Annals of Case Reports
Zheng J, et al. Ann Case Rep: 7: 1017.
www.doi.org/10.29011/2574-7754.101017
www.gavinpublishers.com

Case Report

Treatment of Acrodermatitis Continua of Hallopeau with Guselkumab in a Patient without IL36RN Mutations: A Case Report and a Literature Review

Jianfeng Zheng, Ying Zhang, Yangfeng Ding*, Yunlu Gao*

Department of Dermatology, Shanghai Skin Disease Hospital; Institute of Psoriasis, Tongji University School of Medicine, Shanghai, China

***Corresponding author's**: Yangfeng Ding and Yunlu Gao, Department of Dermatology, Shanghai Skin Disease Hospital; Institute of Psoriasis, Tongji University School of Medicine, 1278 Baode Road, Jingan District, Shanghai 200443, China

Citation: Zheng J, Zhang Y, Ding Y, Gao Y (2022) Treatment of Acrodermatitis Continua of Hallopeau with Guselkumab in a Patient without IL36RN Mutations: A Case Report and a Literature Review. Ann Case Report. 7: 1017. DOI: 10.29011/2574-7754.101017

Received Date: 28 October 2022; **Accepted Date**: 01 November 2022; **Published Date**: 04 November 2022

Abstract

Acrodermatitis continua of Hallopeau (ACH) is a rare, sterile pustular psoriasis variant refractory to many conventional treatments. The eruption typically occurs after local trauma or infection; other etiologies include neural, inflammatory, and genetic causes. Herein, we reported a single case of a 61-year-old patient with ACH that was successfully treated with guselkumab for 76 weeks. At first, the patient was misdiagnosed with onychomycosis. Due to the worsening of nail lesions, the patient was admitted to our hospital. Subungual pustules were observed, and multiple cultures of the pustules were all negative. Thus, a diagnosis of ACH was made. The patient was treated with 100 mg guselkumab post admission. Four weeks after the first infusion, the patient showed minimal improvement; eight weeks after the second infusion, the patient showed clinical improvement and was still under treatment. Meanwhile, whole exome sequencing was performed for our patient, revealing no rare coding variant in IL36RN, CARD14, or AP1S3. This case report is associated with a review of recent data on ACH with biological treatments and gene mutations.

Keywords: Acrodermatitis continua of Hallopeau; Pustular psoriasis; Guselkumab; IL36RN; Case report

Introduction

Acrodermatitis continua of Hallopeau (ACH) is a rare condition that was first described by Henri Hallopeau in 1890. It is characterized by sterile pustules on the distal phalanges of the fingers and toes. [1] Continuous inflammation results in severe finger and toe damage, onychodystrophy, and sometimes anonychia and osteolysis. Histological findings usually show the formation of neutrophilic pustules, degenerative changes in epidermal cells, and moderate lymphohistiocytic infiltration. [2] Due to the overall rarity of ACH, larger clinical studies of high methodological quality are not available. Previous studies suggested using multiple therapies, including topical ointments, photochemotherapy, methotrexate, systemic retinoids, cyclosporin A, and biologics for ACH. [3] Among them, biologics appears to be the most effective approach. However, the longer-term effects of this agent are still not fully understood. [4-6] herein, we reported a single case of a 61-year-old patient with ACH that was successfully treated with guselkumab for 76 weeks.

Case Report

A 61-year-old male with no personal or known family history of psoriasis had recurrent episodes of redness, swelling, and purulent discharge on all fingers and toes with progressive degeneration of

the nails. Despite negative findings on bacteriological/mycological examinations at another dermatological center, the patient was treated with local antibacterial and antifungals in April 2020 and then with oral Iitraconazole (200 mg bid) for 7 days every-four-weeks for 3 months. The patient monitored the evolution of the disease for over half a year, after which he consulted our clinic in September 2020. Cutaneous clinical picture, erythema, pustules, and crusting were observed on the soles of the feet. The diagnosis of eczema was considered and was administered local steroids and oral antihistamines.

