper-suppressor and NK cell ratio over time after the initiation supports the existence of a precipitating, cell-mediated immune response with only a short eliciting period (3,4). More recent studies have shown that dysfunctional neutrophils and monocytes may also be involved in the pathogenesis of HS, still, no primary abnormalities of the innate or acquired immune system can be held to be causal in every case (3–6).

Because of increasing evidence suggesting that keratinocytes (KCs) not only participate in cutaneous immune responses but may in fact play key initiation roles (7), one must also consider the contribution of KCs to HS pathogenesis. KCs are able to recognize a wide variety of micro-organisms through their pattern recognition receptors (PRRs) and have evolved mechanisms to distinguish between skin commensals and pathogens. Signalling through specific PRR combinations provides selectivity and specificity to immune response. As a result, KCs produce a wide range of antimicrobial peptides, proinflammatory cytokines/chemokines and inducible enzymes (8). The secretion of antimicrobial peptides is indeed crucial, as skin lesions characterized by low levels of such host-defence peptides are more susceptible to infections. By exhibiting chemoattractant activity, KC-derived cytokines/chemokines and antimicrobial peptides can recruit T cells, neutrophils and dendritic cells into sites of infection, thus providing an improved immune response against pathogens (7,8). These findings indicate a close interdependence of KCs and inflammatory infiltrate as well as a balance between the innate and acquired immune systems. Any perturbation in this system, for example dysregulation and abnormal expression of inflammatory mediators or their receptors in KCs, can lead to the pathogenesis of chronic inflammatory skin diseases, such as HS.

The significance of bacterial involvement in the pathogenesis of HS is also controversial. It is likely that chronic inflammation is because of secondary bacterial colonization (5). This is further supported by the fact that routine cultures from the surface of the lesions are often negative. Still, bacteria are likely to be involved in the pathogenesis of the disease as numerous species are most frequently isolated from lesions (6,9). Most of bacteria identified in HS lesions, such as Propionibacterium acnes and coagulase-negative staphylococci, are part of the normal microflora, but have also gained attention as pathogens. These findings highlight a possible polymicrobial nature and predominance of anaerobic bacteria, supporting the role of bacterial infections as a possible pathogenic event in HS. However, interpreting the results of previous studies is difficult, as potential differences amongst recently discovered phylogeneic groups and/or ecotypes have not been taken into account. Notably, the existence of philogenetically distinct P. acnes clusters have recently been demonstrated (10). Importantly, these clusters differ in the production of secreted proteins (11), and induce different immune responses in KCs and sebocytes (12,13).

These findings challenge our current understanding of the pathogenic nature of bacteria involved in HS pathogenesis and raise the exciting possibility that bacterial strains, or group of strains, with greater potential to cause opportunistic infection in HS may exist. This may explain, in part, the apparent controversy with respect to the role of bacterial infection in HS.

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References