*Hong Kong J. Dermatol. Venereol.* (2018) **26**, 5-9

Original Article

# Management of hidradenitis suppurativa: experience from a Singaporean dermatologic institute

## 化膿性汗腺炎的治療：一所新加坡皮膚科院所的經驗分享

ECE Choi 蔡慈恩 and NS Chandran 素綠

Hidradenitis suppurativa (HS) is a chronic inflammatory disorder of the follicular epithelium that runs a chronic course and can be difficult to treat. We studied 58 patients with HS treated at the National University Hospital, Singapore over a 13 year period, and described the treatment regimes used. We looked at the response to treatment and the second and third-line agents used in our institute. We describe the benefits and limitations of our care, and discuss possibilities and avenues for improvement.

化膿性汗腺炎是一種毛囊上皮細胞的慢性炎症性疾病，病情長久持續及難以控制是其特性。我們在新加坡國立大學醫院對 13 年間在本院治療化膿性汗腺炎的 58 名患者進行研究，並描述了他們所使用的治療方案。我們檢視了治療的成效及所用的二線和三線藥物，同時描述了我們的護理的好處和局限性，進而討論改進的可能性和途徑。

**Keywords:** Acne inversa, Asian, Hidradenitis suppurativa, Treatment

**關鍵詞**：反常性痤瘡、亞洲人、化膿性汗腺炎、治療

## Introduction

Hidradenitis suppurativa (HS) is an inflammatory disorder of the terminal follicular epithelium of apocrine-gland bearing skin. It runs a chronic relapsing and remitting course with inflammation, abscess formation and scarring in the involved skin.[1,2]

**Division of Dermatology, University Medicine Cluster, National University Hospital, Singapore**
ECE Choi, MRCP, MMed(IM)
NS Chandran, MRCP, MMed(IM)

Correspondence to: Dr. NS Chandran
5 Lower Kent Ridge Road, Singapore 110974

The European guidelines recommend consideration of medical, surgical and adjuvant treatment.[3] Medical treatment includes topical antibiotics, oral antibiotics, retinoids and biologics; while surgical interventions include deroofing, local excision and wide surgical excision. Adjuvant therapies include weight loss, smoking cessation and pain management.

Recent evidence supports the use of the biologics adalimumab and infliximab in the treatment of HS. In 2015, adalimumab became the first biologic agent approved by FDA for the treatment of HS,[4] and in August 2016, an NEJM article reported significantly higher clinical response rates in patients treated with weekly adalimumab

compared to placebo in two phase three trials.[5] A randomised controlled cross-over trial comparing infliximab with placebo in 38 participants found significant objective and subjective improvement in the infliximab arm.[6] A Cochrane review on interventions for HS in 2015 reported moderate quality evidence for adalimumab and infliximab.[7] The European guidelines recommend adalimumab as a first-line treatment option for patients with moderate to severe HS unresponsive or intolerant to oral antibiotics, with infliximab being recommended as second-line therapy after failure of adalimumab.[8]

Standard surgical treatments range from simple incision and drainage (I&D) to laser surgery and radical surgical excision. Primary closure may be achieved with flaps and grafts, or lesions may be left to heal with secondary intention. Some procedures aim for 'cure', while others for symptom relief. Simple I&D for HS is often ineffective, providing only temporary relief with high recurrence rates.[9-11] More extensive resection surgeries are often associated with significant post-surgical healing time.[8]

Smaller scale office-based procedures have been described in 2010 by van der Zee et al,[12] Jemec in 2012,[11] and Danby et al in 2015,[10] such as 'punch debridement' and 'unroofing/deroofing' of abscesses and sinus tracts. These are theorised to provide better long term healing than I&D, and are suitable for early and localised disease (Hurley stage I and II), with extensive surgery reserved for extensive Hurley stage III disease.[10]

## Methods

We retrospectively reviewed all patients with HS treated at the University dermatology outpatient clinic of the National University Hospital (Singapore) over a 13-year period between January 2004 to December 2016 with analysis of treatment regimes and outcomes. This study was approved by the hospital ethics review board.

