Medical and Surgical Treatment of Hidradenitis Suppurativa: A Review

Nicolò Scuderi^a Ambra Monfrecola^a Luca Andrea Dessy^a
Gabriella Fabbrocini^b Matteo Megna^b Giuseppe Monfrecola^b

^aDepartment of Plastic, Reconstructive and Aesthetic Surgery, University of Rome "Sapienza," Rome, and

^bSection of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy

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care providers to see patients with this disease owing to its characteristic clinical presentation (inflammatory nodules, abscesses, sinus tract, etc.).

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Abstract

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease presenting with painful nodules, abscesses, sinus tracts, and scarring primarily affecting apocrine gland-rich intertriginous areas. HS prevalence ranges from 0.05 to 1%. The central pathogenic event in HS is believed to be the occlusion of the upper part of the folliculopilosebaceous unit, leading to the rupture of the sebofollicular canal with the consequent development of perifollicular lymphohistiocytic inflammation. The HS treatment choices are influenced by disease severity and its individual subjective impact, involving both medical and surgical interventions. However, given the chronic nature of HS, its destructive impact on social, working, and daily life of patients, its management is often frustrating for both the patient and physician. Hence, prompt and effective management strategies are urgently needed and a multidisciplinary approach is advocated. Therefore, in this article, we highlighted the main features of HS (clinical aspects, epidemiology, pathogenesis, diagnostic criteria, classifications, comorbidities, and treatments), so that awareness of this disease might be heightened in primary care physicians and surgeons, who may be the first health

Introduction

Patients suffering from hidradenitis suppurativa (HS) are often diagnosed late (averaging 7 years) although they urgently require appropriate treatment at the earliest time in order to ensure the best possible course of this stigmatizing and painful disease [1]. This is also due to the fact that HS is often seen by nondermatologists, so the condition may not be easily identified, yet the clinical presentation is distinct and a reliable diagnosis can be made based on simple questions [2]. Therefore, since nondermatologists such as primary care physicians and surgeons may often be the first health care providers to see HS patients due to its peculiar clinical aspects, in the present article we aimed to highlight the main features of HS (clinical aspects, epidemiology, pathogenesis, diagnostic criteria, classifications, comorbidities, and treatments) and the need of a multidisciplinary approach in order to increase the awareness of this disease among different medical specialists, avoid delay in diagnosis and ensure prompt disease management.

Fig. 1. HS lesions: inflamed erythematous papules and nodules.

Definition

HS, also known as acne inversa or Verneuil disease, is a chronic, inflammatory, recurrent, debilitating skin disease of the folliculopilosebaceous unit [3].

Epidemiology

HS is mainly a disease of young adults with a female predominance (the female:male ratio variously reported as 3:1 to 4:1) [4]. European studies estimated HS prevalence to be 1% in the general population [5, 6] and 4% in young adult women [7], whereas epidemiological data from American surveys reported prevalence between 0.05 and 0.20% [8, 9]. The discrepancies between European and American studies may be due to the employment of different study methodologies or diverse diagnostic criteria but may also reflect actual differences in prevalence/incidence of HS. However, it is believed that the overall disease burden is disproportionate to the estimated prevalence, and clinical experience suggests that it is underrecognized.

Clinical Presentation

HS usually presents with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body such as axillae, inguinal and anogenital regions, perineum, and the infra-mammary area of female patients [3]. Particularly, painful or suppurating lesions including nodules (commonly indicated as “boils” or “pimples”), abscesses, draining sinus tracts, and scarring can be observed [10] (Fig. 1, 2). Other typical lesions that are considered to be painful and/or tender include erythematous papules smaller than 1 cm in diameter, dermal contractions and ropelike elevation of the skin, as well as double-ended comedones (Fig. 1, 2) [11–13]. The disease course is characterized by recurrent flares that may involve supuration of foul-smelling discharge, as well as pain-causing significant quality of life impairment. One of the most characteristic features of HS is the restriction to the skin areas affected being essentially limited to the intertriginous areas, although aberrant lesions may occur. The sites affected in the order of decreasing frequency include: axillary, inguinal, perineal and perianal, mammary and

Fig. 2. HS lesions: sinus-tracts, scarring and double-ended comedones.

Table 1. HS disease severity indexes

Scoring systems	Features
Hurley staging system	Disease severity is classified into 3 stages
MSS	Disease severity is indicated by an open scale value
HS-PGA	Disease severity is classified into 6 stages
HSSI	Disease severity is defined by a score ranging from 0 to 19

HS-PGA, Hidradenitis Suppurativa-Physician's Global Assessment; HSSI, Hidradenitis Suppurativa Severity Index; MSS, modified Sartorius score.

inframammary, buttocks, pubic region, chest, scalp, retroauricular, and eyelid [14]. The diagnosis of HS is clinical, and biopsy is rarely needed.

