The use of Goeckerman therapy in managing erythrodermic psoriasis resistant to multiple medications

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Abstract

Erythrodermic psoriasis is a relatively rare, more dangerous inflammatory variant of psoriasis associated with high morbidity and mortality. It can be exceptionally challenging to manage, defeating even the most experienced dermatologist's arsenal of treatment strategies. Goeckerman therapy, a regimen of ultraviolet B phototherapy and crude coal tar, has demonstrable efficacy in severe and recalcitrant plaque-type psoriasis. However, its utility in erythrodermic psoriasis has not been explored within the dermatology literature. Herein, we present a patient with a long-standing history of erythrodermic psoriasis refractory to eleven treatment modalities including four biologic agents, who had his erythroderma 'turned around' following Goeckerman therapy. 'Turned around' is used to describe dramatically reducing a patient's cutaneous inflammation so that previously recalcitrant disease can now respond to maintenance therapy. The importance of a one to three week 'cool down' period of topical corticosteroid therapy prior to phototherapy or crude coal tar use is highlighted in this case as well. Although Goeckerman therapy is no longer regularly used, it remains one of the most efficacious treatments available for intractable psoriasis, attracting patients from all over the country desperate for symptom relief. This case suggests it may be useful in 'turning around' extremely difficult-to-treat erythrodermic psoriasis as well.

Keywords: Goeckerman therapy, erythrodermic psoriasis, treatment resistance, narrow-band ultraviolet B phototherapy, crude coal tar

Introduction

Since 1925, Goeckerman therapy has been used to treat psoriasis using the combination of ultraviolet B (UVB) phototherapy and crude coal tar (CCT), [1]. The overwhelming majority of psoriasis patients that complete Goeckerman therapy achieve complete or near-complete clearance of their cutaneous signs and symptoms [1]. Goeckerman therapy is superior in efficacy to many psoriasis treatment options and has been used to successfully treat psoriasis resistant to biologic agents [2]. Despite it being a very efficacious therapy with few side effects, Goeckerman is no longer regularly used in the U.S. owing to the low number of Goeckerman therapy centers and the significant discipline, commitment, and time that it requires [1,3]. However, for severe and intractable cases that have evaded every option in a dermatologist's tool kit, Goeckerman treatment remains a viable option and our therapy center has received patient referrals from all over the country. Insurance companies often enact special provisions so that the most severe patients can receive coverage for Goeckerman therapy, even if the treatment center is out-of-state or out-of-network.

While Goeckerman therapy is known to be very efficacious in treating plaque-type psoriasis, its efficacy in treating erythrodermic psoriasis is not as widely known. Erythrodermic psoriasis is a rare and intense inflammatory variant of psoriasis that is associated with high morbidity and mortality and can be particularly difficult to clinically manage [4]. Herein, we present a patient with a long-standing history of erythrodermic psoriasis refractory to at least eleven psoriatic treatments, including four

biologic agents. Successful completion of Goeckerman therapy for twelve weeks resulted in 'turning around' his previously recalcitrant erythrodermic disease. 'Turning around' is a term we use to describe aggressive treatment of severely erythematous skin, with the goal of considerably reducing cutaneous inflammation so that previously resistant psoriasis can now respond to maintenance therapy. We also discuss the importance of a 'cool down' period, a week or more of diffuse topical corticosteroid therapy, prior to initiating phototherapy or CCT in erythrodermic or severely inflamed psoriasis patients, to lessen the risk of worsening erythema and edema or pustular conversion, respectively [5,6].

Case Synopsis

A 46-year-old man with a long-standing history of severe, chronic, intractable erythrodermic psoriasis and psoriatic arthritis presented to our center. When he first presented, more than 90% of his body surface area (BSA) was covered by large, thick plaques scattered over his trunk and extremities overlying severe, diffuse background erythema (**Figure 1**). At that time, his treatment regimen included the extensive application of triamcinolone ointment over the body and aclometasone ointment for the face. His psoriasis was intensely pruritic and profoundly disruptive to his daily life. He experienced significant sleep disturbance and had difficulty completing his work owing to his psoriasis symptoms. His psoriatic arthritis manifested as constant stiffness and pain over his spine and neck. He also had many flares of pustular psoriasis throughout his more than 15-year-history. The patient tried and failed at least eleven psoriasis treatment modalities before his first visit to us, with little to no improvement. These treatments included super-potent and other topical corticosteroids, topical vitamin D analogues, narrow-band ultraviolet B (NB-UVB) phototherapy, oral systemic medications (acitretin, cyclosporine, methotrexate, and apremilast), and biologic agents (etanercept, adalimumab, ustekinumab, and secukinumab).

