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# Gram-negative infections in patients with folliculitis decalvans: a subset of patients requiring alternative treatment

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## Abstract

**Background**: Folliculitis decalvans is a neutrophilic cicatricial alopecia whose etiology remains unknown. It is frequently associated with staphylococcal infections. We aimed to determine the rate of gram-negative infections in patients with folliculitis decalvans.

**Methods**: A retrospective chart review was performed of patients with biopsy-proven folliculitis decalvans seen at a tertiary hair referral center. The results of bacterial cultures were evaluated. Subjects were determined to have no infection, gram-positive infections, gram-negative infections, or mixed infections.

**Results**: Thirty-nine subjects were included in the study. Ninety-three cultures were performed. The majority of cultures were positive for staphylococci. Eleven patients (28%) had gram-negative infections of the scalp. Gram-negative infections comprised one-third of all cultures (33%).

**Conclusion**: We present the largest cohort of folliculitis decalvans patients with gram-negative infections, suggesting the need for routine bacterial cultures in patients who are not responsive to standard anti-staphylococcal antibiotics. Awareness of the incidence of these infections may lead to better therapeutic outcomes.

*Keywords: folliculitis decalvans, alopecia, gram-negative infections*

## Introduction

Folliculitis decalvans (FD) is a neutrophil-mediated primary cicatricial alopecia characterized by follicularly based pustules and crusting that is often associated with bacterial infection. It has been reported in the literature that the preponderance of these infections are caused by staphylococci [1, 2]. The pathogenesis of folliculitis decalvans, however, remains unknown. Studies suggest that an alteration in the host immune response may play a role in onset of disease [1]. Loss of epidermal barrier integrity and disruption of endogenous bacterial biofilms leading to an altered subepidermal microbiota are also thought to be triggers of folliculitis decalvans [3, 4]. In this study we aimed to evaluate rates of non-staphylococcal infections in patients with FD.

## Methods

We performed a retrospective chart review of patients with a known diagnosis of folliculitis decalvans, seen at a tertiary hair referral center within Kaiser Permanente Northern California. The diagnosis of FD was based on typical clinical examination findings and history plus histopathologic confirmation in all cases. Histopathologic inclusion criteria were: 1) the presence of a primarily neutrophilic perifollicular and intrafollicular infiltrate in early lesions or lymphocytic perifollicular infiltrates with plasma cells and histiocytes in chronic lesions and 2) loss of sebaceous glands with perifollicular fibrosis. Patients clinically exhibited patches of hair loss with loss of follicular markings, follicular hyperkeratosis, follicular pustules, and perifollicular erythema at the margins of alopecic patches (**Figures 1, 2**). The results of scalp skin bacterial cultures of pustules were evaluated. Subjects were determined to have no infection,