Diagnosis

The criteria for the diagnosis of HS listed below are according to the European S1 Guideline for the Treatment of HS [15].

Primary Positive Diagnostic Criteria

History: recurrent painful or suppurating lesions more than 2 times/6 months.

Lesions: presence of nodules (inflamed or noninflamed), sinus tracts (inflamed or noninflamed), abscesses, scarring (atrophic, mesh-like, red, hypertrophic or linear).

Location: involvement of the axilla, genitofemoral area, perineum, gluteal area, and infra-mammary area in women.

Secondary Positive Diagnostic Criteria

History: family history of HS.

Microbiology: a negative swab or the presence of normal skin microbiota may be indicative of HS.

Classification and Severity Assessment

HS quantification is still clinical. There are several scoring systems for assessing disease severity (Hurley staging, HS-Physician's Global Assessment [PGA], the modified Sartorius score [MSS], Hidradenitis Suppurativa Severity Index [HSSI]) (Table 1) [16–19]; however, all of them have some limitations in daily practice [20].

The Hurley Staging System

The Hurley staging system is the most common, simple, and easily used instrument for HS classification. It classifies patients into 3 stages (stage I: abscess formation, single or multiple, without sinus tracts and scars; stage II: recurrent abscesses with tract formation and scars, single or multiple, widely separated lesions; stage III: diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area) (Fig. 3) [21]. It was originally designed for selection of the appropriate treatment modality in a certain body location and not de-

Fig. 3. HS severity following the Hurley staging system. Hurley stage I (a), II (b), and III (c).

signed for an accurate assessment of the extent of inflammation within each stage which classifies patients into 3 different stages [21]. The Hurley classification is not quantitative, consisting of only 3 stages and based on static disease characteristics such as scarring and fistulas. Hence, it is not suitable for monitoring the efficacy of interventions in clinical trials.

The Modified Sartorius Score

The MSS is more detailed and dynamic being based on the counting of individual nodules and fistulas within 7 anatomical regions. Calculating MSS requires measuring the longest distance between 2 lesions of the same type within each anatomical region, applying predetermined weights to the specific types of lesion characteristics. It was created by Sartorius et al. [22, 23] and was later modified being the first disease-specific instrument for dynamically measuring clinical severity. However, it has been argued that its applicability is limited in severe cases in which separate lesions become confluent. MSS can sometimes be time-consuming and difficult to interpret and may not be optimal for gauging inflammatory manifestations in clinical practice or trials [24].

The HS-Physician's Global Assessment

HS-PGA is frequently used as an assessment tool to measure clinical improvement in clinical trials of medical treatments and is relatively easy to use [17]. It comprises 6 stages (stage 1: clear, no inflammatory or noninflammatory nodules; stage 2: minimal, only the presence of non-inflammatory nodules; stage 3: mild, less than 5 inflammatory nodules or 1 abscess or draining fistula and no inflammatory nodules; stage 4: moderate, less than 5 inflammatory nodules or 1 abscess or draining fistula and 1 or more inflammatory nodules or 2–5 abscesses or drain-

ing fistulas and less than 10 inflammatory nodules; stage 5: severe, 2–5 abscesses or draining fistulas and 10 or more inflammatory nodules; and stage 6: severe, more than 5 abscesses or draining fistulas) [15, 17]. However, marked heterogeneity potentially exists among patients in the most severe category, creating the possibility that patients may experience clinically important improvement but not gain a meaningful reduction in their HS-PGA score.

The Hidradenitis Suppurativa Severity Index

HSSI is another HS-specific severity index [19, 25]. This score incorporates categorical objective parameters with categorical subjective parameters considering body surface area involved, number of skin lesions, pain through a visual analog scale and drainage (number of dressing changes/working hours). Severe disease is defined by an HSSI score ≥ 13 , whereas a score between 8 and 12 and a score between 0 and 7 define moderate and mild disease, respectively.

Pathogenesis

The etiology of HS involves genetic and environmental factors possibly acting as risk elements (cigarette smoking, mechanical stress, etc.) [3, 8, 15, 26, 27]. The importance of genetic factors is highlighted by studies showing that 30–40% of HS patients reported a family history of HS [28, 29] as well as 5% of HS patients presenting with a familial form with mutations in subunits of the γ -secretase proteins [30, 31]. Originally, when first described, HS was thought to be a disease of the apocrine gland because it most commonly occurs in apocrine gland-rich intertriginous areas. However, HS has more

