



An Overview- Hidradenitis Suppurativa: A Rare and Chronic Disease

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ABSTRACT

Hidradenitis suppurativa is a Rare and chronic disease also known as Acne inverse or Verneuil's disease is a chronic inflammation condition affecting skin regions especially bearing apocrine glands. It is represented with painful nodules, abscesses, sinus tracts and scarring. HS is a multifactorial disease in which genetic and environmental factors plays a vital role. It is usually developing after puberty, manifested as painful, deep seated, inflamed lesions, including nodules. In most to patients flares are accompanied by increased pain and suppuration at varying intervals after occurring premenstrual in woman. If untreated, the flares subside within days. Hidradenitis suppurativa is one of the most distressing dermatological conditions and has a significant negative impact on patient's quality of life. The current manuscript focuses on the newly approved drugs and therapies in order to treat this disease together considering a brief into the disease, it's symptoms, Treatment protocol, Pathophysiology, Clinical Treatment, Diagnosis Pattern. This script focuses to give Hidradenitis suppurativa – An overview look.

Keywords: Pathophysiology, Therapy, Pathogenesis, Pathomechanism.

INTRODUCTION

Hidradenitis suppurativa is a chronic inflammatory disease, presented with recurrent inflammatory nodules, abscess formation and subsequent formation of subcutaneous sinus tracts and scars during disease progression. HS is associated with a high burden of disease, impairing the social and economic situation of affected patients. HS all contribute to the remarkable psychosocial impact of the patient's quality of life that can not be overestimated. The occurrence of Inflammatory skin lesions and plaque discharge in the intertriginous areas compromises the sexual life and causes chronic and exacerbating pain.¹

The exact cause of this disease is still unknown, but it is a complex disease with contributory genetic and epigenetic changes and hormonal, mechanical, microbial and lifestyle factors such as obesity and smoking. Multiple immunological Pathways are involved, with a variety of cells and their soluble mediators. Despite the incapacitating nature of HS, the treatment of the disease landscape is limited, leading to inadequate management of the disease for many patients.

LITERATURE REVIEW

HS is a disease with a poor prognosis often misinterpreted as an infection, with the highest impact on the patient's quality of life among all the assessed dermatological disease.

Symptoms of HS:

Hidradenitis suppurativa can effect one or several areas of the body. In this disease several breakouts can be seen on

skin which looks like pimples or boils. often, these breakouts clear for a while later new breakouts develop in the same area. sometimes, the breakouts develop in exactly the same spot.²⁻¹⁰

Signs and symptoms of this disease include:-

1. Blackheads – blackheads appear in small, pitted areas of skin, often appearing in pairs.
2. Painful pea sized lumps – The condition usually starts with a single, painful lump under the skin that persists for weeks or months. more bumps may be formed later, usually in the areas where you have more sweat and oil glands or where the skin rubs together, such as the armpits, groin and breast
3. Leaking bumps or sores – some bumps or sores yet bigger, break open and drains pits with an odour.
4. Tunnels – overtime, tunnels might form under the skin, connecting the lumps. These wounds heals slowly, drains blood and pus.
5. Itch – HS on the groin, armpits, or thighs tends to be itchiest.
6. Painful conditions- The deep lumps and tunnels that develop beneath the skin can be painful. Some people need prescription strength painkillers to help manage the pain.
7. Depressions – Medical studies have found that people who have HS tend to develop depression more often very easily.



8. Anxiety – these sudden bump appearance tend to develop anxiety very easily causing stress.
9. Skin cancer – some people with HS have an increased risk of developing a type of cancer called as Squamous cells carcinoma (SCS)

Some people with this condition experience only mild symptoms. The cause of disease is highly variable. Excess weight and being a smoker are being the one facing worst symptoms, but people who are thin and do not smoke faces severe symptoms.

Etiology:

The etiology of HS appears to have genetic, environmental and behavioral influences. 33 to 44 % of individuals with HS report an effect first degree relative, suggesting a heredity component with an autosomal dominant transmission pattern. In small subset of affected families, researchers have identified a mutation of the gamma-secretase notch signaling pathway.