In November 2020, onychodystrophy was observed with frank pustules present in the nail's bed and the feet' soles (Figure 1a-c). The patient reported the maximum score on a 10-point pain visual analog scale (PAIN VAS).

Before starting treatment, echographic examination showed moderate enthesitis with effusion. Remarkable nail dystrophy was detected with the disappearance of the anatomical space between cuticle and lunula. Complete laboratory and instrumental tests, including chest X-ray, electrocardiogram (ECG), complete blood count, complete liver profile, creatinine, autoantibodies (ANA, anti-dsDNA, ENA, LAC, anti-cardiolipin, anti-citrulline) showed a C-reactive protein (CRP) level of 1.3 mg/L and an erythrocyte sedimentation rate (ESR) of 17 mm/h. No other abnormalities were noted. Whole exome sequencing was performed, revealing no rare coding variant in IL36RN, CARD14, or AP1S3.

In early December 2020, the patient was given the following treatment: guselkumab (GUS) at a dose of 100 mg at weeks 0/4 and then 100 mg every 8 weeks. The patient showed an important reduction of discomfort and pain after 4 weeks, experiencing marked improvement in the skin and nails lesions from 6 weeks (Figure 1d-f). Also, a second echographic examination showed a reduction of the size of the dystrophic nail and reappearance of the anatomical space between the cuticle and nail lunula.

After 76 weeks of GUS treatment, the patient's clinical picture was resolved and the nail lesions showed almost complete resolution.

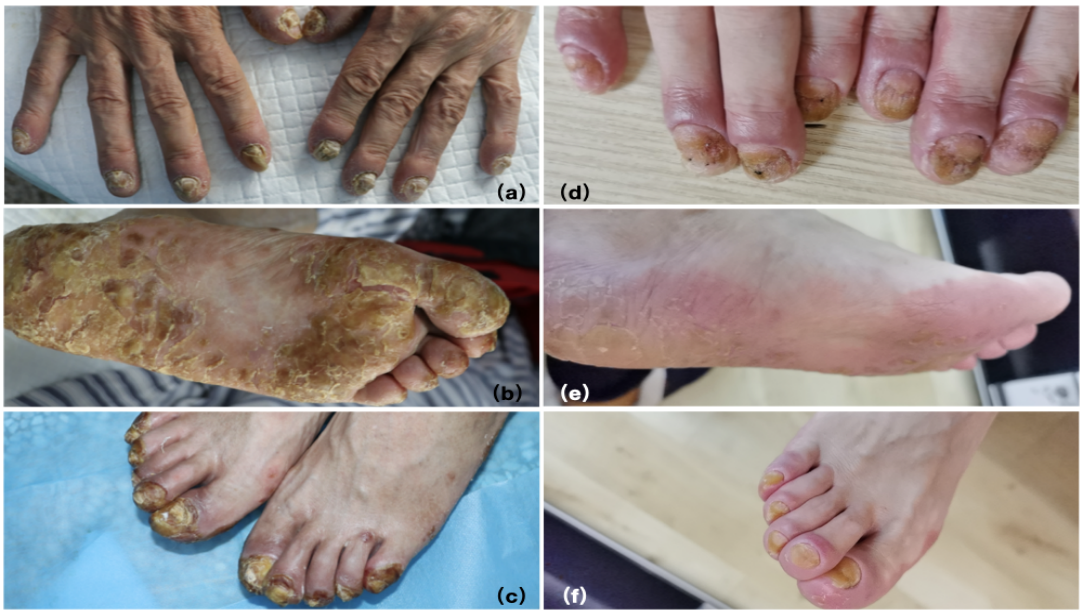

Figure 1. Clinical presentation of ACH before and after GUS treatment. **(a, b, c)** multiple subungual and palmoplantar pustules on the day of admission. **(d, e, f)** significant improvement of the pustules two weeks after the second infusion.

