

3 Cases of Dissecting Cellulitis of the Scalp Treated With Adalimumab

Control of Inflammation Within Residual Structural Disease

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Background: Dissecting cellulitis of the scalp (DCS) is a chronic inflammatory disease of scalp hair follicles manifesting as multiple painful nodules and abscesses that interconnect via sinus tracts. The disease tends to run a progressive course that eventually results in scarring alopecia. The condition is thought to represent a follicular occlusion disorder. Sebaceous and keratinous material within dilated pilosebaceous units accumulates until follicles burst, with subsequent neutrophilic inflammatory reaction and abscess formation. Treatment remains unsatisfactory. While oral antibiotics, intralesional corticosteroids, isotretinoin, or dapsone are insufficient, in this case series the inflammation responsible for scarifying tissue destruction was directly targeted by means of the tumor necrosis factor antagonist adalimumab.

Observation: Clinical signs of inflammation as well as burden of disease measured by a score of 0 to 10 ($P < .04$) was reduced rapidly by adalimumab. Histopathologic characteristics demonstrated marked improvement of inflammation, despite persistence of underlying structural disease. Relapse was observed following discontinuation of adalimumab.

Conclusions: Adalimumab is effective for treatment of DCS. Relapse on discontinuation of therapy can be expected depending on persisting structural disease. Continuous treatment or combined surgical resection of involved areas could be necessary for definitive resolution of disease.

Arch Dermatol. 2010;146(5):(doi:10.1001/archdermatol.2010.16)

DISSECTING CELLULITIS OF the scalp (DCS), also known as dissecting folliculitis, perifolliculitis capitis abscedens et suffodiens, or Hoffmann disease, is a rare but well characterized chronic inflammatory disease of the scalp leading to scarring alopecia. Most of those affected are young black males; about 10% of cases involve white males. Association with acne conglobata was described as early as 1903.¹ Today, DCS is considered to be part of the follicular occlusion triad, along with acne conglobata and hidradenitis suppurativa,^{2,3} although isolated scalp disease can occur. Deep inflammatory nodules develop on the occipital scalp or vertex and can evolve to extensive confluent boggy plaques with sinus tract formation. Hairs overlying the nodules can be easily plucked, and sinus tracts may discharge purulent material. Ultimately, a multifocal scarring alopecia ensues that is potentially disfiguring.

Pathogenetically, a defect in follicular keratinization is blamed, leading to poral obstruction and accumulation of sebaceous

and keratinous material within dilated pilosebaceous units. Subsequently, follicles burst, and an intense neutrophilic inflammatory reaction with abscess and sinus tract formation follows. The histopathologic features vary according to the stage of disease: early lesions are characterized by acneiform distention of the follicular infundibula with intrafollicular and perifollicular neutrophilic infiltrates. On progression of the lesions, prominent, deep-seated abscesses eventually form in the adventitial dermis and subcutis, and foreign body giant cells and granulation tissue may be present. Late-stage lesions include scarring and sinus tracts partly lined with squamous epithelium. Sinus tracts that transport purulent material can interconnect lesions up to several centimeters apart. Secondary bacterial infection frequently occurs, with both opportunistic strains such as *Propionibacterium acnes* and coagulase-negative *Staphylococci* and, less frequently, overt pathogenic bacterial strains such as *Staphylococcus aureus*. It has been suggested also that the pathogenesis of this disorder may include an abnormal host response to bacterial antigens.

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Table. Clinical and Laboratory Data

Characteristic	Patient No.		
	1	2	3
Age at presentation, y	30	29	27
Duration of disease, y	1	4	7
Prior treatments	Antibiotics	Antibiotics, tetracyclines, isotretinoin, 4 mo	Antibiotics, tetracyclines, levofloxacin, isotretinoin 3 y
Comorbidities	None	None	Inguinal suppurative hidradenitis
Dermatopathologic findings before treatment with adalimumab	Inflammatory infiltrate (+++), fibrosis and cicatrization (++)	Inflammatory infiltrate (++), fibrosis and cicatrization (-)	Inflammatory infiltrate (+++), fibrosis and cicatrization (-)
Dermatopathologic findings after treatment with adalimumab	Inflammatory infiltrate (+), fibrosis and cicatrization (+++)	Inflammatory infiltrate (++), fibrosis and cicatrization (-)	Inflammatory infiltrate (+), fibrosis and cicatrization (+)
Bacteriologic findings	Coagulase-negative staphylococci	Coagulase-negative staphylococci	Coagulase-negative staphylococci, propionibacterium acnes

Abbreviations: -, absent; +, detectable; ++, intermediate; +++, pronounced.

