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Updates in therapeutics for folliculitis decalvans: A systematic review with evidence-based analysis

To the Editor: Folliculitis decalvans (FD) is the most common neutrophilic scarring alopecia, causing painful, recurrent purulent follicular exudation.[1] Currently, there is a paucity of data regarding the efficacy of FD-specific treatments. This study aimed to provide an evidence-based analysis of current treatment efficacy for FD. Using PRISMA (Preferred Reporting Items for Systemic Reviews and Meta-Analyses) guidelines. PubMed, Medline, Scopus, and the Cochrane library were searched for articles published in English during 1998-2018. Data regarding treatment regimen and efficacy was graded according to the American College of Physicians grading system (Supplemental Fig 1; available at http://www.jaad.org).[2], Treatment efficacy of FD was discussed in 20 studies that included 282 patients, of which 73.4% were male. The highest level of evidence was grade 3, encompassing 7 studies with 263 patients (Table I).[3-8] A multicenter, retrospective study showed that 15 patients treated with a 10-week course of clindamycin and rifampicin achieved the longest disease remission at an average of 7.2 months. The remission period was shorter among those treated with doxycycline or azithromycin for 3-6 months, who subsequently received adjunct topical antibiotics and intralesional corticosteroids.[3] Powell et al demonstrated that a 10-week course of clindamycin and rifampicin achieved remission in 10 of 18 (55.6%) patients for 2-22 months, and 5 additional patients responded after 2-3 more courses.[4] Similarly, Miguel Gomez et al demonstrated a 91% response rate and longer duration of response (5 months) in cases initially refractory to tetracycline treatment.[5] Conversely, a retrospective study by Tietze et al showed 8 of 12 patients treated with a 10-week course of clindamycin and rifampicin relapsed, and 2 had no clinical response.[6] In another retrospective study, 7 of 10 patients treated with combination tetracycline, clobetasol propionate lotion, and intralesional triamcinolone for an average of 7 months were in disease remission for up to 4 years. Continued treatment with oral antibiotics, intralesional triamcinolone, or clobetasol propionate was needed in 11 of 23 patients to maintain remission.[7] Tietze et al[6] demonstrated that isotretinoin treatment for 5-7 months resulted in disease remission for 4-24 months in 9 of 10 patients, 3 of whom required low-dose maintenance. Of note, treatment of FD with isotretinoin was associated with hyperlipidemia (14/39) in another retrospective review.[8]

Newer therapeutic options have been described in case reports and case series in recent years, and accordingly, the level of evidence is very low (grade 4) (Table II).[1] Red light photodynamic therapy resulted in clinical improvement in 9 of 10 patients, with 6 patients exhibiting disease remission.[1] Additional treatments with lowest evidence were tacrolimus ointment, external beam radiation, isotretinoin, human immunoglobulin, adalimumab, infliximab, and long-pulse neodymium:yttrium aluminum garnet.

Overall, all studies evaluated had small sample sizes, lacked control groups, and randomization. In addition, given the retrospective nature of the included studies, blinding was not possible so observer bias might have occurred. Combination of clindamycin and rifampicin was the most commonly used treatment in reviewed studies. However, based on low quality of evidence, we are unable to discern whether it is the most efficacious treatment. The lack of higher grade evidence highlights the need for stronger studies performed to assess the efficacy of various treatments used for folliculitis decalvans, though the rarity of FD makes this challenging.

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Table I. Grade 3 studies with low quality of evidence