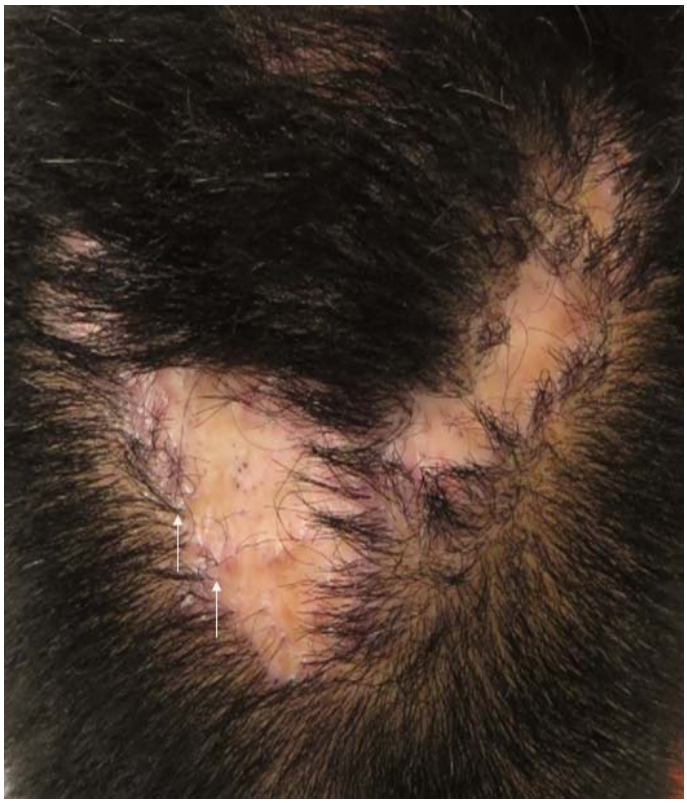

**Figure 1**. *Subject 1 with folliculitis decalvans. Note the follicular pustules and crusting (arrows). This subject had multiple cultures over the course of 12 years, which were positive for Pseudomonas aeruginosa, Serratia marcescens, Klebsiella pneumoniae, Klebsiella oxytoca, methicillin-resistant S. aureus, and S. lugdunenesis.*

gram-positive infections, gram-negative infections, or mixed infections.

## Results

Thirty-nine patients with biopsy proven folliculitis decalvans were identified for inclusion in the study. The majority of patients were male (77%), in keeping with the epidemiology of the disease (1). Average age was 46 with a range of 26-70 years. Race was self-reported as white (41%), black (28%), Hispanic (18%), Asian (8%), and unknown (5%). Five patients did not have cultures. Of the remaining 34 patients, 93 bacterial cultures were done. The majority of cultures showed staphylococci: *S. aureus* (15), methicillin-resistant *S. aureus* (15), *S. lugdunenesis* (4). Eleven of the 34 patients with cultures (32%) had gram-negative rod infections (**Table 1**). Gram-negative infections comprised 33% of all cultures. Cultures were positive for: *Escherichia coli* (7), *Enterobacter aerogenes* (6), *Klebsiella pneumoniae* (6), enteric gram-negative rods (5*), Pseudomonas aeruginosa* (2), *Enterobacter cloacae* (1), *Klebsiella oxytoca* (1), *Proteus mirabilis* (1), *Citrobacter koseri* (1), and *Serratia marcescens* (1).

## Discussion

Folliculitis decalvans is a rare chronic, neutrophlic scarring alopecia most often considered to be either induced by or resulting in chronic staphylococcal infections. Optimal eradication of staphylococci is obtained with one of the following antibiotic regimens: 1) a ten-week course of clindamycin and rifampin 2) doxycycline for three-to-6 months or 3) azithromycin three times a week for three months [5]. Our study provides the largest cohort, to our knowledge, to date of folliculitis decalvans patients with culture proven gram-negative infections. Recent research has documented the presence of commensal biofilms in the infra-infundibular