Treatment of DSC remains unsatisfactory. With response to oral antibiotics, intralesional corticosteroids, isotretinoin, or dapsone being unpredictable and at best temporary, in willing patients with medically intractable, symptomatic, and cosmetically disfiguring disease, radical surgical resection or, more recently, selective follicular destructing by photothermolysis using laser⁴ represent the single definitive treatment modalities.

Because the pathogenetically related hidradenitis suppurativa has been shown to respond favorably to tumor necrosis factor (TNF) targeted therapy,^{5,6} we decided to treat DCS with the monoclonal anti-TNF antibody adalimumab. Moreover, we were encouraged by a recent single case report⁷ of successful treatment of DCS with the monoclonal anti-TNF antibody infliximab. At the same time, we questioned the sustainability of such an exclusively anti-inflammatory monotherapy in view of the underlying structural disease of DSC. We treated 3 cases of DSC with adalimumab, and assessed clinical and subjective responses, as well as histopathologic changes.

METHODS

Three white male patients, 27, 29, and 30 years of age, were referred to the Hair Consultation Clinic of the Department of Dermatology, University Hospital of Zürich, Switzerland, for treatment of DSC of 1, 4, and 7 years' duration, respectively, in 1 case associated with inguinal hidradenitis suppurativa (**Table**).

After ruling out latent tuberculosis and hepatitis B, we started adalimumab at a dose of 80 mg administered subcutaneously followed by a dose of 40 mg 1 week later and an additional 40 mg every second week. As is customary at our department, at every visit approximately every month patients were asked to indicate their subjective burden of disease on a scale of 0 to 10, with 0 indicating that the patient is free of disease and 10 indicating maximal burden of disease. Nonsystematic retrospective case studies such as this qualify as off-label use not requiring ethics committee review in Switzerland.

RESULTS

In all 3 patients, boggy and fluctuant infiltrates (**Figure, A-C**) with purulent secretion were present, and the diagnosis of DSC was confirmed by biopsy. Microbiologic findings showed colonization of pus with coagulase-negative *Staphylococci* in all cases and *Propionibacterium acnes* in 1 case. All 3 patients had previously been treated with antibiotics and 2 of the 3 with isotretinoin without success.

During treatment with adalimumab, clinical symptoms subsided within 8 weeks of treatment in all 3 patients. After 3 months, clinical activity (**Figure, D-F**) and patients' subjective symptoms (**Figure, G**) were effectively reduced. However, biopsy findings during treatment demonstrated that although the inflammatory infiltrate was reduced in 2 of the 3 patients (patients 1 and 3), preexisting pathologic residual structures such as subcutaneous sinus tracts remained unchanged (**Figure, H and I**). Ultimately, when treatment with adalimumab was paused in patient 3 after 4 months of successful treatment, disease activity returned within 4 weeks, and adalimumab had to be restarted.

COMMENT

The biologic agent adalimumab binds to TNF, preventing it from activating TNF receptors. Tumor necrosis factor inactivation has proven to be important in down-regulating the inflammatory reactions associated with a number of immune-mediated diseases. In 2008, adalimumab was approved by the US Food and Drug Administration for treatment of severe chronic psoriasis. Because biologic agents often are at the forefront of biomedical research, they are typically used to treat medical conditions for which no other satisfactory treatments are available. They have given us the possibility to reduce inflammation in many dermatoses easily and quickly. Often, the rapid reduction of symptoms and clini-

