Acrodermatitis continua of Hallopeau successfully treated with adalimumab: A case report

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Abstract
Acrodermatitis continua of Hallopeau is a chronic, inflammatory, and relapsing condition that presents as pustules of the fingers and toes, often with nail involvement. This condition is infrequently reported, difficult to treat, and often misdiagnosed. Various anti-psoriatic therapies have been used, but literature is limited to case studies with equivocal results. Biological therapy is revolutionizing the management of many dermatologic conditions and is believed to be a promising option for acrodermatitis continua of Hallopeau patients who have failed conventional therapy. We report the 4-year treatment course of a 70-year-old woman with acrodermatitis continua of Hallopeau that was initially unsuccessful with conventional treatments but successfully treated with the tumor necrosis factor alpha inhibitor adalimumab, in combination with altretinoin and clobetasol propionate. This case adds to the current understanding of acrodermatitis continua of Hallopeau and the potential of biological therapy, in our case, adalimumab, for acrodermatitis continua of Hallopeau management. Literature should continue growing to ascertain the safety and efficacy of biologic therapy for patients with acrodermatitis continua of Hallopeau.

Keywords
Acrodermatitis continua of Hallopeau, psoriasis, biological therapy, adalimumab

Introduction
Acrodermatitis continua of Hallopeau (ACH) is a chronic, inflammatory, and relapsing condition that presents as sterile pustules of the fingers and toes and often involves the nail beds. Owing to the infrequency of reports as well as the complexity of ACH, this condition is associated with a broad differential diagnosis and can be challenging to treat.¹ No standardized guidelines have been developed for ACH management and although various topical and systemic anti-psoriatic therapies have been used, literature is limited to case studies that have yielded equivocal results.¹,² Biological therapy has revolutionized the treatment of many dermatologic conditions, including the treatment and management of plaque psoriasis, and is believed to be a safe and efficacious option for ACH.¹ This case study reports the 4-year treatment course of a patient with ACH that was successfully treated with the biologic adalimumab, after failing treatment with conventional therapies.

Case report
A 66-year-old female presented in June 2014 with hypoplasia and onychodystrophy leading to trachyonychia of all fingernails. She also presented with diffuse erythema of the proximal and lateral folds and extreme pain. Her medical history included rheumatoid arthritis, osteoarthritis, osteoporosis, and anorexia nervosa. Her medications included misoprostol, naproxen, and multivitamins. She had a family history of unspecified arthritis. The patient was seen once prior in December 2009 regarding fragile fingernails and fingertip fissures and was prescribed hydrocortisone cream and fluocinonide ointment. She had also used petrolatum and moisturizing cream. Between June 2014 and October 2018, the patient had many rheumatology and dermatology consultations regarding her fingernail dystrophy (Table 1). Her final diagnosis was ACH but various
differential diagnoses over her treatment course included various infections, chronic dermatitis involving the fingertips and nails, lichen planus, Raynaud’s disease, and Bazex syndrome which highlights the difficulty in confirming a diagnosis of ACH. A negative workup for aerodigestive malignancy indicated that it was unlikely Bazex disease. She had negative testing on two occasions for connective tissue disease. She also presented to many clinic visits with secondary infection with bacterial and candidal colonization which complicated her course.

Initial treatments between 2014 and 2017 included topical agents (calcipotriol-betamethasone, tazarotene, clobetasol propionate, and mupirocin), as well as systemic agents acitretin, methotrexate, and phototherapy, all with little benefit. Acitretin seemed to worsen her condition. Her course was complicated by several small ulcerations on the fingers (not typical of distal ulcerations of Raynaud’s), which were treated unsuccessfully with fusidic acid 2% ointment on ulcers. A biopsy demonstrated candidiasis. Fluconazole orally and clotrimazole topically were given with great response as the ulcerations healed and there was nail growth. A subsequent flare-up in winter 2016 led to violaceous swollen fingers and nails that had become resistant to further treatment with fluconazole and clotrimazole. Subsequent cultures grew Klebsiella oxytoca and Staphylococcus aureus and were treated with sulfamethoxazole/trimethoprim. Of note, she never presented with the pustules or lakes of pus typical of this condition.

The patient began acitretin, in addition to mupirocin ointment, in April 2017. She alternated between doses of 10 and 30 mg daily due to side effects of dry eyes and conjunctival inflammation, which were treated with ocular lubricant and suitable eye hygiene. Her fissures and ulcers responded well to acitretin; however, her nails remained thin or nonexistent. In addition, the condition seemed to worsen again with winter 2017. A bacterial swab of a finger ulcer revealed Pseudomonas aeruginosa, which was treated with ciprofloxacin (acitretin on hold). Dilute acetic acid washes were recommended but not tolerated. Acetaminophen was used to manage pain. During this care period, the patient was hospitalized for cellulitis in the left arm and had open wounds on fingers and nail beds, which was treated with cephalxin.