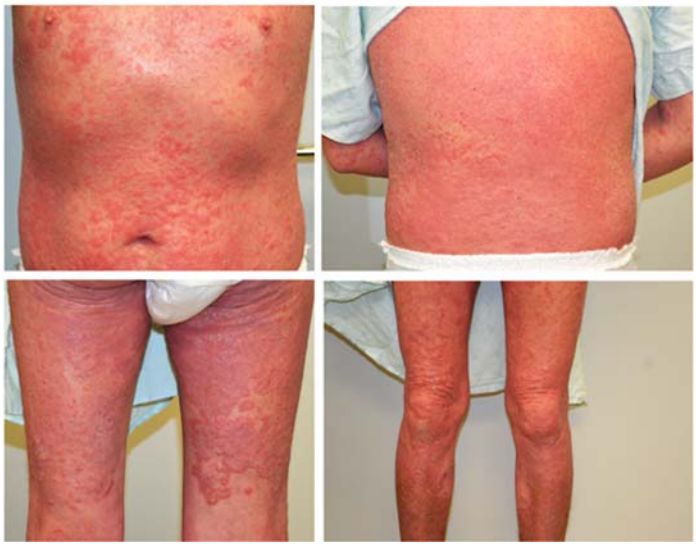

Figure 1. *Over 90% body surface area involvement of erythrodermic psoriasis in the patient prior to Goeckerman therapy.*

The patient was considered an ideal candidate for Goeckerman therapy owing to his severe, recalcitrant disease and his motivation to complete the time-intensive regimen. The Goeckerman regimen at the University of California, San Francisco's (UCSF's) Psoriasis and Skin Treatment Center requires approximately six hours (with at least four hours in the tar) of treatment per day, five days a week, for a minimum of six weeks [7]. Prior to beginning Goeckerman therapy, the patient completed a three week 'cool down' period in which he applied triamcinolone 0.1% cream diffusely. During Goeckerman therapy, the patient received daily NB-UVB phototherapy (beginning cautiously at the low dose of 30mJ UVB and increasing as tolerated) followed by application and Saran Wrap occlusion of 2-10% CCT that was later washed off with mineral oil. During this time, he also used 20% liquor carbonis detergens (LCD) in Aquaphor at home. After more than twelve weeks of therapy, totaling 62 days of Goeckerman treatments, the patient achieved significant improvement, 'turning around' his psoriasis with no residual pruritus (**Figure 2**). The patient transitioned to risankizumab-rzaa for long-term maintenance therapy and has maintained disease clearance three months later.

Case Discussion

This case highlights the utility of Goeckerman therapy as an effective option for long-standing erythrodermic psoriasis that defied many treatment

options. Following a comprehensive review, we found that only one case report (N=2), [8] and two retrospective reviews (N=53 and N=23), one at Mayo clinic [2] and one at UCSF [9], have been published describing Goeckerman therapy's efficacy in treating psoriasis refractory to one or more biologic agents when used as monotherapy or as an adjuvant to biologic therapy. This case report is unique, however, given the severe, extensive, and debilitating nature of this patient's disease and his erythrodermic subtype of psoriasis.

Erythrodermic psoriasis is an uncommon and severe variant of psoriasis, present in 1-2.25% of psoriasis patients [10]. Erythrodermic psoriasis presents with a generalized inflammatory erythema involving at least 75% BSA [4]. Systemic symptoms are sometimes seen, such as fever, tachycardia, dehydration, fatigue, arthralgia, myalgia, diarrhea, and constipation. Erythrodermic psoriasis is associated with both increased morbidity and potential mortality. Although rare, patients can present with high output heart failure related to water loss and edema [11,12]. Another serious and possibly fatal complication that has been reported is sepsis from skin pathogens [13]. The pathogenesis of erythrodermic psoriasis is not yet completely understood, but it is thought to involve a complicated interaction of Th1-, Th17-, and Th2-driven inflammatory responses, with a skew towards Th2 [4]. Management of these patients is often challenging and may necessitate a multidisciplinary approach or supportive management to correct electrolyte or thermoregulatory imbalances [4].

