

Characteristics of inflammatory eye disease associated with hidradenitis suppurativa

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Abstract

Objective: Hidradenitis suppurativa (HS) is an inflammatory skin condition that can cause profound morbidity. Patients can present with recurrent nodules, sinus tract formation, abscesses, and/or scarring, mainly affecting the intertriginous areas. Case reports have documented the coexistence of HS and inflammatory eye disease (IED). Herein, we aimed to assess the types of IED associated with HS and the outcomes of IED treatment in patients with HS.

Methods: All the cases with a diagnosis of HS and any IED were identified. Patients with episcleritis and sicca were excluded, and only those with chronic IED were included. An independent ophthalmologist reviewed notes to ensure accuracy of IED diagnosis. Demographics, IED patterns, comorbidities, treatments, and outcomes were retrieved from patient charts.

Results: Twenty patients [16 females (80%); 12 African Americans (60%)] were included in this study after the exclusion of 436 cases due to lack of data. The mean age at the diagnosis of HS and IED was 42.1 and 43.6 years, respectively. Thirteen patients had uveitis (65%), six had scleritis (30%), and one had peripheral ulcerative keratitis. Thirteen out of 20 patients (65%) had multiple autoimmune and/or inflammatory comorbidities, including inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis, multiple sclerosis, and lupus. Seven patients (35%) did not have any comorbid inflammatory/autoimmune conditions.

Conclusion: One-third of the patients with HS and IED did not have any autoimmune or inflammatory comorbidity that could explain the eye involvement. The potential association between HS and IED might be a manifestation of a common immune dysregulation phenomenon. Furthermore, the management of IED required an escalation of therapy to systemic immunosuppressive agents in 70% of patients with HS.

Keywords: Hidradenitis suppurativa, inflammatory eye disease, uveitis, biologics



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Cite this article as: Saygin D, Syed AU, Lowder CY, Srivastava S, Maya JJ, Hajj-Ali RA. Characteristics of inflammatory eye disease associated with hidradenitis suppurativa. *Eur J Rheumatol* 2018; 5(3): 165-8.

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Submitted: 29 September 2017

Accepted: 9 February 2018

Available Online Date: 22 June 2018

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Introduction

Hidradenitis suppurativa (HS), also known as acne inversa and Verneuil's disease, is a chronic inflammatory skin condition that can profoundly impact the life of patients. It is a chronic follicular occlusive disease involving the follicular portion of folliculopilosebaceous units (FPSUs) of apocrine gland-bearing skin. Patients can present with recurrent nodules, sinus tracts formation, abscesses, and/or scarring. It mainly affects the intertriginous skin areas of the axillary, groin, perianal, perineal, and inframammary regions, although it can occur in any skin area that contains FPSUs (1, 2). The prevalence of HS has been reported to range from >1% to 4%. No racial predilection has been identified, but it has been found to be more common in women and obese patients and more severe in smokers (3, 4).

The pathogenesis of HS is not fully understood; however, it is believed that follicular occlusion, rupture, and the resultant immune response are important events in the development of the clinical manifestations of HS. Apart from the activation of the innate and adaptive immune systems in response to the release of antigens and other proinflammatory stimuli from a ruptured follicular duct, the role of immune system dysregulation in HS is thought to be similar to that in the pathogenesis of Crohn's disease (5).

An association between HS and several other inflammatory and genetic disorders have also been reported in the literature, including acne conglobata, spondyloarthropathies, pyoderma gangrenosum, synovitis-acne-pustulosis-hyperostosis-osteitis syndrome, Dowling-Degos disease, fox den disease, florid steatocysto-

ma multiplex, pyoderma vegetans, and pityriasis rubra pilaris (6-14). Of note, multiple case reports have documented the coexistence of HS and inflammatory eye diseases (IEDs), including peripheral ulcerative keratitis (PUK) and uveitis (15-1). The eye is a commonly affected organ in several systemic inflammatory diseases including Crohn's disease. Given that

HS is believed to be a disease with systemic immune dysregulation similar to Crohn's disease, IED may be a rare manifestation of HS. In this study, we sought to investigate the spectrum of IEDs in patients with HS and to describe the extent of eye involvement, diseases associated with IED, and treatment outcomes of IED in patients with HS.

