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Folliculitis Decalvans: A Review of Treatment Modalities

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ABSTRACT

Background: Folliculitis decalvans (FD) is a rare subtype of neutrophilic cicatricial alopecia, firstly described by Quinquad in 1888, as inflammatory scalp disease usually affecting young adults. The exact etiopathology of the disease is not fully understood, however the presence of *Staphylococcus aureus*, dysfunction of the host's immune response, genetic factors, previous trauma of the scalp, as well as Epidermal Growth Factor Receptor inhibitors (EGFRi) use seem to play a role. Clinically, FD presents with scarring alopecic patches with follicular pustules, crusts and tufted hair.

Objectives: As the full etiology of the disease is unknown and most data in the literature is based on retrospective date, therapeutic management is not precisely established. The objective of this review is to describe therapeutic options, as well as highlighting potential new therapeutic modalities reported in the literature.

Limitations: Because FD is a rare disease, the main limitation is lack of randomized control trials, evaluating therapeutic modalities.

Methods: An exhaustive search of references related to FD published in PubMed between 2017 and 2024 was undertaken, using the search term: "folliculitis decalvans". Articles with large patient cohorts and reviews were included, as well as case reports and case series, that reported novel treatment approaches for FD.

Conclusions: The management of FD poses a challenge. Systemic antibiotics, particularly rifampicin and clindamycin, are considered the first-line agents and are commonly used in combination with local therapies. Systemic isotretinoin yields sustained remission in some cases, while biological agents exhibit promise in managing severe FD. Novel therapeutic modalities, incorporating, among others, botulinum toxin A injections, Platelet-Rich-Plasma (PRP), or surgical procedures, necessitate randomized double-blind trials to evaluate their safety and efficacy.

INTRODUCTION

Epidemiology

Folliculitis decalvans is a rare subtype of primary neutrophilic cicatricial alopecia, affecting both genders, with a slight predominance of male (62-63 %). Depending on the source, the mean age of onset of FD differs from 35 to 40 years old [1,2].

Etiopathogenesis

Although the literature reports various hypotheses regarding the etiopathogenesis of FD, it is still not precisely defined. Factors such as *Staphylococcus aureus (S.aureus)* colonization, bacterial biofilms, abnormal microbiota, loss of epidermal barrier integrity, previous scalp trauma, congenital abnormalities of follicular orifices, dysfunction of the local immune system, as well as use of EGFRi may play a role in the development of the disease [1,2,3,4,5].

The role of *S. aureus* and abnormal microbiota. In many studies, *S. aureus* has been isolated from pustules [1,2,6] as well as nasal swabs [1] of patients with FD. Recent investigations indicate that *S. aureus* likely acts as an opportunistic rather than a specific pathogen in FD, as the obtained strains lack any particular pathogenicity [3]. Researchers suggest that either unknown changes in hair follicles or the impairment of the immune system enable the existence of dysbiotic flora, composed mainly of opportunistic *S. aureus*. Abnormal microbiota lead to a significant neutrophil migration, associated with the activation of innate immune signals, such as inflammasomes: NALP1, NALP3 and interleukin-1β (IL-11β), however fail to control the *S. aureus* burden. Prolonged inflammation in hair follicles, precipitates local immune collapse, resulting in the exposure of follicular antigens and immune-mediated damage to the hair follicles. Additionally, the persistence of abnormal microbiota, despite antibiotic treatment, elucidates the chronic course of the disease [3,4,6].

Genetic factors. Researchers describe familial cases of FD, implying genetic involvement in the etiopathogenesis of FD [1,2]. The disease was documented in a pair of 32-year-old male twins, who lived separately. Neema et al. reported a case where both a 32-year-old and their 8-year-old son developed FD [7]. Moreover, a newly identified TRAF3IP2 variant has been described as the cause of scarring alopecia exhibiting a combination of features characteristic

of discoid lupus erythematosus and FD [8]. It is important to consider that although genetics may contribute, unknown environmental factors could also influence familial FD cases.

Previous trauma. According to numerous studies, the development of FD may occur at the site of a previous scalp injury [1,2]. In the case described by Brodovskaya et al. the development of FD occurred 20 years after a dog bite, with the onset of FD in the 20th week of pregnancy [9].

The EGFRi use. The EGFR is a crucial receptor in cell proliferation, apoptosis, and epithelial differentiation. Since its overexpression has been linked with various pathways involved in cancer cell division, angiogenesis, and metastasis, it became a therapeutic target for the treatment of non-small cell lung carcinoma (NSCLC), head and neck squamous cell carcinoma (HNSCC), as well as breast cancer. Presence of EGFR in various dermal structures implicates EGFRi in inducing several dermatological side effects, including acneiform papulopustular rash, xerosis, and, rare, folliculitis decalvans. In reported cases of EGFRi-induced FD, the median duration from the initiation of EGFRi to the onset of symptoms was 4 months, with a range from 1 to 23 months. Researchers suggest that folliculitis decalvans following EGFRi use stems from disrupted processes of keratinocyte maturation and differentiation, as well as the neutrophil chemotaxis induced by EGFRi. Bacterial superinfection, facilitated by the compromised antimicrobial defense of the skin due to EGFR inhibition, may also play a role [5].

