Hidradenitis Suppurativa: Current Views on Epidemiology, Pathogenesis, and Pathophysiology

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Abstract

Hidradenitis suppurativa (HS) is a disease characterized by chronic follicular occlusion and secondary inflammation of the apocrine glands. The disease is uncommon but not rare. Further epidemiologic study is required to better determine HS prevalence in various populations. Women are affected three times more often than men, although HS tends to be more severe in men. The typical age of onset is in the second and third decades; HS is rare prior to puberty, and the prevalence is lower in older adults. A number of factors (particularly cigarette smoking) and comorbid conditions (especially obesity) are associated with HS, but causative relationships have not been established.

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Keywords

Autosomal dominant inheritance; cigarette smoking; comorbidities; hidradenitis suppurativa; obesity

From the time hidradenitis suppurativa (HS) was first described as a disease, it has been misnamed and misunderstood. Because lesions typically are found in anatomic areas rich in apocrine sweat glands, hidradenitis suppurativa—as the name implies—was thought to be a disease characterized by apocrine gland dysfunction. More than a century and a half later, HS is thought instead to be a disease of chronic follicular occlusion with secondary inflammation of the apocrine glands. The results of research published within the past decade have provided a better understanding, if not a complete articulation, of the underlying inflammatory process. In addition, epidemiologic studies have provided a clearer picture of those affected (**Table**).[1]

Epidemiology and Demographics

The prevalence of HS has been estimated to be as low as 0.00033%[2] and as high as 4%.[3] More recent studies have estimated the risk to be 1%[4] or less.[5,6] This variation may be explained by the fact that substantial differences in prevalence exist among various subpopulations, which may be under- or overrepresented in particular studies. For example, a large Danish study estimated the point prevalence of HS from a sample of 507 consecutive patients undergoing screening for sexually transmitted diseases.[3] The relatively high prevalence of HS in this group (4.1%) may well be explained by the comparatively young age of those included. Attempts to estimate the prevalence of HS from claims databases and electronic health records may be limited by the potential for misdiagnosis and inaccurate coding among the various medical specialties that interact with and care for patients with HS.

Thus, the potential is high for methodologic problems in studying the epidemiology of HS. The pathophysiology of the disease is still not well characterized, so confounding variables likely exist that are not identified and controlled for. Nevertheless, there is widespread agreement, based on both available epidemiologic data and the preponderance of experience among clinicians, that HS most commonly occurs in individuals in the second and third decades of life and is seen more frequently in women than in men. Differences among ethnic populations are less clear.

Age

The disease is rare prior to puberty, and the prevalence is lower among older adults. In a study of 302 French patients with HS, the median age of disease onset was 20 years (19 years in men, 21 years in women), and the median age of evaluation for the study was 30.4 years (30.2 years in men and 33.5 years in women).[7]

Sex

The female-to-male ratio of patients with HS is approximately 3:1,[5,7] and the highest incidence has been reported to be among women 20 to 29 years of age.[1] Interestingly, the presentation of HS also appears to differ by sex in both anatomic distribution and severity, with more severe disease and more perianal and atypical disease locations seen in men. (A more detailed discussion of presentation is available in the article "Natural History, Presentation, and Diagnosis of Hidradenitis Suppurativa" on page S51 of this supplement[8])

Ethnicity

Some have suggested that the disease is more common and/or more severe in patients of African ancestry than in those of European descent. However, the available data do not support this notion.[9]

Underlying Pathogenesis in HS

Arguments supporting a number of possible pathogenetic mechanisms in HS have been proposed; behavioral, genetic, infectious, hormonal, and/or host defense factors may be involved.

Behavioral "Risk Factors" for HS

A number of factors have been associated with HS, including the most frequently cited—smoking, obesity, and mechanical and environmental factors. However, a causative relationship

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has not been firmly established for these associations. Although the term "risk factors" is commonly used, further research is needed to characterize these relationships.

Smoking

A number of studies have revealed that a high percentage of patients with HS are cigarette smokers. Some studies have shown a prevalence of cigarette smoking as high as 70% to 88.9% among patients with HS, findings that are consistent across various populations.[9] In a multivariate analysis, Revuz et al[4] reported the odds ratio of self-reported smoking among patients with HS to be 4.16. The quantity of cigarettes smoked did not appear to be relevant. Meanwhile, smoking cessation was not shown to improve the disease.

Obesity

Body weight has a strong positive correlation with HS. As many as 50% of those with HS are obese.[9] The odds ratio for HS is 1.12 for each increase of one unit of body mass index.[4] The proposed mechanisms underlying this association include follicular occlusion and trauma/friction.

Mechanical and Environmental Factors

Clinical experience and a variety of studies have implicated a number of mechanical and environmental insults that seem to have an effect on HS. Among the factors cited in this category are skin-on-skin friction in intertriginous areas (especially in obese patients), irritation from the use of antiperspirants, and shaving of axillary hair, activities that may traumatize hair follicles. Whether these effects play a role in causation or simply exacerbate the disease has not been established, and there are no data that prove the associations. However, patient reports and clinical observation suggest that all of these factors may at least worsen the symptoms of patients with HS.