recently been shown to be a disease that centers on the hair follicular unit, resulting in follicular occlusion and inflammation [32]. The central pathogenic event in HS is believed to be the occlusion of the upper part of the folliculopilosebaceous unit by increased outer root sheath keratinocyte proliferation leading to the rupture of the sebofollicular canal and extrusion of contents, including corneocytes, bacteria, yeast, sebum, and pilar residua ruptured hair follicles into the surrounding dermis, with the consequent development of perifollicular lymphohistiocytic inflammation [3, 15, 33–36]. The basis for follicular occlusion in HS has yet to be fully defined. However, recently impaired notch signaling has been proposed as the major pathogenic mechanism of HS. Appropriate notch signaling is of pivotal importance for maintaining the inner and outer root sheath of the hair follicle and skin appendages [37–39]. Indeed, Melnik and Plewig eloquently described the concept of HS as an autoinflammatory disease with dysregulation of the γ -secretase/notch pathway [40]. Particularly, mutations of the γ -secretase-notch pathway have already been shown to be involved in the molecular pathogenesis of familial HS among Chinese, British, Japanese, and French families [30, 31]. Moreover, deficient notch signaling is able to switch the fate of outer root sheath cells, resulting in the conversion of hair follicles to keratin-enriched epidermal cysts, and compromise apocrine gland homeostasis also leading to stimulation of toll-like receptor (TLR)-mediated innate immunity by damage-associated molecular pattern molecules released by either ruptured epidermal cysts exposing keratin fibers or altered structural components of less maintained apocrine glands, supporting and maintaining chronic inflammation. Particularly, it is believed that stimulation of TLRs on macrophages and dendritic cells (DCs), the most abundant cells in HS lesions, leads to increased amounts of proinflammatory cytokines (tumor necrosis factor [TNF]- α , interleukin [IL]-1 β) and activation of DCs, which secrete IL-23 promoting Th17 cell polarization (IL-17-producing T helper cells were found to infiltrate the dermis in chronic HS lesions) [40–46]. Due to deficient notch signaling, impaired notch-mediated feedback inhibition of innate immunity by reduced activation of MAPK phosphatase-1 may result in chronic inflammation and Th17-driven auto-inflammation leading to progressive tissue destruction and IL-17-mediated neutrophil attraction in HS [40, 41]. Therefore, as shown above, deficient notch signaling seems to be implicated in the genesis of established HS lesions and their peculiar features (follicular plugging, follicular cysts, reduced volume of sebaceous glands, sinus tracts lined by a stratified

epithelium, and neutrophilic abscesses) [47]. Therefore, inappropriate notch signaling may not only initiate inflammation in HS but may lead to insufficient feedback inhibition of overstimulated innate immunity. In this context, TNF- α is considered as one of the major actors in TLR-activated innate immunity in HS. Indeed, its overexpression has been observed in lesional and perilesional skin of HS together with a positive correlation with disease severity, providing a rationale for HS treatment with biologic drugs such as inhibitors of TNF- α [48, 49] whose use, particularly adalimumab, has been shown to suppress the overexpression of most of the upregulated cytokines in HS such as IL-1 β , CXCL9, B-lymphocyte chemoattractant, as well as the number of inflammatory CD11c+ DCs in HS lesional skin [41]. Hence, it is clear that HS is a follicular disease showing some defect in keratin clearance with resultant follicular occlusion, where defective innate cellular immunity plays an important role [24, 44]. This fact is also highlighted by the increased expression of antimicrobial peptides (AMPs) such as cathelicidin (LL-37), psoriasin and human β -defensin (HBD)-2 and HBD-3 observed in HS skin [50–52]. Particularly, AMPs can activate the adaptive immune system inducing keratinocyte migration and proliferation, providing a basis for the development of follicular occlusion [32]. Moreover, AMPs are part of a complex production network of cytokines and chemokines (notably HBD-2 and HBD-3 expression are under control of IL-1 β and TNF- α) [53] and their presence, absence, or abnormality of one of any of the AMPs could explain the infectious and inflammatory features of HS, being directly involved in its pathophysiology. As a result of increased AMPs in HS skin, HS is not a classic infectious disease as highlighted by the fact that bacterial sampling of HS suppurative lesions are frequently negative or showing several members of the normal skin flora [54, 55]. Moreover, bacteria found in HS lesions are various; they have been considered either as contaminants of the normal skin flora or as the result of a secondary infection of an initially sterile process, and samples collected at the surface of lesions entail the risk of contamination by the resident or transitory (*Staphylococcus aureus*) flora [15]. Some studies, usually circumventing the risk of contamination by aspirating pus from deep parts or by vaporization level by level with CO₂ laser showed that coagulase-negative staphylococci and anaerobic bacteria were the main bacteria recovered from HS lesions [56–58]. Therefore, bacterial infection is considered to be implicated in the secondary pathogenesis of HS, and since patients with HS often require long courses of antibiotics with only partial

improvement in their skin, it seems likely that HS is a bio-film disease [59–62]. Biofilms are specialized communities of bacteria showing irreversible binding to external substrates through secretion of a sticky polysaccharide matrix that surrounds and protects the community from outside insults, including antibiotics [62]. Biofilms adherent to sinus tract epithelium and hair follicles have been reported in HS, supporting the hypothesis that biofilms may play a secondary role in the pathogenesis of HS, thereby making bacterial eradication more difficult [60, 61]. Although this concept is very fascinating and promising, more research efforts are needed to clarify its role in HS pathogenesis.