Comorbidities. In some patients, coexisting diseases are present, such as hypertension, dyslipidemia, thyroiditis, as well as dermatologic conditions including atopic dermatitis, androgenetic alopecia, hidradenitis suppurativa, seborrheic dermatitis, vitiligo, alopecia areata, and psoriasis. However, the vast majority of patients (65-74%) are healthy and their laboratory parameters remain within normal range [1,2].

CLINICAL FEATURES & DIAGNOSIS

Clinical Features

FD is characterized by a focus of scarring alopecia with the presence of erythematous papules and perifollicular pustules, often accompanied by crusting. A distinctive feature of FD, termed

"brush signs" is present in up to 88% patients [1]. It refers to multiple hair shafts merging into one common infundibulum, exceeding the typical count of five [1,2,10]. The most frequently affected area is the vertex (56% of patients); however, the disease can also involve the parietal, occipital, and frontal regions, as well as multiple scalp regions (30%). It can present as a solitary alopecia patch or as up to five disease foci in the same or different areas of the scalp. The beard and eyebrows can also be affected, whereas hair follicles in other body sites are typically spared. Additional clinical manifestations of FD include: facial papules, erythema and seborrhea. Regarding clinical symptoms, literature reports presence of pruritus, as well as trichodynia (pain of the scalp), however some patients report no symptoms. Typically, this condition follows a chronic and recurrent course. Hair regrowth is typically not expected [1,2].

Diagnosis

The diagnostic methods for FD typically involve the physical examination, trichoscopy, skin biopsy and the bacterial cultures of scalp pustules and nasal mucosa, assessing the antibiotic sensitivity [9].

Trichoscopy. Trichoscopy is a non-invasive technique used for diagnosing FD. To perform trichoscopy correctly, the evaluation should focus on hair shafts and follicular openings, perifollicular surface, interfollicular surface, as well as scalp blood vessels. It should be also emphasized that trichoscopic features vary depending on the inflammatory state [11].

In trichoscopy, following features can be observed:

1) **Hair shafts and follicular openings.** The predominant finding is hair tufting, although pili torti and broken hairs may also be observed.
2) **Perifollicular surface.** Perifollicular erythema, follicular pustules, perifollicular hemorrhages, perifollicular hyperkeratinization, and yellow tubular hyperkeratinization are observed around the hair follicles.
3) I**nterfollicular surface.** Yellow crusts and white interfollicular hyperkeratinization are common findings of the interfollicular surface.
4) **Scalp blood vessels.** Some patients present elongated capillary loops. Well-defined, thin arborizing vessels (thinner than hair shafts) have also been observed and are associated with disease improvement [11].

Skin biopsy. Histologically, early stages of FD are characterized by intrafollicular and perifollicular neutrophil infiltrations, as well as perifollicular acanthosis and fibrosis-depressed, fused infundibula. Loss of sebaceous gland is also described. In advanced stages of FD, there is a mixed inflammatory infiltration characterized by neutrophils, lymphocytes, and plasma cells [1,2,12]. A recent study conducted by Uchiyama et al. revealed that inflammatory neutrophilic infiltration is more pronounced around the infundibulum and isthmus compared to the lower part of the hair follicle [12].

Bacterial cultures. Due to the potential involvement of *S. aureus* in the etiopathogenesis of FD, bacterial cultures from pustules should be performed [1,13]. Some authors advocate for routine nasal cultures in patients diagnosed with FD to assess potential nasal colonization by *S. aureus,* which should be eradicated if detected [1]. Moreover, antibiotics targeting *S. aureus* may lead to the microbiome balance by targeting commensal coagulase-negative staphylococci and *Propionibacterium acnes*. This could result in the excessive proliferation of Gram-negative bacteria and worsen FD symptoms. Therefore, bacterial cultures should be considered in patients with active disease to evaluate the presence of non-staphylococcal infections that may require adjustments in the treatment approach [13].

SEVERITY OF THE DISEASE

The maximum diameter of the largest patch

Severity of FD can be determined by the maximum diameter of the largest alopecic patch as follows: grade I: <2 cm, grade II: 2-4.99 cm, grade III: 5 cm or more. Grade I and II are considered as mild/moderate FD, and grade III corresponds to severe FD [1]. Factors such as onset before 25 years old, the presence of pustules in the alopecic patch and “brush signs” may be associated with more advanced FD [1,2].

Trichoscopy activity scale for folliculitis decalvans

To assess the activity of the disease, the trichoscopy activity scale for folliculitis decalvans proposed by Saceda-Corallo et al. can be utilized (Table 1).

Table 1. Trichoscopy activity scale for folliculitis decalvans proposed by Saceda-Corallo et al. [11].

Trichoscopic sign	Trichoscopy finding	Punctuation
Yellow signs	Follicular pustules	+2
	Yellow tubular hyperkeratinization	+1
	Yellow crusts	+1
Red signs	Perifollicular erythema (>50% of the follicular units)	+1
	Perifollicular haemorrhages	+1
	Thin arborizing vessels (thinner than hair shafts)	-1
Total		max. 6

The results should be interpreted as follows: **3 points and above:** severe flare-up, **2 points:** moderate flare-up, **1 point:** slight reactivation, **0 points:** disease controlled.