Discussion

ACH is a variant of pustular psoriasis with limited effective treatment options. Topical treatments (topical steroids, calcipotriol, topical tacrolimus) are classically prescribed as first-line therapy; systemic treatments such as acitretin (ACI), methotrexate (MTX), or cyclosporin (CyA) can be effective in some cases. [2, 7] However, the lack of treatment guidelines reflects the rarity of the disease and the challenges in management. In recent years, many biologics have been used for the treatment of ACH, and the results are encouraging. In Japan, Christian et al. identified 39 patients with ACH from five university medical centers and analyzed disease characteristics and treatment experience, which is also the largest case series of patients with ACH investigating patient characteristics and treatment outcomes in a real-world setting. The mean age of ACH onset was 54.4 years, and 22 (56.4%) patients were female. Among non-biologics, the excellent response was noted in 21.1% (4/19) of treatment courses with MTX, followed by ACI (13.3%; 2/15). For biologics, GUS (excellent response: 100%; 2/2), secukinumab (SEC) (excellent response: 42.9%; 3/7) and adalimumab (ADA) (excellent response: 20.0%; 2/10) were most efficacious [8].

To further evaluate treatment outcomes of biologics in patients with ACH, we conducted an electronic literature search to identify studies, case reports, and case series of ACH treated with biologics. The female/male ratio was close to 1:1; the age of ACH onset ranged from 6 to 85 years old, with a mean age of 47.0 years. Among 44 patients, 5 patients developed the first episode by 18 years of age, and 39 patients after 18. Nine patients had a family history of psoriasis or a history of psoriasis vulgaris (PsV). There were also 10 patients (22.7%) with arthritis, while 11 patients (26.2%) had a history of smoking.

In 2004, successful treatment of ACH with infliximab (INX) was first reported in a 54-year-old woman following 23 monthly infusions of INX. [9-22] Since then, anti-tumor necrosis factor (TNF) α biologic therapy has been used in a number of such cases. This review included 40 patients who were treated with one or more biological anti-TNF α drugs (18 with etanercept (ETA), 26 with ADA, and 18 with INX), where the effectiveness of anti-TNF α drugs was 53.2% (50% with ETA, 57.7% with ADA, and 50% with INX). A total of 62 systemic treatment courses were analyzed, with ADA monotherapy as the most common therapy (32.3%). Anti-TNF treatments were reported to induce or maintain remission in 32 cases. Of note, in 1 patient treated with ETA, there was a rapid loss of efficacy (within 4 months) after initial clearance of the lesions when ETA was decreased from 100 mg weekly to 50 mg weekly. [9] In 2 patients treated with ADA, A 43-year-old man with a half-a-year history of ACH showed an excellent response to ADA 40 mg every two weeks but did not respond after 1 year of ADA treatment; [23] while a woman with a 1-year history of PPP and a 3-year history of PsA showed an excellent clearance of the lesions after an initial loss of efficacy when ADA was increased from 40 mg every 2 weeks to 40 mg weekly. [24-49] In 2 patients treated with INX, the treatments had to be discontinued because of the development of high antinuclear antibody titers (ANA).20, 42 One of these patients received ADA at 40 mg on a weekly basis in addition to acitretin 50 mg daily. After one month, a dramatic improvement was observed, and the condition remained very well controlled. In 11 cases, clearance was achieved following a combination of a variety of systemic treatments (MTX, ACI or CyA). In 8 reported patients, a second-line anti-TNF treatment was efficient after failure or loss of efficacy of another anti-TNF α. One of these patients was a 9-year-old girl with a 3-year history of ACH, who did not respond to etanercept 50 mg when given twice weekly but showed an excellent response within 8 weeks to ADA 40 mg every two weeks. [4] Finally, there were 3 patients with ACH refractory to the 3 available anti-TNF α treatments. Details of the cases summarized below are presented in (Table 1).