Comorbidities

Literature is constantly enriched by surveys showing the complex yet established link between the metabolic syndrome and HS [63–67]. Consequently, comorbidities and metabolic alterations associated with HS include overweight, obesity, diabetes, insulin resistance, glucose intolerance, hyperlipidemia [64–66, 68–70], as well as dysregulated adipokine levels [32, 71], which may all be possible modulators of disease activity (e.g., obesity is related to increased levels of proinflammatory circulating cytokines TNF- α and IL-1 β secreted by visceral fat macrophages [13, 72]; insulin resistance, which is strongly linked to obesity, is aggravated by TNF- α -IKK β -mediated inhibitory phosphorylation of insulin receptor substrate-1 [73], etc.). Therefore, clinicians should take into account that HS patients may have 1 or more undiagnosed components of the metabolic syndrome despite their young age, thus requiring appropriate targeted screening. Indeed, HS patients have a significantly higher prevalence of the metabolic syndrome (odds ratio [OR] 4.46) and almost all of its criteria, namely central obesity (OR 5.88), hypertriglyceridemia (OR 2.24), hypo-HDL-cholesterolemia (OR 4.56), and hyperglycemia (OR 4.09), compared to healthy controls [74]. Particularly, a recent study showed a link between severe anogenital HS and metabolic syndrome components (hypertension and diabetes above all), also highlighting their negative impact on treatment outcomes [75].

On the other hand, the point prevalence of HS is quoted at 18% amongst bariatric surgery patients [76], with an odds ratio for the metabolic syndrome of 3.89 for a hospital HS cohort [67]. Elevated BMI is considered as a risk factor for HS whose severity has been also correlated with the degree of BMI [22, 74, 77]. Patients affected by HS

Table 2. HS treatment

HS treatment	Indications
Acitretin	Hurley stage I–III
Biologics (adalimumab, infliximab)	Hurley stage II and III
Cyclosporin A	– ^a
Clindamycin (topical)	Hurley stage I
Clindamycin + rifampicin	Hurley stage I–III
Dapsone	– ^a
Isotretinoin	– ^a
Doxycycline or minocycline or tetracycline	Hurley stage I–III

Adapted from Megna et al. [79]. ^a Possible role as adjuvant treatment: literature lacks evidence for significant improvement.

may benefit from early dietary interventions aimed at the metabolic comorbidities that may predispose the patient to HS itself, reducing weight as a secondary benefit. Moreover, since the strict link with metabolic abnormalities, HS patients have also been shown to present a higher cardiovascular risk compared to controls [78].

Treatment

The HS treatment choices should be influenced by disease severity and its individual subjective impact. The degree of HS clinical involvement is usually performed according to the Hurley staging system which classifies the disease into stages I, II, and III (Table 2) [21, 79]. HS treatment is very challenging. Both topical and systemic drug treatments may show significant improvement, but complete response rates are relatively low and relapses are common. Nevertheless, as there is currently no evidence that severe HS complications like squamous cell carcinoma and amyloidosis can be prevented by drug therapy, it is reasonable to state that their incidence can be limited by adequate medical treatment through providing longer remission period, limiting disease severity, body area involved, and chronic inflammation. Moreover, even if several treatments are available for HS, they are often used off-label, since randomized controlled trials (RCTs) are scant. Hence, the text will only focus on the main HS treatments considering existing European guidelines, Cochrane meta-analysis, and clinical experience, highlighting that both medical and surgical interventions are needed for adequate HS treatment [15, 79, 80].

General Measures

Smoking, obesity, and overweight have been recognized as well-known major HS risk factors which can also negatively impact HS course and severity. Therefore, lifestyle modification including smoking cessation, diet, and weight loss have been proposed to enhance anti-HS drugs' efficacy, limiting HS severity, and favoring longer remission periods [76, 81]. Particularly, smoking is not only a comorbidity but a well-established HS-aggravating factor. Indeed, nonsmoker HS patients tend to respond much better to any of the treatment options than active smokers. Smoking cessation is even more important when a patient is considering surgery because smoking undermines healing and significantly worsens surgical outcomes [82]. As regards obesity, it can show a deep negative effect on several outcomes since weight gain and related insulin resistance may favor the development of new HS lesions, especially in abdominal or submammary folds [75, 81]. In addition, weight loss also leads to decreased friction in body folds, which is a proposed trigger factor for new HS lesion development [32]. Moreover, dramatic weight loss due to bariatric surgery has been observed to possibly be able to induce a rapid improvement of long-standing treatment-refractory HS with a long remission period [83].