TREATMENT

As hair regrowth is unlikely, the main goals of treatment focus on symptom reduction, inflammation suppression and halting the disease progression.

Local Treatment

1. Topical Agents

Antimicrobials and anti-inflammatory agents. Topical agents utilized in FD include mainly anti-inflammatory medications, such as corticosteroids and tacrolimus, as well as antimicrobials, such as mupirocin, fusidic acid or ozenoxacin [2,14,15]

Dapsone. Dapsone demonstrated efficacy in the treatment of disorders characterized by abnormal neutrophil recruitment [16]. In many studies, its oral administration has been

utilized in FD, yielding varying outcomes [14]. A recent retrospective study conducted by Melian-Oliviera et al. investigated its topical application (5% gel) in 14 patients. The drug was applied three times a week, showing positive outcomes defined by a reduction in the number of flare-ups. Additionally, topical dapsone was well-tolerated by all patients. Hence, it emerges as a potential novel therapeutic approach for reducing the frequency of flare-ups. Further studies are needed to assess both its efficacy and safety profile comprehensively [14,16].

Other topical agents. Vitamin D derivatives (calcipotriol) are indicated for desquamation and seborrhea, salicylic acid for hyperkeratosis, and minoxidil for cases associated with androgenic alopecia. Other topical agents highlighted in the literature encompass zinc oxide, lidocaine, azelaic acid, medical honey and chlorhexidine [2,14,17]. However, evaluating the efficacy of these treatments is challenging due to their frequent concurrent use with other systemic therapies [14].

2. Intralesional Treatment

Intralesional Triamcinolone Acetonide (ILTA). ILTA involves the injection of triamcinolone acetonide directly into the affected area of the scalp. Miguel et al. recommend the utilization of ILTA for mild or moderate forms of FD once every three months, particularly when slight inflammation is present [2]. The literature describes the use of ILTA in combination with other agents such as topical corticosteroids, oral antimicrobials, or PRP, with variable results [14, 18].

PRP. PRP is commonly utilized in various forms of alopecia. To date, the literature documents two cases of folliculitis decalvans where PRP application was pursued following the failure of prior treatment modalities. In both cases, PRP was combined with other forms of the treatment, which included, among others, ILTA, oral doxycycline, and topical agents. The administration of PRP resulted in a notable reduction in erythema, hyperkeratinization, and pustules, with stabilization of hair loss. However, the observed clinical improvement was not sustained upon discontinuation of the treatment.

Two mechanisms are postulated to underlie the potential efficacy of PRP in the treatment of FD. Firstly, the release of anti-inflammatory cytokines such as IL-3, IL-10, and TGF-beta by activated platelets explains the alleviating effect of PRP on inflammation. Secondly, the

release of antimicrobial peptides with a broad spectrum of activity against pathogens, including *S. aureus*, further supports PRP's potential effectiveness. Additionally, the antibacterial action is elucidated through release of oxygen metabolites that kill bacteria by activated platelets [18].

Botulinum Toxin A Injections. Numerous studies have confirmed the effectiveness of botulinum toxin A as an alternative therapeutic approach for androgenic alopecia. However, there is limited data on its application in FD, with only one case report detailing its use. A 34-year-old patient with a 2-year history of FD underwent four intradermal sessions of 100 IU botulinum toxin A at one-month intervals. Previous therapeutic modalities, including tetracyclines and ILTA were ineffective. Following the implemented treatment, the patient reported a reduction of inflammatory lesions and alleviation of pruritus. Furthermore, no relapse was observed during a 5-year follow-up period.

The researchers suggest that the effect of botulinum toxin A may stem from its capacity to inhibit TRPV1 (transient receptor potential vanilloid-1) receptors and therefore modulate the release of CGRP (calcitonin gene-related peptide). TRPV1 receptors are located in nociceptive C fibers, hair follicles, and immune cells of the scalp, contributing to dysregulated immune responses and the activation of mediators affecting hair growth. Consequently, the inhibition of these receptors may result in restoring homeostasis in the hyperactive immune response, thus ameliorating disease manifestations [19].

3. Photodynamic therapy (PDT)

PDT is based on the localized or systemic application of photosensitizers, such as 5-aminolevulinic acid or benzoporphyrin derivatives, which accumulate within cells. Upon exposure to light of an appropriate wavelength, these photosensitizers become activated, what leads to destruction of pathological skin cells. PDT is extensively utilized in the management of various skin conditions, including skin cancers and inflammatory skin diseases. Additionally, PDT has demonstrated effectiveness in addressing drug-resistant bacterial skin infections as well as improving skin healing [20,21]. Miguel-Gomez et al. recommend utilization of PDT in certain cases of FD. Their proposed protocol involves an initial series of four PDT sessions spaced four weeks apart. If patients respond well to the treatment, further PDT sessions can be implemented if clinical symptoms reappear [2]. However, the

therapeutic efficacy of PDT varies among different studies. Some patients experience favorable outcomes while others show no response or even worsening of symptoms [21-24].

