GUIDANCE IN HIDRADENITIS SUPPURATIVA MANAGEMENT

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Summary

Hidradenitis suppurativa (HS) is a chronic, inflammatory skin condition characterized by painful nodules, abscesses, and fistulas in intertriginous areas. Immune-mediated inflammation is thought to be involved, necessitating early and appropriate therapy due to its significant impact on quality of life. Diagnosis relies on clinical examination, with staging systems aiding in severity assessment. Treatment options include topical and systemic medications like clindamycin and tetracyclines, as well as surgical interventions such as deroofing and excision. Biological agents, including anti-TNFs and anti-IL therapies, show promise in HS management. A multidisciplinary approach, combining various therapies tailored to each patient, is essential for optimal outcomes. Ongoing research into novel biologic therapies is crucial for improving treatment efficacy and patient well-being.

Key words: *Hidradenitis Suppurativa (HS), deroofing, biologic therapy.*

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Introduction

Hidradenitis suppurativa (HS), formerly known as acne inversa, is a chronic, recurrent, incapacitating inflammatory skin condition characterized by the presence of painful, resilient, nodules, abscesses, and fistulas located in cutaneous folds of the axilla, groin, gluteal, and perianal regions.[1]

Although the exact cause of HS is still unknown, immune-mediated inflammation (IMID) is currently thought to be its pathophysiology. The choice of the proper therapy is crucial for these patients due to the marked decline in their quality of life and their late initiation of treatment. Although there are numerous approaches to treat HS, no particular therapy has been shown to be consistently successful.[2]

Etiology

The exact etiology is unknown, but genetic and environmental factors have been incriminated.[3]

Overweight and obesity have been incriminated as risk factors for HS,, an increased friction of the skin negatively affecting the disease course. Smoking has been reported in people with more severe forms of HS, probably due to increased follicular plugging.[4]

Epidemiology

Hidradenitis suppurativa appears to affect 1% of the general population. Although hidra-

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denitis suppurativa is generally believed to be more prevalent in females than in males, data analysis on sex prevalence are debatable. Actually, females are far more likely to have a family record of hidradenitis suppurativa, whereas men have a higher risk of severe disease and acne. The age when hidradenitis suppurativa presents spans from 11 to 50 years.[5-7]

Pathophysiology

The pathologic course of hidradenitis suppurativa starts when an abnormal hair follicle gets blocked and breaks apart, releasing its components, which include keratin and bacteria, into the dermis.[8]

Immunological anomalies were also noticed. Increased levels of inflammatory cytokines, such as tumour necrosis factor-alpha and multiple interleukins, have been observed in hidradenitis suppurativa lesions, suggesting potential targets for future treatments.[9, 10]

Clinical

The diagnosis is mostly clinical and often delayed; there is no pathognomonic test, and biopsy is rarely necessary, particularly in advanced lesions.[7]

Clinical diagnosis demands identification of the lesions (deep, inflamed, painful papule or nodules, double ended comedones sinus tracts, scars), characteristic distribution (intertriginous areas, apocrine gland-containing areas), and recurrences.[7,9]

After a proper history and clinical examination, the Hurley staging may be applied as follows, as it is the most widely used form of categorizing HS. There are also other useful scales and tools that can be used (Sartorius HS score, Visual Analogue scale, Dermatology Life Quality Index, Hidradenitis Suppurativa Impact Assessment, Hidradenitis Suppurativa Symptom Assessment, Acne Inversa Severity Index) and the new **International Hidradenitis Suppurativa Severity Score System (IHS4)**.[11, 12]

Treatment

Standard & local hygiene is mandatory. No harsh products are recommended for washing.