Topical Antibiotics

Clindamycin is the only antibiotic that has been studied as a topical agent for HS [84, 85]. No data are available on the topical use of any other antibiotics. The most significant effect of topical clindamycin treatment was observed on superficial lesions (folliculitis, papules, pustules), whereas the outcome was very low for deep lesions (nodules and abscesses), suggesting its indication in localized Hurley Stage I or mild stage II disease [15].

Systemic Treatments

Systemic treatment is indicated when more severe or widely spread lesions are present (moderate to severe disease) [15, 79].

Clindamycin – Rifampicin

The combined use of systemic clindamycin and systemic rifampicin (300 mg of clindamycin, given in combination with rifampicin [600 mg daily given either as 1 or 2 doses] for 10 weeks) has been proven beneficial, with variable results, in more widely spread Hurley stage I or mild stage II disease [86–89]. Particularly, a study conducted by van der Zee et al. [88] showed that 47% of treated HS patients reported total remission after 10 weeks

with an additional 35% of subjects experiencing at least some improvement whereas another survey reported that 70/116 patients (almost 70%) had significant improvement after 10 weeks of treatment [85].

Tetracycline

Tetracycline (500 mg b.i.d) has not been proven to show any difference in either physicians' or patients' assessment of overall effect, soreness, nodules, or abscesses compared to topical clindamycin in more widely spread Hurley stage I or mild stage II disease [85]. The alternative use of doxycycline (100 mg daily) or minocycline (50–100 mg b.i.d.) is also reported [79].

Acitretin

Acitretin is indicated in early HS stages (Hurley I or mild II); however, it seems reasonable that this medication could also be advocated in the chronic stages of HS with recurrent abscesses with sinus tracts (even interconnected) and/or scarring [90–92].

Regarding dosage and duration of treatment with acitretin for HS patients, daily doses of 0.25–0.88 mg/kg for 3–12 months have been used [91, 91]. Studies involving acitretin treatment included in total 32 patients, reporting a high response rate with 21 of 32 subjects (65.6%) significantly improving after therapy [90–96].

Biologics

According to the current lines of evidence, adalimumab and infliximab, 2 different monoclonal antibodies against TNF- α , are effective in the treatment of moderate to severe HS (Hurley II–III) as well as in improving the quality of patient life, with adalimumab being more tolerable [97–99]. There are different rates of response to adalimumab reported in case series and in a current, prospective controlled study. Administration of adalimumab with a cumulative response rate of 58% (improvement $\geq 50\%$ in 23 patients) has been reported in case reports with 42 patients with moderate-to-severe HS [19, 100–103]. Adalimumab efficacy in HS is also supported by prospective open studies [19, 104] and prospective, randomized, double-blind, placebo-controlled surveys [17, 105] involving over 800 HS patients, the vast majority of whom were included in 2 phase III studies [106]. Moreover, the European Medicine Agency has recently accepted HS as an indication for adalimumab. As regards infliximab, even if the first RCT phase II crossover study on 38 patients (15 treated and 28 placebo) was published in 2010 [25], no additional phase III RCT studies have been published. A cumulative response rate of 58% (improve-

ment $\geq 50\%$ in 42 patients) has been reported in case reports with 73 patients with moderate to severe HS [107–116]. Infliximab is administered intravenously over a period of 2 h, whereas adalimumab is administered subcutaneously. Long-term therapy is as follows: infliximab 5 mg/kg body weight on days 0, 2, and 6 and then regularly every 8 weeks; adalimumab 40 mg once weekly (after induction doses) [15, 17].

Surgical Therapy

Surgical treatment of HS is still a challenging experience for plastic surgeons. Indeed, the optimal surgical treatment in HS is controversial, and there is no unique opinion and enough clarity in the literature about which is the best surgical option for each of the most affected areas. Generally, patients with Hurley stage III or severe stage II may benefit most from surgical than medical treatments [117]. The acute or chronic nature of the disease, the affected site, the extent of the disease, and patient's comorbidities are all factors used to determine the appropriate operative approach. An important task for the plastic surgeon is to treat an HS condition in a remission phase, with active inflammation processes reduced to the minimum. To obtain this, a strict collaboration with the dermatologist and a multidisciplinary approach are advocated. In the acute phases, surgery, if required, should be limited to incision, drainage, and deroofting; major surgery should be performed only in a silent chronic phase. The risk of recurrence is greater with simple excision than with wide excision [118]. Parks and Parks [119] recommend that wide excision should be performed by removing all the apocrine glands from all hair-bearing skin to the deep underlying fascia. In this case, mapping techniques such as iodine-starch and methylene blue can be a way to remove lesions completely during excision. However, reconstruction after wide excision is important in terms of wound healing time and cosmetic results, and represents the real challenge for the plastic surgeon in HS treatment. Reconstructive strategy should follow the reconstructive ladder, starting from the simplest method towards the most complex (secondary healing > primary suture > grafts > pedicled flaps > free flap). An important support to the reconstructive strategy is given by recent and less invasive methods such vacuum-assisted closure (VAC therapy), platelet-enriched plasma, and dermal substitutes. Furthermore, the operative procedure of HS is closely related to the location and extension of the disease and whether the excision is sufficient [117–121].