In this case, we describe the patient's chronic erythrodermic psoriasis as 'turning around' with Goeckerman therapy. In patients that have erythrodermic or intensely erythematous psoriasis, aggressive treatment is often necessary to dramatically reduce one's skin inflammation prior to starting maintenance therapy. Maintenance therapy, such as systemic or biologic monotherapy, used when a patient is extraordinarily inflamed can be ineffective. Instead of undergoing repeated failed trials of various treatment modalities, one approach is to temporarily bring to bear a more intensive and efficacious regimen, such as Goeckerman therapy, to rapidly reduce the patient's intensity of inflammation. Once the skin is less inflamed, it is more likely to respond to long-term treatment agents, such as rizankizumab-rzaa in this case.

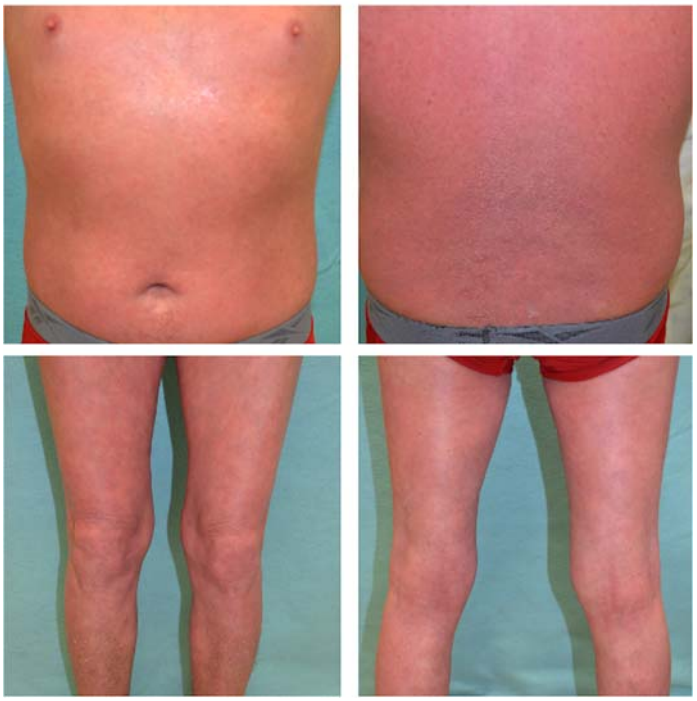

Figure 2. *Resolution of erythrodermic psoriasis in the patient following a 12-week Goeckerman regimen.*

Importantly, this patient underwent a 'cool down' period before starting Goeckerman therapy to reduce cutaneous inflammation. A 'cool down' period is meant to describe one or more weeks of diffuse topical steroid therapy prior to beginning phototherapy or CCT application for erythrodermic or most intensely erythematous psoriasis. If such patients begin phototherapy without a cool down period, there is risk of aggravating cutaneous inflammation, triggering even more intense erythema or edema which could lead to dehydration, temperature dysregulation, or electrolyte imbalances possibly necessitating hospitalization [5]. In this case of chronic erythrodermic psoriasis, a more than three-week cool down period was necessary prior to initiating phototherapy, which began extremely cautiously and was titrated up as tolerated. This cool down period is necessary prior to starting CCT therapy as well, as CCT has a risk of triggering pustular disease when it is applied to extremely erythematous

psoriasis [6]. Although topical corticosteroid under impermeable, whole-body occlusion was used to 'cool down' the inflamed skin of this patient, the author (JK) has found that high dose cyclosporine is an effective alternative as well [5].

In treating psoriasis, Goeckerman therapy is likely effective because of the synergistic effects of phototherapy's and CCT's mechanisms of action. The therapeutic efficacy of phototherapy is believed to relate to an interplay of several physiologic responses, including downregulation of the Th1 and Th17 immune response, induced apoptosis of epidermal and dermal T lymphocytes, keratinocytes, and other skin cell types, and altered cytokine profiles favoring the Th2 versus the Th1/Th17 axis [14]. As for CCT, its composition and anti-inflammatory activity is not yet completely understood as it is composed of over 10,000 chemicals. However, research suggests that the aryl hydrocarbon component may play a role in regulating epidermal, keratinocyte, and Th17 and Treg cell differentiation [15].

