Frontiers in Dermatology and Cosmetology

CASE REPORT

Extra-digital Acrodermatitis Continua of Hallopeau in a Patient with Pre-existing ACH Confined to Right Great Toe

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Introduction

Acrodermatitis Continua of Hallopeau (ACH) is rare, recalcitrant condition consisting of sterile, pustular eruptions of the digits. It is recognized by a variety of names including pustular acrodermatitis, acrodermatitis continua suppurativa, acrodermatitis perstans and dermatitis repens. The etiology of this entity remains elusive, yet, most cases are preceded by local trauma or injury; however, other etiologies have been postulated including infectious, inflammatory, and neural causes. Acute presentation is characterized by small pustules that upon rupturing, coalesce into larger "lakes of pus" with resulting onychodystrophy and subsequent anonychia [1-6]. The affected digit then becomes erythematous with a shiny, glossy appearance, with noticeable hyperkeratosis, scaling and persistent pustulation. Chronic ACH can lead to osteolysis of affected digits, with subsequent proximal spread into the hand or foot. The diagnosis of ACH is primarily made on clinical grounds and can often be misdiagnosed due to its presentation and purulence mimicking bacterial, fungal or viral etiologies [7]. Histopathological examination of biopsies concerning for ACH demonstrate features consistent with pustular psoriasis, exhibiting subcorneal neutrophilic pustules and spongiform pustules that are formed by the degeneration and thinning of upper layer epidermal cells [8].Given the overlapping clinical presentation with other cutaneous diseases, other diagnoses warrant consideration before a firm diagnosis of ACH can be made. To date, there are no definitive treatment guidelines to aid in treating ACH. Current literature does support, however, the use of biologics and other therapies commonly used in psoriatic patients including the use of cyclosporine [9-13]. We report a unique case of ACH with an atypical presentation of the left ala in a patient with pre-existing ACH confined to the right great toe.

Case Report

A 62-year-old male presented to clinic with complaints of a tender, erythematous lesion on his left ala. The patient sustained a superficial laceration to this area while he was using a weed eater and had been washing with soap and water with judicious application of hydrogen peroxide. Medical history is notable for acrodermatitis continua of Hallopeau (ACH) of the right great toe treated with prednisone 5 mg daily and 20 mg as needed for flares. The patient is a former smoker with a history of staphylococcal infections. Initial physical examination revealed a crusty plaque with pustules on the left ala. The patient was started on Bactrim 800 mg BID and mupirocin 2% topical cream to be applied BID to the left alar region and nares for 10 days. Bacterial cultures obtained at initial visit were negative for staphylococcal bacteria. The patient returned to clinic 3 months later for follow-up with physical examination demonstrating a 2.5 cm crusty, hyperkeratotic plaque on left ala extending to the nasal tip (Figure 1). The patient resumed Bactrim 800 mg BID for 10 days with clobetasol 0.05% topical cream to be applied to left ala BID for seven days. Additional bacterial cultures were obtained at this visit and found to be negative. At the follow-up visit two weeks later, the patient reported a

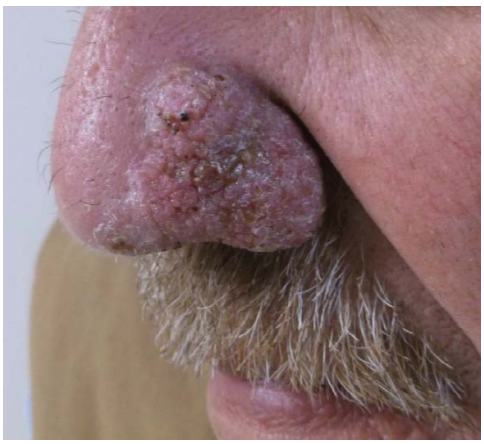

Figure 1: 2.5 cm hyperkeratotic, crusty plaque of left ala

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significant improvement in appearance of the left alar lesion within 72-hours after starting clobetasol 0.05% topical cream. Physical examination revealed a 1.5 cm crusty plaque on the left ala with significant reduction in erythema and size (Figure 2). The patient was advised to continue clobetasol 0.05% topical cream with application BID for 2 weeks in conjunction with Vaseline. A working diagnosis of acrodermatitis continua of the left ala was determined at this visit. At the follow-up visit three weeks later, physical examination revealed a pebbly, flat plaque on the left ala (Figure 3). The right great toe was noted to have moderate swelling with a dystrophic nail. The patient was instructed to take prednisone 20 mg PRN for ACH flare of right great toe (Figure 4). Clobetasol 0.05% topical cream was discontinued and patient instructed to apply Vaseline to left ala. At the time of this report, the patient has not had any more inpatient follow-up visits and reports continued improvement of left alar lesion.