Authors	Age (year)/Sex	Dosage
Adas A et al.[9]	61/M	ETA effective at 100mg weekly for 3 months, ETA ineffective after 1 month of decrease to 50 mg weekly
Saunier J et al.[10]	53/M	ADA ineffective at 40 mg every 2 weeks for 4 months; ETA ineffective at 50 mg twice/week + ACI 35 mg/day for 8 weeks; INX ineffective at 5 mg/kg + MTX 10 mg/week for 3 months
Puig L et al.[11]	72/F	ETA success, 10 months of treatment, 50 mg twice/week; ADA success, 3 months of treatment, 80 mg at week 0, 40 mg at week 1, and then 40 mg every 2 weeks.
Thielen AM et al.[12]	64/M	Failure of induction therapy on INX 5 mg/ kg at weeks 0, 2, and 6. ETA success, 9 months of treatment, 25 mg twice/week.
Adisen E et al.[13]	40/M	ETA ineffective at 25 mg twice weekly for 1 week, then 50 mg twice weekly for 11 weeks
Weisshaar E et al.[14]	50 /F	ETA success, 9 months of treatment, 25 mg twice/week
Kazinski K et al.[15]	65/M	ETA success, 12 weeks of treatment + ACI
Bonish B et al. [16]	NA/NA	ETA success
Silpa-arch N et al.[17]	24/F	ETA success, 6 months of treatment + ACI
Nikkels AF et al.[18]	74/M	ETA success, 12 weeks of treatment, 50 mg twice/week + ACI 50 mg/day
Rubio C et al.[19]	60/F	ETA ineffective INX success, 32 months of treatment, 5 mg/kg at 0, 2, and 6 weeks, followed by maintenance doses at 8-week intervals+ ACI 0.25mg/kg + prednisone 10 mg daily for the first 2 weeks
Ahmad K et al.[20]	78/F	INX Success, 5 mg/kg at 0, 2, and 6 weeks, followed by maintenance doses at 8-week intervals, discontinued at 40 months because of high ANA titre development
Din V et al.[4]	9/F	ETA ineffective at 50 mg twice weekly for 3 months ADA success, 12 months of treatment, 80 mg at week 0, 40 mg at week 1, and then 40 mg every 2 weeks
Mang R et al.[22]	58/M	INX success, 23 months of treatment, 3 mg/kg at week 0, followed by 4 mg/kg at 4-week intervals.
Okumo K et al.[23]	29/M	INX success, 48 months of treatment, 5 mg/kg at 0, 2, and 6 weeks, followed by maintenance doses at 8-week intervals + MTX 6 mg/week
Okumo K et al.[23]	55/F	INX success
Kioka M et al.[24]	22/M	INX success, 18 months of treatment, 5 mg/kg at 0, 2, and 6 weeks, followed by maintenance doses at 8-week intervals

