Skin Appendage Disorders

Novel Insights from Clinical Practice

Skin Appendage Disord 2022;8:342–345
DOI: 10.1159/000521860

Received: November 4, 2021
Accepted: December 29, 2021
Published online: February 9, 2022

An Anti-Interleukin-17A Monoclonal Antibody, Ixekizumab, in the Treatment of Resistant Hidradenitis Suppurativa: A Case Series

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Established Facts

- Hidradenitis suppurativa is a chronic and relapsing inflammatory skin disease of the hair follicles, negatively impacting patients' quality of life.
- Recent advances in disease pathogenesis have expanded our understanding of elevated levels of several pro-inflammatory cytokines, including serum levels of IL-17.
- Recently, inhibition of pathogenic IL-17 blockade has shown promising results in isolated case reports.

Novel Insights

- Ixekizumab may be effective for hidradenitis suppurativa, even in adalimumab-resistant cases.

Keywords
Hidradenitis suppurativa · Biologic · Adalimumab · Ixekizumab · IL-17

Abstract

Introduction: Although adalimumab is the only approved biologic for the treatment of hidradenitis suppurativa (HS), the treatment response may not be satisfactory in all patients. Recently, many other biological agents, including interleukin 17 inhibitors such as ixekizumab, have shown promise. ***Case Presentations:*** Five severe HS (Hurley stage III) patients resistant to conventional treatments and adalimumab for at least 3 months were recruited. Patients were prescribed ixekizumab with a scheme approved for psoriasis (160 mg once, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12.) The primary outcome measure was achieving the Hidradenitis Suppurativa Clinical Response (HiSCR) score following 12 weeks. Secondary outcome measures included the patient-reported Dermatology Life Quality Index (DLQI) and visual analog scale (VAS). Four of 5 patients (80%) achieved HiSCR. While improvement was observed in the VAS and DLQI scores of 4 patients, the decline was limited in 1 patient. No adverse event was recorded related to ixekizumab. ***Conclusion:*** The result of our observation suggests that ixekizumab may be effective for HS, especially in challenging cases.

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Introduction/Literature Review

Hidradenitis suppurativa (HS) is a severe and debilitating skin disease characterized by painful subcutaneous nodules in intertriginous areas. The clinical course and disease severity are highly variable with substantial negative impacts on quality of life. Although numerous therapeutic approaches exist to treat HS, clinical management is still quite challenging, with existing therapies having limited efficacy [1].

Although the pathogenesis of HS has not been fully elucidated, aberrant expression of pro-inflammatory cytokines such as tumor necrosis factor, interleukin (IL)-1β, and IL-17 play a central role [2, 3]. Adalimumab is the only approved biologic for the treatment of HS; many other biological agents, including IL-17 inhibitors, appear promising [4, 5]. There are case reports of HS improved with ixekizumab [6–8]. We present the clinical characteristics and the course of 5 HS patients treated with 12 weeks of ixekizumab.

Case Presentations

Severe HS patients resistant to conventional treatments and adalimumab for at least 3 months were recruited. Off-label use of ixekizumab (Copellor®) was considered and discussed with the patients. Ixekizumab was used with a scheme approved by the US Food and Drug Administration for psoriasis (160 mg once, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12.) The primary outcome measure was achieving the Hidradenitis Suppurativa Clinical Response (HiSCR) score following 12 weeks. Secondary outcome measures included the patient-reported Dermatology Life Quality Index (DLQI) and visual analog scale (VAS).

All patients were Hurley III previously treated with adalimumab (Table 1). Four of 5 patients (80%) achieved HiSCR (2 patients at week 8 and the other 2 at week 12; Table 1; Fig. 1). One patient (patient 1) was unresponsive, and treatment was stopped at the 12th week due to lack of effectiveness and increased discharge. While improvement was observed in the VAS and DLQI scores of 4 patients, the decline was limited in patient 1 (Table 1). No serious adverse events such as new-onset inflammatory bowel disease or candidiasis were recorded due to the use of ixekizumab.

Discussion

Although weekly adalimumab is effective for HS, approximately 40–60% of patients do not achieve benefit after 3 months of treatment, indicating primary treatment failure [9]. Considering the additional secondary failure in the following period, there is still a huge unmet need for HS treatments.

The IL-17 pathway has been implicated as a potential therapeutic target in HS, prompting clinical trials with various IL-17 inhibitors (secukinumab, brodalumab, and ixekizumab) [4]. While data are increasing regarding secukinumab and brodalumab, the literature on ixekizumab is limited [4, 6–8]. Ixekizumab, a humanized monoclonal immunoglobulin G 4 antibody, specifically binding to IL-17A, is very effective in treating moderate to severe psoriasis [4]. We found 3 case reports of ixekizumab for HS.

Table 1. Clinical characteristics and medical history of the patients and their responses to ixekizumab

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gender/age	M/53	M/34	M/29	M/47	M/56
Hurley stage	III	III	III	III	III
Disease duration, years	6	4	10	18	20
Diagnostic delay, months	24	36	84	120	180
Smoking history, packet-years	10	15	16	10	20
Medical comorbidities	–	–	–-	HT, DM	HT, DM
Previous treatments, weeks					
Adalimumab	12	24	24	36	108
Certolizumab pegol	–	–	–	–	48
Rifampicin-clindamycin	12	10	–	10	12
Antibiotics (≥3 cycle)	+	+	+	+	+
Achieved HiSCR, week	–	12	8	12	8
DLQI					
Baseline	16	21	24	18	18
Week 12	10	12	9	8	10
VAS					
Baseline	10	9	10	9	10
Week 12	8	4	2	3	3

DM, diabetes mellitus; HT, hypertension.