A recent retrospective study conducted by Yang et al. involved 13 Asian patients with FD who underwent PDT. The treatment utilized 5-aminolevulonic acid with an initial irradiation intensity of 100 mW/cm³ and consisted of three therapeutic sessions spaced 10-14 days apart. Following the completion of three sessions, total disappearance of inflammatory lesions was observed in 4 patients, lesions reduction of ≥70% with significant symptom improvement in 7 cases, and lesions reduction of ≥30% with slight symptom improvement in 2 cases. Follow-up evaluations conducted at 12 months post-treatment revealed that the condition was well controlled in 9 out of the 13 cases, with no recurrence. In the case of 3 patients experiencing a recurrence, the use of oral medications (isotretinoin, clarithromycin), or topical treatments (selenium dioxide) allowed for alleviation of the disease symptoms.

It should be emphasized that prior to this treatment, the patient should be informed about the necessity of shaving the affected scalp and potential local burning discomfort experienced during irradiation. Furthermore, it is recommended to avoid water contact in the treated area for 24 hours and strictly avoid light exposure for 48 hours [20].

4. Neodymium:yttrium aluminium garnet (Nd:YAG) laser

The literature reports two cases where neodymium:yttrium aluminium garnet (Nd:YAG) laser treatment was implemented for recurrent FD, resulting in positive outcomes and long-lasting improvement. Researchers suggest that the efficacy of this approach is based on the removal of all affected hair follicles, what leads to the elimination of inflammatory focus [25].

Systemic Treatment

1.Antimicrobials

Given the frequent presence of *S. aureus* in bacterial cultures obtained from FD-affected hair follicles, eradicating this bacterium is a key goal of the therapy.

Rifampicin & Clindamycin. One of the most effective treatment approaches for FD involves a 10-week course combining rifampicin (300 mg/ twice daily) and clindamycin (300 mg/ twice daily). Rifampicin, an antimicrobial agent, exhibits notable activity against *S. aureus*

and exerts immunomodulatory effects by suppressing T-cell function. However, given concerns regarding the emergence of drug resistance, rifampicin should be administered in combination with clindamycin [1,2,14,26,27]. Powell et al. reported that 55.6% (10/18) of patients achieved remission following a single 10-week course, with remission rates rising to 83.3% (15/18) after 2-3 additional 10-week courses. Notably, no recurrence was documented within 2-22 months [26]. Vano-Galvan et al. confirmed the efficacy of this combination, with 100% of patients (15/15) showing disease improvement, albeit with a shorter mean remission duration of 7.2 months. According to the researchers, the difference in remission duration across studies may be due to the use of a single 10-week course of therapy in Vano-Galvan's study compared to previous research [1]. Furthermore, Miguel-Gomez reported remission in over 90% of cases, as well as efficacy in managing disease recurrences. Notably, this treatment regimen exhibited the longest disease-free period compared to other therapeutic modalities [2].

Azithromycin. Azithromycin is another antimicrobial used in FD therapy. Its effectiveness is similar to the combination of rifampicin and clindamycin; however, it presents a shorter duration of remission, lasting 4.6 months. Therefore, azitromycin administered at a dose of 500 mg/day three times a week for three months, is suggested for use in cases of slight and moderate severity, especially when resistance to previous therapeutic regimens occurs [1,2,14].

Tetracyclines. Tetracyclines represent therapeutic options for FD, as delineated across several studies [1,2,14,27]. Beyond their antimicrobial properties, they also exert immunomodulatory effects. The therapeutic regimen involving tetracyclines comprises the use of minocycline/doxycycline at a dose of 100-200 mg/day for 8-12 weeks, or tetracycline at a dose of 500 mg twice daily for up to 7 months [1,2,14]. In a study conducted by Vañó-Galván et al. doxycycline demonstrated efficacy in achieving remission in 90% of patients (35/39), while minocycline showed remission in 86% (6/7 patients). In another study wherein tetracyclines were combined with clobetasol propionate lotion and intralesional triamcinolone for an average duration of 7 months, patients remained in disease remission for up to 4 years. Nonetheless, 11 out of 23 patients necessitated continued treatment with oral antibiotics, intralesional triamcinolone, or clobetasol propionate to sustain remission [14].

Another therapeutic alternative from the tetracycline group is lymecycline. Apart from properties such as enhanced gastrointestinal absorption, improved tissue penetration, and slower elimination compared to tetracycline, it also possesses the ability to modulate skin microbiota [27]. A study conducted by Melo et al. revealed a 70% efficacy in pain reduction and attenuation of inflammatory activity following a 90-day lymecycline therapy at a dosage of 300 mg/day. The authors of this study advocate for the medication's usage for a minimum of 3 months, as positive outcomes were associated with longer treatment durations.

Upon initiating tetracycline therapy, the potential side effects, such as epigastralgia, diarrhea, headaches, and phototoxicity must be considered [14,27].

Fusidic acid. Topical fusidic acid is commonly utilized as an adjunctive treatment. However, data concerning its oral administration are limited, and the outcomes vary across studies. Some authors suggest its potential effectiveness in achieving remission when administered at a dose of 500 mg three times daily, particularly when combined with topical zinc oxide or with topical betamethasone, salicylic acid, and azelaic acid. In the case described by Pimenta et al., the application of fusidic acid in conjunction with betamethasone dipropionate 0.05% and salicylic acid 3% lotion, as well as azelaic acid 5% lotion for a period of two months, resulted in clinical improvement and no recurrences after 6-months of follow-up [28].

