Hidradenitis suppurativa

Debilitating and challenging to treat

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Hidradenitis suppurativa is a debilitating chronic skin disease of intertriginous areas, which may be misdiagnosed as boils or ingrown hairs in the early stages. Treatment often requires a combination of lifestyle modifications, medications and laser or surgical interventions.

KEY POINTS

- Hidradenitis suppurativa (HS) is a debilitating chronic skin disease characterised by inflammatory nodules, abscesses, sinus tracts, comedones and fibrotic scarring.
- HS lesions are most common in the axillae but can occur in any intertriginous area.
- The cause of HS is not completely understood and is likely to be multifactorial; contributing factors may include obesity, smoking, hormonal fluctuation, inflammation and genetics.
- The main clinical features supporting an HS diagnosis are a history of recurrent painful or suppurating lesions (typically deep-seated inflammatory nodules) in intertriginous areas, with a chronic or relapsing course.
- There is no single efficacious therapy for HS and a combination of lifestyle modifications, medical and laser or surgical interventions is often required.
- Referral to a dermatologist is recommended for patients with moderate to severe HS.

Hidradenitis suppurativa (HS) is a debilitating chronic skin disease. It is characterised by painful nodules that may progress to abscesses and in severe cases can lead to sinus tract formation, fibrotic scarring, dermal contractures and skin induration. HS causes significant morbidity because of its painful remitting and relapsing course. The pathogenesis is not completely understood but primarily involves occlusion of terminal hair follicles and subsequent hyperkeratinisation and inflammation.[1] There are a number of theories to explain these histological changes, which implicate factors such as obesity, tobacco smoking, genetics, inflammation and hormonal variation. There is currently no single effective therapy for this condition, and management often involves a combination of medical and surgical options.

Epidemiology

The estimated prevalence of HS is 1 to 4% of the population.[2] HS tends to occur in the second or third decades of life and is significantly more common in women than in men (female to male ratio of 3 to 1).[3]

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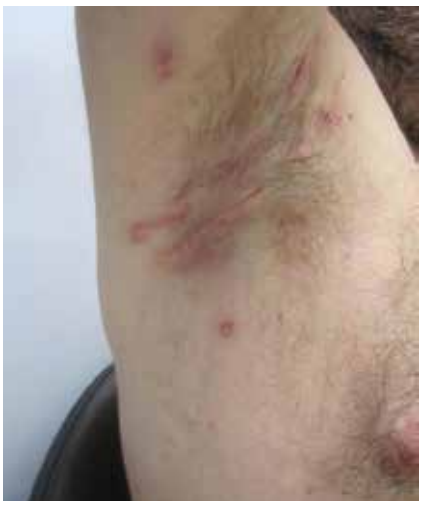
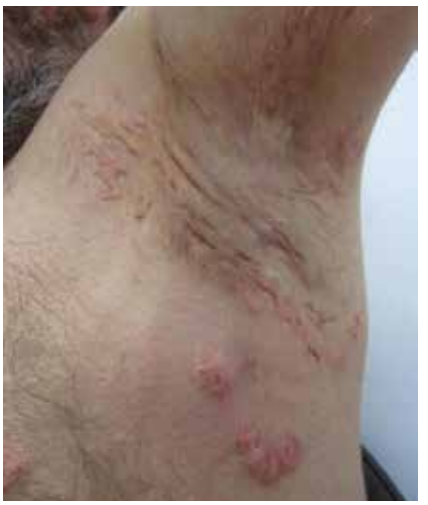
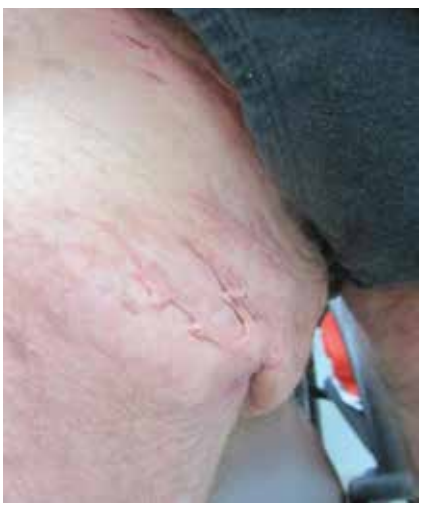
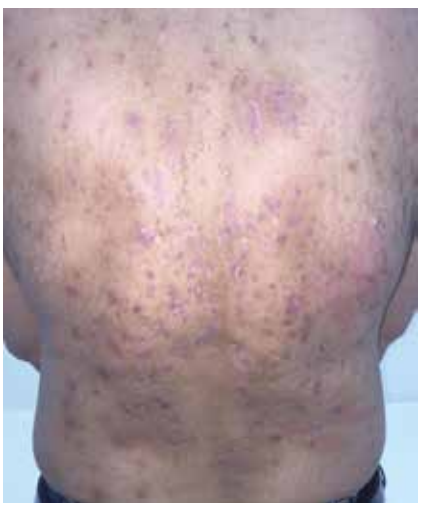