The process of Goeckerman therapy at the UCSF Psoriasis and Skin Treatment Center is described in detail in patient and provider guides by Zhu et al. [1] and Gupta et al. [7], respectively. It involves NB-UVB phototherapy followed by the application of CCT to the body's affected areas and LCD for the scalp, if needed. Plastic wrap, an impermeable material, is used to occlude the body, arms, and legs. Impermeable occlusion is utilized as it increases the penetration and concentration of active drug within the skin, enhancing its therapeutic effect [16]. Impermeable gloves are used for the hands, whereas shower caps are used for the scalp and the feet (kept in place with tube socks). The tar is left on for at least four to five hours before it is washed off in the shower using mineral oil and soap. Before the patient leaves the daycare center, 20% LCD in Aquaphor is applied and repeated by the patient at bedtime. Each day, Goeckerman patients are assessed by in-house providers to monitor for improvement of their condition and screen for adverse events, such as burning because of aggressive phototherapy or skin irritation related to tar or plastic wrap sensitivity. This regimen is followed by patients five days a week for at least four to six weeks, as interruptions in therapy can cause delays in achieving therapeutic response or shorten patients' remission times [1]. On weekends, patients are instructed to apply 20% LCD in Aquaphor at bedtime, ideally with some form of impermeable occlusion that they can manage.

Nearly all patients who complete Goeckerman therapy see complete or almost complete improvement in their psoriasis [1]. A 2005 study performed at the UCSF Psoriasis and Skin Treatment Center found that 100% of consecutively-treated patients (N=25) receiving Goeckerman therapy achieved 75% or greater improvement in their psoriasis area and severity index scores (PASI 75), [17]. Long periods of disease remission are also seen following completion of Goeckerman therapy. In a two-center study involving 300 patients who had completed day-long Goeckerman regimens for three weeks on average, 90% remained clear for eight months and 75% for one year [18]. Goeckerman therapy is also evidenced to improve patients' overall quality of life and psychosocial distress, with significant decreases in Psoriasis Disability Index (PDI) and Hospital Anxiety and Depression Scale (HADS) scores observed in moderate-to-severe psoriasis patients on Goeckerman (N=48) versus conventional therapy (N=36), [19]. Interestingly, similar efficacy and safety has been seen with Dead Sea Climatotherapy at psoriasis clinics in Israel and Jordan. This regimen involves the combination of balneotherapy in Dead Sea salt- and mineral-rich water and heliotherapy [20]. Finally, Goeckerman therapy is not only efficacious in treating psoriasis, but has demonstrated efficacy in treating atopic dermatitis [21], generalized prurigo nodularis [22], and generalized pruritis [23], as well.

Conclusion

This case is first to report the use of Goeckerman therapy in treating erythrodermic psoriasis in a patient with particularly recalcitrant disease resistant to four biologic agents and seven other treatment modalities. This case illustrates how the Goeckerman regimen can be modified with a 'cool down' protocol prior to initiating crude coal tar and light therapy so

that it may be efficacious for erythroderma. Despite Goeckerman therapy's considerable efficacy and safety, it is a time-intensive treatment and to date only three Goeckerman facilities remain in the U.S: UCSF (San Francisco, CA), Mayo Clinic (Rochester, Minnesota), and University of Miami (Miami, Florida). Although the emergence of biologic therapy has further limited its use, in cases of biologic-resistant disease Goeckerman therapy may be the most efficacious treatment available for turning around a patient's stalemate situation. Our therapy center at UCSF receives patient referrals from all over the country and insurance companies regularly enact provisions to allow coverage of Gockerman therapy for the most severe patients. In patients that have severely debilitating psoriatic disease, such as intractable erythrodermic psoriasis, dermatologists may end up in a difficult position in which they have run out of treatment options. In these situations, Goeckerman therapy is an available option and may be worth recommending to desperate treatment resistant patients. Providing this as an option may give the patient hope rather than being left with "there is nothing more to do, you just have to live with this."