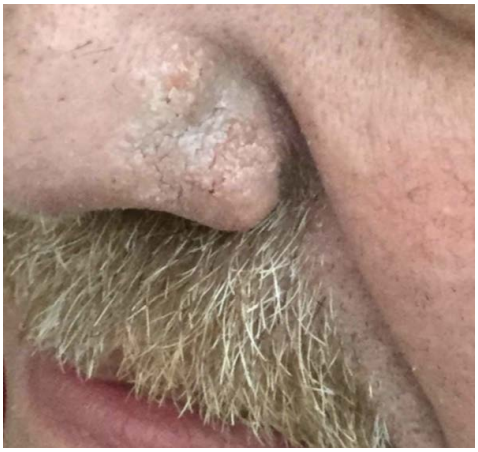

Figure 2: 1.5 cm crusty plaque on left ala following two weeks of topical clobetasol 0.05% cream

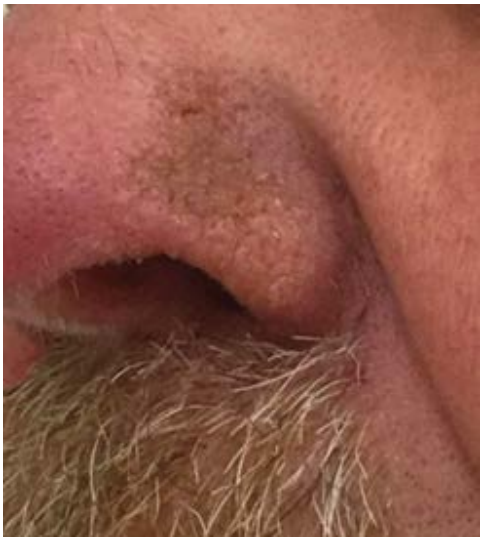

Figure 3: Pebbly, flat plaque of left ala following five weeks of topical clobetasol 0.05% cream and Vaseline

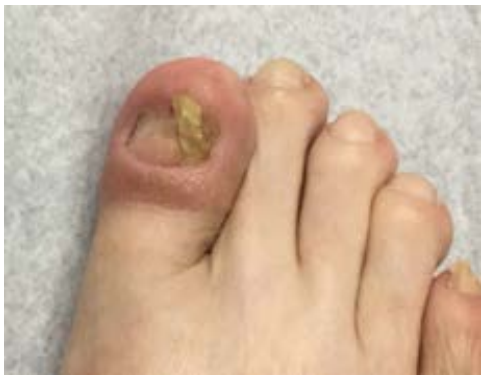

Figure 4: Acrodermatitis of right great toe with erythema and anonychia

Discussion

ACH is an uncommon disease as evidenced by the paucity of published data detailing its etiology and the limited amount of published case reports. ACH is believed by some to be a distinct entity while others consider it to be a variant of pustular psoriasis. Pustular psoriasis is a group of severe inflammatory skin conditions with sustained, painful eruptions of pustules containing neutrophils. There are 3 variations of pustular psoriasis, all of which can present with concurrent psoriasis vulgaris (PV). Generalized pustular psoriasis (GPP), which manifests as acute episodes of systemic pustulation; palmoplantar pustulosis (PPP), which involves chronic skin eruptions of the palms and soles; and acrodermatitis continua of Hallopeau (ACH), acute or chronic involvement of the fingers and toes, often involving the nail bed [14].

Mutations in IL36RN, AP1S3 and CARD14 have been found in patients with PPP, GPP and ACH, which indicates a common genetic component [15-18]. Several large studies have observed these genetic defects in homozygous and compound heterozygous individuals along with single heterozygous changes having been reported as well [19].Our patient was not subjected to genetic sequencing.

Marrakchi et al demonstrated a possible genetic factor contributing to the development of pustular psoriasis. The authors performed homozygous mapping and direct sequencing of nine Tunisian multiplex families with autosomal recessive pustular psoriasis. Their study revealed a missense mutation in IL36RN, encoding for the interleukin-36-receptor antagonist, an antiinflammatory cytokine. The interleukin-36-receptor antagonist binds to the interleukin-36 receptor, blocking agonist binding, and preventing biological activity. Nuclear factor-κB and mitogen activated protein (MAP) kinases, both proinflammatory pathways, are halted and this inhibition leads to the avoidance of exuberant inflammatory responses. The authors also found that persons with DITRA (deficiency of interleukin thirty-six receptor antagonist) have an increased production of interleukin-8 within keratinocytes from agonist binding to interleukin-36 receptor [20]. IL-8 is a chemoattractant and activator of neutrophils in inflamed

regions and has been implicated in the inflammatory process of psoriasis [21-24].

