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Proceeding report of the Third Symposium on Hidradenitis Suppurativa Advances (SHSA) 2018

Claudia J. Posso-De Los Rios¹, Akua Sarfo², Mondana Ghias³, Raed Alhusayen⁴, Iltefat Hamzavi⁵, Michelle A. Lowes^{6,*}, Afsaneh Alavi^{1,*}

¹Department of Medicine, Division of Dermatology, University of Toronto, Toronto, ON, Canada

²Department of Dermatology, Pennsylvania State University College of Medicine, Hershey, PA, USA

³Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY, USA

⁴Division of Dermatology, Sunnybrook Research Institute, Toronto, ON, Canada

⁵Department of Dermatology, Henry Ford Hospital, Detroit, MI, USA

⁶The Rockefeller University, New York, NY, USA

Abstract

The 3rd Annual Symposium on Hidradenitis Suppurativa Advances (SHSA) took place on October 12–14, 2018 at the Women's College Hospital in Toronto, Ontario, Canada. This symposium was a joint meeting of the Hidradenitis Suppurativa Foundation (HSF) founded in the USA, and the Canadian Hidradenitis Suppurativa Foundation (CHSF). This cross-disciplinary meeting with experts from around the world was an opportunity to discuss the most recent advances in the study of hidradenitis suppurativa pathogenesis, epidemiology, classification, scoring systems, radiologic diagnosis, treatment approaches, and psychologic assessment. Two special sessions this year were HS as a systemic disease and HS management guidelines. There were focused workshops on wound healing and ultrasound. There were two sessions primarily for patients and their families in the HS School program: one workshop focused on mindfulness, and the second involved discussion among clinicians and patients about various disease aspects and the latest management.

Correspondence: Claudia J. Posso-De Los Rios. Dermatology department. Sunnybrook Health Sciences Centre. 2075 Bayview Avenue. M-wing, 1st floor, M1-700. Toronto, ON. M4N 3M5, possoclaudia@gmail.com.

*These authors contributed equally to this manuscript.

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Performed the research: CP, AS, MG, RA, IH, MAL, AA

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Conflict of interest

AA has been advisor and investigator for Abbvie, Janssen, InflaRx, Novartis and Incyte.

IH is the President of the HS Foundation, in a non-compensated role; has been principal investigator for Lenicura (equipment received to institution) and GE (research funding, paid to institution); he has received fees as a consultant from Incyte, UCB, and Novartis.

MAL has received fees for participating in advisory boards for AbbVie and Janssen, and consulting fees from Incyte, BSN and XBiotech.

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To facilitate networking between clinical and research experts and those early in their career, a mentoring breakfast was held.

Keywords

epidemiology; pathogenesis; classification; diagnosis; treatment

Introduction

The 3rd Annual Symposium on Hidradenitis and Suppurativa Advances (SHSA) was held at the Women's College Hospital in Toronto, Canada from October 12 – 14, 2018. This symposium was a joint meeting of the Hidradenitis Suppurativa Foundation (HSF Inc.) founded in the USA, and the Canadian Hidradenitis Suppurativa Foundation (CHSF). The conference was opened with an introduction by Dr. Afsaneh Alavi and Dr. Michelle Lowes, scientific co-chairs of the meeting, Dr. Raed Alhusayen, president of the Canadian HS Foundation (CHSF), and Dr. Iltefat Hamzavi, president of the HS Foundation USA (HSF). This annual meeting brought together experts from multiple disciplines from different countries, to discuss the most recent advances in basic science, clinical characteristics, diagnosis and management of hidradenitis suppurativa (HS). Reports from previous meetings are available.^[1,2] There were a total of 230 attendees from 18 countries including 25 patients at the meeting. There is an e-supplement that complements this main document.

Background

Hidradenitis suppurativa/acne inversa (HS) is a chronic, inflammatory, recurrent, debilitating skin disease of the hair follicle that usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillae, inguinal and anogenital regions.^[3] The disease has a wide spectrum of clinical presentation. Treatment response is variable. This condition is not completely characterized from different perspectives. Multidisciplinary teams are preferable to optimize treatment of HS patients.

