Folliculitis decalvans: Effectiveness of therapies and prognostic factors in a multicenter series of 60 patients with long-term follow-up

Laura Miguel-Gómez, MD, PhD,[a] Ana R. Rodrigues-Barata, MD,[a] Ana Molina-Ruiz, MD, PhD,[b] Antonio Martorell-Calatayud, MD, PhD,[c] Pablo Fernández-Crehuet, MD, PhD,[d] Ramón Grimalt, MD, PhD,[e] Didac Barco, MD,[f] Salvador Arias-Santiago, MD, PhD,[g] Cristina Serrano-Falcón, MD,[h] Francisco M. Camacho, MD,[i] David Saceda-Corralo, MD, PhD,[a] Pedro Jaén-Olasolo, MD, PhD,[a] and Sergio Vañó-Galván, MD, PhD[a]

Madrid, Valencia, Cordoba, Barcelona, Granada, and Sevilla, Spain, and Andorra

Background: Folliculitis decalvans (FD) is a rare neutrophilic cicatricial alopecia that poses a therapeutic challenge.

Objectives: To describe the therapeutic response in a large number of cases of FD with long-term follow-up and analyze potential prognostic factors associated with severity of form and with a better therapeutic response.

Methods: This multicenter prospective study included patients with FD who had a minimum of 5 years of follow-up. Severity was assessed by the maximum diameter of the cicatricial area. Therapeutic response was evaluated according to stabilization of the size of the cicatricial areas and the improvement in clinical symptoms.

Results: A total of 60 patients (37 men [61.7%] and 23 women [38.3%]) with a mean age of 40 years were included. Earlier age of onset (P = .01) was statistically associated with severity of form. Treatment with rifampicin and clindamycin, tetracyclines, and intralesional steroids was the most effective. No statistically significant prognostic factors predicting a better therapeutic response were found.

Limitations: Because FD is a rare disease, the main limitation was the sample size.

Conclusions: An earlier age of onset was associated with the severe form of the disease. The proposed specific therapeutic protocol can be a very useful tool in clinical dermatologic practice. (J Am Acad Dermatol 2018;79:878-83.)

Key words: clindamycin; follicutis decalvans; pustules; quality of life; rifampicin; scarring alopecia; tetracyclines; tufted hairs.

Folliculitis decalvans (FD) is a rare primary cicatricial alopecia.[1] Its etiopathogenesis is unclear; however, the presence of *Staphylococcus aureus* and alteration of the patient's local immune response have been suggested as possible triggers.[1,2] In the early stages, an

Abbreviations used:

AGA:	Androgenetic alopecia
FD:	folliculitis decalvans
PDT:	photodynamic therapy
QOL:	quality of life

From the Dermatology Department, Ramon y Cajal University Hospital, Madrid[a]; Dermatology Department, Fundación Jiménez Diaz Hospital, Madrid[b]; Dermatology Department, Manises Hospital Valencia[c]; Dermatology Department, Reina Sofía Hospital, Cordoba[d]; Dermatology Department, Universitat Internacional de Catalunya, Barcelona[e]; Dermatology Department, DermAndTek Clinic, Andorra[f]; Dermatology Department, Complejo Universitario Hospital, Granada[g]; Dermatology Department, La Inmaculada Hospital, Granada[h]; and Dermatology Department, Virgen Macarena Hospital, Sevilla.[i]

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Correspondence to: Laura Miguel-Gómez, MD, PhD, Dermatology Department, Ramon y Cajal Hospital. Carretera Colmenar Viejo km 9.100, 28034 Madrid, Spain. E-mail: lmg_0007@hotmail.com.