Table HURLEY staging

Stage	Clinical aspect
I	Abscess formation No sinus tracts No scarring
II	Recurrent abscesses with sinus tracts and cicatrisation, scarring
III	Diffuse or almost diffuse involvement Multiple interconnected sinus tracts and abscesses[13]

Ordinary or even antiseptic soaps are meant to be used. Warm compresses with sodium chloride solution or Burow solution could be used in order to clean the affected areas.[14]

Obese patients should lose weight in order to decrease the fold lines and inflammation. Weight loss can also increase their self-esteem known to be low in patients with HS.[15]

Patients with HS should wear loose-fitting clothes in order to prevent friction. They should also avoid wearing tight or synthetic clothing to prevent skin trauma and the frequent changing of the clothes should be advised as a means to prevent soaking. They could also use gauze underneath their garments to prevent oozing them.[13]

Shaving hair is not recommended because the hair plays a role in the pathology of HS and clipping the hair might be a possible option. Laser hair removal has been reported to be a good alternative.

Smoking increases the severity of the disease and cessation is imperative. It is also advised that patients with HS have to quit smoking because this habit it has been linked with a poor response to therapy.[16]

Psychological support

Given its long-term recurrent course, characterized by challenging lesions and foul-smelling discharge, HS has a major effect on the life of the patient, and medical care may be necessary. Esmann et al. noted a greater chance of social isolation caused by feelings of shame and anxiety of discrimination so, the patients need psychological counselling.[17]

Topical treatment

In cases of suppurative hidradenitis, TOPICAL THERAPY is the first line of treatment used worldwide. The majority of these treatments are currently used in practice as a result of small, few, and rare studies; unfortunately, there are few randomized studies on this kind of treatment. The clinical observation and historical association between acne vulgaris and hidradenitis suppurativa laid the ground-work for Verneuil's disease topical therapy.[18, 19]

Clindamycin 1% used twice daily for a period of 3 months proved to be beneficial for milder cases. In a 1998 study there were no significant differences between topical clindamycin and systemic tetracycline.[20] As part of the adverse reaction, burning or itching are described. It remains the first line of therapy for Hurley I and II stages although it can cause bacterial resistance. A 2023 study comparing clindamycin with clindamycin-peroxide benzoyl gel showed similar results in efficacy, but decreasing the potential bacterial resistance advising to switch to the combination for further therapy safety.[21]

Azelaic acid 15-20% has bacteriostatic and antifungal properties and works well in pediatric patients if used in the early stage of the disease. There is insufficient evidence for azelaic acid but empiric data show a safe and good response for an initial treatment.[12, 22]

Fusidic acid is a selective antibiotic and the sole distributed part of the fusidane group which indicated favorable outcomes in a perspective cohort study.[23]

Resorcinol 15% is a benzenediol or phenol that acts as a chemical peeling and has antibacterial and antipruritic properties. However, given the drug's pharmacokinetics, antiseptic properties outweigh keratolytic activities at the HS concentrations. A cross sectional study showed an increased patients satisfaction with this topical drug. Patients with Hurley stage 1 and 2 disease noticed improvement of visible lesions, discomfort, and erythema after applying twice daily for 30 days. The new concept of treatment regarding the association of biologic therapy, surgical therapy can be completed with topical resorcinol 15% on inflammatory nodules.[24]

Adapalene needs more evaluation in the efficacy in HS but shows promising result due to the anti-inflammatory properties. There isn't any official assessment of topical retinoids' success in HS.[19]

Ruxolitinib 1,5% cream is a JAK 1&2 inhibitor commonly used in the treatment of myelofibrosis, polycythemia vera, and steroid-refractory acute graft-versus-host disease which is still in trials for the treatment of HS. There is an on-going interventional phase 2 study with satisfactory results, with 50% decrease of inflammatory lesions in patients with early stages of HS.[25, 26]

Silver sulfadiazine is a topical antibiotic spray or cream used in HS, mainly in the pediatric population.[27]

Intralesional **triamcinolone** injection is the most commonly used therapy for keloid scars, either before or after surgical excision. When active nodules and abscesses in HS cause pain, intralesional triamcinolone is a useful adjuvant medication. In contrast, intralesional steroids did not appear to be any more effective than placebo (saline) injections, according to a recent placebo-controlled trial.[28-30]