In a study by Twelves et al, 473 DNA samples from patients with pustular psoriasis were sequenced for disease alleles known to be associated with the pustular forms of psoriasis. The authors' note that mutations in IL36RN were the most frequently observed across all subjects. GPP and ACH were observed to harbor a higher proportion of the IL36RN mutation (23.7% and 18.2%, respectively) when compared to PPP patients (5.2%). While it has been published in the literature that pustular psoriasis can present concurrently with psoriasis vulgaris, Twelves et al note that they did not observe a consistent effect of IL36RN mutations on PV concurrence [25].

Patients with underlying psoriasis can have progression to the pustular form as well as a combination or evolution of one pustular form to another. It has also been reported that evolution of one pustular form to another can take place without underlying PV. Ranugha et al report a patient with pustules confined to the fingertips for 3 years who acutely developed a generalized pustular eruption throughout the entire body with high-grade fevers. Skin biopsies showed hyperkeratosis, parakeratosis with concurrent subcorneal neutrophilic pustules a consistent finding of pustular psoriasis. The diagnosis of ACH with progression to GPP was made and gradual improvement of generalized pustules was noted following cyclosporine treatment. Pustulation of the fingertips was less responsive and a potent topical steroid was added with continued improvement [26].

Our patient was unique in having pre-existing ACH of the right great toe and new onset lesion confined to the left ala suspicious for ACH. While there have been many proposed theories on how ACH develops, science to date does not provide a definitive answer. We find it worthy to mention that our patient denied having similar lesions prior to the trauma he sustained to his face from projectile debris while performing yardwork. It has been postulated that trauma can be an inciting factor in the development of ACH, and while speculative, we propose the development of ACH in our patient's face was a result of local trauma he endured. Literature supports a possible genetic link between pustular forms of psoriasis and as the suspected culprit of their development. Studies have also shown that while mutations have been identified and appear consistent across disease sub-types, they represent only a minority of potential genes that could play a role in psoriasis and its variants. Further, one could ask if genetic mutations increase the probability of disease progression or evolution into another form of pustular psoriasis? Do genetic mutations leave one susceptible to an increase in disease severity when an individual with underlying pustular psoriasis is subjected to trauma, infection or other cutaneous or systemic perturbations? Our patient was not found to have pustules elsewhere on his body aside from his right great toe and left ala. While evolution of one pustular form into another has been report, we did not observe this to be occurring in our patient but rather a new presenting location of pre-existing ACH. The reporting of this case is an effort to contribute to the already published work investigating the etiology, progression and presentation of this rare form of pustular psoriasis, in hopes it will further advance understanding and clinical recognition.