Table 1. Characteristics of patients with concomitant hidradenitis suppurativa (HS) and inflammatory eye disease (IES)

	Mean (\pm SD) or Number of cases/ Total number of cases (%)
Mean age at diagnosis of HS, years	42.1 (\pm 11.9)
Mean age at diagnosis of IED, years	43.6 (\pm 12.5)
Gender (F/M)	16/4
Race (Caucasian/African American/Others)	7/12/1
IED pattern	
Scleritis	6/20 (30%)
Uveitis	13/20 (65%)
Peripheral ulcerative keratitis	1/20 (5%)
Associated comorbidities	
Inflammatory bowel disease	8/20 (40%)
Crohn's disease	5/20 (25%)
Ulcerative colitis	1/20 (5%)
Undifferentiated colitis	2/20 (10%)
Rheumatoid arthritis	2/20 (10%)
Systemic lupus erythematosus	1/20 (5%)
Ankylosing spondylitis	1/20 (5%)
Multiple sclerosis	1/20 (5%)

HS: hidradenitis suppurativa; IED: inflammatory eye disease

Methods

Patients

An electronic search was performed for patients visiting Cleveland Clinic between January 2005 and January 2016 with the International Classification of Diseases (ICD)-9 and 10 codes for HS (705.83) and IED (scleritis, uveitis, iridocyclitis, iritis, keratitis, and conjunctivitis).

This article does not involve any studies with human participants or animals that were performed by any of the authors. For this type of study, a formal consent is not required.

Study factors

A retrospective chart review was performed to identify demographics, IED patterns, associated conditions, treatments, and outcomes.

The remission was defined as inactive IED for at least 3 months without any steroid treatment. Approval from the institutional review board was obtained prior to initiating the study. Descriptive statistical analysis was performed us-

Table 2. Characteristics of the patients without a history of concomitant comorbid inflammatory disease

Case ID	Age at diagnosis of HS, years	Age at diagnosis of IED, years	Sex	Race	Type of IED	Laterality	Treatment	HS stage
1	41	53	Female	African-American	Iridocyclitis	Bilateral	Improved	II
2	52	59	Female	African-American	Anterior uveitis	Unilateral	Topical steroid → remission	I
3	49	56	Male	African-American	Scleritis	Unilateral	Topical steroid for 3 months → failed → 2 months of 60 mg daily prednisone → remission → topical steroid for 3 years → remission	I
4	38	41	Female	African-American	Scleritis	Unilateral	Topical steroid for 9 months → failure → 60 mg daily prednisone for 1 year → failure → adalimumab stopped due to financial problem	
5	37	33	Female	Caucasian	Scleritis	Unilateral	Topical steroid → improved	II
6	49	48	Female	Caucasian	Iritis	Unilateral	Methotrexate 10-15 weekly → not known Topical steroid → improved	
7	51	46	Female	Caucasian	Panuveitis	Bilateral	Topical steroid → improved	

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Table 3. Treatment of IED in patients with HS

Treatment	Remission rate ¹ (%)
Topical steroid	5/17 (29%)
Systemic steroid	1/7 (14%)
Infliximab	4/4 (100%)
Adalimumab ²	2/4 (50%)
Methotrexate	2/7 (29%)
Intraocular steroid injection	0/1

¹number of cases achieving remission/total number of patients who used the specified medication

²one of the two patients did not achieve remission with adalimumab and received only two doses because of rash and itching; the other patient used adalimumab intermittently for 3 years owing to financial issues

ing the JMP statistics software (JMP[®], Version 13. SAS Institute Inc.; Cary, NC, 1989-2007). Qualitative variables were described as measures of frequency.

Results

In total, 483 patients who had ICD-9 codes entered for both HS and any IED were identified. After a careful screening, 436 patients were excluded because of at least one of the following: episcleritis, keratoconjunctivitis, keratitis, conjunctivitis, corneal ulcers, hyphema, vitreous degeneration, vitreous hemorrhage, and retinal neovascularization. Additionally, 27 patients were excluded due to lack of data for re-assessment of IED diagnosis. A total of 20 patients with concomitant IED and HS were identified and included in this study. The study population included 16 female (80%) and 4 male patients (20%) with a majority of them being African American (12 African Americans, seven Caucasians, and one Asian; Table 1). HS was diagnosed before the IED in 11 out of 20 patients (55%). The mean age at HS diagnosis was 42.15 years, whereas the mean age at IED diagnosis was 43.65 years.

Out of the 20 patients with concomitant IED-HS, 13 had uveitis (65%), six had scleritis (30%), and one had PUK. Of note, 13 out of the 20 patients (65%) had multiple autoimmune and/or inflammatory comorbidities (Table 1). Forty percent of the patients had inflammatory bowel disease (IBD). One patient had both Crohn's disease and psoriasis. Further, two patients had undifferentiated IBD in association with other diseases such as common variable immunodeficiency and lymphoma. Two of the 20 cases (10%) with concomitant IED-HS were diagnosed with rheumatoid arthritis. Other associated diseases included multiple sclerosis

in one patient, systemic lupus erythematosus in one patient, and ankylosing spondylitis and common variable immunodeficiency in one patient (Table 1). Seven patients (35%) did not have any concomitant, comorbid inflammatory/autoimmune condition (Table 2).