Study design, study	Previous treatment failure	Cohort description	Treatment regimen	Treatment adverse effects	Treatment outcome	Outcome from ACP grading
1) Retrospective, multicenter review [Vano-Galvan et al; J Eur Acad Dermatol Venereol. 2015; 29(9):1750-57]	Not mentioned	82 total patients; 52 were men; mean age 35 y; 17 (21%) had severe disease	39 patients doxycycline for 3-6 mon 15 patients clindamycin and rifamicin for 10 wk 6 patients azithromycin 3x/wk for 3 mon	None	Doxycycline: 90% improvement, remission (mean 4.8 mon) Clindamycin and rifampicin: 100% improvement, remission (mean 7.2 mon) Azithromycin: 100% improvement, remission (mean 4.6 mon)	Grade 3
2) Retrospective, single-center, observational study [Tietze et al; J Eur Acad Dermatol Venereol 2015; 29(9):1816-21]	Clindamycin, rifampicin, clarithromycin, dapsone	28 total patients; 26 were men; age range 19-64 y	IST (0.2-0.5 mg/kg) for 5-7 mon Dosage tapered after remission achieved to 10 mg 2-3x/wk in 3 patients Follow-up range 2 mon-15 y	None	Complete remission with IST in 9 (90%) patients for 4 mon-2 y 3 (30%) patients required maintenance on low-dose IST Relapse rates with antimicrobials: clindamycin and rifampicin 8 (80%) patients, clarithromycin 6 (67%) patients, ciprofloxacin or doxycycline 7 (78%) patients, dapsone 4 (57%) patients	Grade 3
3) Retrospective, single-center, observational study [Bunagan et al; J Cutan Med Surg. 2015; 19(1):45-9]	Not mentioned	23 total patients; 6 men; follow-up period 3 mon-13 y	A. ILT + clobetasol propionate lotion + (doxycycline 100 mg bid, minocycline 100 mg bid, or tetracycline 500 mg bid) (n = 10) B. Cephalexin + ILT + clobetasol propionate lotion (n = 6) C. Clindamycin + rifampicin (n = 1)	None	A. FD in remission in 7/10 (70%) patients, treatment discontinued FD inactive in 3 (30%) patients with continued treatment B. FD inactive in 6/6 patients with continued treatment	Grade 3

Continued

Table I. Cont'd

Study design, study	Previous treatment failure	Cohort description	Treatment regimen	Treatment adverse effects	Treatment outcome	Outcome from ACP grading
			D. ILT + clobetasol propionate lotion (n = 1)		C. FD in remission in 1/1 patient, treatment discontinued D. FD in remission in 1/1 (100%) patient, treatment discontinued (The ILT+clobetasol proprionate lotion n=1 line)	
			E. Multiple combinations (cephalexin, minocycline, tetracycline, rifampicin, clindamycin, ciprofloxacin, IST, dapsone) (n = 5)		E. FD under control in 2/5 (40%) patients with continued treatment, FD still active in 3/5 (60%) patients despite treatment	
4) Single-center case series; nonblinded, nonrandomized study [Sillani et al; Int J Trichol Jan 2010; 2(1):20-3]	Not reported	13 total patients; 11 were male; mean age 30.1 (range 15-66) y	Mild FD (n = 8): minocycline 100 mg po bid	1 patient developed nausea and vertigo from rifampicin	Mild FD: minocycline 100 mg bid for average of 5.7 wk cleared inflammatory scalp lesions in 7/8 patients, 1/8 needed 2-wk acitretin rescue therapy, 1/8 exhibited FD relapse after 8 mon	Grade 3
			Moderate FD: minocycline 100 mg po bid + rifampicin 150-300 mg bid Adjuvant drugs used included topical fusidic acid or mupirocin, selenium sulfide shampoo, oral compound glycyrrhizin, and zinc gluconate		Moderate FD cases: combination of minocycline and rifampicin for average of 11.7 wk effective in treating 3 patients, clarithromycin + rifampicin for average of 10 wk effective in clearing scalp lesions in 2 patients (1 mild FD, 1 moderate FD) 9/13 patients partial hair growth responders (<75%)	