1. Scientific Session 1: Epidemiology and Burden of Disease

Moderators: Neil Shear, Canada, and Lynne Margesson, USA

1.1 Update on epidemiology of Hidradenitis Suppurativa

Amit Garg, USA

The true prevalence and incidence of HS are still unknown. Prevalence estimates vary significantly across the world (0.00033% to 4.1%). The data disparity could be explained by factors including geographic location where the study is performed, sampling method, method of data acquisition, and burden of undiagnosed disease. Other diseases such as acne, vitiligo and psoriasis show variability in prevalence depending on method of data collection (e.g. diagnostic codes versus self-report). The conclusion was that HS is an uncommon but

not a rare disease. If the prevalence of 1% is considered, this condition would be as common as psoriatic arthritis, lichen planus and hyperthyroidism, and 20–50 times more common than vitiligo, inflammatory bowel disease (IBD), systemic lupus erythematosus, type 1 diabetes, sarcoidosis and discoid lupus erythematosus.^[4,5]

1.2 Psychosocial Burden of Hidradenitis Suppurativa

Łukasz Matusiak, Jacek C. Szepietowski (presenter), Poland

It was estimated that almost 60% of HS patients have a decreased quality of life as measured by Dermatology Life Quality Index (DLQI).^[6–8] The impact of HS on DLQI was greater than other diseases such as chronic idiopathic urticaria, alopecia, acne vulgaris, and mild to moderate psoriasis. QoL impairment was directly correlated with Hurley stage, number of affected areas, and involvement of the anogenital area.^[9] Depression and anxiety were more commonly seen in HS patients, and more prevalent in women than men.^[10] There were profound disturbances of sexual health in patients with HS.^[11] Stigmatization was statistically significant when HS lesions were on visible areas such as the head and neck.^[9] Work disability (absences, dismissal, and lack of work promotion) has been documented in HS patients.^[6,12]

1.3 Pediatric Hidradenitis Suppurativa

Irene Lara-Corrales, Canada

HS in the pediatric population has not been well characterized. A recent publication from the Henry Ford Hospital showed a higher percentage of affected prepubescent boys than girls, but HS was more common in post pubescent girls than boys, proposing that the role of ovarian hormones in prepubescent disease is less important.^[13] Currently, the Pediatric Dermatology Research Alliance (PeDRA) has started an international collaborative study in 10 centers around the world to characterize HS in the pediatric population. Treatment guidelines for the pediatric population are lacking; a therapeutic approach based on Hurley stage was reviewed.^[14]

1.4 A Study of Survival in Patients with Hidradenitis Suppurativa

Mark Davis, USA

The Rochester Epidemiology Project, based on population-based research, determined the first population-based cohort finding that HS was less prevalent than suggested by previous reports, at 6–11.4 per 100,000.^[15,16] Using the same population, death records for incident cases of HS and age- and sex- matched controls from the County were reviewed to determine if HS patients have a higher mortality rate. The results showed that the risk of death due to any cause was over two times higher for the patients with HS in analyses both unadjusted and adjusted for age, race and Charlson index. The risk of cardiovascular or cerebrovascular death was also significantly higher for the patients with HS. This data was comparable with previous studies.^[17–19]

1.5 Development of the Hidradenitis Suppurativa Quality of Life (HiSQOL) Measure

Joslyn S. Kirby (presenter), Linnea Thorlacius, Bente Villumsen, Amit M. Garg, Solveig Esmann, John Ingram, Jerry Tan, Gregor Jemec

HS has a large negative impact on health-related quality of life (HRQOL). Generic HRQOL instruments do not assess the multiple and serious impacts that HS patients experience. There is a need for a fully validated and reliable instrument to evaluate HS-specific HRQOL (HiSQOL) for use in clinical research as well as in clinical practice. North American and Danish investigators are currently collaborating within IDEOM/HISTORIC^[20] to develop and validate a tool aligned with guidance from the US Food and Drug Administration. Preliminary psychometric testing showed the HiSQOL has high content and construct validity as well as high internal consistency and intrarater reliability. This initiative will open numerous research opportunities in this area.

2. Scientific Session 2: Hidradenitis Suppurativa as a Systemic Disease

Moderators: Amit Garg, USA, and Gregor Jemec, Denmark

This session is available as an e-supplement.