Figures 1a and b. Patient with Hurley stage III hidradenitis suppurativa in the axillae, showing inflammatory nodules and hypertrophic scarring.

Figures 2a and b. a (left). Patient with chronic hidradenitis suppurativa in the groin after treatment with biologic therapy, showing hypertrophic scarring from multiple previous lesions. b (right). Patient with Hurley stage II hidradenitis suppurativa after treatment with biologic therapy, showing extensive involvement of the back with inflammatory nodules and scarring.

Presentation

HS is characterised by deep-seated tender subcutaneous inflammatory nodules. The onset of HS is often insidious, with sporadic solitary nodules that persist for several days to months. Episodes of nodules may recur in the same location or general area. Early symptoms of HS include pain, pruritus, heat and hyperhidrosis. Patients often present in general practice with early-stage lesions, which are commonly misdiagnosed as boils (furuncles) or ingrown hairs caused by waxing or shaving. However, HS lesions differ from furuncles as they are deep-seated and round-topped, lacking the typical pointed appearance of furuncles.

An HS nodule may progress to an abscess and rupture at the skin surface, exuding a foul-smelling discharge. Alternatively, HS nodules may regress without rupture or persist deep within the skin, leading to sinus tract formation. As the disease process continues, fibrosis, dermal contractures and induration of the skin can occur. HS commonly causes significant impairment of quality of life.[2]

HS lesions are most common in the axillae but can occur in any intertriginous area, including the inguinal area, inner thigh, mammary and inframammary regions, buttocks, pubic region, scrotum, vulva and chest.

Diagnosis

HS is a clinical diagnosis that can be made through careful history taking and examination, informed by knowledge of the characteristic clinical manifestations. Investigations such as skin swabs or biopsies are not necessarily indicated. Microscopy of swabs of lesions predominantly has negative results, showing either contaminants of normal skin flora or occasionally secondary bacterial infections.[4] Skin biopsy may be warranted to exclude differential diagnoses such as cutaneous Crohn's disease and ulcerated squamous cell carcinoma (Marjolin's ulcer). Imaging such as ultrasound examination may be of clinical benefit for preoperative planning.

Diagnostic criteria

Primary diagnostic criteria for HS include:

- a history of recurrent painful or suppurating lesions (typically deep-seated inflammatory nodules), with
- at least two episodes over a six-month period.[4]

The signs of HS include:

- nodules, comedones, sinus tracts, abscesses and/or fibrotic scarring, particularly in patients with chronic disease (Figures 1a and b)
- lesions in characteristic locations, such as the inguinal area, inner thigh, mammary and inframammary regions, buttocks, pubic region, scrotum, vulva and chest (Figures 2a and b).

A positive family history is a secondary

diagnostic criterion. In addition, a negative swab result or the presence of normal skin microbiota suggests HS.