Environmental and behavioral factors also influence individual with HS are more commonly overweight or obese. Obesity leads to greater intertriginous surface area and skin friction, increased sweat production and retention and hormonal changes leading to relative androgen excess, all associated with HS. Metabolic syndrome is more common in obese individual and thus is also seen more commonly in HS.

Smoking is also prevalent among these diagnosed with HS. Causation is unclear, however; nicotine may cause increased follicular plugging. As the obesity, disease progression and severity are worse in those who smoke¹¹⁻¹⁵

The influence of hormones can be seen in HS. There is a greater prevalence in females than males, with the age of primary occurrence most commonly between puberty menopause. In addition, there are fluctuations of acute symptomatic episode and severity with menstrual cycles.



Figure 1: Symptomatic stages of Hidradenitis Suppurativa

Pathophysiology:

The pathophysiology process of HS begins when a defective hair follicle becomes occluded and ruptures, spilling its contents, including keratin and bacteria into the surrounding dermis. A chemotactic inflammatory response by surrounding neutrophils and lymphocytes can lead to a abscess formation and subsequent destruction of the unit and other adjacent structures. Other possible antimicrobial peptides, abnormal secretion of apocrine glands, abnormal invaginations, and deficient number of sebaceous glands.¹⁶⁻²⁰

Immunological abnormalities have also been observed. Elevated levels of inflammatory cytokines, including tumor necrosis factor- alpha and various interleukins, have been detected in the lesions of HS and provide possible targets for emerging treatments. Bacteria do not occur to be causative. Aspirate from an unruptured lesion typically yield to a sterile culture. However, bacterial infection and colonization during the process can secondarily worsen HS.

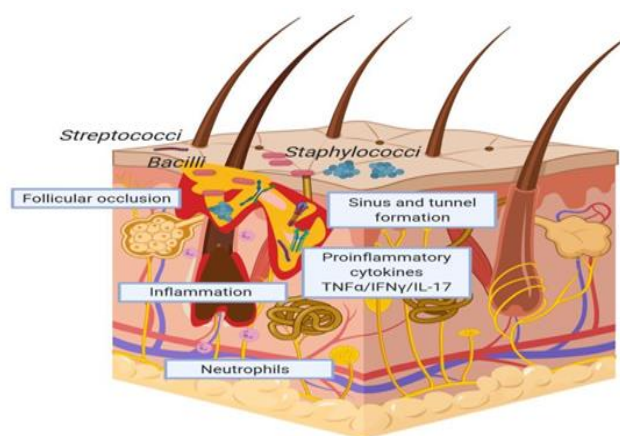


Figure 2: Pathophysiology of HS (Formation of tunnels, bumps)

Treatment:

1. Weight Control – There are studies correlating obesity with the coarse and severity of HS. The influence of obesity in the process of systematic inflammation and risk of

systematic inflammation and risk of comorbidities is known. In the case of HS, obesity, influences the disease directly through the mechanical effects friction, rubbing of hair shaft] and the coexistence of hormonal changes [polycystic syndrome and glucose intolerance]. in view of these considerations, weight loss is recommended in the approach of the patient with HS, with or without disease activity.^{21–25}

2. Management of pruritus – It is not common to ask about pruritus when seeing patients with HS. however, great part of the patients complains of pruritus that can even unpair sleep and consequently the quality of life, studies demonstrate that pruritus; as erythema and local pains are considered prodromal symptoms for flares. Pruritus control in recommended with or without disease activity, with the primary goal of improving the quality of life of these patients.

3.Smoking – even though there are no randomized studies establishing the casual relationships between smoking and HS, many studies point to a high prevalence of smoking among HS patients, beside increased severity of the disease in those who smoke. Tobacco seems to influence the genetic predisposition of HS, leading to the formation of follicular plugs and the inflammatory process triggered by the neutrophils, smoking cessation is important in the approach of the patient with HS.

4. Local antiseptic – it is known as that HS is an inflammatory disease and when an infectious process occurs it is secondary. There is the hypothesis that follicular occlusion could be a site for bacterial colonization, triggering an exacerbated inflammatory reaction to the local microbiome. Advice on adequate local hygiene should be given, although there is no need to exhaustively remove germs or to use soaps with high concentrations of chlorhexidine.