## Results

In this study, 58 patients were included. Their demographic and clinical characteristics are shown in Table 1.

The number of patients prescribed with the various treatment modalities are shown in Table 2. Lifestyle modifications such as smoking cessation were recommended as a standard for all patients.

**Table 1.** Demographics of patients

| | | n | % |
|---|---|---|---|
| Gender | Male | 34 | 58.6 |
| | Female | 24 | 41.4 |
| Race | Chinese | 24 | 41.4 |
| | Malay | 7 | 12.1 |
| | Indian | 17 | 29.3 |
| | Others | 10 | 17.2 |
| Worst Hurley stage during follow up | I | 18 | 31.0 |
| | II | 33 | 56.9 |
| | III | 7 | 12.1 |
| Disease involvement at presentation | Axilla | 49 | 84.5 |
| | Groin | 25 | 43.1 |
| | Buttock | 23 | 39.7 |

**Table 2.** Number of patients prescribed with the various treatment modalities

| Treatment modality | Number of patients (total 58) |
|---|---|
| Topicals (antiseptic/antibacterial) | 50 |
| Oral suppressive antibiotics | 44 |
| Metformin | 16 |
| Immunomodulators/ Immunosuppresants | 5 |
| Prednisolone | 3 |
| Isotretinion | 2 |
| Oral hormonal contraceptives | 2 |
| Biologic agents | 1 |
| Surgery by dermatologist | 3 |

Topical agents and oral suppressive antibiotics were prescribed in the majority of patients (Table 3). Two patients had stopped oral antibiotics in less than five days due to side effects. Antibiotics were commonly switched if patients failed to respond. Fifteen patients had at least two or more different courses of antibiotics. The median duration of each course of antibiotics was 5.25 months (IQR: 3-10.8 months).

Of the 16 patients on metformin, only seven were prescribed metformin for the sole indication of HS. The rest were on metformin for diabetes, prior to the diagnosis of HS.

Immunomodulators such as ciclosporin and methotrexate were used for those not responsive to oral antibiotics (Table 3). Only one patient had received a biologic agent. This patient had Crohn's disease for which he was prescribed infliximab by his gastroenterologist. Biologics were offered in another six patients but none were initiated on treatment.

**Table 3.** Type of suppressive antibiotics and immunomodulators prescribed

| Antibiotic | Number of patients |
|---|---|
| Doxycycline | 36 |
| Rifampicin and clindamycin | 8 |
| Minocycline | 9 |
| Erythromycin | 4 |
| Tetracycline | 1 |
| Metronidazole | 1 |
| Clarithromycin | 1 |
| Trimethoprim and Sulfamethoxazole | 1 |
| Ciprofloxacin | 1 |
| Clindamycin | 1 |
| Linezolid | 1 |
| Immunomodulator | |
| Ciclosporin | 2 |
| Methotrexate | 2 |
| Azathioprine | 1 |

While many patients had previous I&Ds under the surgical or emergency department prior to being seen by dermatologists, of which only seven patients (stage I disease: 1 case; stage II disease: 4 cases; stage III disease: 2 cases) were offered further surgical intervention either by a dermatologist or plastic surgeon. Three of these patients (stage I: 1 case; stage II disease: 2 cases) proceeded with simple excision of the most fluctuant nodules by a dermatologist. Patients with more extensive disease were referred to plastic surgery for resection with flaps or grafts, however none had proceeded.

The median duration of follow up was 8.2 months (range 0-93 months). Thirty-nine patients were followed up. Of these, 23 had an overall improvement, 15 had no change, and one had worsening disease severity at latest follow-up.

Of the 29 patients who were prescribed long-term antibiotics: 17 showed improvement, eight had stable disease and four had worsening disease.

Of despite a prolonged the four patients with worsening disease despite prolonged course oral antibiotics:

One patient was given prednisolone with good response at a dose of 60 mg daily, and subsequently started on methotrexate with a gradual tapering of prednisolone over 10 months with good response.

