Hidradenitis Suppurativa: A Frequently Missed Diagnosis, Part 1: A Review of Pathogenesis, Associations, and Clinical Features

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Editor’s note: This is the first part of this continuing education topic. “Hidradenitis Suppurativa: A Frequently Missed Diagnosis, Part 2: Treatment Options” will be published in the August 2015 issue.

PURPOSE:
To provide information about the etiology, diagnostic evaluations, and clinical features of hidradenitis suppurativa (HS).

TARGET AUDIENCE:
This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.

OBJECTIVES:
After participating in this educational activity, the participant should be better able to:
1. Identify the prevalence, pathophysiology, and risk factors associated with HS.
2. Describe diagnostic evaluations, staging, and comorbid disorders associated with HS.
ABSTRACT

Hidradenitis Suppurativa (HS) is a recurrent inflammatory follicular disease that commonly affects the apocrine-bearing skin. The aim of this continuing education article is to review the pathogenesis and clinical presentations of HS. The spectrum of clinical presentations ranges from subcutaneous nodules to draining sinus and fistula. The pathogenesis of HS remains unknown.

KEYWORDS: hidradenitis suppurativa, pathogenesis, wound care

INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic, recurrent inflammatory disease that presents with tender subcutaneous nodules, draining sinuses, abscesses, ulcers, and fistulas (Figure 1). Hidradenitis suppurativa is a primary defect of the hair follicle that commonly affects the axilla, groin, perianal, perineal, and inframammary regions in females. These lesions cause significant interference with everyday activities from pain, drainage, odor, and scar formation. Individual nodules may spontaneously rupture or coalesce to form deep dermal intensely painful abscesses that ultimately heal with contracted and indurated dermal fibrotic scars (Figure 2). Appropriate local wound care is an integral part of the HS ulcer management. Persons with HS often receive suboptimal pain control and suffer from persistent unpleasant odor from the exudates. The time from onset of HS lesions to diagnosis can be years; in the authors’ series, it took an average of 5 years, with some patients having their disease undiagnosed for 25 years.1

Unscheduled emergency visits, inadequate debridement of active lesions, suboptimal antibiotic treatment for secondary infection, and poor wound management all facilitate the chronicity of this condition.

THE SCOPE OF THE PROBLEM AND EPIDEMIOLOGY

Estimates of the prevalence of HS have varied, ranging from 1% to 4% of the general population depending on the studied population.2 However, many cases of HS remain undiagnosed or misdiagnosed, suggesting the true prevalence is likely to be higher than previously estimated. Typically, HS develops in otherwise healthy young individuals after puberty with a female-to-male ratio of 3.3:1.2,5,4 Although HS is more common among females, males tend to have a more severe disease.5 Consistent with these previous estimates, a recent analysis by Schrader et al5 of 845 Dutch patients calculated 72.6% of them to be female. In fact, females were more likely to have a family history of HS, and men had a tendency for more severe HS disease and associated severe acne.5 Canoui-Poitrine et al5 stated, “the front part of the body was predominantly involved in female patients (inguinal, mammary) in contrast to involvement of the back of the body (gluteal, inguinal, and atypical regions, including the posterior thigh), which was a hallmark of male patient involvement” (Figure 3).

UPDATE ON THE PATHOPHYSIOLOGY OF HS

The exact pathogenesis of HS is not fully understood. Historically, HS was considered to be a disorder of the apocrine glands and therefore was given its name derived from the Greek hidros, meaning “sweat,” and aden, meaning “glands.” Recent data, however, indicate that HS is predominantly a defect of the follicular epithelium.7 Yet, HS does not produce sebaceous secretions as seen in acne vulgaris, and there is a concern that the alternate name, acne inversa, may suggest a minor disorder rather than a life-altering major illness. Hidradenitis suppurativa is commonly grouped as part of the follicular occlusion tetrad, also including severe acne, dissecting cellulitis of the scalp, and pilonidal sinus.8 These conditions may share a common pathological process initiated by follicular occlusion.