Georgakapoulos JR et al.25	68/M	INX success, 6 months of treatment 5 mg/kg at weeks 0 and 2. Followed by maintenance doses at 8-week intervals + cyclosporine 200 mg twice daily for weeks 0 and 2
Di Costanzo L et al.[26]	53/M	ADA success, 40 weeks of treatment, 40mg every 2 weeks
Di Costanzo L et al.[26]	62/F	ADA success, 3 months of treatment, 40mg every 2 weeks
Crowley EL et al.[27]	66/F	ADA success, 7 months of treatment, 80 mg at week 0, and then 40 mg every 2 weeks
Sopkovich JA et al.[28]	79/M	ADA success, 1 months of treatment, 80 mg at week 0, 40 mg at week 1, and then 40 mg every 2 weeks
Ryan C et al.[29]	72/F	INX ineffective: 5 mg/kg at 0, 2, and 6 weeks, followed by maintenance doses at 8-week intervals + MTX 10 mg/week for 13 weeks ETA ineffective: 50 mg twice/week + cyclosporine 5 mg/kg/day ADA success, for 12 months of treatment 40 mg weekly, after 7 weeks of decrease to 40 mg every 2 weeks
Ryan C et al.[29]	61/F	ETA ineffective: 50 mg twice/week + MTX 15 mg/week for 4 months Success on ADA on 40 mg/week for 44 weeks; after 44 weeks ADA dosage decreased to 40 mg every 2 weeks + cyclosporine 3 mg/kg/day
Ryan C et al.[29]	NA/F	ADA ineffective at 40 mg every 2 weeks for 13 weeks, Effective after 10 weeks of increase to 40 mg weekly for 25 months
Lutz V et al.[30]	59/M	ETA ineffective, for 3 months INX ineffective + MTX 20 mg/week ADA ineffective at 40 mg every 2 weeks + MTX 20 mg/week
Palacios-Alvarez I et al.31	67/M	ADA without efficiency, 40 mg every 2 weeks (treatment period not provided) ETA effective at 50 mg weekly + MTX 15 mg/week, Ineffective after 7 month of ETA treatment INX effective at 5 mg/kg every 8 weeks + MTX 17.5 mg/week, and then 5 mg/ kg every 6 weeks after 4 months, discontinued at 6 months because of an infusion reaction.
Smirnova LM et al.[32]	53/F	INX ineffective, 5 mg/kg at weeks 0,2 and 6 weeks
Miller AC et al.[33]	31/F	ADA without efficiency
Bardazzi F et al.[34]	43/M	ADA effective, 40 mg in week 0/1, and then every 2 weeks, Ineffective after 1 year of ADA treatment
Caputo F et al.[35]	68/M	ADA success, 2 months of treatment, 160 mg at week 0, 80 mg at week 2, and 40 mg weekly beginning at week 4
Conti A et al.[36]	75/F	ADA success, 4 weeks of treatment, 80 mg at week 0, 40 mg at week 2, and 40 mg every 2 weeks + prednisone 25 mg/day
Inoue S et al.[37]	15/F	ADA ineffective, 16 weeks of treatment, 80 mg every 2 weeks
Lefkir S et al.[5]	26/M	ADA success, 12 months of treatment, 40 mg every 2 weeks + MTX 20 mg/week
Milani-Nejad N et al.38	60/M	INX without efficiency ADA without efficiency

Mueller RB et al.[39]	20/F	ADA success, 40 mg every 2 weeks + prednisolon 30 mg/day, and then decrease to 5 mg/day after 4 weeks
Megna M et al.[40]	15/F	ADA biosimilar success, 9 months of treatment, 40 mg every 2 weeks
Samotij D et al.[41]	72/F	ADA without efficiency INX success, 2 weeks of treatment, 5 mg/kg + ACI 50 mg/day, and then decrease to 35 mg/day
Tobin AM et al.[42]	55/F	INX success, 3 infusions of treatment, discontinued at the fourth infusion because of a severe urticarial reaction with high ANA titre development ADA success, 40 mg weekly + ACI 50mg/day, and then decrease to 35 mg/day
ACI: Acitretin; ADA: Adalimumab; ANA: Antinuclear antibody; ETA: Etanercept; F: Female; INX: Infliximab; M: Male; MTX: Methotrexate.		

Table 1: Summary of ACH cases treated with TNF-blocking agents.

Furthermore, 21 patients were treated with biologic non-anti-TNF α drugs. A total of 30 systemic treatment courses were analyzed with SEC monotherapy as the most common therapy (42.9%), where the effectiveness of non-anti-TNF α drugs was 52.4% (66.7% with SEC, 62.5% with UST, and 60% with ixekizumab (IXE)). Non-anti-TNF α drugs were reported to induce or maintain remission in 20 cases (SEC: 6; UST: 5; IXE: 3; brodalumab: 3; risankizumab: 1; GUS: 1; anakinra: 1). Among 2 patients treated with the IL-1 inhibitor, anakinra, there was 1 case report of UST-resistant ACH reporting rapid improvement with anakinra, [30] and conversely, another report of a failure to anakinra with subsequent response to UST. [10] The two patients were also refractory to the 3 available anti-TNF α treatments. There were 3 patients treated with the IL-17-receptor A inhibitor, brodalumab. [34, 38, 50] Although they all showed excellent responses, Milani-Nejad et al. reported the case of a patient whose ACH was refractory to the 2 available anti-TNF α treatments (INX and ADA), the 2 available anti- IL-17 treatments (SEC and IXE), UST, and GUS. Anti-IL-23 had been reported to induce remission in 4 patients (GUS: 3; risankizumab: 1). [8, 51] Although treatment was unsuccessful in 1 case with GUS38 and the literature on GUS treatment of ACH is limited by sample size, GUS showed an excellent response that aligns with our patient. Details of the cases summarized below are presented in (Table 2).