Cephalexin. In one study, the combination of cephalexin with ILTA and clobetasol propionate lotion led to remission in 100% of patients (6/6). However, specific details regarding the duration of treatment and the disease-free period after treatment were not specified [14].

2. Isotretinoin

Isotretinoin is a retinoid derivative of vitamin A, used in various dermatological conditions, including acne vulgaris, rosacea, hidradenitis suppurativa and psoriasis. It is hypothesized that due to its inhibitory effects on neutrophils migration to the skin and downregulation of toll-like receptor 2, a mediator of the immune response against gram-positive bacteria, isotretinoin may demonstrate efficacy in the treatment of FD. A retrospective study conducted by Aksoy et al. revealed that oral isotretinoin used in monotherapy for a median duration of 2.5 months, resulted in complete remission in 82% of patients. Notably, individuals receiving oral isotretinoin at a dosage of ≥0.4 mg/kg/day for over three months exhibited a higher response

rate and 66 % of them did not encounter a relapse. It is worth mentioning that the use of isotretinoin for FD treatment was linked to hyperlipidemia in 14 out of 39 cases in another retrospective study [14, 29].

3. Tumor Necrosis Factor-alpha (TNF-alpha) inhibitors

Adalimumab. Adalimumab is a fully human, recombinant monoclonal antibody with specificity for human TNF-alpha, the mediator of inflammation. TNF-alpha is a key target for treating different skin conditions, including certain types of skin inflammation like pyoderma gangrenosum or dissecting cellulitis. Many studies have reported the use of adalimumab in FD [30].

A case series by Iorizzo et al. involved 23 patients treated with adalimumab due to the ineffectiveness of conventional treatments. The medication was administered via subcutaneous injections, with an initial dose of 160 mg at week 0 and 80 mg at week 1, followed by 80 mg every two weeks thereafter. Clinical improvement was observed in all patients, beginning as early as the first month of treatment and continuing throughout. The duration of adalimumab therapy ranged from 6 to 24 months. Only two patients discontinued treatment due to inadequate improvement, both of whom had mixed-culture bacterial culture with the presence of *S. aureus* and gram-negative bacteria [31].

Infliximab. Infliximab, a chimeric monoclonal antibody targeting TNF-alpha, is commonly utilized in managing Crohn's disease, ulcerative colitis, and severe chronic plaque psoriasis [32]. In a study by Dupent et al., nine patients received infliximab (5 mg/kg) every 4-8 weeks, while two patients received adalimumab (40 mg) every 2 weeks. Most patients received concurrent topical agents alongside this treatment. The therapy led to improvement in half of the patients, particularly in alleviating pruritus. The treatment was well tolerated by the majority of patients, however, one patient reported lower-limb vasculitis and another moderately elevated liver parameters. Compared to the aforementioned study, positive results were achieved after a longer duration of therapy. The authors attribute this difference to the inclusion of predominantly severe cases of folliculitis decalvans in this study, and regarding adalimumab, to lower doses [33].

Certolizumab pegol. Certolizumab is a pegylated fragment of a recombinant human monoclonal antibody that acts as a TNF-alpha inhibitor. Literature reports a single case of its utilization in the management of FD. Due to the failure of previous therapeutic approaches, the 42-year-old man received 400 mg of certolizumab subcutaneously for the first 3 injections, followed by 200 mg injections every two weeks thereafter. The implemented treatment resulted in improvement within one month, characterized by a reduction in trichodynia, pruritus, and, as the treatment was continued, reduction in scalp erythema, as well as scalp pustules was observed [34].

4. Secukinumab.

Secukinumab is a human monoclonal antibody targeting the interleukin-17 receptor. This medication is used in the treatment of certain forms of plaque psoriasis, rheumatoid arthritis, and ankylosing spondylitis. In the case described by Ismail et al. secukinumab was administered to a 30-year-old female patient with a 14-year history of FD, who had previously undergone various forms of therapy, such as topical and systemic treatments, including tofacitinib, central scalp reduction, as well as laser hair removal, all of which, however, proved to be ineffective. The patient received secukinumab at a dose of 300 mg subcutaneously at weeks 0, 1, 2, 3, and 4, followed by 300 mg every 4 weeks thereafter, in conjunction with cyclosporine at a dose of 100 mg twice daily. After 2 months, due to some clinical improvement, cyclosporine was discontinued. Reduction in active folliculitis decalvans was observed after 4 months, and treatment with 4-weekly injections was continued with a sustained response after 7 months. No adverse effects were reported [35].

5. JAK inhibitors

Baricitinib. Oral administration of baricitinib (3.4-6.8 mg/day), a selective and reversible JAK-1/2 inhibitor, was utilized in 4 patients with FD. It was combined with other topical medications (such as antimicrobials or corticosteroids) and systemic treatments (oral minoxidil, finasteride), resulting in sustained improvement throughout the therapy. However, one patient presented a relapse after self-discontinuation; another experienced exacerbation of symptoms upon attempting to reduce the dose to 3.4 mg/day. Mild hypercholesterolemia and transient facial and back acne were reported as adverse effects, but overall, the medications were well-tolerated by the patients [36].

