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CASE REPORT

Long-Term Efficacy of Guselkumab in an Adolescent Hidradenitis Suppurativa Patients: A Case Report

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Abstract: Managing HS has long posed a significant challenge for dermatologists. Adalimumab stands as the sole biologic drug sanctioned for HS, receiving approval in 2015 as an anti-tumor necrosis factor (TNF)-α drug. Real-life evidence over the years has debated its efficacy, suggesting a success rate hovering around 70%. However, the variability in existing treatments and the chronic-recurrent nature of the condition make its treatment and management exceedingly challenging. Hence, identifying new therapeutic targets for HS in the future becomes imperative. Recently, on October 31, 2023, the FDA approved secukinumab for moderate-severe HS, marking a significant development. There has been substantial discourse on the potential of anti-interleukin-23 drugs as new therapeutic avenues for treating HS in recent years. Here, we report a case of 17-year-old man successfully treated with Guselkumab. The results were confirmed at week 52.

Keywords: hidradenitis suppurativa, anti-IL23, guselkumab, adalimumab, secukinumab

Introduction

Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent, and disabling skin condition that affects hair follicles. It is characterized by painful lesions affecting areas of the body where apocrine glands are present.[1,2] While the precise underlying pathogenic mechanism of HS remains uncertain, initial follicular hyperkeratosis within the pilosebaceous-apocrine unit is considered the primum movens. Recent studies have provided new insights into the role of pro-inflammatory cytokines in HS pathogenesis, helping to address some existing gaps in our understanding of the development of this condition.[3,4] To date, the first FDA-approved biologic drug for HS is adalimumab, an anti-tumor necrosis factor (TNF)-α approved in 2015. Several real-life studies have highlighted a mean clinical success rate of approximately 70%.[5,6] However, primary or secondary lack of efficacy may occur.[7–10] Secukinumab, an anti-interleukin 17A drug approved for moderate to severe psoriasis and psoriatic arthritis (PsA), has shown promising results in clinical trials by improving signs and symptoms of HS with a good safety profile, maintaining a positive response for up to 52 weeks.[11] Even a few real-life data already align with these studies.[11] Recently, the European Commission (EC) approved secukinumab for use in adults with active moderate to severe HS,[12] while FDA approval was granted just a few months ago (October 31, 2023). Managing HS still remains challenging due to the variable outcomes of available treatments, and its chronic-recurrent nature; there is a huge need of new therapeutic targets for HS in order to take control of the disease in long-term. In this context, significant attention has been directed toward understanding the role of anti-IL-23 drugs in treating HS, thanks to the real-life studies and experiences recently published in literatures. Presently, there are three Phase 2 studies investigating these drugs alongside several case studies and case series, showcasing highly variable outcomes[12] Indeed, different drugs with diverse mechanism of action are being tested for HS (eg spesolimab, porvocitinib and bimekizumab).[13–15]

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Case Report

Here, we report a case of 17-year-old man affected by HS since 3 years presenting nodules and fistulous routes in the axillary cavity, inguinal region, and on the buttocks (Hurley stage II, IHS4 16) (Figure 1A–C). His medical history was unremarkable except heart failure (NYHA1) related to surgery performed in childhood for a congenital atrial shunt. His family history was negative for inflammatory disease except for Crohn's disease (father). The patient had already been on several courses of antibiotics with rifampicin (600 mg) and clindamycin (600 mg) for up to 8 weeks or tetracyclines up to 8 weeks without receiving substantial benefit. Hence, we decided to start Guselkumab following the dosing for adult psoriasis, 100 mg at week 0 and week 4 followed by a maintenance dose every 8 weeks[16–18] avoiding adalimumab and secukinumab due to possible contraindications (heart failure and Crohn's disease familiarity, respectively). At week 16 HiSCR (Hidradenitis Suppurativa Clinical Response) was achieved (IHS4 6), lesions were reduced in both numbers and soreness, and there was no need to add antibiotic and/or cortisone therapy for management of recurrence or inflammation. The results were confirmed at week 52 (IHS4 5) (Figure 1D–F). The patient had no adverse events for ongoing therapy.