Authors	**Age (year)/ Sex**	**Dosage**
Saunier J et al.[10]	53/M	Anakinra ineffective at 100 mg daily for 7 weeks UST success, 12 months of treatment, 45mg at week 0 and 4, followed by every 12 weeks, Updated to 90 mg every 12 weeks + ACI 30 mg/day after 1 year of UST treatment
Lutz V et al.[30]	59/M	UST ineffective + ACI 50 mg/day + colchicine 1 mg/day Anakinra success, 5 months of treatment, 100mg daily with ACI 50mg/day.
Adas A et al.[9]	61/M	UST success, 18 months of treatment, 45mg at week 0 and 4, followed by every 12 weeks, updated to 90 mg every 8 weeks.
Georgakapoulos JR et al.25	68/M	UST ineffective, for 6 months of treatment, 90mg every 8 weeks.
Adisen E et al.[13]	50/M	UST success, 90 mg at week 0, then 45 mg at weeks 4, and then every 12 weeks.
Palacios-Alvarez I et al.31	67/M	UST Success, 21 months of treatment, 45 mg at week 0/4, followed by 45 mg every 12 weeks.
Cymerman RM et al.43	NA/F	UST success, 7 months of treatment, 45mg at week 0/4, and then 90 mg every 12 weeks after the second injection.
Baron JA et al.[44]	42/F	SEC success, 1-time treatment one 300 mg injection.

Galluzzo M et al.[45]	27/F	SEC success, 1 year of treatment, 300 mg at weeks 0/1/2/3/4 and then 300 mg every four weeks.
Smirnova LM et al.[32]	53/F	SEC success, 8 weeks of treatment, 300 mg at weeks 0, 1, 2, 3, then 300 mg monthly.
Balestri R et al.[46]	43/M	SEC success, 10 months of treatment, 300 mg at weeks 0/1/2/3/4, and then 300 mg every four weeks.
Inoue S et al.[37]	15/F	SEC success, 8 months of treatment, 300 mg every 4 weeks.
Muggli D et al.[47]	87/M	SEC success, 6 weeks of treatment, 300 mg in weeks 0, 1, 2, 3, 4 and then every 4 weeks.
Bardazzi F et al.[34]	43/M	SEC ineffective 300 mg in weeks 0, 1, 2, 3, and 4, then 300 mg every 4 weeks for 1 year Brodalumab success, 12 months of treatment, 210 mg in weeks 1, 2, 3 and then 210 mg every 2 weeks.
Miller AC et al.[33]	31/F	IXE success, 3 months of treatment, 80 mg at week 0, and then 80 mg every two weeks.
Battista T et al.[48]	31/F	IXE success, 7 months of treatment, 160 mg at week 0, and then 80 mg every two weeks.
Pilz AC et al.[49]	60/F	IXE success, 3 months of treatment, 160 mg at week 0, 80 mg every 2 weeks, and then 80 mg every 4 weeks after 12 weeks
Langer N et al.[50]	60/F	SEC without efficiency IXE without efficiency GUS success, 10 months of treatment.
Langer N et al.[50]	67/M	Risankizumab success, 6 months of treatment.
Milani-Nejad N et al.[38]	60/M	UST without efficiency SEC without efficiency IXE without efficiency GUS without efficiency. Brodalumab success, 6 months of treatment, 210 mg in weeks 0, 1, 2 and then every 2 weeks.
Passante M et al.[51]	37/F	Brodalumab success, 6 months of treatment, 210 mg in weeks 0, 1, 2 and then every 2 weeks.