Tofacitinib. Oral administration of tofacitinib, a selective JAK 1/3 inhibitor, (2.5 mg/day), combined with other forms of topical and systemic therapy, resulted in significant improvement in 3 patients within 3-5 months of initiating treatment, with remission lasting 1-10 months after treatment cessation. Elevated total cholesterol and mild eosinophilia were observed in 1 patient as adverse effects of JAKi [37].

5. Cyclosporine

Cyclosporine, a calcineurin inhibitor, is utilized in various inflammatory disorders, including skin conditions like psoriasis or atopic dermatitis. It is proposed that its ability to inhibit IL-2, leading to decreased activation and proliferation of skin T-lymphocytes responsive to superantigens and microbial antigens, could explain its efficacy in FD. Thus, Jarjen et al. employed cyclosporine in three patients at doses ranging from 0.81 to 2.25 mg/kg body weight per day for 6 to 28 months. Each patient received cyclosporine in combination with other medications, including among others, topical and oral antimicrobials, topical/intralesional corticosteroids, as well as isotretinoin or finasteride. In one patient, despite treatment effectiveness, cyclosporine was discontinued due to abnormal kidney parameters after 6 months, leading to disease relapse after 4 months. Among patients receiving longer treatment, remissions were achieved for up to 5 months. The authors suggest that cyclosporine could be considered a therapeutic option for folliculitis decalvans, especially in cases where activity persists despite antibacterial treatment or conventional immunosuppression [14,38].

6. Apremilast

Apremilast, a phosphodiesterase 4 selective inhibitor, has demonstrated effectiveness in treating conditions such as psoriasis and Behçet's disease, characterized by neutrophilic inflammation. In a case reported by Fassler et al., a 28-year-old male with FD underwent multiple treatment modalities including topical agents, systemic rifampicin combined with clindamycin, lymecycline, dapsone gel, isotretinoin, PDT, adalimumab, and systemic corticosteroids, all of which proved ineffective. The implementation of apremilast, at a dosage used in psoriasis, led to significant improvement, confirmed in trichoscopy. Nevertheless, upon discontinuation of the treatment, disease relapse occurred, necessitating the reinitiation of apremilast to achieve remission [39].

Surgical Procedures

The literature reports few cases of surgical procedures in the treatment FD. Excision with second-intention healing aided by guarded high-tension sutures in 5 patients resulted in sustained remission during long-term follow-up (10-21 months) [40]. Adipose tissue transplant has been also described in a 41-year-old female patient who underwent this procedure twice, with a 5-month interval, due to the ineffectiveness of prior therapeutic modalities. Following treatment, the patient did not present new folliculitis lesions and reported the absence of trichodynia or burning sensations in the affected area. Furthermore, discontinuation of antibiotic therapy was possible and hair regrowth at the periphery of alopecia was observed. Despite the positive outcomes of the above mentioned methods, it should be emphasized that FD often occurs following scalp injury or scalp and hair restoration surgery. Therefore, surgical intervention should be approached with caution [41].

SUMMARY

FD poses a challenge in clinical management. The exact etiopathogenesis of this condition is not completely elucidated, and most available data regarding treatment modalities have been obtained retrospectively, based on descriptions of case reports or small case series. Therefore, standardized treatment guidelines are still not established. Systemically administered antibiotics are commonly used as first-line therapy. In the described studies, the most effective therapeutic regimen consists of rifampicin and clindamycin combination. Treatment with tetracyclines, azithromycin, or cephalexin may be considered in subsequent lines of therapy in cases where previous treatment methods have proven ineffective or intolerable. Systemic therapies are often used in combination with anti-inflammatory and antimicrobial topical agents or ILTA. Since isotretinoin administered at a dose of ≥0.4 mg/kg/day for over 3 months demonstrated sustained remission, pivotal in managing FD's chronicity and relapsing nature, it also can be considered in systemic treatment. Regarding the reduction of flare-ups, the use of topical dapsone gel appears promising. TNF-alpha inhibitors, IL-17 receptor inhibitors, and Janus kinase inhibitors may also demonstrate efficacy, especially in severe forms FD or refractory to previous treatment modalities. However, further randomized clinical trials are necessary to assess their safety and efficacy. Photodynamic therapy can be also considered in some FD cases. Intralesional botulinum toxin A and PRP, as well as

surgical procedures, necessitate more extensive investigation due to limited evidence in the literature.

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References:

1.Vañó-Galván S, Molina-Ruiz AM, Fernández-Crehuet P, et al. Folliculitis decalvans: a multicentre review of 82 patients. *Journal of the European Academy of Dermatology and Venereology*. 2015;29(9):1750-1757. doi:https://doi.org/10.1111/jdv.12993

2.Miguel-Gómez L, Rodrigues-Barata AR, Molina-Ruiz A, et al. Folliculitis decalvans: Effectiveness of therapies and prognostic factors in a multicenter series of 60 patients with

long-term follow-up. *Journal of the American Academy of Dermatology*. 2018;79(5). doi:https://doi.org/10.1016/j.jaad.2018.05.1240

3.Matard B, Jean Luc Donay, Matthieu Resche-Rigon, et al. Folliculitis decalvans is characterized by a persistent, abnormal subepidermal microbiota. *Experimental Dermatology*. 2020;29(3):295-298. doi:https://doi.org/10.1111/exd.13916

