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Rapid and sustained response to apremilast in a patient with long-standing acrodermatitis continua of Hallopeau

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To the Editor:

Acrodermatitis continua of Hallopeau (ACH) is a rare form of localized pustular psoriasis primarily affecting the distal phalanges of the fingers and toes [1]. This disabling condition is characterized by chronic inflammation and recurrent crops of sterile pustules that result in pain, progressive destruction of the nail apparatus, and even osteolysis and anonychia in severe cases [1,2]. Acrodermatitis continua of Hallopeau is usually refractory to multiple treatments and currently there are no standardized treatment guidelines available [2].

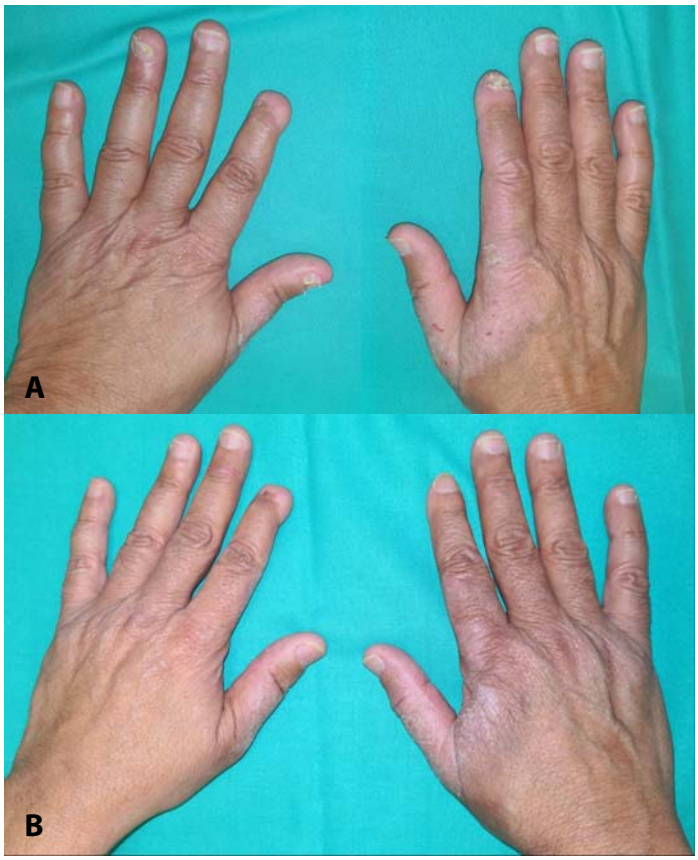

Figure 1. ***A)*** *Patient at baseline showing severe affectation of the first finger of the left hand and the second finger of the right hand.* ***B)*** *Complete resolution of nail lesions at three months of follow-up.*

A 61-year-old woman was referred to our dermatology department to assess treatment of long-standing recurrent painful lesions in various fingers. Her medical history was positive for ACH diagnosed at the age of 30, with repeated episodes of osteitis that had led to the amputation of the distal phalanx of the second finger of the left hand. She complained of repeated episodes of periungual inflammation in various fingers, with almost constant pain and permanent nail dystrophy. Treatment with oral acitretin and subcutaneous methotrexate had been attempted multiple times resulting in little improvement and poor tolerance. No improvement was obtained with topical corticosteroids and vitamin D3 analogues. Local PUVA therapy had resulted in partial and transient improvement of lesions but persistence of pain.

Physical examination revealed onychodystrophy, grouped pustules, and periungueal inflammation on the first finger of the left hand and the second finger of the right hand; onycholysis and periungueal inflammation on the fourth finger of the left hand was also present. A psoriasiform plaque affected part of the dorsum of the right hand and the dorsum of the left thumb (**Figure 1A**). A chronic hepatitis B virus infection, which was not detected in previous screenings, was incidentally found in the biological

Table 1. *Reported patients with acrodermatitis continua of Hallopeau treated with apremilast and response to treatment.*