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infundibular acneiform dilation accompanied by an intrafollicular and perifollicular infiltrate composed of neutrophils is observed. As the condition progresses, the infiltrate is mixed and extends to the adventitial dermis. In the late stages, periadnexal dermal fibrosis predominates.[3,4] Clinically, FD causes pustules, crusts, "tufted hairs" (more than 5 hairs emerging from the same follicular opening), and perifollicular hyperkeratosis, causing scarring alopecic patches over the scalp.[1,5,6] Combined topical and oral antibiotics are the main treatment used, with frequent relapses occurring in most patients.[7-9]

The main objective of our study was to describe the therapeutic response in a large series of patients with FD with long-term follow-up and to analyze potential prognostic factors associated with severity of form and with a better therapeutic response. As a secondary objective, the economic impact of FD and patients' quality of life (QOL) were evaluated.

CAPSULE SUMMARY

- Folliculitis decalvans causes scarring alopecia with an unclear prognosis, and there is no specific treatment.
- An early age of onset is associated with the severe form of folliculitis decalvans.
- We propose a specific therapeutic protocol for use in daily practice by clinicians.

MATERIALS AND METHODS

Study design

A retrospective multicenter study was designed; it included patients with FD and a minimum follow-up period of 5 years. The study included patients evaluated in 9 Spanish medical centers between 1995 and 2015. The diagnosis of FD was confirmed by histopathology in all patients. The following details of all patients were recorded in a database: epidemiologic (sex, age, race, comorbidities, family history, and associated trigger), clinical (age of onset, size, affected areas, symptoms, signs, and alterations in blood test results), diagnostic (results of skin biopsy and microbial culture of pustules over alopecic patches and the nose), and therapeutic (therapies, response and duration of response, and adverse effects).

As reported in the study of Vañó-Galván et al,[2] the severity of FD was calculated on the basis of the maximum diameter of the largest alopecic patch and categorized as being of 1 of 3 grades: I, mild (<2 cm); II, moderate (2-4.99 cm); and III, severe (≥5 cm). The intensity of symptoms was evaluated as asymptomatic, occasional symptoms, and daily symptoms. Response to therapy was quantified as a greater than 75% improvement in symptoms and inflammatory signs without any increase in the alopecic patch. The effectiveness of the treatment was evaluated during patients' medical visits every 2 to 3 months.

To evaluate the economic impact associated with FD, monthly costs (including the costs of drugs, private medical visits, and cosmetic treatments such as hair prostheses) were estimated. Patients' QOL was measured according to the validated Dermatology Life Quality Index.[10] The 12-Item Short Form Health Survey, version 1, questionnaire was also used. It provides a general profile of the health quality perceived by evaluating 12 items and assesses the degree of well-being (mental health) and functional capacity (physical health).[11]

Statistical analysis

In the descriptive analysis, the data are presented as means plus or minus standard deviations, medians, or crude numbers, depending on whether they were quantitative or ordinal variables and depending on the normality of their distribution. The Student *t* test, Mann-Whitney U test, and Kruskal-Wallis test were used for comparison of quantitative variables. The differences in qualitative variables were analyzed by using the χ^2, likelihood ratio, or Fisher's exact test as needed. Two models of multiple logistic regression were performed with an estimation approach. The selection criteria of the variables in the models were as follows: relevance of the collected scientific literature, clinical criteria of the author, and relevance found in the previous analysis of the variables. *P* values less than .05 were considered statistically significant. The statistical software packages SPSS Statistics (version 21, IBM Corp, Armonk, NY) and Stata v14 (StataCorp LP, College Station, TX) were used for data analysis.

RESULTS

A total of 60 patients (37 males [61.7%] and 23 females [38.3%]) with a median age of 40 years (range, 23-83) were included in the study. Fifty-eight patients (96.6%) were white, 1 (1.6%) was Hispanic, and 1 (1.6%) was of African origin.

The associated comorbidities were as follows: hypercholesterolemia in 8 patients (13.3%), arterial hypertension in 7 patients (11%), pollen allergy in 3 patients (5%), obesity in 2 patients (3.3%), and non-Hodgkin lymphoma in 1 patient (1.6%). There were no associated comorbidities in 39 patients (65%). Associated dermatologic diseases were identified in

29 patients (48%) as follows: androgenetic alopecia (AGA) in 14 patients (23.3%); atopic dermatitis in 4 patients (6.6%); seborrheic dermatitis in 2 patients (3.3%); psoriasis in 2 patients (3.3%); and hyperhidrosis, alopecia areata, interstitial granulomatous dermatitis, hidradenitis suppurativa, basal cell carcinoma, vitiligo, and acne in 1 patient (3.3%) each.