5) Case series study [Powell et al; Br J Dermatol. 1999; 140(2): 328-33]	Flucoxacillin, erythromycin, minocycline	18 total patients; 13 were men; age range 18-62 y	Clindamycin 300 mg bid and rifampicin 300 mg bid for 10 wk	1 patient developed rash from clindamycin	FD in remission for 2-22 mon in 10 (55.6%) patients after 10-week course; FD in remission in 15 (83.3%) patients after 2-3 more 10-week courses	Grade 3
6) Retrospective, multicenter review [Miguel-Gomez et al; J Am Acad Dermatol. 2018; Epub ahead of print]	Not reported	60 total patients; 37 were men; median age 40 (range 23-83) y	Topical steroids (n = 48), topical antibiotics (n = 37), tetracycline (n = 36), intralesional steroids (n = 25), rifampicin and clindamycin (n = 21), oral isotretinoin (n = 15), photodynamic therapy (n = 8), oral steroids (n = 5), azithromycin and dapsone (n = 4), topical tacrolimus (n = 3), hydroxychloroquine and minoxidil (n = 2)	Epigastralgia, diarrhea, and headache associated with tetracyclines in 4 patients; hypercholesterolemia, arthralgias, and epistaxis in 3 patients treated with isotretinoin	Tetracyclines used in moderate and severe FD patients (n = 36) had 91% response rate; in refractory cases, rifampicin + clindamycin most effective, with 90.5% response rate and longer response duration (5 mon)	Grade 3
7) Retrospective, case series study [Aksoy et al; Int J Dermatol. 2018; 57(2):250-253]	Not reported	39 total patients, all male; mean age 37.85 (range 16-82) y	Oral isotretinoin 0.1-1.02 mg/kg/d for median 2.5 (range 1-8) mon; patients responding to treatment (n = 36) were subgrouped by daily dose (<0.4 mg/kg, ≥0.4 mg/kg) and duration (<3 mo, ≥3 mo)	Hyperlipidemia (35.9%), intractable xerosis (10.3%)	36 patients had partial and complete response after isotretinoin treatment, 61.5% patients had response to IST within 1 mon; 66% patients receiving IST <3 mo relapsed; patients that received oral IST ≥0.4 mg/kg/d for ≥3 mo had best response to IST, 66% no disease relapse	Grade 3

BID, Two times a day; *FD*, folliculitis decalvans; *ILT*, intralesional triamcinolone; *IST*, isotretinoin; po, per oral.

Table II. Grade 4 studies with very low level of evidence

Study design	Previous treatment failure	Patient description	Treatment regimen	Treatment adverse effects	Treatment outcome	Outcome from ACP grading
1) Retrospective, case report [Collier et al; Clin Exp Dermatol. 2017; doi: 10.1111/ced.13238]	Doxycycline, rifampicin, clindamycin, IST, acitretin, CS, CsA	26-year-old man	Systemic PDT with ultraviolet light (100-140 J/cm^2) with 1 mg/kg porfimer sodium	None	FD in remission at 25 mon follow-up	Grade 4
2) Retrospective, case series [Burillo-Martinez et al; J Am Acad Dermatol. 2016;74(4): e69-70]	Oral and intralesional CS, antibiotics	3 patients; all men; mean age 30 y	PDT; mean of 11 sessions over mean 9 mon; concurrent treatment with sulfamethoxazole-trimethoprim	All patients experienced pain and erythema; 1 patient exhibited worsening of condition	2 patients mild improvement after PDT session but relapsed before next cycle; 1 patient worsening of FD during treatment, required oral CS	Grade 4
3) Retrospective, case report [Elsayad et al; Strahlenther Onkol. 2015; 191(11): 883-8]	Tetracycline, rifampicin, cefaclor, clarithromycin, linezolid, CS, CsA, IST	45-year-old man	First course radiotherapy: 5 Gy in 5 fractions; second course radiotherapy: 6 Gy in 5 fractions 5 mon later	Mild pain, erythema, and transient increased scalp exudate	FD and associated symptoms significantly improved especially pain and pruritus at 12 mon follow-up	Grade 4
4) Prospective, single-center, case series [Miguel-Gomez et al; J Am Acad Dermatol. 2015;72(6): 1085-7]	Doxycycline, IST, rifampicin	10 patients; 5 men	PDT with MAL (methyl aminolevulinate hydrochloride)* 160 mg/g cream at 4-wk interval; area treated with red light at 630 nm with total light dose of 37 J/cm^2; 2 patients concurrent doxycycline and intralesional CS	6 (60%) patients experienced local reaction post-PDT and pain	FD in remission for 9 (90%) patients; duration of remission 2-36 months (mean 9.9 mon); No. of patients and (no. sessions): 1(13), 1(9), 1(6), 1(5), 3(4), 1(3)	Grade 4
5) Retrospective, case report [Ismail et al; J Dermatolog Treat 2015; 26(5):471-2]	Clindamycin, rifampicin	27-year-old man	IVIG 2 g/kg first month then reduced to 1 g/kg from second to fourth month; concurrent flucloxacillin up to 3 infusions	None	FD in remission at 6 mon follow-up	Grade 4