Discussion

Guselkumab, a human monoclonal immunoglobulin G1 (IgG1) lambda antibody targeting IL-23, has obtained approval for treating moderate-to-severe plaque psoriasis and PsA. Extensive studies in both psoriasis and PsA have demonstrated the efficacy and safety of this drug in long term.[19,20] The literature also includes several reports concerning HS, specifically encompassing two recent phase 2 studies and multiple case reports or series. Dudink et al[21] conducted a 24-week open-label, multicenter, phase IIa trial, enrolling 20 patients and divided into 16 weeks of treatment followed by an 8-week follow-up. The primary endpoint was achieving HiSCR at week 16. Approximately 65% of patients (13 out of 20) reached HiSCR, while 35% (7 out of 20) attained a 75% improvement in HiSCR. The authors concluded that while guselkumab demonstrated effectiveness in specific subtypes of HS patients, IL-23 inhibition might not be central to HS pathophysiology. Kimball et al[22] conducted a phase 2, multicenter, randomized, placebo-controlled, double-blind study with 184 enrolled patients. The trial spanned 36 weeks and comprised four arms: guselkumab, intravenous guselkumab, guselkumab from weeks 12 to 36, and a placebo group. Primary endpoints included HiSCR at weeks 16 and 40, with

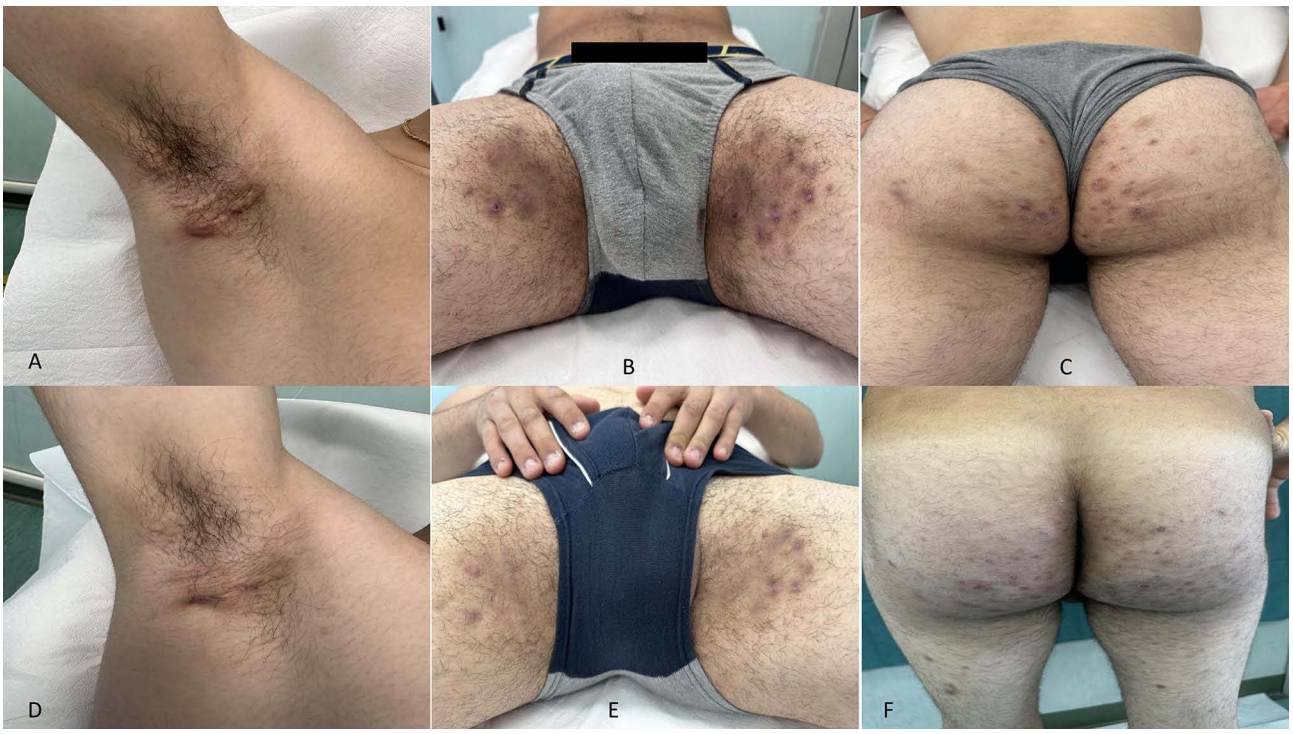

Figure 1 (A–C) Patient at baseline (**D–F**) Patient after 52-week of treatment with Guselkumab.

a follow-up four weeks after treatment cessation. Secondary endpoints involved IHS4 and AN count at these same time points. While guselkumab sc or guselkumab iv demonstrated numerically higher HiSCR rates versus the placebo at Week 16 (50.8%, 45.0%, 38.7% respectively), statistical significance was not reached. These trends persisted at week 40, leading the authors to conclude that guselkumab did not demonstrate efficacy, as the primary endpoint was not met. More encouraging data come from real life experiences with case reports and case series; Casseres et al[23] performed a retrospective chart review involving 8 patients, comprising 4 with Hurley stage III and 4 with Hurley stage II, all of whom had previously experienced treatment failure with adalimumab, secukinumab, ustekinumab, and ixekizumab. The authors observed improvement in 5 patients (63%) following 4 months of therapy, although specific score data detailing the improvement were not provided. Vilchez et al[24] presented a case series involving 4 patients undergoing treatment with guselkumab at a dosage of 100 mg administered every 4 weeks. These patients had prior exposure to adalimumab, secukinumab, or ustekinumab. The authors documented a moderate reduction in IHS4, VAS for pain, and DLQI after 12 weeks of treatment.