A family history of FD was observed in 4 males (2 pairs of brothers). In 6 patients (10%), the onset of FD was associated with stress, and in 5 patients (8.3%), it was associated with local trauma. The mean age of onset of FD was 32 years (range, 10-75 years), with a higher mean age of onset in females than in males (37 vs 30 years, respectively).

Clinically, 14 patients (23.3%) had grade I FD; 24 (40%) had grade II FD; and 22 (36.6%) had grade III FD. The most frequently affected area was the vertex (in 33 patients [55%]), followed by the interparietal area (in 9 patients [15%]), whereas 18 patients (30%) presented with 2 or more affected areas of the scalp. Pruritus was present in 42 patients (70%) and trichodynia was present in 28 patients (46.6%). Pustules and crusts were present in 42 patients (70%), seborrhea in 23 (38.3%), facial papules in 2 (3.3%), tufted hairs in 51 (85%), erythema in 44 (73.3%), and perifollicular hyperkeratosis in 34 (56.6%). Intensity of symptoms was evaluated in 55 of the 60 patients (91.6%); 6 patients (11%) were asymptomatic, 34 (61.8%) had occasional symptoms, and 15 (27.2%) had daily symptoms.

Only 8 patients (13.3%) had alterations in their laboratory blood test results: hypercholesterolemia was found in 5 patients and thalassemia minor, iron deficiency anemia, and antithyroid antibodies were found in 1 patient each.

After multivariate analysis, the unique independent factor associated with a severe from of FD (grade III) was the onset of FD before 25 years of age (odds ratio, 7.33; 95% confidence interval, 1.5-35.0; P = .01). Other factors that were also included in multivariate analysis were tufted hairs, AGA, trichodynia, and pruritus.

Microbiologic cultures of the alopecic patch were performed in 32 patients (53.3%). *S aureus* was isolated in 23 of them (72%) and *Staphylococcus epidermidis* was isolated in 1 patient (3%). Cultures were negative in 8 patients (25%). Nasal bacterial cultures were studied in 10 patients (16.6%). Cultures positive for *S aureus* were obtained in 4 of them (40%), whereas the remaining cultures were negative (60%).

The most frequently used treatments were as follows: topical steroids in 48 patients (80%); topical antibiotics in 37 (61.6%); doxycycline or minocycline in 36 (60%); intralesional steroids in 25 (41.6%); rifampicin and clindamycin in 21 (35%); oral isotretinoin in 15 (25%); photodynamic therapy (PDT) in 8 (13.3%); oral steroids in 5 (8.3%); azithromycin and dapsone in 4 (6.6%); topical tacrolimus in 3 (5%); hydroxychloroquine and minoxidil in 2 (3.3%); and finasteride, cyclosporine, acitretin, trimethoprim-sulfamethoxazole, ciprofloxacin, fusidic acid, and rifampicin in 1 patient (1.6%) each. Adverse effects were assessed in 25 of the 60 patients (41.6%) and were present in 9 of them (in 36%). Epigastralgia, diarrhea, and headache were associated with tetracyclines in 4 patients; hypercholesterolemia, arthralgias, and epistaxis with isotretinoin in 3 patients; and increased alopecic patch and local pain with PDT in 2 patients.

After multivariate analysis, we did not find any statistically significant prognostic factors (age of onset younger than 25 years, tufted hairs, AGA, trichodynia, or pruritus and treatment with rifampicin and clindamycin vs with doxycycline and isotretinoin) that could predict a better therapeutic response.

Monthly cost associated with FD was studied in a subgroup of 25 patients (41.6%). The median monthly cost in patients with mild and moderate forms of the disease was 20€ (range, 5€-25€), whereas in patients with severe FD, it was 80€ (range, 27.5-170), with a statistically significant difference (P = .004).

