Hydroxychloroquine for the treatment of hidradenitis suppurativa

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Key words: acne inversa; antimalarial; case series; hidradenitis suppurativa; hydroxychloroquine; treatment.

BACKGROUND

Hidradenitis suppurativa (HS) is a debilitating and mutilating disease, and its pathogenesis is still poorly understood. It involves the development of recurrent, painful nodules in intertriginous areas that become inflamed, form abscesses that may rupture, and develop chronic fistula tracts. The cause of HS is thought to be multifactorial and may begin with follicular occlusion and rupture, leading to a cascade of inflammatory responses in susceptible individuals. The disease has been associated with high body mass index, smoking, and genetic predisposition. There is a known association between HS and the metabolic syndrome, an association that remains after controlling for body mass index.[1] HS predominantly affects women and ethnic minorities,[2,3] and the prevalence is thought to be as high as 2%, although embarrassment and lack of awareness may lead to underestimation of the true burden of the disease. Consent for the publication of all patient photographs and medical information was provided by the authors at the time of article submission to the journal stating that all patients gave consent for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available.

Although HS is a fairly common disease, relatively little is understood about its pathogenesis. Immune dysregulation is thought to play a role in disease development. Increased levels of interleukin (IL)-12, IL-17, IL-23, tumor necrosis factor-α, IL-10, and IL-1β were found to be expressed in lesional skin of patients with HS.[4,5] Recent studies have also identified elevated levels of IL-17 in the serum of patients with HS.[6]

Abbreviations used:

HS: hidradenitis suppurativa
IL: interleukin

HS is associated with a significant impact on patients' quality of life.[7] Patients experience both the physical and psychological impact of the disease. Many therapies have been used to treat HS, from topical antibiotics to oral retinoids to radical surgeries; however, all have limited efficacy. Despite efforts to control disease, many patients live with chronic wounds and disability. The decision about appropriate therapy for HS, especially in the early stages, is mainly based on expert opinion, anecdotal evidence, and small studies. Topical and systemic antimicrobial treatments are often used as first-line therapies, although studies have repeatedly shown that abscesses of HS are sterile or contain only normal flora. The mechanism of improvement with antimicrobials may be through alterations in the local microbiome. Significant improvement in disease has been seen with dual therapy with twice-daily use of 300-mg rifampicin and 300-mg clindamycin,[8] neither of which have a Food and Drug Administration indication for use in HS. Doxycycline is used frequently in HS; however, little evidence supports this. Despite success with the above therapies, the risk of antimicrobial resistance is real and increased with frequent and prolonged use of these medications in patients with HS.[9] Teratogenic effects, gastrointestinal upset, and photosensitivity with the use of tetracyclines, the risks of *Clostridium difficile* colitis with clindamycin and antimicrobial resistance

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Funding sources: None.
IRB approval status: Approved.

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JAAD Case Reports 2023;37:64-7.
2352-5126

https://doi.org/10.1016/j.jdcr.2023.05.017

with rifampicin highlight a need for safer and more effective therapeutic options for the treatment of early HS.

For more advanced disease (Hurley stage II and III), the tumor necrosis factor inhibitor adalimumab is the only Food and Drug Administration–approved biologic treatment option for HS. It has shown promise in severe disease; however, only ~50% of patients achieved a clinical response at 12 weeks, and this clinical response declined over time.[10] Additionally, newer biologic therapies have been used in small numbers of patients with HS, with variable results. Although biologic treatments can have a tremendous benefit, they come with a high cost, and this can limit accessibility.

Hydroxychloroquine, initially developed as an antimalarial, has been used successfully for >70 years in the treatment of autoimmune disease. Its mechanism of action is still poorly understood; however, it has been shown to have many varied immunomodulatory properties.[11] Evidence has suggested that hydroxychloroquine has an effect on inflammatory disease through decreasing levels of TNF-α[12] and Th-17 cytokines (including IL-6, IL-17, and IL-22).[13] Additionally, studies have shown a beneficial effect of hydroxychloroquine on lipid metabolism and glucose.[14] Patients with rheumatoid arthritis (which, similar to HS, has an independent association with cardiovascular disease) who were treated with hydroxychloroquine had an overall decreased incidence of cardiovascular events.[15] Hydroxychloroquine has a relatively benign safety profile, with retinopathy being the most concerning long-term side effect. The retinopathy caused by hydroxychloroquine is reversible if identified early, and standard protocols for the use of this medication include yearly ophthalmologic examinations.

The objective was to evaluate the feasibility and efficacy of hydroxychloroquine as a treatment option for HS.

METHODS

This was an institutional review board–approved clinical trial. Sequential patients with HS who presented to the Department of Dermatology, University of Pittsburgh, were enrolled. Treatment included 200-mg of hydroxychloroquine twice daily for 6 months. Patients were evaluated at baseline and at 3 and 6 months using Hurley staging (I-III), Sartorius scoring, and the Dermatology Life Quality Index (DLQI) survey. Patients were allowed to continue topical therapies during treatment; however, no other oral or injectable HS treatments could be used. Participants had to be 18 years of age and had to be able to understand written informed consent. Patients could not have evidence of active infection, regardless of the degree of severity or localization. Patients with porphyria cutanea tarda, known retinal disease, psoriasis, or thrombocytopenia were excluded. Comparisons were to be performed using the 2-sided *t* test, with a *P* value of <.05 for statistical significance.