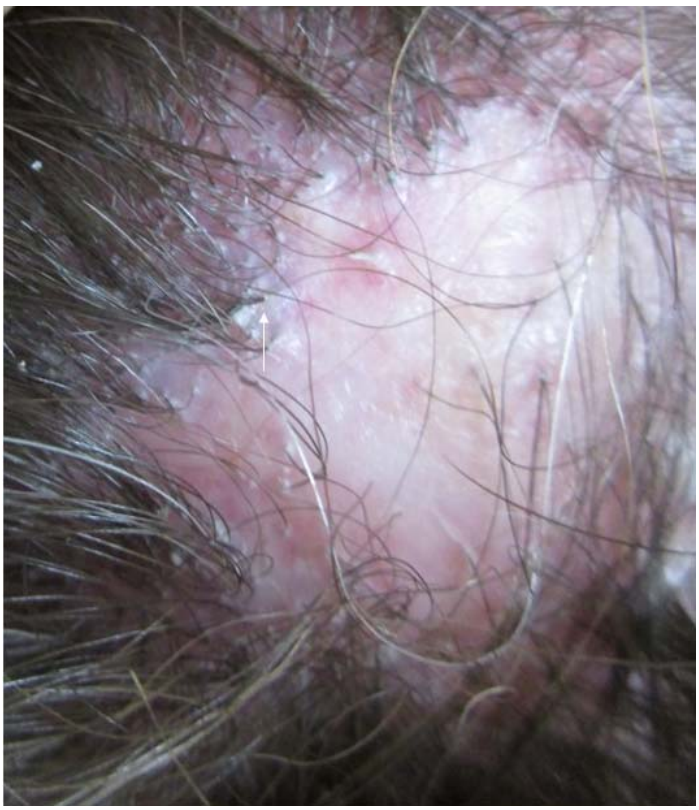

**Figure 2**. *Subject 2 with folliculitis decalvans. Note the perifollicular crusting (arrow). This subject had culture positive for Pseudomonas aeruginosa, Klebsiella pneumoniae. and Escherichia coli. This subject also had a gram-negative folliculitis of the chest.*

(anaerobe) portion of normal hair follicles and in patients with FD [4]. The presence of biofilms could explain chronicity of disease and why there are frequent recurrences after appropriate antibiotic therapy. *Propionibacterium acnes* and coagulase negative staphylococci almost exclusively characterize the subepidermal microbiota of scalp skin [3, 6]. The presence of *P. acnes* and coagulase negative staphylococci in biofilms help maintain the integrity of the hair follicle [3, 4]. Epidermal barrier dysfunction has also been proposed as a contributing factor in disease progression. One study showed that the microbiota in FD patients post-antibiotic therapy is not fully restored to that of healthy controls suggesting a persistent defect in the epidermal barrier [3]. Antibiotics effectively reduce the bacterial load to a level that will not trigger the innate immune system. However, an unbalanced microbiota remains. It is plausible that disruption of the host immune response is also an etiologic component of disease.

Depressed cell-mediated immunity, altered humoral immunity, and diminished levels of alpha-1 antitrypsin resulting in impaired complement 3 (C3) activity have been shown to play a role in pathogenesis of gram-negative folliculitis [7, 8]. Gram-negative folliculitis is believed to be a complication of long-term antibiotic treatment in acne and rosacea patients, the etiology of which has been hypothesized to be the result of suppression of normal commensal flora of the nasal mucous membranes and facial skin [7]. Similarly, gram-negative infections in FD patients may be the result of decreased protective *P. acnes*, which responds well to anti-staphylococcal antibiotics, and coagulase negative staphylococci. Overproduction of sweat and sebum create a favorable environment for gram-negative rod infections [8]. The most frequently found gram-negative bacteria in gram-negative folliculitis are *Klebsiella spp*, *E. coli*, and *Enterobacter spp*. Other gram-negative bacteria such as *Proteus spp, Citrobacter spp*, and *Serratia spp* occur at a less frequent rate [7-9]. Our data support findings of previous studies in patients with gram-negative folliculitis.

**Table 1**. *Culture results. The number of patients with normal skin cultures versus those with gram positive infections, gram negative infections, and mixed infections is shown.*

| Number of patients with cultures | Number normal (%) | Number gram positive (%) | Number gram negative (%) | Number mixed gram negative and positive (%) |
|---|---|---|---|---|
| 34 | 10 (29) | 13 (38) | 5 (15) | 6 (18) |

## Conclusion

In this cohort, the rate of gram-negative rod infections was high and likely represents a referral bias of patients who did not respond to standard treatment. Potential causes for these infections includes long-term antibiotic use as well as nosocomial/environmental exposure and disruption of the normal epidermal barrier related to ongoing inflammation. We conclude that regular bacterial cultures should be considered in patients who have ongoing/active disease to evaluate for the presence of non-staphylococcal bacterial infections. Additionally, treatments including appropriate antibiotics, eradication of the potential source of the infection, topical or systemic retinoids, and re-establishment of the epidermal barrier may be necessary for disease control. As hair regrowth is not possible, the goal of any treatment should be to treat the inflammation thus halting disease progression.

## Potential conflicts of interest

The authors declare no conflicts of interests.

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