Most of the patients (85%) were on topical steroids for IED management (Table 3). Forty percent of them were on tumor necrosis factor (TNF) inhibitors, 35% were on methotrexate, and 35% were on systemic steroids. Intraocular steroid injection was used in one patient (5%). All the cases that were treated with infliximab (3/3) were found to achieve remission. Two out of four cases achieved remission with adalimumab. Two patients on adalimumab did not achieve remission; one patient had to stop the medication due to bacteremia after 1 month, and the other patient had irregular injections and had to stop adalimumab due to financial problems. Systemic steroids, topical steroids, and methotrexate had 14%, 29%, and 29% remission rates, respectively. One patient receiving intraocular steroid injection did not achieve remission (Table 3).

Discussion

In this study, we demonstrated the spectrum of IEDs that can be encountered in patients with HS. Majority of these patients had other systemic autoimmune and/or inflammatory diseases besides HS that could explain the presence of IED; however, 35% of the patients did not have any other concomitant, chronic systemic disease. We believe that this finding supports the hypothesis of a common pathogenic link between IED and HS.

Uveitis was the most prevalent form of IED in patients with HS, which was followed by scleritis and then PUK. IBD, particularly Crohn's disease, was the most prevalent disease among these patients. As expected, other inflammatory conditions were also seen in this cohort, including sarcoidosis, rheumatoid arthritis, ankylosing spondylitis, and systemic lupus erythematosus, all of which have a clear association with IED.

Consistent with our results, HS has been reported to be associated with Crohn's disease in literature (18). The pathogenic link between the two diseases remains unclear; however, there are some clinical and pathogenic similarities in these diseases. First, the studies performed in patients with familial HS showed impaired Notch signaling, which appears to suppress Toll-like receptor 4-triggered proinflammatory, macrophage cytokine expression, which in

turn may explain the excessive proinflammatory cytokine production [TNF- α , interleukin (IL)-1b, and IL-23] seen in some forms of HS (19, 20). Similarly, the pathogenesis of Crohn's disease involves several hypotheses, including disruption of mucosal barrier with environmental stimuli; activation; proinflammatory cytokine release; and excessive retention of macrophages, neutrophils, and T cells as well as dysbiosis (21). Clinically, Crohn's disease is a systemic, inflammatory disease with cutaneous, articular, and ocular manifestations. Both HS and Crohn's disease occur in body areas rich in bacteria, are characterized by chronic inflammation, can be treated with antibiotics and TNF inhibitors, and may cause squamous cell carcinoma as a long-term complication. With this study, we showed that IED may be seen in patients with HS, similar to Crohn's disease.

Regarding therapy, topical steroids are typically considered as the first-line treatment for IED. However, in this cohort with HS, most patients did not achieve remission with topical treatment. The escalation of the therapy with systemic immunosuppressive agents was often necessary. The anti-TNF- α therapy is of particular interest considering their higher rate of remission in this study group. Apart from this, several of these patients also experienced an improvement in the HS symptoms with immunosuppressive therapy.

Although our study has some strengths, it also has multiple limitations; our cohort represented a small number of patients, and additional studies with higher number of patients are necessary to confirm the possible association of HS and IED and the long-term outcomes of IED treatment in patients with HS. Secondly, the retrospective nature of this study precluded the documentation of skin response to immunosuppressive medication. Lastly, the low number of patients treated with anti-TNF agents preclude any strong recommendation for these agents in the treatment of IED in patients with HS but do indicate that there is a therapeutic potential in this particular group.

In conclusion, this study expands on previously limited case reports. Ultimately, clinicians should be aware of a possible association between HS and IED, which might also be a manifestation of an immune dysregulation phenomenon.

Ethics Committee Approval: N/A.

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - J.J.M., R.A.H., C.Y.L., S.S.; Design - R.A.H., C.Y.L., S.S.; Supervision R.A.H.; M.A., Ö.T.Y., T.S.; Data Collection and/or Processing - R.A.H., C.Y.L., S.S.; Analysis and/or Interpretation - A.U.S., D.S., J.J.M.; Literature Search - A.U.S., D.S.; Writing Manuscript - A.U.S., D.S.; Critical Review - R.A.H.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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