References

1. Smith MP, Ly K, Thibodeaux Q, Bhutani T, Liao W et al. (2019) Acrodermatitis continua of Hallopeau: clinical perspectives. *Psoriasis: Targets and Therapy 9*: 65. [View Article]
2. Bachelez H (2018) Pustular psoriasis and related pustular skin diseases. *Br J of Dermatology* 178: 614-618. [View Article]
3. Mengesha YM, Bennett ML (2002) Pustular skin disorders. *Am J of clin dermatology* 3: 389-400. [View Article]
4. Jo SJ, Park JY, Yoon HS, Youn JI (2006) Case of acrodermatitis continua accompanied by psoriatic arthritis. *The J of dermatology* 33: 787-791. [View Article]
5. Benjegerdes KE, Hyde K, Kivelevitch D, Mansouri B (2016) Pustular psoriasis: pathophysiology and current treatment perspectives. *Psoriasis (Auckland, NZ)* 6: 131. [View Article]
6. Waller JM, Wu JJ, Murase JE, Dyson SW, Kelly KM (2007) Chronically painful right thumb with pustules and onycholysis. *Clin and Exp dermatology (Print)* 32: 619-620. [View Article]
7. Rosenberg BE, Strober BE (2004) Acrodermatitis continua. *Dermatology online J* 10: 9. [View Article]
8. Sehgal VN, Verma P, Sharma S, Srivastava G, Aggarwal AK et al. (2011) Acrodermatitis continua of Hallopeau: evolution of treatment options. *Int J of dermatology* 50: 1195-1211. [View Article]
9. Gupta AK, Ellis CN, Nickoloff BJ, Goldfarb MT, Ho VC et al. (1990) Oral cyclosporine in the treatment of inflammatory and noninflammatory dermatoses: a clinical and immunopathologic analysis. *Arch of dermatology* 126: 339-350. [View Article]
10. Peter RU, Ruzicka T, Donhauser G, Braun-Falco O (1990) Acrodermatitis continua-type of pustular psoriasis responds to low-dose cyclosporine. *J of the Am Acad of Dermatology* 23:515. [View Article]
11. Lavaroni G, Kokelj F (1994). Hallopeau's acrodermatitis treated with cyclosporin Aa case report. *J of dermatological treatment 5*: 209-210. [View Article]
12. Bugatti L, Filosa G, Nicolini M, Ciattaglia G (1997). Hallopeau's acrodermatitis continua responding to low-dose cyclosporin therapy. *Chronica Dermatologica 7*: 379-384. [View Article]
13. Abbas O, Itani S, Ghosn S, Kibbi AG, Fidawi G et al. (2013) Acrodermatitis continua of Hallopeau is a clinical phenotype of DITRA: evidence that it is a variant of pustular psoriasis. *Dermatology* 226: 28-31. [View Article]
14. Navarini AA, Burden AD, Capon F, Mrowietz U, Puig L et al. (2017) European consensus statement on phenotypes of pustular psoriasis. *J Euro Acad of Dermatology and Venereology* 31: 1792-1799. [View Article]
15. Setta-Kaffetzi N, Simpson MA, Navarini AA, Patel VM, Lu HC et al. (2014) AP1S3 mutations are associated with pustular psoriasis and impaired Toll-like receptor 3 trafficking. *The Am J of Hum Genet* 94: 790-797. [View Article]

16. Berki DM, Liu L, Choon SE, Burden AD, Griffiths CE et al. (2015) Activating CARD14 mutations are associated with generalized pustular psoriasis but rarely account for familial recurrence in psoriasis vulgaris. *J of Invest Dermatology* 135: 2964-2970. [View Article]

17. Mossner R, Frambach Y, Wilsmann-Theis D, L ohr S, Jacobi A, Weyergraf A et al. (2015) Palmoplantar pustular psoriasis is associated with missense variants in CARD14, but not with loss-of-function mutations in IL36RN in European patients. *The J of invest dermatology* 135: 2538. [View Article]

18. Setta-Kaffetzi N, Navarini AA, Patel VM, Pullabhatla V, Pink AE, et al. (2013) Rare pathogenic variants in IL36RN underlie a spectrum of psoriasis-associated pustular phenotypes. *The J of invest dermatology 133*: 1366. [View Article]

19. Hussain S, Berki DM, Choon SE, Burden AD, Allen MH et al. (2015) IL36RN mutations define a severe autoinflammatory phenotype of generalized pustular psoriasis. *J of Allergy and Clin Immunol* 135: 1067-1070. [View Article]

20. Marrakchi S, Guigue P, Renshaw BR, Puel A, Pei XY et al. (2011) Interleukin-36–receptor antagonist deficiency and generalized pustular psoriasis. *New Engl J of Med 365*: 620-628. [View Article]

21. Duan H, Koga T, Kohda F, Hara H, Urabe K et al. (2001) Interleukin-8-positive neutrophils in psoriasis. *J of dermatological sci* 26: 119-124. [View Article]

22. Gillitzer R, Berger R, Mielke V, Muller C, Wolff K et al. (1991) Upper keratinocytes of psoriatic skin lesions express high levels of NAP-1/IL-8 mRNA in situ. *J of invest dermatology* 97: 73-79. [View Article]

23. Nickoloff BJ, Karabin GD, Barker JN, Griffiths CE, Sarma V et al. (1991) Cellular localization of interleukin-8 and its inducer, tumor necrosis factor-alpha in psoriasis. *The Am J of pathol* 138: 129. [View Article]

24. Anttila HS, Reitamo S, Erkko P, Ceska M, Moser B et al. (1992) Interleukin-8 immunoreactivity in the skin of healthy subjects and patients with palmoplantar pustulosis and psoriasis. *J of invest dermatology* 98: 96-101. [View Article]

25. Twelves S, Mostafa A, Dand N, Burri E, Farkas K et al. (2019) Clinical and genetic differences between pustular psoriasis subtypes. *J of Allergy and Clin Immunol* 143: 1021-1026. [View Article]

26. Ranugha PS, Kumari R, Thappa DM (2013) Acrodermatitis continua of hallopeau evolving into generalised pustular psoriasis. *Indian J of dermatology* 58: 161. [View Article]

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