4.Moreno-Arrones OM, Garcia-Hoz C, Rosa Del Campo, et al. Folliculitis decalvans has a heterogeneous microbiological signature and impaired immunological response. *Dermatology*. 2023;239(3):454-461. doi:https://doi.org/10.1159/000529301

5.Nowaczyk J, Fret K, Kaminska-Winciorek G, Rudnicka L, Czuwara J. EGFR inhibitor-induced folliculitis decalvans: a case series and management guidelines. *Anti-Cancer Drugs*. 2023;34(8):942-948. doi:https://doi.org/10.1097/CAD.0000000000001494

6.Eyraud A, Milpied B, Thiolat D, et al. Inflammasome activation characterizes lesional skin of folliculitis decalvans. *Acta Dermato-Venereologica*. 2018;98(6):570-575. doi:https://doi.org/10.2340/00015555-2924

7.Shekhar N, Senkadhir V, Vasudevan B, Krishnan L. Folliculitis decalvans in father and son – genes, environment or both? *Dermatology Practical and Conceptual*. 2023;13(2). doi:https://doi.org/10.5826/dpc.1302a100

8.Nemer G, El-Hachem N, Eid E, et al. A novel *TRAF3IP2* variant causing familial scarring alopecia with mixed features of discoid lupus erythematosus and folliculitis decalvans. *Clinical Genetics*. 2020;98(2):116-125. doi:https://doi.org/10.1111/cge.13767

9.Brodovskaya S, Savelyeva A, Elizaveta Nekrasova, Valeriy Dubenskiy. CLINICAL CASE OF FOLLICULITIS DECALVANS IN A PREGNANT WOMAN. *Archiv Euromedica*. 2022;12(3). doi:https://doi.org/10.35630/2199-885x/2022/12/3.19

10.Wróbel J, Sadowska-Przytocka A, Dorota Jenerowicz, Bowszyc-Dmochowska M, Czarnecka-Operacz M. Folliculitis decalvans – a case study and an overview of literature. *Journal of Medical Science*. 2018;87(3). doi:https://doi.org/10.20883/jms.278

11.Saceda-Corralo D, Moreno-Arrones OM,Rodrigues-Barata R, et al. Trichoscopy activity scale for folliculitis decalvans. *Journal of the European Academy of Dermatology and Venereology*. 2020;34(2). doi:https://doi.org/10.1111/jdv.15900

12.Uchiyama M, Harada K, Rie Tobita, Ryokichi Irisawa, Tsuboi R. Histopathologic and dermoscopic features of 42 cases of folliculitis decalvans: A case series. *Journal of the American Academy of Dermatology*. 2021;85(5):1185-1193. doi:https://doi.org/10.1016/j.jaad.2020.03.092

13.Samrao A, Mirmirani P. Gram-negative infections in patients with folliculitis decalvans: A subset of patients requiring alternative treatment. *Dermatology Online Journal*. 2020;26(2). doi:https://doi.org/10.5070/d3262047408

14.Rambhia PH, Rosalynn R.Z. Conic, Murad A, Atanaskova-Mesinkovska N, Piliang M, Bergfeld W. Updates in therapeutics for folliculitis decalvans: A systematic review with evidence-based analysis. *Journal of the American Academy of Dermatology*. 2019;80(3). doi:https://doi.org/10.1016/j.jaad.2018.07.050

15.Kashikar Y, Saoji V, Madke B, Chandak MS, Meghe S. Successful Management of Folliculitis Decalvans. *Curēus*. Published online January 24, 2024. doi:https://doi.org/10.7759/cureus.52881

16.Melián-Olivera A, Burgos-Blasco P, Selda-Enríquez G, et al. Topical dapsone for folliculitis decalvans: A retrospective cohort study. *Journal of the American Academy of Dermatology*. 2022;87(1). doi:https://doi.org/10.1016/j.jaad.2021.07.004

17.Yeh JE, Hartman RI, Xu J, Hoang M, Yasuda MR. Resolution of folliculitis decalvans with medical honey. *Dermatology online journal*. 2019;25(8).

18.Suh S, Nguyen C, Zhao L, Atanaskova Mesinkovska N. The role of platelet-rich plasma therapy in refractory folliculitis decalvans. *JAAD Case Reports*. 2021;12:85-87. doi:https://doi.org/10.1016/j.jdcr.2021.04.008

19.Neri S, Franzolin MR, Luiza C, Michalany NS, Michalany AO, Domingos MO. Botulinum toxin A as an alternative treatment for folliculitis decalvans. *JAAD Case Reports*. 2023;35. doi:https://doi.org/10.1016/j.jdcr.2023.02.022

20.Kwiatkowski S, Knap B, Przystupski D, et al. Photodynamic therapy – mechanisms, photosensitizers and combinations. *Biomedicine & Pharmacotherapy*. 2018;106:1098-1107. doi:https://doi.org/10.1016/j.biopha.2018.07.049

21.Collier NJ, Allan D, F. Diaz Pesantes, Sheridan L, Allan E. Systemic photodynamic therapy in folliculitis decalvans. *Clinical and Experimental Dermatology*. 2018;43(1). doi:https://doi.org/10.1111/ced.13238

22.Castaño-Suárez E, Romero-Maté A, Arias-Palomo D, Borbujo J. Photodynamic therapy for the treatment of folliculitis decalvans. *Photodermatology, Photoimmunology & Photomedicine*. 2012;28(2):102-104. doi:https://doi.org/10.1111/j.1600-0781.2011.00639.x