Results obtained in the Dermatology Life Quality Index questionnaire showed that approximately 25% of the patients had moderate or severe worsening of their QOL. When scores obtained with the 12-Item Short Form Health Survey, version 1, questionnaire were analyzed and stratified by sex, the Mental Component Summary was found to be lower in females than in males, with a statistically significant difference (P = .01). At the same time, it was observed that in the older age groups, the Physical Component Summary and Mental Component Summary of patients decreased.

DISCUSSION

Our study was based on patients with FD and a follow-up period of more than 5 years, and it was intended to deepen the knowledge of this disease. We have proposed a specific therapeutic protocol that could be very useful in the daily practice of the dermatologist (Table I).[1,2,7-9]

FD affects young patients, with a discrete male predominance.[2,6,8,9,12-15] In our study, the detected comorbidities and laboratory tests performed reflect the fact that the disease has no association with immunodeficiency disorders that could explain the chronicity of *S aureus* infection in hair follicles. We

Table I. Proposed therapeutic protocol

Form of FD	Type of treatment	Protocol
Slight or moderate clinical forms	Local	a) Topical corticosteroids: 2 or 3 times per week continuously in combination with topical antibiotics b) Topical antibiotics: 2 or 3 times per week continuously c) Topical tacrolimus: in selected patients, d) Intralesional corticosteroids: once every 3 months if there is slight inflammation e) Others according to symptoms: vitamin D derivatives (calcipotriol) if desquamation and seborrhea, salicylic acid if hyperkeratosis, and minoxidil if associated with androgenic alopecia
	Oral	a) Tetracyclines (doxycycline or minocycline): 100 mg/24 h for 8-12 wk for a mild-to-moderate inflammatory outbreak b) Azithromycin: 500 mg/24 h on 3 d/wk for 3 consecutive weeks when there is resistance to previous antibiotics c) Other antibiotics: fusidic acid, trimethoprim-sulfamethoxazole
Severe clinical forms	Local	Same as for mild or moderate clinical forms
	Oral	a) Rifampicin plus clindamycin: 300 mg/12 h each for 10 wk b) Oral corticosteroids: in association with other treatments when there is severe inflammation c) Isotretinoin: if the response is not maintained with previous treatments c) Dapsone d) Other: cyclosporine, etc
	PDT in selected cases. Initial protocol: 4 sessions of PDT at 4-wk intervals. In patients with adequate response to therapy, sessions can be repeated if clinical symptoms reappear. PDT should be administered in combination with topical and systemic treatment	

FD, Folliculitis decalvans; *PDT*, photodynamic therapy.

did not analyze the association of concomitant dermatologic diseases with the severity of FD; however, in our own experience, these diseases do not correlate with the evolution of FD.

In our study, most cases of FD were sporadic. Regarding the age of onset and the area most frequently affected (the vertex), our findings were similar to those of other studies published in the literature.[1,2,6,8,9,12,14,16]

In the univariate analysis, the presence of tufted hairs was associated with the severe form of FD (P = .04). This relationship had not been described previously. Polytrichia and tufted hairs originate when perifollicular and intrafollicular infiltrate of neutrophils, lymphocytes, and plasma cells surround the upper segment around the infundibulum. Several follicular openings fuse, and more than 5 hairs emerge through the same follicular orifice. We believe that the presence of tufted hairs entails an intense inflammation and, therefore, further progression of scarring alopecia. Early age of onset (<25 years old) (P = .02) and duration of disease (P = .008) were also associated with the severe form of the condition.