Intramuscular immunoglobulin. A retrospective review indicates that intramuscular HIG can be utilized alone or in conjunction with other treatments to address resistant suppurative skin conditions.[30]

Botulinum toxin A. A 2022 systematic review showed that for individuals with hidradenitis suppurativa who are not responding to typical therapy, botulinum toxin stands for a possible helpful and secure substitute.[31]

A report of a case that used perilesional granulocyte-macrophage colony-stimulating factor (GM-CSF) in association with surgery was

reported to have a successful endpoint but further studies are to be made.[32]

Photodynamic therapy for the treatment of HS yields inconsistent outcomes.[33]

Cryotherapy

When treating persistent HS nodules that are resistant to drug therapy, cryotherapy is a quick, cheap, easy, and safe alternative to surgery or laser therapy, but with disputable results.[34]

Carbon dioxide laser excision combined with second-intention healing can be secure and efficient treatment but for early stages of HS.[35]

Systemic treatment

Patients with Hurley stages 1 and 2 should start *systemic* treatment with **tetracyclines** if there is little or no response by applying local therapy.

Besides their antibiotic effect **tetracyclines** are known for their anti-inflammatory properties.[36] Gastrointestinal side effects, including diarrhea, nausea, vomiting, and esophageal ulceration are the most frequent.[37]

During this treatment patients should avoid exposing themselves to the sun because of photosensitivity. Usually, they are prescribed for a duration of roughly four months. They can cause brown or yellow staining of the teeth or damage to the dental enamel.[38]

Drug	Dosage	Duration
Doxycycline	100 mg x 2/day	4 months
Tetracycline	500 mg x2/day	4 months
Minocycline	100mg x2/day	4 months

Patients who do not respond to tetracycline can use **clindamycin** and **rifampicin** in conjunction. A common adverse reaction is diarrhea but the most fearful one is colitis, the drug combination therapy being contraindicated in the latter.[27, 39]

Drug	Dosage	Duration
Clindamycin+ Rifampicin	300 mg x2/day+ 300 mg x2/day or 600 mg/day	6 months

Retinoids Isotretinoin/ Acitretin 35,9% of the patients responded well to isotretinoin[40], though it has been discovered with the help of a retrospective study in 12 patients that acitretin [41] is a more successful therapy.[27]

Drug	Dosage	Duration
Isotretinoin	~0,59 mg/kg daily	4-10 months
Acitretin	0,5-1 mg/kg daily	9-12 months

Anti androgens

There are some reports about cyproterone acetate working well in women.[42]

Spironolactone

A single-center chart review on females showed that low dose spironolactone can add good results in HS.[43]

In a 2016 review it showed that finasteride could be useful in HS while the exact mechanism is still unknown. It should be used with caution especially in young males due to the reports of adverse reactions regrading fertility.[44]

Drug	Dosage	Duration
Spironolactone	75 mg/day	7 months
Finasteride	5 mg/day	6-16 months
Cyproterone acetate	100 mg/day	12 months

Dapsone

A 2022 systematic review revealed that lower doses of dapsone seem to be working effectively in HS, but further studies need to be made. The patient needs to be monthly monitored for adverse reactions such as methemoglobinemia. The dosage was variable, varying from 50-200mg/day, for 1-3 months, with hematological screening.[45]

Cyclosporine

Refractory HS could benefit from cyclosporine, though there are only a few reports in literature. It should be used at least 2.0 mg/-kg/day.[46]

Corticosteroids

There is minimal evidence to back up the use of low dose corticosteroids for HS, so they must be used carefully. A case series showed improvement with low dose betamethasone but further studies need to be made.[47]

Surgical therapy

There are many different types of surgical therapy, from minimally invasive procedures to major surgery. This kind of surgery is customized based on the requirements, features, and preferences of the individual patient.[48]

In order to relieve symptoms, large, fluctuating abscesses that cause excruciating pain may be incised and drained. Because most patients relapse, this kind of treatment is only symptomatic and transient.[49]