5. Hair Removal – Laser hair removal leads to reduction in the number of hair follicles and bacteria in the affected areas. It is an adjustment therapy for the management of HS, reducing the number of flares and preventing the appearance of lesions.

Many studies have showed that laser hair removal is effective in the control of HS. A controlled, randomized, prospective study with 22 patients. Hurley I TO III using Nd: yag laser demonstrated a 65% improvement after three monthly treatments. Another randomized study compared contralateral sites s controls and reduction in HS severity was of 65.3% and 72.7% after laser, treatment when compared to 75% and 22.9% for controlled sites treated topically with 10% benzoyl peroxide and 1% clindamycin. other lasers, such as diode and intense pulsed light have successful reports in smaller series of patients.

TOPICAL TREATMENTS

- **Clindamycin** -1% clindamycin gel is the only topical antibiotic with randomized studies comparing its efficacy to the use of a systemic medication,

tetracycline. There was no difference in efficacy of after 3 months of treatment. During the use of topical clindamycin, superficial lesions (pustules, folliculitis) showed better response when compared to deeper lesions (nodules and abscesses). In view of these considerations, the use of 1% clindamycin gel in HS lesions is recommended for Hurly stage I or in case with superficial lesions during exacerbation periods.^{26–30}

- **Fusidic acid** – the use of fusidic acid was evaluated through case reports and one perspective study where Hurley stage I patients were assessed. They were submitted to conservative therapy with fusidic acid, beside local antiseptics until the inflammatory nodules were under control, and more than 70% of cases achieved control. Comparing with gentamycin and mupirocin fusidic acid has a higher minimum inhibitory concentration in deeper layers of the skin.
- **Other topical antibiotics** – there are enough studies to support the use of gentamycin in HS. Some studies evaluated that the use of gentamycin for the postoperative period with the aim of assessing the rates of recurrence and local complications. A reduction in short term complication was seen (8 weeks), however, there was no success in the long-term rates of occurrence. The use of gentamycin in HS lesions would only be indicated if the use of other topical antibiotics is not possible.
- **Benzoyl peroxide associated to clindamycin** – Topical treatment with 10% clindamycin gel associated to 1% clindamycin gel or lotion was compared to the topical treatment associated to Nd- Yag laser hair removal in a controlled, prospective study with 22 Hurley I to III patients. Progressive improvement in the activity of the diseases was seen, more markedly during the 4 months of treatment, which was maintained in the past treatment 2 month followed up 2 months. The improvement was 72.7% on the side treated with laser and 22.9% on the control side, suggesting the topical treatments improve with HS, although less than when associated to laser hair removal, there are no studies with benzoyl peroxide alone.
- **Resorcinol cream** – topical resorcinol cream was studied in a prospective study.12 patients with Hurley stage I or II were instructed to apply 15% resorcinol cream twice daily on a active HS lesion. In all patients, the use of resorcinol resulted in reduction of pain and reduction in the mean duration of painful accesses. topical resorcinol (m-dihydroxybenzene) is an exfoliant with keratolytic antipruritic and antiseptic activity. It can be useful to shorten the mean duration of a painful nodule. There is still no control, randomized studies on its efficacy.
- **Biological treatments** – biological drugs have a well established role for the treatment of inflammatory diseases such as rheumatoid arthritis, psoriasis. The first reported case of HS responsive with the treatment



of crohn's disease was in 2001. This publication revolutionized the perception of the disease and subsequent studies lead to a change in paradigm of the pathogenesis and treatment of hidradenitis, is a pro inflammatory cytokine with a central role in the pathogenesis of HS³¹⁻³⁵

Cytokines become an important target for inflammation control, integrating the armamentarium employed in the management of HS, what was acknowledged in the consequences, reviewed and guidelines for the management of the disease has already published in many countries. TNF – alpha blockers, including adalimumab, infliximab and etanercept were the first biologics studied for the treatment of HS, adalimumab is one with more complete studied, with better level for the treatment of HS.