23.Lin X, Zhou S, Wang X, Zhu X. Aminolevulinic acid photodynamic therapy for folliculitis decalvans: A case report. *Dermatologic Therapy*. 2020;33(3). doi:https://doi.org/10.1111/dth.13358

24.Burillo-Martinez S, Maroñas-Jimenez L, Sara Isabel Palencia-Pérez, Vanaclocha-Sebastián F, López-Gómez S. Failure of photodynamic therapy (PDT) in 3 patients with folliculitis decalvans. *Journal of the American Academy of Dermatology*. 2016;74(4):e69-e70. doi:https://doi.org/10.1016/j.jaad.2015.09.075

25.Meesters AA, van, Wolkerstorfer A. Long-term remission of folliculitis decalvans after treatment with the long-pulsed Nd:YAG laser. *J Dermatolog Treat*. 2014;25(2):167-168. doi:https://doi.org/10.3109/09546634.2013.826340

26.POWELL, DAWBER, GATTER. Folliculitis decalvans including tufted folliculitis: clinical, histological and therapeutic findings. *British Journal of Dermatology*. 1999;140(2):328-333. doi:https://doi.org/10.1046/j.1365-2133.1999.02675.x

27.

Daniel Fernandes Melo, Carla Jorge Machado, Naiara Luiza Bordignon, Silva, Paulo Müller Ramos. Lymecycline as a treatment option for dissecting cellulitis and folliculitis decalvans. *Dermatologic Therapy*. 2020;33(6). doi:https://doi.org/10.1111/dth.14051

28.Pimenta R, João Borges-Costa. Successful treatment with fusidic acid in a patient with folliculitis decalvans. *Acta Dermatovenerologica Croatica*. 2019;27(1).

29.Aksoy B, Asli Hapa, Mutlu E. Isotretinoin treatment for folliculitis decalvans: a retrospective case-series study. *International Journal of Dermatology*. 2018;57(2). doi:https://doi.org/10.1111/ijd.13874

30.Alhameedy M, Alsantali A. Therapy-recalcitrant folliculitis decalvans controlled successfully with adalimumab. *International Journal of Trichology*. 2019;11(6). doi:https://doi.org/10.4103/ijt.ijt_92_19

31.Iorizzo M, Starace M, Vano-Galvan S, et al. Refractory folliculitis decalvans treated with adalimumab: A case series of 23 patients. *Journal of the American Academy of Dermatology*. 2022;87(3). doi:https://doi.org/10.1016/j.jaad.2022.02.044

32.Papamichael K, Lin S, Moore M, Papaioannou G, Sattler L, Cheifetz AS. Infliximab in inflammatory bowel disease. *Therapeutic Advances in Chronic Disease*. 2019;10:204062231983844. doi:https://doi.org/10.1177/2040622319838443

33.Dupont A, Eyraud A, Milpied B, et al. Efficacy and safety of tumour necrosis factor-α antagonists for folliculitis decalvans: A retrospective case-series pilot study. *Acta Dermato-Venereologica*. 2023;103. doi:https://doi.org/10.2340/actadv.v103.3713

34.Hoy M, Böhm M. Therapy-refractory folliculitis decalvans treated with certolizumab pegol. *International Journal of Dermatology*. 2022;61(1). doi:https://doi.org/10.1111/ijd.15914

35. Ismail FF, Sinclair R. Successful treatment of refractory folliculitis decalvans with secukinumab. *Australasian Journal of Dermatology*. 2020;61(2). doi:https://doi.org/10.1111/ajd.13190

36.Moussa A, Asfour L, Eisman S, Bevin Bhoyrul, Sinclair R. Successful treatment of folliculitis decalvans with baricitinib: A case series. *Australasian Journal of Dermatology*. 2022;63(2). doi:https://doi.org/10.1111/ajd.13786

37.Jerjen R, Meah N, Trindade L, Wall D, Sinclair R. Folliculitis decalvans responsive to tofacitinib: A case series. *Dermatologic Therapy*. 2020;33(6). doi:https://doi.org/10.1111/dth.13968

38.Jerjen R, Meah N, Trindade L, Wall D, Shyamalar Gunatheesan, Sinclair R. Effective treatment of folliculitis decalvans with cyclosporin: A case series. *Australasian Journal of Dermatology*. 2021;62(2). doi:https://doi.org/10.1111/ajd.13532

39.Fässler M, Radonjic-Hoesli S, Feldmeyer L, et al. Successful treatment of refractory folliculitis decalvans with apremilast. *JAAD Case Reports*. 2020;6(10). doi:https://doi.org/10.1016/j.jdcr.2020.08.019

40.Umar S, Waterman A, Ton D, Shitabata P. Refractory folliculitis decalvans treatment success with a novel surgical excision approach using guarded high-tension sutures. *Clinical, Cosmetic and Investigational Dermatology*. 2023;16. doi:https://doi.org/10.2147/CCID.S422077

41.Tedesco M. Adipose tissue transplant in recurrent folliculitis decalvans. *International Journal of Immunopathology and Pharmacology*. 2018;32. doi:https://doi.org/10.1177/2058738418814688