The new gold standard treatment is **deroofing**, which works extremely well when combined with biologic therapy. The process entails removing the "roof" from every sinus tract or abscess and exposing the lesions' floor in the afflicted regions. All communicating tracts are detected with a metal probe or scissors, and they are then deroofed. A curette, scalpel, or soaked gauze is then used to remove the gelatinous expanding sinus tissue. The floor stays intact, which promotes rapid healing of the wound resulting in secondary intention healing. [50, 51]

Another option is excision, which can be limited or expanded based on the patient's needs and the type of lesion or severe cases or for those where there is no longer functionality, mobility or it bothers the patient a lot from an aesthetic point of view, skin grafts or even skin flaps can be used.**[52]**

The treatment of chronic inflammatory diseases has made far-reaching changes by monoclonal antibody therapy. There are scarcely any comparative studies between biologic agents this being a potential ground to conclude which one is a better option.

Anti TNF agents

Tumour necrosis factor alpha (TNF-α) inhibitors, also known as anti-TNFs, have transformed therapies in medicine that impact the gastrointestinal tract, joints, skin, and eyes since only three decades ago. Anti-TNFs continue to be the mainstay of treatment despite the fact that their arsenal of therapeutic tools is constantly growing.

Adalimumab is the first FDA approved monoclonal antibody for moderate to severe HS. [53]

Drug	Dosage	Study
Adalimumab	40 mg weekly	PIONEER I, II
Infliximab	5-10 mg/kg	
Etanercept	50 mg sc twice weekly	Clinical Trial by Penn State University

Infliximab - Overall, we noticed that infliximab is a beneficial therapy for people with HS stages Hurley 2 and 3.[54]

Golimumab is a fully human,*anti-TNF* monoclonal antibody that showed in a retrospective cohort study that with a higher dose (2 mg/kg) than normally used in other maladies HiSCR can be reached. It is noted that the cases included in the study were biological experienced ones, previously treated with other biological agents.[55]

Certolizumab was described in 6 cases reports in current literature with promising results.[56]

Anti IL-17

In October 2023 FDA approved **secukinumab**, a human IgG1 monoclonal antibody, for the treatment of hidradenitis suppurativa. SUNSHINE and SUNRISE were identical, multicenter, randomized, placebo-controlled, double-blind phase 3 trials which unfolded that used every 2 weeks secukinumab offers an ideal risk profile and is proved to be clinically successful in promptly alleviating hidradenitis suppurativa manifestations.[57]

Further studies need to be made about other IL-17 receptor antagonists, brodalumab, bimekizumab and ixekizumab, because few trials showed promising results.[58-60]

Anti IL-12/23

Ustekinumab,a monoclonal antibody targeting interleukin (il)-12 and il-13 showed in a systematic review a very good improvement in the patients' disease but further evaluation needs to be made in order to use this biologic agent on a larger scale.[61]

Anti IL-23

Guselkumab showed modest results in a phase II, open-label, mode-of-action study because it only helped a small number of patients.[62]

Other monoclonal antibodies targeting IL-23 (*risankizumab*, *tildrakizumab*) were studied in small trials but didn't show promising results suggesting that interleukin 23 does not play an important role in HS, like in psoriasis.[63, 64]

The best option in HS treatment consists in combined therapy, depending on the stage and patient profile. Following an accurate and thorough examination to determine all comorbidities and patient expectations, a treatment plan is started based on the patient's receptivity, the disease's stage, and the treatment's level of safety. The first step in treating this disease is to combine topical and systemic therapy with advanced surgical techniques to increase patients' functionality. New biological discoveries have led to encouraging outcomes for patients, including genuine assurances that they can lead normal lives with a satisfactory DLQI.

Because the physiopathology behind the scenes of the great actor called hidradenitis suppurativa is not yet known exactly, a singular 100% effective and safe treatment is yet to be discovered. Consequently, in order to fully understand the emergence of this disease and identify additional agents that function against different interleukins – biological therapies that hold great promise for treating a variety of dermatological diseases in the future – further research on these topics is imperative.

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Conflict of interest
NONE DECLARED

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