Clinical staging

The Hurley clinical staging system is frequently used in clinical trials to differentiate patients with HS into three severity groups:[2]

- stage I – abscess formation (single or multiple) without sinus tracts and cicatrisation or scarring
- stage II – recurrent abscesses with sinus tracts and scarring, single or multiple widely separated lesions
- stage III – diffuse or almost diffuse involvement, or multiple interconnected sinus tracts and abscesses across the entire area.

Assessment of disease severity in patients with HS requires a combination of Hurley staging and physician assessment combined with patient perception and experience of disease. This can be objectively assessed using a validated tool such as the Dermatology Life Quality Index.

Differential diagnosis

Other diseases that cause inflamed nodules, recurrent abscesses or sinus tracts and may be mistaken for the different stages of HS are listed in the Box.

Pathogenesis

The pathogenesis of HS is not fully understood. However, there is now greater understanding of the disease from the explosion of research on the topic over recent years. The histopathology of HS has shown the origin of the pathological process is from follicular occlusion and subsequent inflammation.[1] Essentially, the hair follicles become occluded then rupture and re-epithelialise with an associated immune response. Recent studies have suggested that the interleukin-12 to interleukin-23 pathway and tumour necrosis factor alfa (TNF-α) are involved in the pathogenesis of HS, adding credence to the theory that it is an immune or inflammatory disorder.[5] The cause of the follicular occlusion and subsequent inflammation is thought to be multifactorial and includes obesity, smoking, hormonal fluctuation, genetics and inflammation.

Contributing factors

Obesity and metabolic syndrome

An association between obesity and HS has been well established. There is extensive research to suggest that obesity is linked to both the likelihood of developing HS and the severity of disease, and that weight reduction can improve symptoms. A proposed mechanism for this correlation follows the observation that HS typically occurs in intertriginous areas and involves follicular occlusion. With the increased surface area and skin folds in obese patients there is greater shear mechanical stress, pressure and friction on skin that could contribute to follicular occlusion and rupture.[6] Interestingly, there is a growing body of research that identifies an association between metabolic syndrome and HS.[7]

DIFFERENTIAL DIAGNOSIS OF HIDRADENITIS SUPPURATIVA

Early HS lesions

- Acne
- Cellulitis
- Dermoid cyst
- Folliculitis, furuncles, carbuncles
- Lymphadenopathy
- Perirectal abscess
- Pilonidal cyst

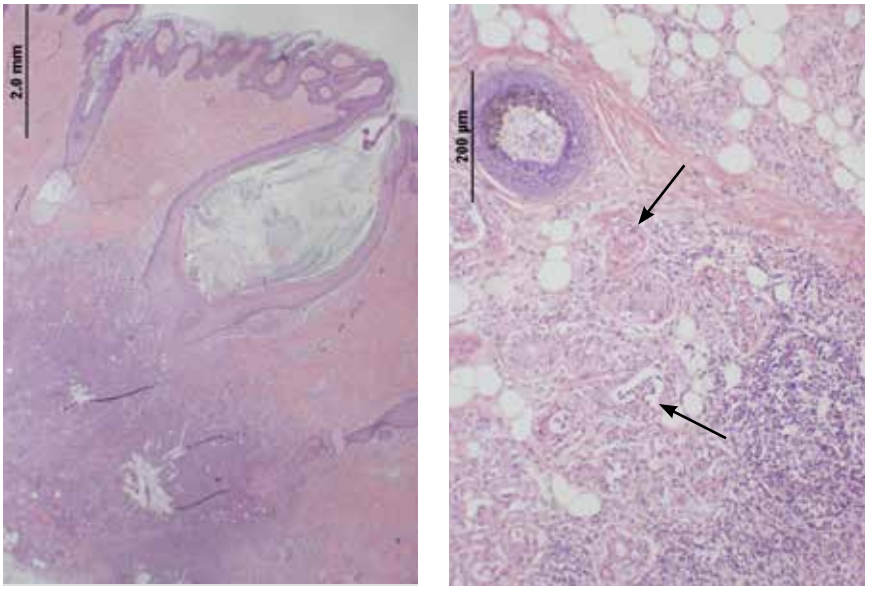
Late HS lesions

- Anal fistula
- Cutaneous Crohn's disease
- Granuloma inguinale
- Ischiorectal abscess
- Ulcerated squamous cell carcinoma (Marjolin's ulcer)

Abbreviation: HS = hidradenitis suppurativa.