3. Scientific Session 3: Pathophysiology of Hidradenitis Suppurativa

3.1 Update on Pathogenesis of Hidradenitis Suppurativa

Michelle A. Lowes, USA

A current model of HS considers the pathogenesis as two phases, initiation and progression. Although the initiation phase has yet to be elucidated, it may involve follicular occlusion and cyst formation in the context of aberrant keratinocyte reactions, genetic factors, and immune dysregulation. The progression phase consists of a chronic inflammatory state with abundant immunoglobulin transcripts, antimicrobial peptides (AMP), interferons, plasma cells in lesional skin, and complement dysregulation. These findings in conjunction with prior findings in HS of excess neutrophils, B cells, plasma cells, TLR2 and IL-32 suggest an over exuberant immune response to eradicate commensal bacteria in HS, which may be unique aspects of HS pathophysiology. Additionally, there may be shared immune responses with other chronic cutaneous diseases including abundant AMPs, inflammatory cytokines (IL-1, IL-6, IL-17, IL-12/23), and Th17/T-reg dysregulation. These findings propose several molecular targets for therapeutic interventions in HS.^[21–23]

3.2 Update on Bacteriology and Microbiome in Hidradenitis Suppurativa

Haley B. Naik, USA

Bacteria have been proposed to play a role in HS due to the abscesses and chronic malodorous suppurative drainage, positive bacterial cultures from some HS lesions, and therapeutic effect of antibiotics.^[24,25] However, several studies also found that 50% of lesional specimens were culture negative with no specific organism identified in all cases. HS does not fulfill Koch's postulates. HS is not contagious and there are usually no typical

complications of infection, such as sepsis or cellulitis. Commensal microbiota in altered abundances may result in dysbiosis.^[26] In a study analyzing lesional, non lesional, and healthy skin control biopsies, sequencing data identified different proportions of commensal bacteria in each specimen.^[27] This data suggests bacteria may be secondary drivers in HS, with some evidence of microbiome alterations in HS lesional skin compared to healthy volunteers.

3.3 Advanced Molecular Approaches for Studying Defective MicroRNA Processing and MicroRNA Dysregulation in Hidradenitis Suppurativa

Neil Renwick, Canada

MicroRNAs (miRNAs) are small molecules that negatively regulate gene expression and serve as effective biomarkers due to their abundance, cell-type and disease-stage specificity, and stability in clinical samples. Prior studies showed that miRNA processing factors (including Drosha and Dicer),^[28] as well as components of the RISC complex (AGO proteins)^[29] are distinctly and progressively downregulated from normal, perilesional, to lesional HS skin. The presence of many inflammatory miRNAs in lesional HS suggests a typical inflammatory response obscuring keratinocyte contribution.^[30] New tools to comprehensively characterize miRNAs could shed light on their role in HS.

4. Scientific Session 4: Clinical Presentations of Hidradenitis Suppurativa and Measuring Disease Severity

4.1 Update on Clinical Phenotypes

Afsaneh Alavi, Canada

HS consists of many phenotypic presentations including: classic vs. atypical, inflammatory vs. occlusive follicular, early vs. late onset, and indolent vs. fulminant.^[31,32] Further studies of the genetic background of the disease, clinical presentations, pathophysiology, and associated co-morbidities guide the understanding of the natural history of the disease. The heterogenic nature of HS with regards to variations in populations with known genetic mutations,^[33] the bimodal age distribution of disease onset, and gender/weight differences suggest multi-divergent pathway involvement in disease pathogenesis.^[34,35]

4.2 Update on Pregnancy and Hidradenitis Suppurativa

Jennifer Hsiao, USA

Although preliminary data suggests that HS symptoms improve for a subset of patients during pregnancy, most patients do not experience a change in their disease course. Levels of progesterone and estrogen both rise through pregnancy (progesterone>estrogen). Progesterone suppresses the development and function of Th1 and Th17 cells. Serum levels of anti-inflammatory molecules and TNF-alpha receptors also increase during pregnancy. However, pregnancy weight gain may exacerbate HS due to increased friction and adipocyte secretion of pro-inflammatory cytokines.^[36,37] Medical therapies that may be utilized during pregnancy depends on the severity of the disease, for mild disease topical and oral

antibiotics (clindamycin, erythromycin, metronidazole) and metformin can be used. For severe, recalcitrant disease, antibiotics such as ertapenem and biologics such as adalimumab and infliximab may be considered.^[38] Surgical excision using lidocaine alone is safe; other procedures such as laser and cryoinsufflation are not classified.^[39] Tetracycline, oral retinoids, spironolactone, and oral contraceptives are contraindicated during pregnancy. The most recent FDA classification for pregnancy and lactation was reviewed.^[40]

