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Management of mild hidradenitis suppurativa: our greatest challenge yet

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Hidradenitis suppurativa (HS) is a debilitating, chronic, inflammatory disease originating from hair follicles.[1] When thinking of this disease, images of a patient with extensive tunnel formation and continuous foul-smelling drainage spring to mind. The immense impact on the quality of life of these patients is evident. These images have been the driving force behind increasing scientific interest in this disease over the past 10 years, resulting in one approved biologic (adalimumab) and multiple ongoing clinical trials for patients with moderate-to-severe disease.

However, according to the most commonly used severity classification (Hurley stage), the majority of patients (70%) do not fit into that image, instead having mild disease consisting of recurrent nodules and abscesses (Hurley 1), rather than tunnel formation (Hurley 2/3), which 30% of patients have.[1] Even though the majority of patients present with limited disease this does not mean there is only minor impact on their quality of life.[2] A recent study has shown that in patients with HS classified as mild according to Hurley stage the disease can have a similar impact on quality of life to those classified as have moderate or severe HS depending on the number of active lesions.[2] Even a single abscess can cause extreme pain and impair physical functioning, and have a large psychological impact. In addition, as HS usually starts around 20 years of age and often only gradually fades away after the age of 50 years, even patients with mild HS have to cope with unpredictable, active disease for $\geq$ 30 years.[1]

Nonetheless, this group with clinically mild disease, the majority of patients with HS, are clearly missing out on the scientific advancements. Only a limited number of treatment options are currently available to treat these patients. Current guidelines advocate only the use of topical clindamycin or recurrent courses of oral antibiotics for mild disease.[1] However, none of these treatment options achieves the targets that either physicians or patients desire: prolonged disease remission and prevention of disease progression. This is especially striking as preventing disease progression and the development of tunnel formation could spare patients large, impactful surgeries. In addition, frequent courses of antibiotics for a period of 30 years of active disease are highly undesirable due to bacterial resistance. Treatment of mild HS should ideally reach the aforementioned targets while having limited side-effects, be relatively low cost, and be suitable for long-lasting use. Potential treatment options that could meet these criteria, now or in the future, are oral metformin, definitive depilation, oral or topical retinoids, and adalimumab or other biologics. However, to date none of these has been adequately assessed in mild HS.

This is understandable as assessing the effectiveness of these potential treatments in mild disease raises a whole new challenge: the primary outcome measure. The current gold standard Hidradenitis Suppurativa Clinical Response (HiSCR) and the internationally accepted International Hidradenitis Suppurativa Severity Score System (IHS4) are unsuitable for clinical trials in mild HS. HiSCR by definition requires at least three nodules or abscesses, which are often not present at one timepoint in patients with mild disease.[3] In contrast, the IHS4, which was created by an international consortium of HS specialists, can in essence be calculated from only one lesion.[4] Even though the IHS4 works reasonably well in moderate and severe HS with higher IHS4 scores, the lower the scores (mild patients are deemed those with an IHS4 score $\leq$ 3) the more difficult it is to find a statistically significant difference between scores at different timepoints. Additionally, mild HS is characterized by a strong waxing and waning of nodules or abscesses and it is not uncommon to find no active lesions during physical examination. Therefore, providing patients with mild HS with scientifically proven effective treatments will require a different way of thinking about outcome measures and treatment targets. More meaningful outcomes in this patient group could be the number of flares over a period of time or the cumulative abscess–nodule count in that period. However, the lack of a specific and measurable definition of HS flare is still a barrier.[5]

This perspectives letter serves as a call to action for both researchers and pharmaceutical companies to invest in the largest group of patients with HS. This group of patients with mild HS is currently overlooked but deserves our help. We need to find effective treatment options for this group, and in order to achieve this goal we will need to develop new outcome measures. Adequate treatment of mild HS might be our greatest challenge yet.

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