6) Retrospective, single-center, case series [Kreutzer et al; J Dtsch Dermatol Ges 2014;12(1): 74-6]	Clindamycin, rifampicin, dapsone, methotrexate, oral CS, IST	2 patients; all women; age 58 and 50 y	Adalimumab 40 mg every 2 wk	None	FD in remission after 2-3 mon treatment; long-term follow-up unavailable	Grade 4
7) Case report [Meesters et al; J Dermatolog Treat 2014;25(2): 167-8]	Tetracycline, erythromycin, doxycycline, flucloxacillin, IST	34-year-old man	Long-pulsed Nd:YAG 1064-nm laser; started at 30 J/cm^2 for 50 ms; dose increased to 50 J/cm^2 with reduced pulse duration to 30 ms; total of 9 treatments, 8−12-wk interval	Pain and mild crusting but relived with topical lidocaine ointment and oral tramadol 50 mg during treatment	FD in remission at 1.5 y follow-up	Grade 4
8) Retrospective, case report [Mihaljevic et al; J Dtsch Dermatol Ges 2012;10(8): 589-90]	IST, oral CS, oral antibiotics, dapsone and zinc	45-year-old man	Infliximab 5 mg/kg every 4-6 wk	None	FD in remission after 3 infusions until 12 mon follow-up	Grade 4
9) Retrospective, case report [Castano-Suarez et al; Photodermatol Photoimmunol Photomed. 2012;28(2): 102-4]	Topical CS, IST, dapsone	32-year-old woman	PDT with MAL (methyl aminolevulinate hydrochloride);* 630 nm delivered at 37 J/cm^2; 3 cycles over 8-wk period; each cycle involved 2 treatments 2 wk apart	Mild itching	FD in remission at 12 mon follow-up after last treatment	Grade 4
10) Retrospective, case series [Bastida et al; Int J Dermatol. 2012; 51(2): 216-20]	Acitretin, dapsone, oral and topical CS, antibiotics	4 patients; 3 were women; age 23-40 years	Tacrolimus (0.1%) ointment bid; 1 patient had combination treatment with doxycycline 100 mg/d	None	FD in remission at follow-up (range 2 mon-2.5 y); relapse occurred shortly after treatment discontinued	Grade 4

Continued

Table II. Cont'd

Study design	Previous treatment failure	Patient description	Treatment regimen	Treatment adverse effects	Treatment outcome	Outcome from ACP grading
11) Retrospective, case report [Parlette et al; Dermatol Surg. 2004;30(8): 1152-4]	Dicloxacillin, tetralysal, doxycycline, minocycline, levofloxacin, ILT, IST, 1 course radiation	26-year old man	Nd:YAG laser at 28 J/cm2, 3-msec pulse duration, a 12-mm spot, and dynamic cryogen spray cooling set at 50-msec spray and 20-msec delay; patient received 8 treatments at 4-wk to 6-wk intervals	Significant pain during treatment	FD in remission at 6 mon follow-up	Grade 4
12) Retrospective, case report [Gemmeke et al; Acta Dermatovenerol Alp Pannonica Adriat. 2006; 15(4):184-186]	Prednisolone, ampicillin	27-year-old man	IST 30 mg/d, oral clindamycin 300 mg/d for 6 wk, prednisolone 20 mg/d tapered within 3 wk	None	At 3 wk, marked reduction in inflammation and partial regrowth in nonscarred scalp areas; at 6-mon follow-up, no disease progression	Grade 4
13) Retrospective, case report [Kaur et al; J of Dermatol. 2002;29(7): 180-181]	Multiple short courses of low-dose corticosteroids and antibiotics	42-year-old man	Rifampicin 600 mg po 1x/d; topical 2% mupirocin ointment	None	At 2 wk, pain and folliculitis disappeared, and no new pustules formed; alopecia did not extend but scarring persisted; complete resolution of FD at 6-mon follow-up	Grade 4
14) Retrospective, case report [Kunte et al; J Am Acad Dermatol. 1998;39(5 Pt2): 891-3]	Flucloxacillin, IST, topical superpotent CS	27-year-old man	Dapsone 100 mg/d	None	FD in remission for 18 mon	Grade 4