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Zhu TH, Nakamura M, Farahnik B, Abrouk M, Singh RK, Lee KM, et al. The Patient's Guide to Psoriasis Treatment. Part 4: Goeckerman Therapy. *Dermatol Ther.* 2016;6:333–9. [PMID: 27474032].
2. Serrao R, Davis MDP. Goeckerman treatment for remission of psoriasis refractory to biologic therapy. *J Am Acad Dermatol.* 2009;60:348–9. [PMID: 19150284].
3. Moscaliuc ML, Heller MM, Lee ES, Koo J. Goeckerman therapy: a very effective, yet often forgotten treatment for severe generalized psoriasis. *J Dermatol Treat.* 2013;24:34–7. [PMID: 22329632].
4. Singh RK, Lee KM, Ucmak D, Brodsky M, Atanelov Z, Farahnik B, et al. Erythrodermic psoriasis: pathophysiology and current treatment perspectives. *Psoriasis Auckl NZ.* 2016;6:93–104. [PMID: 28856115].
5. Nguyen TV, Wu JJ, Lim HW, Koo JYM. Acute Exacerbation of Erythrodermic Psoriasis with Phototherapy: Pathophysiology and Results of a National Psoriasis Foundation Survey regarding Photo-Management of Erythrodermic Skin. *J Psoriasis Psoriatic Arthritis.* 2016;1:142–6.
6. Zelickson BD, Muller SA. Generalized pustular psoriasis. A review of 63 cases. *Arch Dermatol.* 1991;127:1339–45. [PMID: 1892402].
7. Gupta R, Debbaneh M, Butler D, Huynh M, Levin E, Leon A, et al. The Goeckerman Regimen for the Treatment of Moderate to Severe Psoriasis. *JoVE J Vis Exp.* 2013;77:e50509. [PMID: 23892536].
8. Soares TF, Davis MDP. Success of Goeckerman treatment in two patients with psoriasis not responding to biological drugs. *Arch Dermatol.* 2007;143:950–1. [PMID: 17638750].
9. Fitzmaurice S, Bhutani T, Koo J. Goeckerman regimen for management of psoriasis refractory to biologic therapy: the University of California San Francisco experience. *J Am Acad Dermatol.* 2013;69:648–9. [PMID: 24034372].
10. Boyd AS, Menter A. Erythrodermic psoriasis. Precipitating factors, course, and prognosis in 50 patients. *J Am Acad Dermatol.* 1989;21:985–91. [PMID: 2530253].
11. Rosenbach M, Hsu S, Korman NJ, Lebwohl MG, Young M, Bebo BF, et al. Treatment of erythrodermic psoriasis: from the medical board of the National Psoriasis Foundation. *J Am Acad Dermatol.* 2010;62:655–62. [PMID: 19665821].
12. Stinco G, Errichetti E. Erythrodermic psoriasis: current and future role of biologicals. *BioDrugs Clin Immunother Biopharm Gene Ther.* 2015;29:91–101. [PMID: 25752640].
13. Green MS, Prystowsky JH, Cohen SR, Cohen JI, Lebwohl MG. Infectious complications of erythrodermic psoriasis. *J Am Acad Dermatol.* 1996;3:911–4. [PMID: 8621827].
14. Tami Wong BS, Leon Hsu BA, Wilson Liao MD. Phototherapy in Psoriasis: A Review of Mechanisms of Action. *J Cutan Med Surg.* 2013;17:6–12. [PMID: 23364144].
15. Sekhon S, Jeon C, Nakamura M, Afifi L, Yan D, Wu JJ, et al. Review of the mechanism of action of coal tar in psoriasis. *J Dermatol Treat.* 2018;29:230–2. [PMID: 28814117].
16. Vickers CF. Stratum corneum reservoir for drugs. *Adv Biol Skin.* 1972;12:177-89. [PMID: 4579191].
17. Lee E, Koo J. Modern modified "ultra" Goeckerman therapy: a PASI assessment of a very effective therapy for psoriasis resistant to both prebiologic and biologic therapies. *J Dermatol Treat.* 2005;16:102–7. [PMID: 16019624].
18. Menter A, Cram DL. The Goeckerman regimen in two psoriasis day care centers. *J Am Acad Dermatol.* 1983;9:59–65. [PMID: 6886105].
19. Chern E, Yau D, Ho J-C, Wu W-M, Wang C-Y, Chang H-W, et al. Positive effect of modified Goeckerman regimen on quality of life and psychosocial distress in moderate and severe psoriasis. *Acta Derm Venereol.* 2011;91:447–51. [PMID: 21537818].
20. David M, Efron D, Hodak E, Evan-Paz, Z. Treatment of psoriasis at the dead sea: why, how, and when? *Isr Med Assoc J.* 2000;2:232-234. [PMID: 10774275].
21. Farahnik B, Beroukhim K, Danesh M, Nakamura M, Abrouk M, Zhu TH, et al. Successful use of a modified Goeckerman regimen in the treatment of chronic severe atopic dermatitis: A prospective pilot study. *J Am Acad Dermatol.* 2016;75:1068–71. [PMID: 27745637].
22. Sorenson E, Levin E, Koo J, Berger TG. Successful use of a modified Goeckerman regimen in the treatment of generalized prurigo nodularis. *J Am Acad Dermatol.* 2015;72(1):e40-42. [PMID: 25497953].
23. Nakamura M, Koo J, Bhutani T. Uremic pruritus treated successfully with the Goeckerman Program. *Dermatol Online J.* 2016;22):13030/qt3cp819gj. [PMID: 27617950].