DIAGNOSIS

Diagnosis is clinical in essence based on the modified criteria of Dessau. For such, it is important to define lesions and typical sites besides recurrence or chronicity, translated by the occurrence of 2 or more episodes in 6 months. for didactic purpose, the consensus suggests the following description for HS lesions;

- **Nodules**- raised, palpable, edematous lesion, larger than 1cm
- **Abscess**- painful, larger lesions larger than 1 cm in diameter, with an inflammatory aspect, not necessarily septic.
- **Tunnel** – longitudinal, raised, painful, fluctuant mass, with variable length and depth, ending on the skin surface and occasionally with fluid discharge (pus, blood, serum) . this demonstration included fistulas, draining and no draining sinus tracts.

Typical sites are axillae, inguinal regions, inframammary regions and intermammary and gluteal clefts even though atypical sites can also be involved (face, neck, back, thighs)

Complementary exams such as biopsy and culture of the lesions are indicated in the cases of diagnosis uncertainty, suspicious chronic lesions can also require malignancy screening imaging studies (ultrasounds and nuclear magnetic resonance) can be beneficial for a better characterization of the lesions and surgical programming . ultrasounds evaluation can also contribute to past surgery follow up if recurrence is suspected.

Differential Diagnosis³⁶⁻⁴⁰

- Follicular pyoderma (including folliculitis, furuncles, earbunches)
- Granuloma inguinale
- Noduloulcerative syphilis
- Tuberculous abscess
- Actinomycosis
- Acne vulgaris

- Lymphogranuloma venereum

Objectives of medical treatment

1. Control the inflammation and inter current infections
2. Avoid progression to advanced stages with fibrosis and scarring and involvement of extension or multiple areas.
3. Improve the quality of life, particularly in regards to pain and discharge.
4. Prepare for surgical procedure, reducing inflammation and delimitating the lesion.
5. Approach extensive, disseminated ulcerated or surgically difficult to treat clinical forms.
6. Treat syndromic cases, in which HS is associated to other conditions such as acute inflammatory disease and inflammatory bowel disease

Current Newly Drug Approval^{41- 45}

Basel, October 31, 2023 – Novartis, a global leader in immune dermatology and rheumatology has launched Cosentyx to treat moderate to severe HS in adults. It is the only drug to treat moderate to severe HS in adults.

Others

Adalimumab (ADA) is the only biotechnology drug approved for management of Hidradenitis Suppurativa (HS)

Topical clindamycin 1% applied twice daily for 12 weeks represent first line therapy in mild to moderate HS.

DISCUSSION

this systematic review discussed the available therapeutic options for hidradenitis suppurativa. We investigated the published literature on several medical, radiation and surgical modalities. Several of these modalities showed good efficacy and tolerability in the included studies. We further performed a meta-analysis of the safety and efficacy of adalimumab in hidradenitis suppurativa patients. The analysis showed that adalimumab is effective when given weekly rather than at every other week. Surgery is reserved for advanced stages, unresponsive cases and extensive scarring^{46- 48}

Compared with general population, hidradenitis suppurativa patients have a 50% higher risk of any type of cancer. These epidemiological studies have also indicated that some cancers such as squamous cell carcinoma, hepatocellular cancer and buccal cancer occur more specifically than others in these patients. However, these findings should be considered with care as smoking was not controlled for in these patients, which is a confounding factor for both the conditions. Finding safe and effective treatments for those patients is therefore necessary.

CONCLUSION

Numerous medical treatments are available for hidradenitis suppurativa such as antibiotics, retinoids, antiandrogens,



immunosuppressive and anti-inflammatory agents and radiotherapy for early lesions. A dalimumab, an anti-tumor necrosis factor antibody, was superior to placebo in reducing Sartorius score and pain, when given weekly (not every other week). Combination therapies (such as antibiotics and hyperbaric oxygen therapy) have been tested and showed promising results that are yet to be confirmed. On the basis of quality of evidence, the most recommended treatments for hidradenitis suppurativa include adalimumab and laser therapy. Surgery (either by simple excision or complete local excision followed by skin graft) is the first choice for intractable disease presenting at late stages. The evidence on most of these treatments is deficient and further randomized controlled trials are needed to establish the most efficient therapies for hidradenitis suppurativa management.

In this article we have showed the detailed study of this disease including symptoms, medical treatment and diagnosis. We have showed newly drugs been approved on the treatment of this disease also reflecting the effect of various suggested drugs on HS.^{49,50}

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