Mechanism

The follicular occlusion in HS appears to result from a combination of an increase in ductal keratinocyte proliferation (follicular epithelial hyperplasia) and a failure to shed these keratinocytes, leading to occlusion and subsequent inflammation.8 Von Laffert et al7 suggested 2 different areas of inflammation: at the terminal follicles and the interfollicular epidermis. Keratinocyte proliferation may cause structural weakness of the follicular walls leading to follicular rupture and the formation of sinus tracts characteristic of HS.9 These sinus tracts can eventually open to the skin surface where commensal skin colonization can lead to deep and surrounding infection.

RISK FACTORS

Immune Dysregulations

Clinically, HS shares several similarities with many well-described autoimmune disorders, including exacerbations that are preceded by periods of stress and coexistence with other immune-mediated diseases including thyroid disease, Crohn disease (CD), and pyoderma gangrenosum (PG).11

The administration of antagonists to the proinflammatory tumor necrosis factor (TNF-) is often beneficial, suggesting a key role for TNF- in the pathogenesis of the disease.12 Van der Zee et al12 reported HS patients having a 5-fold enhancement in TNF-expression in lesional and perilesional skin areas compared with control subjects. Typical TH1 and TH2 cytokines, such as interferon , interleukin 4 (IL-4), IL-5, and IL-13, do not appear to be involved in HS, differentiating the inflammatory profile in HS from psoriasis and atopic dermatitis.11 Involvement of the IL-23/TH17
pathway has also been documented. The role of the immune system and the actual pathogenic pathway remain unclear. Further studies are necessary to clarify the impact of HS-associated immune dysregulation.

Genetics
Genetic susceptibility has been shown to be an associated factor in the development of HS. Approximately one-third of HS patients have a family history of HS. Familial HS is transmitted with an autosomal dominant inheritance pattern. Schrader et al also reported that in patients with a family history of HS the disease developed earlier and lasted longer.

Obesity
Although HS is not limited to overweight or obese individuals, HS patients generally have a higher average body mass index (BMI) and in the morbidly obese population, the prevalence of HS appears to be approximately 10 times higher than the general population. Obesity increases skin-on-skin contact (friction, moisture) in the deep skinfolds, leading to follicular hyperkeratinization and occlusion aggravated by local desquamation. The moist microenvironment promotes bacterial growth and colonization of affected sites.

Miller et al conducted a hospital-based study that demonstrated a positive association between HS and metabolic syndrome and the individual metabolic syndrome components including:

- A for A1c elevation associated with type 2 adult-onset diabetes mellitus
- B for blood pressure elevation (hypertension)
- C for cholesterol and triglyceride abnormalities (eg, low levels of high-density lipoprotein, dyslipidemias, and so on)
- D for diet and increased BMI.

Abdominal Obesity
There is mounting evidence that obese adult patients who lose weight may improve their HS. Kromann et al found a significant post–bariatric surgery weight reduction was associated with decreased HS disease severity. This finding is supported by a case study that demonstrated rapid improvement of longstanding treatment-refractory HS following bariatric surgery and subsequent dramatic weight loss. In addition, the authors highlighted the close relationship between active obese patient HS inflammation and the development of genital lymphedema. Inflammation and subsequent fibrosis from HS impair the lymph drainage routes, resulting in lymphedema that also increases infection risk by compromising tissue immunity.

Figure 1. HIDRADENITIS SUPPURATIVA PRESENTING WITH ACNEIFORM ERUPTIONS UNDER THE AXILLA

Figure 2. HIDRADENITIS SUPPURATIVA PRESENTING WITH SCAR AND SINUS FORMATION OF THE AXILLA
Smoking
There is a strong association between tobacco smoking and HS. In earlier studies, smoking has been reported at rates of 70% to 90% in populations of patients with HS. Using a postal follow-up survey with uncomplicated factual questions, Kromann et al determined that more than 90% of the HS survey respondents were active or former smokers. Previous studies have presented a host of potential mechanisms of cigarette smoking in the pathogenesis of HS, most acting as a proinflammatory stimulus or follicular occlusion promoter. Schrader et al determined increased HS disease severity with a greater number of smoking pack-years and longer HS disease duration.