RESULTS

A total of 17 patients were enrolled in the trial. The average age of the patients enrolled was 39 years. Of those enrolled, 82% were women, 82% of were Caucasians, and 18% were Black. The mean age of onset was 25 years, with a standard deviation of 13 years, and the mean duration to diagnosis was 8.4 years.

Nine patients were Hurley stage I, 5 were stage II, and 3 were stage III. The mean baseline Sartorius score was 23.3 ± 16.3. The mean baseline DLQI scores were 14.7 ± 11. Of the patients, 47.1% were current everyday smokers, 41.1% were never smokers, and 11.8% were former smokers. Eight patients had a family history of HS, 8 patients had a history of acne, 6 patients had a history of pilonidal cyst, and no patients had a history of dissecting cellulitis of the scalp.

Prior treatments included the following: 70.6% doxycycline, 35.3% oral clindamycin alone, 5.9% rifampin alone, 5.9% oral clindamycin/rifampin combination, 5.9% adalimumab, 17.6% isotretinoin, 58.8% chlorhexidine wash, 23.5% minocycline, 52.9% topical clindamycin, 47% incision and drainage, 29.4% excision, 11.8% spironolactone, 5.9% azithromycin, 5.9% benzoyl peroxide wash, 5.9% intralesional triamcinolone, 5.9% trimethoprim-sulfamethoxazole, and 5.9% zinc.

At the 3-month follow-up, 7 patients were still on treatment, 3 were Hurley stage II, and 4 were Hurley stage I. Three patients were still on treatment at the 6-month follow-up, 2 were Hurley stage II, and 1 was Hurley stage I. The reasons for medication discontinuation included blurred vision, no improvement in disease, nausea, headache, hives, and depressed mood. Seven patients were lost to follow-up.

Response to hydroxychloroquine

Given the small size of our study and high dropout rate, it is difficult to perform statistical analysis on our data. Using data from those who continued in the trial, however, there was a strongly downward trend in both mean DLQI (from 14.7 ± 11 to 4.4 ± 5.2) and Sartorius score (from 23.3 ± 16.2 to 13 ± 6.6) from the baseline to 3 months. From the baseline to 6 months, the mean DLQI changed from

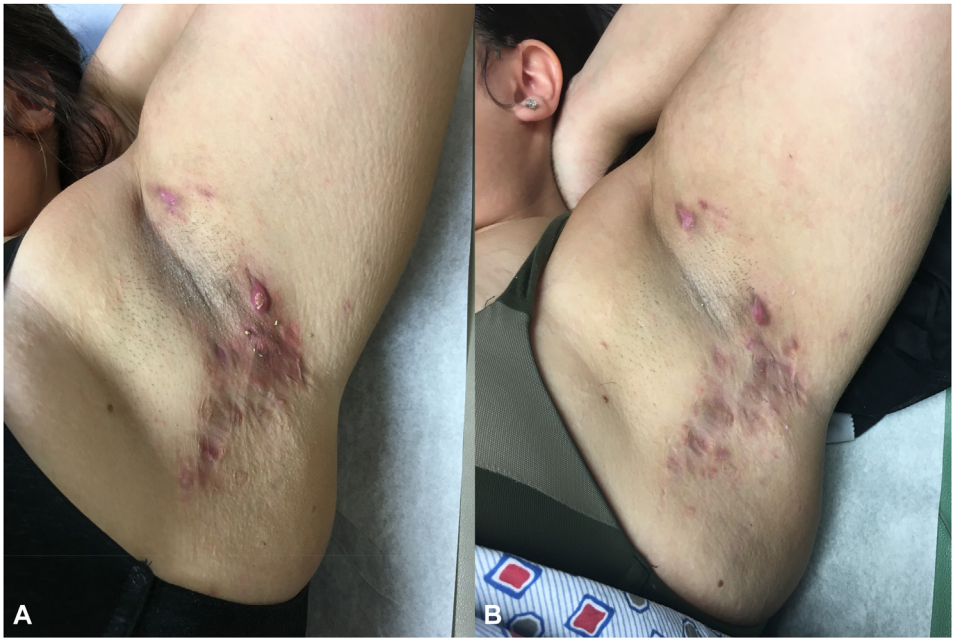

Fig 1. A, Patient disease at baseline. **B,** Patient disease after 6 months of treatment with hydroxychloroquine.

14.7 ± 11 to 6 ± 7.9 and mean Sartorius score decreased from 23.3 ± 16.2 to 17.6 ± 14.4, based on 3 patients who completed the trial (Fig 1).

No persistent side effects were associated with treatment with hydroxychloroquine in the 6 months of the study or the 6-month follow-up period.

The limitations were small sample size, open-label study, and no placebo control.

CONCLUSION

The cost, availability, and dearth of treatment options for HS are tremendous barriers to the management of this disease. Hydroxychloroquine is a widely available and inexpensive treatment with low toxicity. Although this was a small case series, there was a trend toward improvement in DLQI and Sartorius scores. Larger studies are required to determine the true efficacy of this treatment. However, our results suggest that hydroxychloroquine is an accessible alternative or adjunctive treatment option for patients with any stage of disease. It could also potentially be used as a bridge to other therapies while awaiting necessary laboratory testing and insurance approval.

Conflicts of interest

None disclosed.

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