Author (publication year)	Patient characteristics	Previous treatments	Response to apremilast and follow-up	Ref
Baron et al. 2017	42-year-old woman 2 fingers affected, 3 years from onset of symptoms	Topicals (corticosteroids, calcipotriol, tazarotene, tacrolimus), intralesional triamcinolone, systemic antibiotics, prednisone	Treatment failure. Poor tolerance to treatment (nausea, vomiting, and anorexia)	[5]
Smirnova et al. 2019	53-year-old woman Multiple fingers of both hands and feet affected, 3 years from onset of symptoms	Local psoralen UVA therapy, isotretinoin, methotrexate, infliximab	Treatment failure (regression of pustules and infiltration improvement after 2 months, no re-growth of healthy nail plates)	[2]
Lanna et al. 2019	58-year-old man Multiple fingers of both hands affected, 1 year from onset of symptoms	Topicals (antibiotics, antimycotics, corticosteroids), systemic antimycotics	Complete resolution of lesions after 1 month of follow-up. No side effects	[6]
Calleja Algarra et al. 2019	75-year-old man Multiple fingers of both hands and feet affected, 1 year from onset of symptoms	Topicals (antibiotics, antimycotics, corticosteroids), systemic antibiotics	Partial resolution of symptoms and nail lesions after 6 months of follow-up. No side effects	[7]
Kurihara et al. 2019	62-year-old man Multiple fingers of both hands affected, 2 years from onset of symptoms	Topicals (corticosteroids), narrowband ultraviolet B phototherapy, methotrexate	Complete resolution of lesions after 3 months of follow-up. No side effects	[8]
Megna et al. 2022	72-year-old man 1 finger affected, unknown time from onset of symptoms	Topicals (corticosteroids)	Partial resolution of symptoms and nail lesions after 4 months of follow-up. No side effects	[9]
Fustà-Novell et al. 2022	61-year-old woman Multiple fingers of both hands affected, 31 years from onset of symptoms	Topicals (corticosteroids, calcipotriol), local psoralen UVA therapy, acitretin, methotrexate	Complete resolution of symptoms and nail lesions after 3 months. No recurrences after 2 years of follow-up. No side effects	CR

CR, current report; Ref, reference.

therapy pre-treatment screening tests and treatment with entecavir was started on the recommendation of the gastroenterology and hepatology department. The patient was concerned about initiating biologic therapy due to the recent hepatitis B infection diagnosis and the epidemiological situation of the COVID19 pandemic in Spain at that time. Apremilast 30mg twice daily was started, resulting in an almost immediate complete disappearance of pain, marked improvement of skin lesions, and complete resolution of onychodystrophy after three months (**Figure 1B**). The patient has remained asymptomatic, with no recurrences and with excellent tolerance to treatment after two years of follow-up.

The etiology and pathogenesis of ACH remain poorly understood and its treatment is still challenging. Biologic therapies are showing good results in an increasing number of cases reported. The largest number of successes have been recorded with tumor necrosis factor (TNF) and IL17 inhibitors [3-5]. However, ACH molecular profiling has yet to be established. Apremilast is an oral phosphodiesterase-4 inhibitor that modulates proinflammatory pathways in favor of anti-inflammatory activity, which includes findings of increasing intracellular cAMP levels and decreasing the expression of pro-inflammatory cytokines including TNF, IL17, and IL23 [6]. To date, less than 10 cases of ACH treated with apremilast have been

reported, with variable results (**Table 1**), [2,5-9]. A rapid but partial improvement of lesions has been observed in most of these cases within a few weeks of follow-up [6-9]. No cases with more than one year of follow-up have been reported. Therefore, long-term efficacy of apremilast in the treatment of ACH remains unknown.

Apremilast may be a safe and effective therapeutic option in patients with ACH, especially when comorbidities contraindicate or make biologic therapy inappropriate. A rapid improvement of symptoms has been shown in the few cases reported but complete resolution of lesions is not always achieved. We report a patient with ACH successfully treated with apremilast with the longest follow-up to date, demonstrating that treatment response may be sustained in ACH apremilast-responders.

Potential conflicts of interest

The authors declare no conflicts of interest.

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