4.3 Ultrasound Assessment

Antonio Martorell, Spain

Due to the limitations of clinical exams for HS staging, ultrasound (US) has been identified as a non-invasive, cost-effective imaging technique to better understand the subclinical anatomical manifestations of HS. US enhances the ability to identify nodules, abscesses, and dermal tracts and to precisely describe the nature of HS lesions.^[41,42] A multi-center study conducted on 143 HS patients to assess the usefulness of US in HS (ECO-HS) found that clinical examinations alone underestimate HS severity, with a greater percentage of patients determined as Hurley stage II and III using US than by clinical exam. Additionally, 82% of patients had modification of their therapeutic management after ultrasound examination. The results of ECO-HS suggest US will guide more personalized clinical and surgical approaches by offering more accurate characterization and staging of disease severity for HS patients.

4.4 Itch in Hidradenitis Suppurativa

Jacek C. Szepietowski, Karolina Kaaz, Łukasz Matusiak (presenter), Poland

Recent studies suggested that pruritus may be an important symptom associated with HS, especially in the prodromal stage.^[43] Histopathology reports found an increase in mast cells in all stages of HS (including perilesional skin) accompanying the inflammation of the involved skin. Mast cells in conjunction with other immune cells secrete a variety of proinflammatory cytokines responsible for the symptoms observed in various skin conditions including cutaneous swelling and pruritus.^[44] A study of 103 HS patients found that 97% noticed pruritus and 62% experienced pain associated with their HS lesions. Additionally, the co-occurrence of pain and pruritus at one location simultaneously was 60%. The intensity of pruritus correlated positively with impairment of quality of life and had a significant influence on the frequency of insomnia.

5. Scientific Session 5: Medical Treatment of Hidradenitis Suppurativa

Moderators: Jerry Tan, Canada, and Haley Naik, USA

5.1 Response to Treatment in Patients with Hidradenitis Suppurativa (Lack or Loss of Efficacy)

Gregor Jemec, Denmark

Much work has been done to improve treatment modalities, diagnosis, and disease stratification in HS, however several challenges still exist. One of the major challenges is

establishing standardized disease scoring methods and determination of outcome measures, which may be used to inform and develop best practices and guidelines for treatment. Clinical manifestations of HS are diverse; clinicians exhibit differences in confidence in identification and classification of disease. To illustrate this point, 46% of physicians queried indicated non-confidence in diagnosing a non-inflamed sinus tract. To address gaps in determining outcomes measures groups such as Hidradenitis Suppurativa cORe outcomes set International Collaboration (HISTORIC) are working to define a core set of agreed-upon outcomes measures for HS. Treatment guidelines for HS are a constantly evolving target and a several studies and case reports exist for various medical and surgical interventions. A comprehensive review of the progress made toward medical and surgical management and a proposed treatment algorithm can be found in Saunté and Jemec.^[45]

5.2 New Studies on Old Drugs

Alexa Kimball, USA

Therapies that target hormonal pathways may be of benefit to some patients with HS. As evidence, HS generally starts during puberty and often abates following menopause in women, with some women experiencing changes in disease activity in association with the menstrual cycle. Several studies of hormone-targeting therapies have demonstrated improvement in HS in female patients.^[46–49] Based on these findings, spironolactone may be a potential therapy in females. To address this, a retrospective chart review of adult females with HS treated with spironolactone showed significant disease improvement regarding pain, number of inflammatory lesions, and hidradenitis suppurativa physician global assessment (HSPGA), though no change was noted in Hurley stage or fistulas. An ongoing study including men and women is looking into outcomes for methotrexate therapy for HS.

