Hidradenitis suppurativa: a review

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ABSTRACT: Hidradenitis suppurativa is a recurrent disease involving apocrine-bearing skin with a predilection for intertriginous areas, including genital skin. It has a highly variable clinical course. Mild cases may present as recurrent isolated nodules, while severe instances of the disease with chronic inflammation may lead to scarring, functional impairment, and rarely, squamous cell carcinoma. While genetic factors, patient characteristics, hormones and infection play a role in disease expression, a comprehensive understanding of the pathogenesis remains to be elicited. Additionally, effective treatment is largely unknown. While the mainstay of therapy had been surgery, and topical or systemic antimicrobial agents, other therapeutic modalities such as retinoids, hormonal therapy and immunosuppressive medications may also hold some promise.

KEYWORDS: apocrine acne, follicular retention triad, hidradenitis suppurativum, inverse acne.

Introduction

Hidradenitis suppurativa (HS) is a disorder of the apocrine-gland-bearing follicular epithelium. It was first described in 1839 by Velpeau (1). It was in 1854 that Verneuil (2) gave a name to this disorder and associated it with the sweat glands. Hidradenitis suppurativa then came to be classified as a member of the follicular occlusion triad, along with acne conglobata and dissecting cellulitis of the scalp (3,4). In 1975, pilonidal sinus was added as a member to this triad, forming the follicular occlusion tetrad (5).

Epidemiology

Hidradenitis suppurativa is common with a point prevalence of up to 4.1%, based upon objective findings, and a one-year prevalence of 1% based on patient recall (6). It is more common in females, with reported female: male ratios ranging from 2 to 5:1. The age of onset may vary from childhood to middle age, with an average of 23 years (7). Pre-pubertal cases are rare (8). Although the disease may develop in any skin bearing apocrine glands, genitofemoral lesions are more common in women, while axillary involvement does not appear demonstrate a gender predilection (6).

Etiology

Surprisingly little is known about the pathogenic basis of HS and few studies have attempted to help to clarify its etiology.

Adnexal structures

Classically, HS was thought to represent a primary disorder of apocrine glands and was also referred to as apocrinitis (3). This concept was supported by Shelly and Cahn (9) through the reproduction of clinical and pathologic lesions using their experimental model. More recently, HS has become regarded as a disorder of the follicular epithelium, with follicular occlusion giving rise to clinical findings. Follicular hyperkeratosis is the initial event, leading to occlusion, occasional secondary apocrine involvement, and follicular rupture with resultant inflammation and possibly secondary infection (10,11). The concept of the follicular occlusion tetrad stems from the concept that HS, acne vulgaris, pilonidal sinus, and dissecting cellulitis, all share follicular occlusion as an initial event leading to disease development.

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Genetic factors
A family history of HS may be elicited in 26% of patients (12). While several studies have failed to demonstrate human lymphocyte antigens (HLA) associations (13,14), others studies have suggested an autosomal dominant mode of inheritance (15–17). The identification of an exact genetic locus remains to be found.

Associated disease
Several disease states have been reported in association with HS. The significance of such conditions remains unknown. Such associations include Crohn's disease (18–21) and Dowling-Degos disease (22), and arthropathy (23–25).

Hormones and androgens
Some authors have suggested that hormones influence HS because it is rarely present prior to puberty. Additionally, the disease may flare up premenstrually in approximately 50% of postpartum cases (22,26), or in association with the oral contraceptive pill (27). Anti-androgen therapy has also demonstrated some therapeutic benefit in some studies (28–31). Some authors have disputed this association. Barth et al. (32) examined 66 women with HS and did not find any evidence biochemical hyperandrogenism. Thus, the influence of hormones on HS remains uncertain.

Obesity
Several studies have examined a pathogenic role for obesity and reports are conflicting. Overall, it is believed that obesity, while not playing a role in the primary pathogenesis of HS, may aggravate disease via occlusion and masceration (22).

Bacterial infection
Bacterial infection has classically been regarded as a pathogenic event in HS, and not surprisingly, antibacterial agents are commonly employed as treatment.

Although disputed by some authors, bacterial involvement is thought to occur secondary to the disease process. Although routine cultures are often negative, numerous bacteria have been recovered from lesions of HS. Staphylococcus aureus and coagulase-negative staphylococci are most frequently isolated (33,34). However, other investigations have managed to identify other bacteria, including streptococci, gram-negative rods, and anaerobes (22,35).

Smoking
The use of tobacco products is more common in patients with HS than in healthy controls. The etiologic basis is unknown (36,37).

Clinical features
Hidradenitis suppurativa is a recurrent disease with a highly variable clinical course. Diagnosis of HS is primarily clinical, rarely necessitating a biopsy. The clinical diagnostic criteria are wide, and include recurrent disease, scarring, and multifocal location.

Hidradenitis suppurativa involves apocrine-bearing skin, with a predilection for intertriginous areas. The most frequently affected sited are the axilla, perineum, and groin, although other areas may be affected. A predilection for genital skin is not surprising, given the high density of follicular structures in this area. Any area of genital skin may be involved, as long as it bears follicular epithelium.