Inflammation

An expanding body of research supports the hypothesis that HS is accompanied by a substantial systemic burden of inflammation. Patients with HS have



Figures 3a and b. Skin biopsy specimen from a 25-year-old man showing some of the classic features consistent with hidradenitis suppurativa. a (left). Sinus lined with stratified squamous cells and a heavy mixed inflammatory cell infiltrate in the lower half of the dermis. b (right). Inflammation of the apocrine glands (arrows) adjacent to a hair follicle.

Images courtesy of Dr Tricia Saurine and Dr Jessica Reagh, Royal North Shore Hospital, Sydney, NSW.

been found to have higher levels of inflammatory markers (erythrocyte sedimentation rate and C-reactive protein) than patients with psoriasis, suggesting that the inflammatory burden of HS is substantial.[2]

Further, HS has been identified as part of a clinical triad comprising pyoderma gangrenosum, acne and suppurative hidradenitis ('PASH'). PASH represents a new disease entity within the spectrum of autoinflammatory syndromes.[8] It is similar to PAPA (pyogenic arthritis, pyoderma gangrenosum and acne) and aseptic abscess syndrome. All are characterised by recurrent noninfectious inflammatory episodes, the absence of autoantibodies and antigen-specific T cells and the presence of neutrophilic infiltrates.[2] However, PASH is distinguished by its predilection for skin and the lack of arthritis and visceral involvement. Different mutations within the *PSTPIP1* gene (which encodes a protein involved in T cell regulation, proline-serine-threonine phosphatase-interacting protein 1) have been noted in the three distinct syndromes, suggesting that the location of the mutation within the gene influences the organ predilection.[8]

Smoking

The link between smoking and HS is well established, with most patients with severe disease being smokers. Further, a recent cross-sectional study involving 212 patients over 22 years noted greater remission on cessation of smoking.[9]

Hormonal factors

A role for hormones in the pathogenesis of HS is suggested by the observation that HS affects mainly women, occurs after puberty and is associated with polycystic ovary syndrome.[10] Additionally, it has been noted that HS may decline in postmenopausal women. It has been postulated that androgens play a role in the aetiology of HS, as apocrine glands have androgen receptors with known cyclical premenstrual exacerbations.

Genetics

Genetic susceptibility appears to be an important contributor to HS. A high proportion of patients with HS have a first- or second-degree relative with the disease, and an autosomal dominant mode of inheritance has been identified.[3]

Management

HS is a persistent and debilitating condition. The chronic clinical course, pain, malodorous discharge and deformity are understandably a considerable psychological burden for patients. In a recent study, patients ranked the morbidity of HS above that of alopecia, mild to moderate psoriasis and several other dermatological conditions.[11]

Principles of management

There are currently no formal guidelines for the treatment of HS. Treatment is driven primarily by expert opinion and isolated case reports or series. To achieve effective outcomes, management usually requires a combination of:

- lifestyle changes
- medical therapy
- laser or surgical intervention
- considerable psychological support.

Baseline therapy for HS should include adequate pain management and appropriate dressings (e.g. absorbent nonirritant bandages for suppurative lesions). Lifestyle modifications that can reduce disease severity include advice and support for smoking cessation and weight loss. The disease has a considerable psychosocial impact, and screening for depression and social isolation may be appropriate in some patients.

As there is a spectrum of HS severity, treatment should be based on both the objective severity and impact of the disease on the patient.[4] Early referral to a dermatologist is important for optimum therapeutic management in all patients except those with mild disease, who may be managed by GPs.