[24] Kovac et al[25] documented a case series involving 3 patients, among whom 2 had previously experienced treatment failure with adalimumab, while the third patient could not receive adalimumab due to cardiovascular concerns. At week 12, all patients were evaluated using IHS4, DLQI, and VAS pain scales. Prior to treatment, the mean IHS4 stood at 21.3, which decreased to 9.3 after 12 weeks of treatment. The authors also noted reductions in DLQI scores and VAS ratings.[25] Certainly, the reports discussing paradoxical HS reactions effectively managed with guselkumab are highly significant.[26–30] They underline the potential utility of this drug, particularly within specific patient subgroups, such as those experiencing paradoxical HS. This data further emphasizes the drug's efficacy in addressing certain subsets of patients grappling with this condition.[26–30]

Other experiences of individual case reports where patients had other comorbidities have been described in the literature where the role of guselkumab in HS is confirmed by presenting good results.[31–33]

In conclusion, certainly among the anti-IL23 drugs, guselkumab has the most numerous reports regarding HS. In recent years, considerable discussion has revolved around the role of IL-23 in this pathology. Several published papers have detailed how the IL23/TH17 pathways might contribute to the pathogenesis of HS. This is notably evidenced by the overexpression of IL-23 in lesions observed in HS patients, coupled with increased serum levels of IL-23 among individuals affected by HS.[31–36]

Conclusion

New knowledge on HS pathogenesis is leading to the development of new selective and effective drugs, with a high profile in terms of safety. To best of our knowledge we report the first case of an adolescent under 18 years old with HS who was successfully treated with guselkumab in long term (52 weeks) in a patient naïve to Adalimumab and Secukinumab; the real limitation of this case is the presence of only one patient reported so this certainly can provide an encouraging finding for the literature by opening new scenarios with new large-scale studies.

Data Sharing Statement

Data are reported in the current study and are on request by corresponding author.

Patient Consent

Written informed consent for publication was obtained from the mother and father of the patient. Parental informed consent includes publication of the images.

Author Contributions

All authors (F.M., T.B., L.P., A.P., N.T. and M.M.) made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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