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Hidradenitis suppurativa: the "bright side" of autoinflammation and hidden diseases

Angelo Valerio Marzano[1], Giovanni Genovese[1], Piergiacomo Calzavara-Pinton[2]

[1] Dermatology Unit, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

[2]Dermatology Department, ASST Spedali Civili di Brescia, University of Brescia, Brescia, Italy.

Corresponding author:
Angelo Valerio Marzano, MD
Associate Professor Of Dermatology and Consultant,
Dermatology Unit, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico,
via Pace 9 - 20122 Milan, Italy
Telephone: +390255036289
Fax: +390255035236
Email: angelo.marzano@unimi.it

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Hidradenitis suppurativa (HS) is a chronic-relapsing, debilitating inflammatory disease primarily affecting the pilosebaceous unit.[1] It is clinically characterized by recurrent, painful, deep-seated nodules, abscesses and sinus tracts ending in hypertrophic scarring that typically involve apocrine gland-rich areas of the body, notably axillary and inguinoperineal regions.[1] HS is estimated to affect 1% of the population,[1] but, in our opinion, the incidence and prevalence of the disease has significantly increased in the last few years. The pathophysiology of HS is the result of a complex interplay between genetic and environmental factors cross-talking with both innate and adaptive immunity dysfunction, as well-described in the review article by Napolitano et al.[2], providing an update on HS pathogenesis. Heterozygous mutations in the γ-secretase genes – presenilin enhancer 2 (PSENEN), presenilin (PSEN1) and nicastrin - were the first reported genetic changes in HS.[3,4] The above mutations cause inactivation of Notch signaling which is responsible for an altered homoeostasis of hair follicle and apocrine gland leading to the production of the so-called damage-associated molecular pattern (DAMP) molecules. These molecules induce an abnormal activation of the inflammasome, a molecular platform triggering the inflammatory process in HS as in the classic monogenic autoinflammatory diseases like familial Mediterranean fever.[5] The important autoinflammatory component in the pathogenesis of the disease is supported also by the upregulation of interleukin(IL)-1β[6,7], which is a pivotal cytokine in autoinflammation.[8] On the other hand, some studies found γ-secretase mutations only in a minority of HS cases,[9,10] suggesting γ-secretase mutation alone is not sufficient to produce the HS phenotype.[11] Interestingly, our group reported mutations involving a number of autoinflammatory genes in the recently described syndromic variant of HS known as PASH (pyoderma gangrenosum, acne, suppurative hidradenitis), [12,13] giving rise to considering HS a polygenic autoinflammatory condition in which innate immunity dysfunction plays a key role. From an immunological point of view, IL-17, cytokine merging innate and adaptive immunity, has also been reported overexpressed in the lesional skin of HS.[14] Of note, with respect to IL-1β and IL-17 expression, HS resembles PASH[15] as well as two prototypic neutrophilic dermatoses, pyoderma gangrenosum and Sweet's syndrome,[16] making justified, to include HS in the spectrum of neutrophilic dermatoses,[17] based also on the high number of skin infiltrating neutrophils especially in later stages of the disease.[7] The interesting article by Pescitelli et al.[18] supports the recent view on HS as a systemic disease linked to several comorbidities, with which HS shares genetic factors, environmental triggers and inflammatory pathways. Reports of elevated circulating levels of tumour necrosis factor (TNF)-α[19] in HS are in line with systemic inflammatory activation. Obesity and metabolic syndrome are the most common associated conditions in HS patients[18] but inflammatory bowel diseases, particularly Crohn's disease,[20] and spondyloarthritis[21] also occur more frequently in these patients than in the general population. Thus, clinical intervention for HS must include consideration of these comorbidities and complications with a multidisciplinary approach that is outlined also in the article by Veraldi et al.[22] Finally, the paper by Lacarrubba et al.[23] reviews and discusses the important contributory role of imaging techniques, particularly ultrasonography.[24] Ultrasonography may reveal features not appreciable at clinical examination, notably fistulous tracts, allowing a more accurate staging, treatment planning and monitoring response to therapy in this debilitating disease.

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