5.3 Combining Antibiotics with Biologics in the Management of Hidradenitis Suppurativa

Raed Alhusayen, Canada

The Pioneer I and Pioneer II studies compared efficacy of adalimumab in treatment of HS. In the latter study, participants were allowed to continue their tetracycline antibiotics, which was not allowed in Pioneer I.^[50] This possibly could explain the higher response rate in the latter study. Dr. Alhusayen proposed that effective HS treatment should target two major drivers of pathogenesis: inflammation and biofilm formation. A combination approach to address these might consist of an antibiotic and anti-TNF agent. Dr. Alhusayen's preliminary data showed promising results by combining anti-TNF therapy with several antibiotic agents including tetracyclines, trimethoprim/sulfamethoxazole, and rifampin plus clindamycin. Current classes of medical therapy for HS include antibiotics, retinoids, anti-androgens, immunosuppression, and miscellaneous drugs and supplements. Future research should investigate the efficacy of combination strategies in the management of recalcitrant HS.

6. Scientific Session 6: Surgical and Laser Management of Hidradenitis Suppurativa

Moderators: Iltefat Hamzavi, USA, and Joslyn Kirby, USA

6.1 Combining Techniques to Achieve Patient Goals in Surgery

Ralph George, USA

HS patients may need surgical interventions as part of their treatment. Recurrence of the disease is seen in 11% of cases (6–15%) as per a systematic review.^[51] There are reports presenting higher rates from 18% to 50% of cases.^[52] Patients with severe disease may require a combination of surgical techniques and therapies including systemic medications such as antibiotics and biologics to control the disease, wide excision, portable negative pressure wound, secondary wound healing, wound care, and ongoing biologic treatments. Ultrasound is an extremely useful tool to assess extent of tunneling, connection of skin lesions and to target lesions appropriately. Dr. George has observed surgical outcomes are much improved now that patients are optimized by medical therapy before surgery, resulting in fewer complications and recurrences.

6.2 Update on Lasers and Light Modalities in Hidradenitis Suppurativa

Iltefat Hamzavi, USA

Adjunctive therapies, such as laser and light-based therapies, have become more commonly used in the management of HS. Different modalities are used for specific purposes, such as: to target the hair follicle or sebaceous gland, for bacterial load reduction, and for tissue debulking.^[53] There appears to be RCT evidence behind using follicular laser ablation for early stage disease.^[54,55] Response to photodynamic therapy is variable;^[56] larger and randomized controlled trials are needed. External beam radiation therapy has an unclear role in the treatment of HS, as there are currently only case reports in the literature.^[57]

6.3 Ultrasound Detection of Early Hidradenitis Suppurativa

Ximena Wortsman, Chile

There are specific sonographic criteria for the diagnosis of hidradenitis suppurativa based on the assessment of hair follicles and the dermis, presence of dermal pseudocystic nodules, fluid collection, and fistulous tracts. Ultrasound-based staging for HS severity has now been published.^[58,59] Ultrasound detection of a variety of subclinical anatomic abnormalities in early HS patients was discussed; these findings may have an important impact on staging of disease severity as well as management and progression of the disease.

7. Scientific Session 7: Wound Healing and Interdisciplinary Approach

Moderators: Raed Alhusayen, Canada, and Hadar Lev-Tov, USA

Update on Wound Healing in Hidradenitis Suppurativa

Hadar Lev-Tov, USA

The current treatment paradigm for wound care in HS involves management of exudate, bacterial colonization, odor, and pain. For the exudative lesions, superabsorbent dressings, gelling fibers made from highly absorbent polyvinyl alcohol fibers, abdominal pads, calcium alginate, foam dressings, and negative pressure wound therapy are effective at controlling draining nodules and fistulas. The bacterial colonization and biofilms present in HS^[36] may benefit from use of gentian violet and methylene blue, polyhexamethylene biguanide (PHMB) cationic antimicrobial dressings, surfactant micro-micelles, and dialkylcarbamoylchloride (DACC)-containing dressing fibers. Odor control is achieved by metronidazole gel 0.8%, oral metronidazole 200 mg TID, topical metronidazole powder, foam silver dressings, superoxide aqueous solution, and hypertonic saline dressings (Mesalt). Finally, pain was best managed with contact layers and non-adherent dressing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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