The second patient was started on isotretinoin, followed by a short tapering course of prednisolone and methotrexate, and subsequently colchicine, all with inadequate control. Biologics were offered but not taken up due to cost issue. At the latest follow-up, he still had worsening disease.

The third patient was put on ciclosporin but was poorly tolerated due to gastrointestinal side effects. Biologics were offered but not taken up due to cost considerations. She was restarted on oral

antibiotics, rifampicin and clindamycin which resulted in a stable disease.

The last patient had the follicular occlusion triad and had responded poorly to antibiotics. He was put on isotretinoin 20 mg daily for two months, followed by prednisolone, which was started at a dose of 20 mg then tapered over three months to a subsequent long-term dose of 2.5-5 mg daily for three years. The disease was largely stable with minimal intermittent flares. However, this patient was non-compliant with his medications.

Biologics were offered to six patients, but was not taken up by any patient due to financial concerns. Radical surgical resection was considered in two of these patients but none proceeded.

## Discussion

The mainstays of treatment in our institute were topical medications, and oral antibiotics. Treatment response to oral antibiotics was satisfactory in approximately half of our patients (58.6%). Reported response rates to antibiotics are variable, ranging from 30-96%.[13-15] These studies however, were heterogeneous with differing outcome measures. The relative low cost and safety profile of oral antibiotics justifies its use as a mainstay or first-line systemic treatment modality for HS (category of evidence IIb).[8]

For those with a poor response to antibiotics, few in our centre proceeded to biologic agents. This is unfortunate given the evidence for its efficacy. The use of biologics for HS in Singapore has only recently been approved and it is anticipated that with better funding, these agents will soon benefit more patients with HS locally.

We noted a limited use of adjunctive treatment such as anti-androgens and metformin. Current evidence for these treatments is limited to primarily small studies documenting positive response of between 55-85%,[16-18] to antiandrogen therapy such as hormonal contraceptives,[17] spironolactone[16,17] and metformin.[18] Due to the limited evidence, hormonal therapy is currently recommended as a third-line agent with (category of evidence IV).[8] However, these relatively safe and low cost options would be worthwhile considerations especially where limitations in resources preclude the use of more effective therapies such as biologics. The presence of comorbidities such as pre-diabetes, diabetes or polycystic ovarian syndrome would be further indications for such therapies.

Few patients underwent surgical interventions: only three patients received simple excision, all in the year 2016. While this is few, the fact that these all occurred in the preceding year suggests the growing role of surgery in our institute. Studies evaluating the outcomes for surgery are generally sparse and heterogeneous, reporting variable results.[8] A systematic review of recurrence rates after surgical management quoted the estimated average recurrence as follows: wide excision, 13.0%, local incision, 22.0% and deroofing, 27.0%. However there were great variations in the patients recruited, surgical technique, duration of follow-up and evaluation of outcomes.[19] Continued improvement of surgical techniques, and increased expertise and training of dermatologists for less invasive, office-based interventions such as 'deroofing' and 'punch debridement' will likely open more surgical treatment options for patients.

Limitations of this study include the relatively small study size from a single dermatological institution, with a high default rate that may limit the generalisability of this study. There was also significant variability in the treatment regimes, which may relate to the long period of study or inter-physician variability.

Treatment modalities for HS are rapidly expanding and the appropriate funding and training will enable them to be used in our institute and other

parts of the world. For now, HS remains a chronic condition with substantial adverse impact on the quality of life.[20]

## Conclusion

Hidradenitis suppurativa is a difficult condition to treat, and typically runs a chronic course with relapses and recurrences. First-line use of long-term antibiotics is appropriate with efficacy in at least half of the patients. The use of biologics and surgical techniques with less morbidity provides more options to patients. Improved funding and surgical training of dermatologists are necessary to improve the outcomes of HS treatment.