From March 2018 to July 2018, the patient had violaceous swollen fingertips bilaterally, atrophic thin nails which were only partially re-growing, erythema, and eroded macerated skin on left and right hand distal digits. A bacterial swab revealed group A streptococcal infection which was treated. Acitretin 10/30 mg was continued, and cephalxin, prednisone, penicillin, acetaminophen,

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Table 1. Summary of treatments, dosage, and response during the case report.

| Date       | Treatment and dosage                                                                 | Response                      |
|------------|--------------------------------------------------------------------------------------|-------------------------------|
| June 2014  | Topical (calcipotriol-betamethasone, tazarotene) OD for 10 months                   | Slight initial response, not sustained |
| December 2014 | Methotrexate (10, 12.5, 15, or 25 mg weekly) with 1 mg OD folic acid supplementation for 18 months | Mixed response, not sustained |
| March 2015  | Topical clobetasol propionate for 11 months                                           | Mixed response, not sustained |
| December 2015 | Ultraviolet B phototherapy 3× weekly for 2 months                                     | No response                   |
| February 2016 | Acitretin 25 mg OD for 1 month                                                            | Worsened                      |
| March 2016  | Fusidic acid 2% ointment on ulcers                                                       | No response                   |
| April 2016  | Fluconazole 150 mg OD and topical clotrimazole OD for 12 weeks                         | Great response, not sustained |
| January 2017 | Fluconazole (first 150 mg, then increased to 200 mg) OD and topical clotrimazole OD for 7 weeks | No response                   |
| February 2017 | Sulfamethoxazole/trimethoprim for infection. Mupirocin ointment bid for 11 months         | Mixed response, not sustained |
| April 2017  | Acitretin (rotating between 10 and 30 mg) OD for 19 months, ongoing                   | Mixed response, not sufficient for control |
| December 2017 | Fluconazole 150 mg OD for 3 days, followed by ciprofloxacin 500 mg bid for 15 days. Acetaminophen PRN | Mixed response, not sustained |
| December 2017 | Dilute acetic acid soaks (one-part acetic acid: three-parts water)                     | Not tolerated                  |
| March 2018  | Cephalxin 500 mg qid for 2 weeks and after 1 week, prednisone 30 mg OD for 2 weeks added. Switched to penicillin 300 mg tid for 10 days | Limited response              |
| March 2018  | Adalimumab loading dose of 80 mg followed by 40 mg weekly for 7 months, ongoing         | Great response                |
| April 2018  | Cephalxin 500 mg qid for 10 days along with acetaminophen 100 mg qid, acetaminophen/codeine #3 q4H PRN, and Naproxen 200 mg bid. Mupirocin ointment tid PRN | Pain and inflammation managed, good response |
| May 2018    | Clindamycin 300 mg qid for 10 days                                                      | Limited response              |
| May 2018    | Oxycodone-acetaminophen                                                                 | Only took once, not required by patient |
| May 2018    | Topical clobetasol propionate for 5 months, ongoing                                    | Good response                 |
mupirocin, and clindamycin were used during this period. Adalimumab 80 mg was initiated as a loading dose to treat an acute flare, and a subsequent 40 mg dose every 2 weeks had a great effect with near normalization within 2–3 months and no side effects. Initial hypergranulation tissue response was treated with clobetasol propionate.

The patient was diagnosed with ACH, a variant of pustular psoriasis with an atypical course and repeated secondary bacterial and candidal infections. Currently, at 70 years of age, her treatment plan comprised adalimumab 40 mg biweekly, alitretinoin 10 mg daily, ocular lubricant, and clobetasol propionate, with great response (see Figure 1).

Figure 1. Patient’s hands (a) before treatment with adalimumab, (b) 1 week after 80 mg loading dose, and (c) 24 weeks after initiation of adalimumab.
Discussion

ACH is a challenging and sometimes difficult to diagnose entity, as exemplified by this case, in which multiple differential diagnoses have to be considered. The use of various topical and systemic anti-psoriatic treatments has been reported, but these are limited to case reports with equivocal results. These therapies include topical agents (corticosteroids, tar, calcipotriol, dithranol, fluorouracil, and calcineurin inhibitors); phototherapy (psoralen ultraviolet A (PUVA) / ultraviolet B (UVB)); and systemic medications (oral corticosteroids, methotrexate, cyclosporine, retinoids, tetracyclines, colchicine, dapson, and various biologics). Our patient failed conventional plaque psoriasis monotherapy, but the initiation of adalimumab, in addition to alitretinoin and clobetasol propionate, provided disease control without side effects other than xerophthalmia.

Adalimumab, the most commonly reported tumor necrosis factor alpha (TNF-α) inhibitor used to treat this condition, is a recombinant fully human IgG1 monoclonal antibody that binds to the surface receptors of cells to block TNF-α function. Similar to our ACH case, many other case studies have reported disease control with 40mg biweekly after the initial loading dose, with or without combination therapy. Some patients have benefited from more frequent dosing, such as 40mg weekly, for improved control.

This case report adds to our current knowledge of ACH and the potential of biological therapies such as adalimumab for successful management of this condition when conventional therapies fail. Literature regarding ACH should continue to grow, including formal clinical trials and additional case reports, to ascertain the safety and efficacy of biological therapy.

Declaration of conflicting interests

E.L.C., K.M., and F.R.-B. have no conflicts to disclose. A.O. has served as an investigator, speaker, or advisory board member for AbbVie, Celgene, Leo Pharma, Janssen, Pfizer, and Sanofi Genzyme. M.J.G. has served as an investigator, speaker, consultant, and/or advisory board member for AbbVie, Actelion, Akros, Amgen, Arcutis, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermira, Eli Lilly, Galderma, GSK, Incyte, Janssen, Leo Pharma, MedImmune, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, UCB, and Valeant.

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Informed consent

Written and verbal informed consent was obtained from the patient.

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