Acute Disease

Incision and drainage (I&D) is a useful procedure when patients present extremely painful fluctuant abscesses. It is beneficial in relieving acute pain and suffering, but this approach has been discouraged for long-term practice because of the high recurrence rate [117–118].

Chronic Disease

Deroofing: Similar to I&D, deroofing and marsupialization is a simple and minimally invasive office procedure that several authors have described in detail. Essentially, tissue deroofing is a tissue-sparing procedure whereby the “roof” of an HS abscess or sinus tract is removed. Multiple methods can be used for deroofing procedures, using blunt scissors and a probe, electrosurgical cutting and a probe, or carbon dioxide (CO₂) lasers. Usually, the wounds are left open for secondary intention healing [119]. The deroofing technique was first described by Mullins et al. [122] in 1959. Afterwards, deroofing was mentioned in many reviews and dermatology textbooks, but its efficacy has never been properly investigated. Van der Zee et al. [123] in 2010, reported the results of an open study on the deroofing intervention in 44 patients with Hurley grade I and II HS disease, with a 5-year follow-up. All 44 HS patients were treated in an open trial with the deroofing technique. Fifteen of 88 (17%) treated lesions showed a recurrence after a median of 4.6 months, and 73 treated lesions (83%) did not show recurrence after a median follow-up of 34 months. According to this study, deroofing presents many advantages such as the fact that it generally makes small defects so that no general anesthesia is needed, single-lesion surgical treatment offers low morbidity, and the chance of creating unacceptable cosmetic results is clearly diminished and scar contractures are prevented. In addition, it is an easy, inexpensive, and early intervention appearing to prevent disease aggravation. Limits concern the indication. Indeed deroofing can only be performed on I and II Hurley stage lesions.

Radical Wide Excision

There is overall agreement that radical wide excision of all involved skin and tissue is the only curative treatment. Because the disease often extends into the fat, in general, excision should be done to ensure removal of all tissue, including skin and subcutaneous fat, down to the deep underlying fascia. A margin of 1 to 2 cm is often es-

essential to ensure a cure. Radical excision can be successfully performed in all HS locations from Hurley stage I to III. When surgeons are uncertain about the extent of the disease, preoperative magnetic resonance imaging or ultrasound can be used. Alternatively, intraoperative color marking of sinus tracts with dyes such as methyl violet and iodine starch can be used to define the operative area [117, 124, 125].

Reconstruction after Radical Wide Excision

The choice of the reconstructive technique largely depends on the size and location of the defects. Reconstruction after radical wide excision is important to maintain function, reduce contracture, and provide good aesthetic outcomes. Nicoli et al. [126] described an innovative treatment for severe HS using an innovative and alternative method with platelet-enriched plasma to promote neovascularization and a dermal substitute named Hyalomatrix (Fidia Advanced Biopolymers, Abano Terme, Italy), a delivery system for hyaluronic acid, to induce neodermis at the wound bed and to stimulate regeneration in a humid and protected environment. The procedure was well tolerated and achieved complete wound healing after 2 months. No recurrence was observed during the 1 year after the surgical procedure, as well as no wound dehiscence and no scar contractures occurred.

Axillary HS: Options for Reconstruction (Table 3)

The “gold standard” management of severe axillary HS has yet to be identified. In the literature, a high rate of postoperative morbidity such as secondary scar contractures, shoulder stiffness with objectively reduced range of movement and prolonged recovery time are reported [127]. Many procedures have been used for reconstruction after wide excision. Historically, extensive severe HS is treated with excision of the affected tissue and the surgical defect either left to heal by secondary intention or grafted with a split thickness skin graft. However, more recently, local, regional, and free flaps, such as the lateral thoracic flap, the fasciocutaneous V-Y flap, Limberg flap, and musculocutaneous flap, have been used for this purpose. In particular, perforator flaps, such as the thoracodorsal artery perforator (TDAP) flap, have been reported as advantageous for the reconstruction of the soft-tissue defect following excision of severe extensive axillary HS [128]. A retrospective study by Calibre et al. [129] described coverage of wide defects of the axilla in 2 steps with a split-thickness skin graft followed