ACI: acitretin; ADA: Adalimumab; CyA: Cyclosporin; F: female; GUS: guselkumab; IXE: ixekizumab; M: male; MTX: Methotrexate; SEC: Secukinumab; UST: Ustekinumab.

Table 2: Summary of ACH cases treated with non-TNF-blocking agents.

ACH is a rare localized pustulosis involving the digits and nails. It remains controversial whether ACH is an independent disease or a localized form of generalized pustular psoriasis (GPP). Variants in many genes have been identified to be involved in the pathogenesis of ACH.

In their study, Setta-kaffetzi et al. sequenced the four IL-36RN coding exons in 9 ACH and identified recessive variants in 2/9 ACH patients, including a 38-year-old woman carrying p.Arg102Trp/p.Ser113Leu variants and a 77-year-old woman carrying p.Ser113Leu variant. [52] In another paper, which included 28 patients with ACH, the mean age of ACH onset was 51.8 ± 20.4 years, of whom 13 (46.4%) had a history of PV. The proportion of IL-36RN mutations in patients with ACH was 18.2%, and the proportion of AP1S3 mutations was 7.1%. [53] Yet, some ACH patients with IL-36RN mutations had a history of GPP or a family history of GPP. For example, Abbas O et al. identified a homozygous missense mutation c.338C>T (p.Ser113Leu) in the IL36RN gene in a male patient with ACH, as well as in his sister who had a history of GPP.7 IL-36RN mutations were also found in 3 Chinese patients with ACH, all of whom had a history of GPP [54].

Our experience suggests that guselkumab could be an effective therapeutic option for patients with ACH, although the efficacy of biotherapies in ACH of the extremities is far from the promising results observed in plaque psoriasis. However, different results of biological therapy illustrated the different molecular

and gene expressions between PV and ACH. In the present study, whole exome sequencing revealed no rare coding variant in IL36RN, CARD14, or AP1S3, which usually occur in GPP patients. Therefore, future research should address the relationship between ACH and GPP.

Acknowledgments

Our patient had agreed for the use of image and publication of her case details; this work was sponsored by grants from Clinical Research Plan of SHDC (SHDC2020CR1014B).

References

1. Muggli D, Maul J-T, Anzengruber F, Fopp MW, Navarini AA (2017) Secukinumab for acrodermatitis continua of Hallopeau. JAMA Dermatol; 153: 336-337.
2. Sehgal VN, Verma P, Sharma S, et al. (2011) Acrodermatitis continua of Hallopeau: evolution of treatment options. Int J Dermatol; 50: 1195-1211.
3. Benjegerdes KE, Hyde K, Kivelevitch D, Mansouri B (2016) Pustular psoriasis: pathophysiology and current treatment perspectives. Psoriasis (Auckl); 6: 131-144.
4. Dini V, Barbanera S, Romanelli M (2013) Efficacy of adalimumab for the treatment of refractory paediatric acrodermatitis continua of Hallopeau. Acta Derm Venereol; 93: 588-589.
5. Lefkir S, Slimani S, Brahimi N, Ladjouze-Rezig A (2015) Successful treatment of acrodermatitis continua of Hallopeau associated with psoriatic arthritis with adalimumab. Eur J Rheumatol; 2: 78-79.
6. Frew JW, Murrell DF (2017) Highly resistant acrodermatitis continua of Hallopeau and pustular psoriasis. Skin Appendage Disord; 3: 179-181.
7. Abbas O, Itani S, Ghosn S, 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.
8. Kromer C, Loewe E, Schaarschmidt M-L, et al. (2020) Treatment of acrodermatitis continua of Hallopeau: A case series of 39 patients. J Dermatol; 47: 989-997.
9. Adas A, Dadban A, Arnault J-P, Chaby G, Lok C (2019) Acrodermatitis continua of Hallopeau response to optimized biological therapy. Dermatol Online J; 25: 13030/qt93s9w1p3.
10. Saunier J, