

Recalcitrant Folliculitis Decalvans Treatment Outcomes With Biologics and Small Molecule Inhibitors

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PRACTICE POINTS

- Tumor necrosis factor inhibitors, Janus kinase inhibitors, phosphodiesterase 4 inhibitors, and monoclonal antibodies have shown success in the treatment of folliculitis decalvans resistant to traditional therapies.
- The true etiology of folliculitis decalvans is still unknown, but possible factors include *Staphylococcus aureus* infection and an impaired host immune system, which may benefit from treatment with biologics and small molecule inhibitors.

Folliculitis decalvans (FD) is a rare primary neutrophilic cicatricial alopecia that commonly displays resistance to traditional therapies and remains challenging to treat. Currently, data are lacking with recommendations for therapy-recalcitrant FD. A systematic review was conducted to analyze biologics, small molecule inhibitors, tumor necrosis factor (TNF) inhibitors, Janus kinase (JAK) inhibitors, phosphodiesterase 4 (PDE4) inhibitors, and monoclonal antibodies utilized in the treatment of recalcitrant FD.

Folliculitis decalvans (FD) is classified as a rare primary neutrophilic cicatricial alopecia occurring predominantly in middle-aged adults. Although the true etiology is still unknown, the pathogenesis behind the inflammatory follicular lesions stems from possible *Staphylococcus aureus* infection and an impaired host immune system in response to released superantigens.¹

The clinical severity of this inflammatory scalp disorder can range from mild to severe and debilitating. Multiple treatment regimens have been developed with the goal of maintaining full remission. We provide a summary of tumor necrosis factor (TNF) inhibitors, Janus kinase (JAK) inhibitors, phosphodiesterase 4 (PDE4) inhibitors, and monoclonal antibodies being utilized for patients with therapy-recalcitrant FD.

Methods

We conducted a PubMed, Medline, and Google Scholar search for the terms *refractory FD*, *recalcitrant FD*, or *therapy-resistant FD* to identify articles published in English from 1998 to 2022. Articles that reported recalcitrant cases and subsequent therapy with TNF inhibitors, JAK inhibitors, PDE4 inhibitors, and monoclonal antibodies were included. Articles were excluded if recalcitrant cases were not clearly defined. Remission was defined as no recurrence in lesions or pustules or as a reduction in the inflammatory process with stabilization upon continuation or discontinuation of the therapy regimen. Two reviewers (T.F. and K.U.) independently searched for and screened each report.

Results

Treatment of recalcitrant FD with biologics or small molecule inhibitors was discussed in 9 studies with a combined total of 35 patients.²⁻¹⁰ The treatment regimens included TNF inhibitors, JAK inhibitors, PDE4 inhibitors, and monoclonal antibodies (Table).

The TNF inhibitors were utilized in 6 reports with a combined total of 29 patients. Treatments included

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Biologics and Small Molecule Inhibitors for Therapy-Recalcitrant Folliculitis Decalvans

Reference (year)	Treatment	No. of patients	Prior treatment	Outcome
TNF inhibitors				
Shireen and Sudhakar ² (2018)	Biosimilar adalimumab	1	Antibiotics, antifungals, corticosteroids	Remission
Iorizzo et al ³ (2022); Kreutzer and Effendy ⁴ (2014); Alhameedy and Alsantali ⁵ (2019)	Adalimumab	26	Antibiotics, retinoids, corticosteroids, DMARDs	Remission in 24 of 26 patients
Mihaljević and von den Driesch ⁶ (2012)	Infliximab	1	Antibiotics, corticosteroids	Remission after 3 infusions
Hoy and Böhm ⁷ (2022)	Certolizumab pegol	1	Antibiotics, corticosteroids	Marked improvement after 1 mo; no complete resolution
JAK inhibitor				
Moussa et al ⁸ (2022)	Baricitinib	4	Antibiotics, corticosteroids, antiandrogens	Remission after 1–3 mo; recurrence in 1 patient after discontinuation
PDE4 inhibitor				
Fässler et al ⁹ (2020)	Apremilast	1	Antibiotics, corticosteroids, TNF inhibitor	Remission at 3 wk
Monoclonal antibody				
Ismail and Sinclair ¹⁰ (2020)	Secukinumab	1	Antibiotics, corticosteroids	Remission at 7 mo

Abbreviations: DMARD, disease-modifying antirheumatic drug; JAK, Janus kinase; PDE4, phosphodiesterase 4; TNF, tumor necrosis factor.

adalimumab or biosimilar adalimumab (27/29 patients), infliximab (1/29 patients), and certolizumab pegol (1/29 patients). Remission was reported in 26 of 29 cases. There were 2 nonresponders to adalimumab and marked improvement with certolizumab pegol without complete resolution. The use of the JAK inhibitor baricitinib in 4 patients resulted in remission. In all 4 patients, baricitinib was used with concurrent treatments, and remission was achieved in an average of 2.25 months. The use of a PDE4 inhibitor, apremilast, was reported in 1 case; remission was achieved in 3 weeks. Secukinumab, a monoclonal antibody that targets IL-17, was utilized in 1 patient. Marked improvement was seen after 2 months, with complete remission in 7 months.

Comment

Traditional treatment regimens for FD most often include a combination of topical and oral antibiotics; isotretinoin; and oral, topical, or intralesional corticosteroids. In the

past, interventions typically were suppressive as opposed to curative; however, recent treatment advancements have shown promise in achieving lasting remission.

Most reports targeting treatment-resistant FD involved the use of TNF inhibitors, including adalimumab, biosimilar adalimumab, infliximab, and certolizumab pegol. Adalimumab was the most frequently used TNF inhibitor, with 24 of 26 treated patients achieving remission. Adalimumab may have been used the most in the treatment of FD because TNF is pronounced in other neutrophilic dermatoses that have been successfully treated with TNF inhibitors. It has been reported that adalimumab needs to be continued, as stoppage or interruption led to relapse.³

Although there are few reports of the use of JAK inhibitors, PDE4 inhibitors, and monoclonal antibodies for FD, these treatment modalities show promise, as their use led to marked improvement or lasting remission with ongoing treatment. The use of the PDE4 inhibitor

apremilast displayed the most rapid improvement of any of the reviewed treatments, with remission achieved in just 3 weeks.⁹ The rapid success of apremilast may be attributed to the inhibitory effect on neutrophils.

Miguel-Gómez et al¹¹ provided a therapeutic protocol for FD based on the severity of disease (N=60). The protocol included rifampicin plus clindamycin for the treatment of severe disease, as 90.5% (19/21) of resistant cases showed clinical response, with remission of 5 months' duration. Although this may be acceptable for some patients, others may require an alternative approach. Tietze et al¹² showed that rifampicin and clindamycin had the lowest success rate for long-term remission, with 8 of 10 patients relapsing within 2 to 4 months. In addition, the emergence of antimicrobial resistance remains a major concern in the treatment of FD. Upon the review of the most recent reports of successful treatment of therapy-resistant FD, biologics and small molecule inhibitors have shown remission extending through a 12-month follow-up period. We suggest considering the addition of biologics and small molecule inhibitors to the treatment protocol for severe or resistant disease.

Limitations—In the articles reviewed, the definition of remission was inconsistent among authors—some characterized it as no recurrence in lesions or pustules and some as a reduction in the inflammatory process. True duration of remission was difficult to assess from case reports, as follow-up periods varied prior to publication. The studies included in this review consisted mainly of small sample sizes owing to the rarity of FD, and consequently, strength of evidence is lacking. Inherent to the nature of systematic reviews, publication bias may have occurred. Lastly, several studies were impacted by difficulty in obtaining optimal treatment due to financial hardship, and regimens were adjusted accordingly.

Conclusion

The relapsing nature of FD leads to frustration and poor quality of life for patients. There is a paucity of data to guide treatment when FD remains recalcitrant to traditional therapy. Therapies such as TNF inhibitors, JAK inhibitors, PDE4 inhibitors, and monoclonal

antibodies have shown success in the treatment of this often difficult-to-treat disease. Small sample sizes in reports discussing treatment for resistant cases as well as conflicting results make it challenging to draw conclusions about treatment efficacy. Larger studies are needed to understand the long-term outcomes of treatment options. Regardless, disease severity, patient history, patient preferences, and treatment goals can guide the selection of therapeutic options.

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