Locally recurring lesions can be treated surgically, whereas widespread lesions are more appropriately managed with medical treatment, either as monotherapy or in combination with surgery.

In patients with advanced HS, a multifaceted approach may be adopted, in which surgical therapy is used to remove chronic HS components that are not expected to respond to medical therapy (e.g. scars, fistulas and sinus tracts), and long-term systemic medical therapy is used to treat the acute or subchronic manifestations (e.g. abscesses and inflammatory nodules).

Pharmacological treatments

There are a number of pharmacological treatment options, including topical and systemic antibiotics, corticosteroids, antiandrogen therapy, systemic retinoids and immunosuppressive agents. Successful use of antiandrogens, oral retinoids and immunosuppressants in patients with HS that did not respond to other treatments has been described in case reports and series, but no controlled studies have been conducted with these agents. The use of oral retinoids appears to have limited therapeutic benefit, although one small case series reported isotretinoin to be of some benefit.[12]

Topical or systemic antibiotics

In HS, bacterial colonisation is a secondary event and even potent antibiotic therapy is often futile in the long term. For superficial lesions topical clindamycin may be of some benefit in combination with benzoyl peroxide and other topical nonsoap antibacterial cleansers. In patients with more severe or widely spread lesions, combination therapy with clindamycin and rifampicin to eradicate staphylococci may be effective.[4] Concurrent fungal infections may occur, particularly in the groin area. Microscopy, culture and sensitivity testing of skin swabs can be of benefit to allow targeted antibiotic therapy in the less common cases of secondary bacterial infection of HS lesions.

Intralesional corticosteroids

Intralesional injections of triamcinolone acetonide (5 to 10 mg/mL) have been

advocated to rapidly reduce inflammation associated with acute flares and to manage recalcitrant nodules and sinus tracts.[4] However, this therapy is contraindicated if bacterial infection is suspected clinically.

Antiandrogen therapy – spironolactone

Despite the strong possibility of a hormonal influence in HS, evidence supporting the use of antiandrogen therapy is still lacking. A number of small case studies have shown promising results. The potassium-sparing diuretic spironolactone has traditionally been used, because of its known antiandrogen activity. A recent case series showed that spironolactone can be considered as first-line treatment in women with mild to moderate HS.[13]

Immunosuppressants – adalimumab, infliximab

The theory that HS involves an immunological abnormality has prompted investigation into the role of treatment with immunosuppressants, including biologic agents. Adalimumab and infliximab block the effects of TNF-α and have been shown to be useful in patients with severe HS (Figures 2a and b).[12] A recent systematic review of the use of immunosuppressive agents and systemic retinoids in treatment of HS found that infliximab and adalimumab were more effective than other immunosuppressive agents such as colchicine, cyclosporin, dapsone and methotrexate, and systemic retinoids.[14] Use of adalimumab and infliximab in patients with HS is currently off-label in Australia.

Laser treatment and surgery

Early definitive surgical intervention has been regarded as one of the most effective treatments for intractable localised disease. For patients with extensive disease, surgical removal of the entire follicular sweat gland apparatus with generous excision margins is currently being advocated as the gold standard treatment.[10] Carbon dioxide laser therapy is another technique used to treat HS by radically removing all keratinocytes in nodules, abscesses and fistulas. However, surgery has been frequently reported to have unsatisfactory outcomes, with results unacceptable to patients. The most common complications are high recurrence rates, scarring and skin graft failure.

Conclusion

GPs are well positioned to identify patients with HS early in the disease course. Given the high morbidity and psychosocial impact of HS, it is important that clinicians identify the characteristic clinical signs and appreciate the difficulty of treating this disease. Early referral of patients with moderate to severe disease to a dermatologist is important for optimum therapeutic management. Further, with our improved knowledge of the factors that contribute to HS, GPs can have a role in improving the overall health of patients with HS through diagnosing and treating common comorbidities such as metabolic disorders and other inflammatory conditions. MT

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