Hormones
The role of hormones in the pathophysiology of HS is controversial. The observation of female predominance, premenstrual flare-ups, and improvement of HS during pregnancy suggest that androgens may be a contributing factor. In addition, the observed therapeutic benefit of antiandrogens, such as finasteride, in the treatment of children with HS gives some support to the potential role of androgens in HS. Barth et al found no differences in levels of plasma androgens, testosterone, and dehydroepiandrosterone sulfate between patients with HS and matched control subjects for BMI and hirsutism. These findings are supported by a more recent study by Buimer et al, who could not demonstrate a significant difference in the expression of estrogen and androgen receptors in skin biopsies of apocrine glands in patients with HS compared with control subjects. Additional studies are necessary to determine the contribution of hormones to the pathophysiology of HS.

THE MICROBIOME OF HS AND THE ROLE OF BACTERIA
There are conflicting data on the role of bacteria in the development of HS. A positive bacterial culture may represent contaminants from the normal skin flora or a secondary infection in a previously sterile process. It is hypothesized that bacterial superinfection contributes to the inflammatory vicious cycle observed in HS by triggering a cascade of pathogen-associated molecular patterns and leading to the stimulation of inflammasomes. Early studies found Staphylococcus aureus to be the primary pathogen in HS lesions, both superficial and deep levels. However, Matusiak et al found S. aureus to be the second most common isolate obtained and coagulase-negative staphylococci (CNS) as the most common. The authors highlighted that most CNS infections have a slow, subacute evolution resembling the course of HS inflammation. Sartorius et al isolated high numbers of CNS but found no S. aureus. The particular propensity for HS patients to develop chronic recurrent skin infections strongly suggests that HS is not primarily an infectious disease, but a predisposing condition that permits less virulent species to infect soft tissue and skin. Jahns et al suggested that the differences in the reported prevalence of bacterial species might be due to different regions being sampled, collection methods, and culture techniques.

THE PSYCHOSOCIAL IMPACT OF HS
An active HS lesion produces pain, drainage, odor, and disfigurement, placing it among the most distressing dermatology conditions. Patients often experience the following:
- embarrassment, low self-esteem, disabling social stigma, and a reluctance to develop interpersonal relationships
- anxiety and sexual distress
- soreness, pain
- major depression correlated with higher disease severity
The authors’ Canadian HS study identified a significant positive correlation between higher disease severity as measured by the Hurley stages (see below) and the impaired Dermatology Life Quality Index. Both physical and mental health compromises were also documented with the SF-36v2 survey. Esmann and Jemec investigated how patients feared stigmatization and isolation from the smell, pain, itching, and scars. Patients with HS require screening for activities of daily living (psychological compromise, reduced sexuality) in an effort to improve social acceptance and treatment results.

LABORATORY INVESTIGATIONS

Although most laboratory investigations were previously reported to be unhelpful, lesional bacterial cultures are appropriate at first presentation to detect resistant organisms. In addition, the following tests may be helpful in the evaluation of HS: complete blood cell count with differential and platelet counts, erythrocyte sedimentation rate, C-reactive protein assay, urinalysis, serum iron level, and serum protein electrophoresis. Patients with acute lesions may have elevated white blood count and erythrocyte sedimentation rate. Because histopathology is nonspecific, there is no role for the diagnostic skin biopsy in these patients. The diagnosis is based on the clinical characteristics of the lesions and body-fold distribution.

HS AND SYSTEMIC ASSOCIATIONS

There is emerging evidence to suggest that HS may be a systemic disease. Accompanying systemic manifestations that have been discussed in the context of HS include obesity and hormonal disturbance, both of which have been described in this article. Hidradenitis suppurativa has been associated with metabolic syndrome, with excess body weight or obesity, and hormonal abnormalities. There are many reported diseases associated with HS, of which the most commonly associated are inflammatory bowel disease and PG.