Table 3. Axillary HS: options for reconstructions

Wide excision and primary closure
Secondary intention healing (dermal substitutes)
Split-thickness skin graft with or without VAC therapy
Local flaps (Limberg trasposition flap, Island TDAP V-Y advancement flap, extended latissimus dorsi rotational V-Y advancement flap, lateral thoracic transposition flap)
Free flaps

by negative pressure at −75 mm Hg for 5 days. They reported a graft survival of 90%, a complete healing obtained within an average of 34 days (20–43 days), with a good quality of scar tissue, no retraction and no limitation of arm’s abduction. A limitation of this study was the small number of patients treated. In 2010, Varkarakis et al. [130] proposed an extension of the technique described by Altmann et al. [131] in 2004. In particular, the authors reported a series of HS patients undergoing wide resection of axillary hidradenitis with reconstruction by Limberg transposition flaps. Limberg flap coverage led to early shoulder motion and stable coverage. The wide resection encouraged by flap coverage resulted in a low incidence of residual disease. According to Nesmith et al. [132], superficial lymphadenectomy with nodal micro-bacterial analysis would remove all infected tissue, eradicate the disease, and allow more specific targeted antibiotic therapy. It is almost a general opinion that flaps are the best options for closing axillary defects. Flaps adjacent to the axilla are preferred because they bring almost hairless skin of similar color, bulk, and texture back into the cupola of the axilla. The island TDAP V-Y advancement flap is a useful alternative that allows unrestricted inseting with primary donor site closure. Angrigiani et al. [133] used this flap based on the thoracodorsal pedicle to help introduce the concept of perforator flaps. Conversely, Rehman et al. [134] showed that only a single TDAP flap from the chest was necessary to thereby minimize the surgical morbidity and extent of scarring, but nevertheless they identified the perforators, they did not dissect them out and basically kept this as a common subcutaneous pedicled advancement flap. Without a doubt, only a single TDAP V-Y advancement flap can close most axillary hidradenitis defects because the entire subaxillary region can be captured by a single dominant perforator. If necessary, this can be converted to an island flap by dissection of the perforator through the latis-

Fig. 4. Algorithm of Kagan et al. [144] for surgical interventions in HS patients (adapted).

Table 4. Genitoperineal HS: options for reconstruction

Wide excision and primary closure (medial thigh lift)
Secondary intention healing (dermal substitutes)
Split-thickness skin graft with or without vacuum-assisted closure therapy
Local flaps (gluteus maximus musculocutaneous flap, Island TDAP V-Y advancement flap from gluteal region, modified abdominoplasty, pedicled gracilis myocutaneous flap, anterior obturator artery perforator flap, triangular closure technique, free style flaps)
Free flaps

simus muscle even back to the source pedicle to allow to reach even the most cephalad wound edge and inseting without tension to avoid impeding shoulder range of motion. Uchikawa et al. [135] also described a unique extended latissimus dorsi rotational V-Y advancement flap based on the concept of the thin extended latissimus dorsi musculocutaneous flap. The difference in this flap, compared to the other, is that it contains a minimal amount of the muscle belly, including the lateral branch of the thoracodorsal artery and a thin cutaneous portion consisting of the tissue superficial to the subdermal plexus. Including the muscle belly ensures that the artery is included in the flap, and detection and dissection of vessels is not strictly required. The lateral thoracic transposition flap is similar, except that it offers a longer flap and a more robust tip with the delay technique as shown by Teo et al. [136] and Egemen et al. [137].

Genitoperineal HS: Options for Reconstruction (Table 4)

The optimal operative management of localized inguinal hidradenitis is also unclear. Wollina et al. [138] analyzed the records of patients with anogenital HS from 2000 to 2010 to evaluate the role of surgery in the treatment of severe anogenital HS, and they concluded that surgery is the cornerstone of treatment for advanced forms of HS, and they underlined the importance of secondary intention healing. Watson [139] noted the need for reoperation in approximately 20% of patients with inguinal disease whether they were treated with excision and primary closure or excision and skin grafting. Harrison et al. [124] reported a 37% recurrence rate of inguinoperineal disease after wide excision without skin grafting. However, Ariyan and Krizek [140] and Thornton and Abcarian [141] recommended excision and secondary healing for patients with more extensive inguinoperineal and/or perianal-perineal disease, respectively, noting that the need for colostomy was rare. Finally, Hyland and Neale [142] and Ramasastry et al. [143] recommended wide excision of perineal disease with delayed skin grafting as a means of reducing patient discomfort and effecting more rapid and stable wound closure.

It is important to note that the majority of these studies were performed 10–20 years ago. Since then, there have been substantive changes in health care, patient education, and patient decision making. In 2005, Kagan et al. [144] developed an algorithm in consideration of not only the extent and location of disease and comorbidity conditions, but also patient preference. In particular, he advocated early excision of localized disease with primary closure to minimize pain and disability. The patients with

Fig. 5. Three different fasciocutaneous flaps designed on the gluteal region. Adapted from Kishi et al. [145].