After multivariate analysis, the independent factor associated with a greater severity of FD was an age of onset younger than 25 years. We believe that the earlier the FD appears, the more aggressive its behavior will be.[2]

Treatment of FD should be focused on controlling outbreaks and preventing irreversible progression of alopecia. In our study, tetracyclines were the most common oral treatment used in patients with moderate and severe forms; it was administered in cycles of 2 to 3 months, with a 91% response rate. In refractory cases, the combination of rifampicin and clindamycin (300 mg each every 12 hours for 10 weeks) was used because it was the most effective treatment (90.5% response rate) and had a longer duration of response (5 months). Although this is a very short response time, we think that it is acceptable for a relapsing disease such as FD (Fig 1, *A* and *B*). In our experience, the combination of rifampicin and clindamycin is a safe therapeutic regimen with a high rate of response and a prolonged duration of response.[1,2,7-9]

Recently, the use of PDT for the treatment of FD has been described with promising results in some patients.[17-19] In our research, we obtained a favorable response in 75% of the patients; thus, PDT may constitute a therapeutic tool complementary to pharmacologic treatment in selected cases. Local

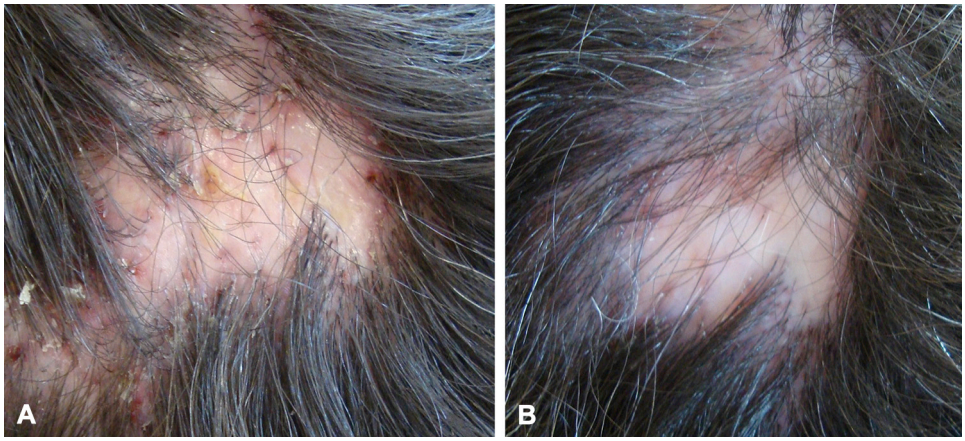

Fig 1. Folliculitis decalvans in a 60-year-old female in whom folliculitis decalvans was diagnosed 4 years ago. **A**, An alopecic patch over the vertex with red and yellowish crusts and erythema and perifollicular hyperkeratosis before initiation of treatment with rifampicin and clindamycin. **B**, Clinical image after treatment with rifampin and clindamycin, 300 mg each every 12 hours for 10 weeks. Clinical improvement with decreased inflammatory signs is observed.

pain related to PDT could be avoided with prior local anesthesia in the affected area. We did not find any prognostic factors associated with a better therapeutic response, and the literature does not currently include any reports analyzing them.

We observed that the economic impact of this chronic disease is considerable. Moreover, in a high percentage of patients, it had a high impact on their QOL and mental health.

Our study has several limitations. Because FD is a rare disease and despite the fact that this was a multicenter study, the recruitment of patients with a minimum period of 5 years of follow-up was difficult. This fact was probably a limiting factor in achieving a larger sample size and therefore more statistically significant results. In addition, there are no validated QOL questionnaires specific to FD; hence, we had to use generic questionnaires.

In conclusion, to our knowledge, this is one of the largest series of patients with FD and a follow-up of more than 5 years that has analyzed the therapeutic responses to the different available treatments. An age of onset of younger than 25 years is associated with a greater severity of FD, and the combination of rifampicin and clindamycin is more effective for refractory cases with a longer duration of response. We have proposed a specific therapeutic protocol with new treatments such as PDT that may be useful in clinical practice. In addition, we have analyzed patients' QOL and the socioeconomic impact of FD to establish how the disease influences patients' lives. One in 4 patients with FD showed a significant worsening of their QOL, and FD had a considerable socioeconomic impact on patients with a severe form of the disease.

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