Crohn Disease and HS

Crohn disease is a chronic inflammatory gastrointestinal disorder with a myriad of cutaneous associations. Before infliximab became a treatment for both HS and CD, the association...
between the two was not well recognized. It is important to distinguish cutaneous CD from HS coexisting with CD. Additional involvement of the axilla favors a diagnosis of HS because cutaneous CD predominantly affects the perineal and perianal area. In 1 study of 1093 patients with inflammatory bowel disease, the prevalence of HS was found to be 23. Possible shared pathogenic factors have been reported in HS and CD. Both are chronic diseases of the epithelia, which are inhabited by commensal flora, both have risk factors that include genetic predisposition and smoking, and both can become complicated by fistula formation.

Pyoderma gangrenosum and HS
Pyoderma gangrenosum is commonly cited as a condition associated with HS. However, only recently has the clinical triad of PG, acne, and HS been described as a new disease entity (called PASH syndrome).

CURRENT STAGING

Staging
A wide variety of treatment options are used in the management of HS, ranging from nonpharmacologic measures (education and support, avoidance of skin trauma, hygiene practices, topical wound dressings, smoking cessation, weight reduction) to topical and systemic medications (antibiotics, retinoids, hormones, corticosteroids, immunosuppressants, metformin, biologies) and surgical procedures. The type and duration of treatment recommended depend on the severity, extent, chronicity, anatomic location, and resistance to treatment of HS lesions. To assess severity of HS disease, there are a variety of clinical measures available (Tables 1 and 2, Figures 4–6).

Although this classic grading system is useful for overall classification of cases, it has been criticized for not being dynamic enough in assessing differences in treatment efficacy. Therefore, Sartorius et al proposed a more dynamic and precise scoring system by adding more clinical details to the staging process.

The Sartorius scoring method factors in the number and type of inflammatory and noninflammatory lesions within 7 anatomical regions. However, this scoring system can be time-consuming and difficult to interpret. The HS Physician’s Global Assessment and Hidradenitis Suppurativa Clinical Response are 2 scores that are mainly used in clinical trials and research.

THE ROLE OF IMAGING
Clinical examination alone may underestimate the severity and disease involvement of HS. In a recent study by Wortsman et al, 34 HS patients with a total of 142 lesional areas were evaluated by ultrasound. The authors noted that sonographic examination revealed diffuse alteration of dermal echogenicity patterns, dermal thickening, dermal pseudocysts, widening of hair follicles, identification of fluid collections, and fistulous tracts that were not detected clinically. Furthermore, as a result of this study,
the management of 82% of the HS patients who participated was modified after the ultrasound examination, and 24% of the cases changed from medical to surgical management. This study demonstrated that imaging can be a potent tool for staging HS and should be used regularly in the assessment of this disease.

CONCLUSION

Hidradenitis suppurativa remains a challenging disease with unknown etiology. A multiprofessional approach is required to address the associated comorbidities and optimize the management. Early diagnosis and optimal treatment alleviate patients’ suffering and decrease the healthcare system burden.

PRACTICE PEARLS

- Hidradenitis suppurativa is a chronic recurrent flexural disease of hair follicles.
- Lesions vary from nodules (Hurley stage 1) to widely spaced abscesses and sinus tracts (Hurley stage 2) to diffuse involvement with scarring (Hurley stage 3).
- Hidradenitis suppurativa is more common in females with obesity, smoking, or adult-onset diabetes/metabolic syndrome, along with Crohn disease and pyoderma gangrenosum.
- Hidradenitis suppurativa is part of a follicular occlusion tetrad that also includes severe acne, pilonidal sinuses, and dissecting cellulitis of the scalp.
- The greater the Hurley stage of hidradenitis suppurativa severity, the greater the effect of Dermatology Life Quality Index.

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