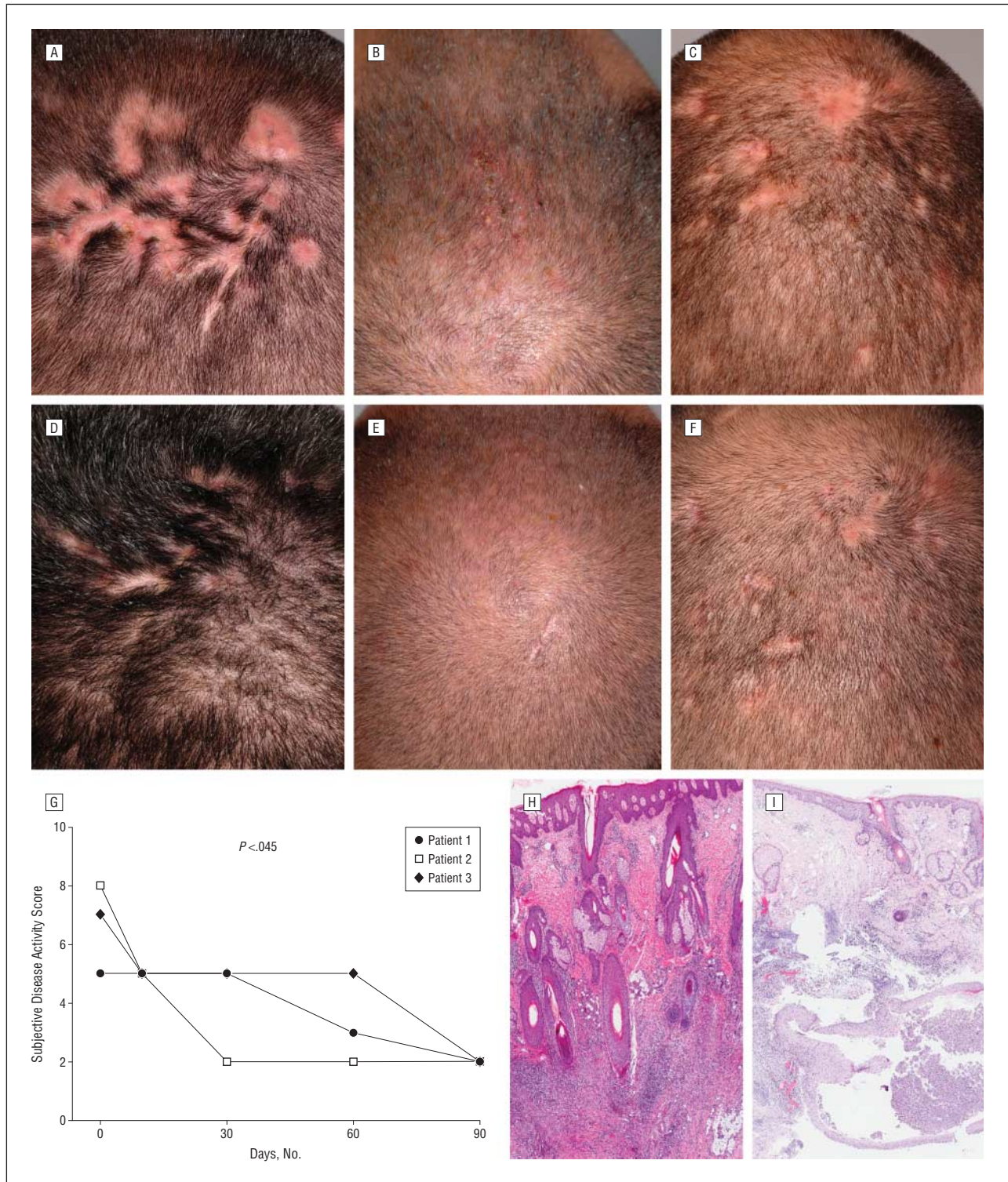


Figure. Patients treated for dissecting cellulitis of the scalp. Patient 1 (A), patient 2 (B), and patient 3 (C) before treatment with adalimumab. Patient 1 (D), patient 2 (E), and patient 3 (F) after 3 months of treatment with adalimumab. Subjective disease activity score from 0 to 10 at the respective days, analyzed with paired 2-sided *t* test (G). Biopsy specimens stained with hematoxylin-eosin (original magnification $\times 20$) of patient 1 before treatment (H) and after 11 weeks of treatment (I) (note persisting epithelialized subcutaneous sinus tract).

cal activity is interpreted as a cure. However, as we know from the experience with psoriasis, on stopping biologic agents, there is a relapse of disease. In fact, biologic agents just suppress the underlying inflammatory process rather than cure the disease. The cases de-

scribed herein demonstrate that clinically successful treatment of DCS with the biologic agent adalimumab is based on control of the inflammatory component of disease, while underlying structural disease remains and represents the point of relapse. In any case, to achieve the goal

of definitively clearing structural pathology-based disease, such as DSC, prolonged treatment⁸ and actual removal of affected tissues⁹ probably remain the only options. The latter could possibly be performed more efficiently after having reduced the inflammation with targeted biologic treatment. In addition, very early anti-TNF treatment could well lead to prevention of chronic inflammation, scarring, and structural disease. Whether a prolonged use of anti-TNF as monotherapy results in actual resolution of subcutaneous epithelialized sinus tracts and whether this can be economically justified remain to be seen.

Accepted for Publication: November 9, 2009.

Published Online: March 15, 2010 (doi:10.1001/archdermatol.2010.16).

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Author Contributions: Both authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Navarini and Trüeb. *Acquisition of data:* Navarini. *Analysis and interpretation of data:* Navarini. *Drafting of the manuscript:* Navarini and Trüeb. *Critical revision of the manuscript for important intel-*

tual content: Navarini and Trüeb. *Statistical analysis:* Navarini. *Obtained funding:* Trüeb. *Administrative, technical, and material support:* Navarini. *Study supervision:* Trüeb.

Financial Disclosure: None reported.

Funding/Support: This study was supported by the Department of Dermatology, University Hospital of Zürich.

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