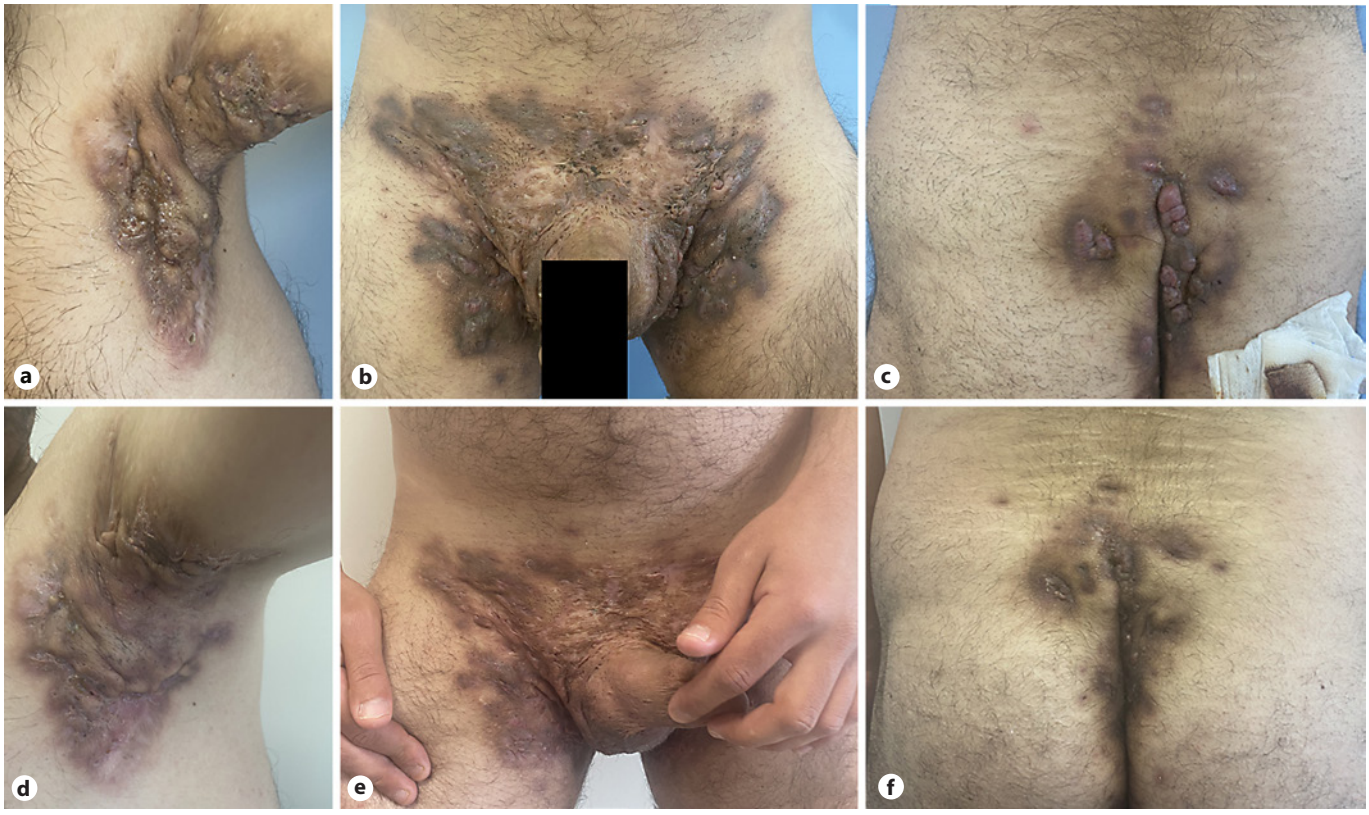

Fig. 1. Clinical appearance of the affected area before and after treatment. A 29-year-old male patient had Hurley stage 3 HS. Before treatment, there were deep swollen inflamed nodules and abscesses, draining sinus tracts, and hypertrophic scar areas in the axilla, inguinal, and perianal regions (**a–c**). After 8 weeks of ixekizumab treatment, there was a reduction in the lesions' inflamed, plump, and discharged appearance (**d–f**). The patient achieved a HiSCR response at week 8.

Detailed information about one of them could not be accessed [6]; in one of the cases, severe HS lesions were unresponsive to adalimumab and improved with 12-week ixekizumab treatment [8]. In the other case, it was reported that simultaneous severe psoriasis and mild HS lesions improved with the standard psoriasis dose of ixekizumab [7]. Our findings also support the potential effectiveness of ixekizumab as a treatment for HS, especially in challenging cases that were not under-controlled with adalimumab.

Statement of Ethics

The local ethics committee provided ethical clearance and approval. Written informed consent was obtained from participants to publish the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors have received no external funding.

Author Contributions

Pelin Esme and Ercan Caliskan: conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; and final approval of the version to be published. Aysenur Botsali: conception or design of the work and the acquisition, analysis, or interpretation of data for the work. Gulsen Akoglu: conception or design of the work; drafting the work or revising it critically for important intellectual content; and final approval of the version to be published.

Data Availability Statement

Data are available on request from the authors.

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