## References


1. Revuz JE, Jemec GB. Diagnosing Hidradenitis Suppurativa. Dermatol Clin 2016;34:1-5.
2. Kurzen H, Kurokawa I, Jemec GB, Emtestam L, Sellheyer K, Giamarellos-Bourboulis EJ, et al. What causes hidradenitis suppurativa? Exp Dermatol 2008;17:455-72.
3. Zouboulis CC, Desai N, Emtestam L, Hunger RE, Ioannides D, Juhász I, et al. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. J Eur Acad Dermatol Venereol 2015;29:619-44.
4. Lee RA, Eisen DB. Treatment of hidradenitis suppurativa with biologic medications. J Am Acad Dermatol 2015; 73(Suppl 1):S82-8.
5. Kimball AB, Okun MM, Williams DA, Gottlieb AB, Papp KA, Zouboulis CC, et al. Two Phase 3 Trials of Adalimumab for Hidradenitis Suppurativa. N Engl J Med 2016;375:422-34.
6. Grant A, Gonzalez T, Montgomery MO, Cardenas V, Kerdel FA. Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: a randomized, double-blind, placebo-controlled crossover trial. J Am Acad Dermatol 2010;62:205-17.
7. Ingram JR, Woo PN, Chua SL, Ormerod AD, Desai N, Kai AC, et al. Interventions for hidradenitis suppurativa: a Cochrane systematic review incorporating GRADE assessment of evidence quality. Br J Dermatol 2016; 174:970-8.
8. Gulliver W, Zouboulis CC, Prens E, Jemec GBE, Tzellos T. Evidence-based approach to the treatment of hidradenitis suppurativa/acne inversa, based on the European guidelines for hidradenitis suppurativa. Rev Endocr Metab Disord 2016;17:343-51.
9. Kohorst JJ, Baum CL, Otley CC, Roenigk RK, Schenck LA, Pemberton JH, et al. Surgical Management of Hidradenitis Suppurativa: Outcomes of 590 Consecutive Patients. Dermatol Surg Off Publ Am Soc Dermatol Surg Al 2016;42:1030-40.
10. Danby FW, Hazen PG, Boer J. New and traditional surgical approaches to hidradenitis suppurativa. J Am Acad Dermatol 2015;73(5 Suppl 1):S62-5.
11. Jemec GB. Clinical practice. Hidradenitis suppurativa. N Engl J Med 2012;366:158-64.
12. van der Zee HH, Prens EP, Boer J. Deroofing: a tissue-saving surgical technique for the treatment of mild to moderate hidradenitis suppurativa lesions. J Am Acad Dermatol 2010;63:475-80.
13. Gener G, Canoui-Poitrine F, Revuz JE, Faye O, Poli F, Gabison G, et al. Combination therapy with clindamycin and rifampicin for hidradenitis suppurativa: a series of 116 consecutive patients. Dermatol Basel Switz 2009; 219:148-54.
14. Alhusayen R, Shear NH. Scientific evidence for the use of current traditional systemic therapies in patients with hidradenitis suppurativa. J Am Acad Dermatol 2015; 73(Suppl 1):S42-6.
15. Jemec GB, Wendelboe P. Topical clindamycin versus systemic tetracycline in the treatment of hidradenitis suppurativa. J Am Acad Dermatol 1998;39:971-4.
16. Lee A, Fischer G. A case series of 20 women with hidradenitis suppurativa treated with spironolactone. Australas J Dermatol 2015;56:192-6.
17. Kraft JN, Searles GE. Hidradenitis suppurativa in 64 female patients: retrospective study comparing oral antibiotics and antiandrogen therapy. J Cutan Med Surg 2007;11:125-31.
18. Verdolini R, Clayton N, Smith A, Alwash N, Mannello B. Metformin for the treatment of hidradenitis suppurativa: a little help along the way. J Eur Acad Dermatol Venereol 2013;27:1101-8.
19. Mehdizadeh A, Hazen PG, Bechara FG, Zwingerman N, Moazenzadeh M, Bashash M, et al. Recurrence of hidradenitis suppurativa after surgical management: A systematic review and meta-analysis. J Am Acad Dermatol 2015;73 (Suppl 1):S70-7.
20. Gooderham M, Papp K. The psychosocial impact of hidradenitis suppurativa. J Am Acad Dermatol 2015; 73(Suppl 1):S19-22.