Genetic Factors

Evidence exists for an autosomal dominant relationship in at least some patients with HS, possibly indicating that HS has a heritable form. In one study, 34% of first-degree relatives of patients with HS also had the disease,[10] demonstrating autosomal dominance with variable penetrance. A potential genetic locus for the disease has also been identified.[11] Subsequently, advances in genetic research have shown that the enzyme γ-secretase is important in skin biology and has a role in a small number of patients with HS, in whom mutations in γ-secretase genes (NCSTN, PSENEN, and PSEN1) have been identified.[12] Further study is needed to enhance the understanding of the genetics of HS.

Infectious Factors

Cultures of samples taken from ruptured or open HS lesions commonly demonstrate a variety of bacterial species, including *Streptococcus viridians*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Peptostreptococcus* and *Bacteroides* species, coryneform bacteria, and Gram-negative bacteria, including *Escherichia coli* and *Klebsiella* and *Proteus* species.[9] Conversely, cultures from early, unruptured lesions may be sterile. To date, none of the organisms recovered from either superficial or deep sampling has predominated. Although some theorizethat staphylococci or other bacteria may play an important role in HS, either by creating an occlusive biofilm or by promoting an inflammatory response,[13,14] it is not possible at this time to state definitively whether bacteria play a primary or secondary role in HS.

TABLE Demographic and Diagnostic Characteristics of Patients With Hidradenitis Suppurativa

Characteristic	Total (N=268)
Gender, n (%)	
Female	189 (70.5)
Male	79 (29.5)
Age at diagnosis, y	
Mean (SD)	32.9 (12.6)
Median	30.6
Range	9.9–78.5
Race, n (%)	
White	241 (90.3)
Nonwhite	26 (9.7)
Unknown	1
BMI (kg/m^2) breakdown, n (%)	
Underweight or normal (<25.0)	49 (19.2)
Overweight (25.0–29.9)	66 (25.9)
WHO class I obesity (30.0–34.9)	49 (19.2)
WHO class II obesity (35.0–39.9)	49 (19.2)
WHO class III obesity (40.0–49.9)	33 (12.9)
Super obese (50+)	9 (3.5)
Unknown*	13
Smoking status, n (%)	
Never	79 (29.8)
Current	153 (57.7)
Former	33 (12.5)
Unknown	3
1st- or 2nd-degree family members affected?	
Yes	22 (8.2)
No	117 (43.7)
Unknown	129 (48.1)
Time between symptom onset and diagnosis, y	
N	156
Mean (SD)	5.1 (5.8)
Median	3.3
Range	0.0–30.0
Diagnosis of HS rendered by, n (%)	
Dermatologist	171 (63.8)
Nondermatologist but meets 4 criteria listed	97 (36.2)

BMI=body mass index; WHO=World Health Organization.
*Of the 19 patients missing BMI, 6 patients had a description of body habitus by the physician that was recorded and abstracted.
Source: Adapted from Vazquez et al.[1]

Hormonal Factors

The possible role of hormones in HS pathogenesis has been proposed but not established, despite numerous studies.[15-17] The age distribution of the disease in women (postpubertal and premenopausal) provides incentive for exploring a hormonal component, at least in women. Although a number of authors suggest that hyperandrogenism, specifically, may be a factor, the increased incidence of HS among women belies this claim, and the evidence available does not support this association.

Host Defense Factors

Dvorak and colleagues[18] concluded more than 35 years ago that host defense mechanisms are not impaired in patients with HS. These investigators found that granulocyte function and cell-mediated immune mechanisms were intact and immunoglobulin levels normal; an important role for an inflammatory process was demonstrated by elevated complement levels in all patients with HS in their study. A more recent study suggested that increased production of oxygen free radicals by neutrophils may play a role in HS.[19] Enhanced expression of toll-like receptors and release of proinflammatory cytokines by macrophages and dentritic cells in HS lesions has also been demonstrated.[20] Within the past decade, increased tumor necrosis factor (TNF)-α expression has been observed in HS, and TNF-α inhibitors have demonstrated efficacy in its treatment, suggesting that that inflammatory pathway may play a role.[21-23] Additionally, both activation of the interleukin-23/T-helper cell type 17 pathway and overproduction of interleukin-1β have been observed in HS lesions and may prove to be important therapeutic targets.[24-26]

Conclusion

Ultimately, HS is probably best thought of as a disease of follicular occlusion and chronic inflammation that is multifactorial and remains incompletely understood. It is not rare in the general population and is a significant source of morbidity among those with the disease. An improved understanding of the factors that contribute to and exacerbate HS is necessary to guide advances in its treatment and management.

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