Disease onset is insidious, usually developing in otherwise healthy post-pubertal individuals. Initially, individuals may experience slight discomfort or pruritus in the affected area. Following this, a tender papule or deep-seeded nodule develops. This nodule may slowly resolve; however, it often expands and coalesces with surrounding nodules to form large, painful inflammatory abscesses that may rupture spontaneously, yielding a purulent discharge. The lesion then heals with fibrosis, dermal contractures, and rope-like elevation of the skin, and double-ended comedones. Sinus tracts may also develop. The process then recurs in an adjacent area.

Complications and associated morbidity
When measured by the Dermatology Life Quality Index (DLQI), patients with HS experience a significant degree of morbidity, with highest scores obtained from pain caused by disease. Additionally, quality of life is lower than other dermatologic diseases which have been investigated using the DLQI (38).

The complications of HS may be either local or systemic. Systemically, infection may develop and lead to septicemia. A case of lumbosacral epidural abscess been reported (39). Hematology parameters may reveal anemia or leukocytosis (40,41).

Locally, scarring may lead to a limitation in mobility. As a consequence of the chronic inflammation of genitofemoral disease, strictures may develop in the anus, urethra, or rectum. Urethral
fistula formation has also been described (42). Additionally, disfiguring persistent genital edema may develop (43), giving rise to functional impairment. Squamous cell carcinoma may rarely develop in chronically inflamed and scarred areas in individuals with long-standing disease. These carcinomas tend to be more aggressive locally and are associated with a higher incidence of metastatic disease (44–50).

One case-control Swedish study found that the overall incidence of malignancy, including non-melanoma skin cancer, to be increased in patients with HS (51).

**Histopathology**

The early lesions of HS demonstrate follicular hyperkeratosis. Other associated dermal features include active folliculitis or abscess, sinus tract formation, fibrosis, and granuloma formation. The histologic features observed in adnexal structures reveal inflammation of the apocrine glands in only 33% of cases. The subcutis may demonstrate some fibrosis, fat necrosis, or inflammation (10,11).

**Management**

**Medical treatment**

Therapy for the early stages of HS consists primarily of systemic antibiotics, topical antiseptics, and compresses. Some authors have advocated long-term suppressive antimicrobial therapy, although supporting evidence is lacking. Topical clindamycin has demonstrated some efficacy in disease management (52). However, a more recent trial comparing topical clindamycin with systemic tetracycline did not demonstrate a difference (53).

Intralesional corticosteroids are of benefit for patients with an isolated number of tender lesions (54). Practically, such treatment may not be appropriate for individuals with extensive disease.

Isotretinoin monotherapy for patients with HS has limited therapeutic benefit. In a study of 68 patients, 23.5% cleared during therapy, while only 16.2% maintained improvement during a follow-up period of up to 6 months (55). One author reported an individual with severe vulvar HS who was treated with prednisolone and then long-term isotretinoin (> 1 year), and remained disease-free at 10 months post-treatment (56). The other systemic retinoids, acitretin and etretinate, have also demonstrated some efficacy in disease management (57,58). Infliximab, a chimeric monoclonal anti-TNF antibody has demonstrated efficacy in a single patient with Crohn's disease and axillary HS (20). Other systemic therapies have been used with varying success, including systemic corticosteroids, azathioprine, and cyclosporine (22,56,59).

Hormonal therapy in HS has some reported success. The anti-androgen, cyproterone acetate (50 mg), in conjunction with ethinyl estradiol (50 µg), has demonstrated some benefit in a double-blind study. Fifty percent of patients experienced complete or partial clearance at 18 months post-treatment (29,30). The 5-alpha-reductase inhibitor, Finasteride (1 mg), may also have a positive effect on disease management (31).

**Surgery**

Surgical removal of all involved tissue, beyond clinically involved margins, is the most effective treatment modality. However, postoperative recurrences do occur. Although usually accomplished via the scalpel, some authors have advocated the use of a CO₂ laser for surgical ablation of tissue. The modality of closure has also been a topic of debate. Overall, healing by secondary intent is thought to provide the best outcome. Primary closure, grafting, or flaps have been extensively utilized, but may be associated with poorer results (60–66).

A more limited surgical approach also plays a role in disease management. De-roofing or marsupialization of recurrent troublesome lesions or sinus tracts may aid with local control. Lancing an inflammatory lesion is of limited benefit and should be avoided (60,67,68).

**Radiotherapy**

Several authors have reported the successful treatment of HS with radiotherapy. Long-term side-effects must be considered (69,70).

**Conclusion**

Hidradenitis suppurativa is a recurrent disease that most commonly involves the genitofemoral area or axillae, areas rich in apocrine glands. The primary pathogenic event is follicular occlusion with subsequent inflammation resulting in the clinical picture. An in-depth understanding of etiology remains limited and uniformly effective treatment is lacking. While surgery may sometimes offer a cure, antibiotics, retinoids, hormonal
treatments, and some immunosuppressive medications offer benefit to some patients.

References

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