more widespread disease were treated with staged excision and split-thickness skin grafting and rarely with excision and secondary healing (Fig. 4). Reconstruction after total skin resection can be performed also with fasciocutaneous flaps. In 2009, Kishi et al. [145] described 3 different fasciocutaneous flaps designed on the gluteal region based on an arterial anatomical study: an island V-Y advancement flap based on the descending branch of the inferior gluteal artery; a rotation V-Y advancement flap based on the first perforator of the deep femoral artery and the descending branch of the inferior gluteal artery; a bilobed flap at each lobe containing either the descending branch or medial branch of the inferior gluteal artery. Flap designs were decided from the size and the location of the skin defect (Fig. 5). The gluteus maximus musculocutaneous flap and its modifications have been widely described by many authors. Among them, the split gluteus maximus musculocutaneous flap seems to be the easiest to elevate and does not leave relevant functional deficit. However, the safety of extending the skin portion beyond the margin of the muscle has not yet been clarified. From the anatomical results, it has been found that it is possible to safely extend the flap beyond the iliac crest several centimeters superiorly, and to the gluteal fold inferiorly, and several centimeters laterally [146]. Patients with HS of the groin frequently have involvement of the labia, buttocks, and mons pubis. These patients often need tailor-made flaps for defect closure after radical excision [147]. Tanka et al. [148] described covering the inguinal defect with a pedicled rectus abdominis musculocutaneous flap. However, the flap appeared bulky and needed secondary contouring. Greenbaum [149] described a modified abdominoplasty as a functional recon-

struction for recurrent HS of the lower abdomen and groin, but these operations are technically demanding and should be performed only in selected cases. The goal of the medial thigh lift as described by Lockwood [150] is an improved slimmed contour of the thigh through tissue resection and lifting of the medial thigh [151]. As a side effect of this aesthetic procedure, the tissue excess of the thigh can be used easily for the coverage of defined and localized groin defects. A number of authors have described technical variations of Lockwood's original technique [152, 153]. All variations have in common the use of anchoring sutures to Colles fascia to avoid the risk of labial deformities. Reconstruction of groin and vulval defect combination of inferior abdominal flap and medial thigh lift has been also described [154]. Another option is the Mutaf triangular closure technique, which was first reported to be used for the closure of a large meningomyelocele in 2007 [155]. In this procedure, 2 skin flaps are elevated in an unequal z-plasty manner and one of these flaps is used for the defect closure, whereas the other one is used for the closure of the donor site of the primary flap (Fig. 6). Using 2 skin flaps designed in an unequal z-plasty manner, this procedure maximizes the amount of tissue relaxation and diminishes the tension in the closure lines. Thus, the defect closure is achieved with a remarkable lesser tension, which is important for prevention of the wound dehiscence and poor scar formation at late term. The pedicled gracilis myocutaneous flap has been introduced as a surgical treatment of HS of the groin and perineum [156], while the anterolateral thigh (ALT) flap has been reported for reconstruction of groin and vulval HD [154]. ALT flap is of adequate size and the donor site can be closed directly. It provides thin pliable skin ideal

Fig. 6. Mutaf's triangular closure technique. Adapted from Mutaf et al. [155].

for resurfacing the groin, and can be thinned if the subcutaneous fat layer is excessive. Furthermore, the anterior obturator artery perforator flap seems to be a safe option for the reconstruction of perineal defects after wide surgical excision of HS [157], although it was not introduced specifically for this disease. When operating in an anatomical region such as the axilla or the inguinal fold, there is a high risk of damaging lymphatic vessels and lymph nodes. Indeed, soft tissue injury during surgery dissection but also, and more frequently, the involvement of lymph nodes by HS chronicle inflammation can result in significant lymphatic disruption and an increased risk for the patient to develop chronic lymphedema. In particular, genital lymphedema seems to be very common in patients with HS and very difficult to manage. Nowadays, the option of microsurgical treatment of lymphedema with vascularized lymph node transfer can improve signs and symptoms of this kind of complication [158, 159].

Submammary HS: Options for Reconstruction

There have been few case reports in the literature regarding surgical treatments of HS lesions in the submammary area. Moosa et al. [160] reported aggressive treatment of HS by performing bilateral mastectomies. Although this is certainly a curative option, the breast contour is disturbed. In 2010, a successful treatment of a patient with HS of the submammary area based on the procedure typical for breast reduction was described. The overall cosmetic result was good with no recurrence and a high degree of patient comfort and satisfaction [160].

Conclusions

HS is a debilitating chronic skin inflammatory disease which can greatly impact quality of life and social and work activities. Nevertheless, prompt treatment is required to reduce and limit HS burden; HS is often diag-

nosed with a considerable delay also because patients may initially seek nondermatologists such as surgeons or primary care physicians. The HS treatment choices involve both medical and surgical interventions, highlighting the need of a multidisciplinary approach. The objective of the present review was to increase the awareness of HS among different medical specialists, avoid delay in diagnosis, and ensure prompt disease management. Indeed, early diagnosis and treatment, which often need the collaboration

of a dermatologist and a plastic surgeon, represent the fundamental medical weapons to fight against this high-morbidity disease.

Disclosure Statement

The authors have no conflicts of interest to declare.

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