ACP, American College of Physicians; *bid*, 2 times a day; *CS*, corticosteroids; *CsA*, cyclosporin; *FD*, folliculitis decalvans; *ILT*, Intralesional triamcinolone; *IST*, Isotretinoin; *IVIG*, Intravenous immunoglobulin; *MAL*, methyl aminolevulinate; *Nd:YAG*, neodymium:yttrium aluminum garnet; *PDT*, photodynamic therapy; *po*, per oral.

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Acute onset/flares of dermatomyositis following ingestion of IsaLean herbal supplement: Clinical and immunostimulatory findings

To the Editor: The use of complementary and alternative medicine has gained popularity over the past few decades.[1] Herbal and dietary supplements—the most common form of complementary and alternative medicine—are known to have various adverse medical and dermatologic[2] effects. Previous literature has reported the acute onset/flare of autoimmune cutaneous disease, including pemphigus vulgaris,[3] dermatomyositis,[3] and systemic lupus erythematosus, with the ingestion of known immunostimulatory herbal supplements. Although tumor necrosis factor-α (TNF-α) is thought to be a mediator[4] in the pathogenesis of autoimmune cutaneous disease, the exact mechanism by which herbal supplements cause the clinical precipitation or exacerbation of these diseases has never been described.

We observed 3 patients with an acute onset (2 cases) or flare (1 case) of their dermatomyositis after ingestion of the widely popular herb-based weight loss product IsaLean (Isagenix, Gilbert, AZ) (Fig 1). Patient 1 had classic dermatomyositis (positive for PM-scl 100 antibody), patient 2 had amyopathic dermatomyositis (negative for Jo-1 antibody), and patient 3 had undifferentiated connective tissue disease with features of amyopathic dermatomyositis and lupus pernio (positive for ANA [titer, 1:320], positive for SS-A (>8), negative for Scl-70, and negative for a myositis panel). The purpose of this study was to investigate and characterize the pathophysiologic mechanism of IsaLean underlying the acute onset or flare of dermatomyositis that was witnessed in all 3 patients.

Peripheral blood mononuclear cells (PBMCs) were isolated from blood samples obtained from 5 patients with dermatomyositis and 5 control subjects. The PBMCs were stimulated with increasing concentrations of IsaLean (0, 0.05, 0.5, and 5 μg/mL) to measure the levels of key pathogenic cytokines (TNF-α, interferon-α [IFN-α], and interferon beta [IFN-β]) secreted. In addition, the effect of anti–Toll-like receptor 4 (TLR4) and 2 antimalarials used in the treatment of dermatomyositis—quinacrine and hydroxychloroquine—on cytokine production was examined after incubation of PBMCs with either lipopolysaccharide (LPS) or IsaLean alone.

Our results showed that IsaLean-treated cells secrete significantly higher levels of TNF-α, IFN-α, and IFN-β. IsaLean significantly increased TNF-α

Treatment Grade	Strength of Evidence
Grade 1	Well-designed randomized, controlled trial (RCT) that yield consistent and directly applicable results. Further research is unlikely to change the level of confidence in the estimate of effect.
Grade 2	Well-designed controlled trial without randomization, well-designed cohort or case-control analytic studies and multiple time series with or without intervention.
Grade 3	Includes observational studies with the risk for bias
Grade 4	Studies with insufficient evidence to determine the net benefits or risks.

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Supplemental Fig 1. American College of Physicians treatment grading guidelines.[2]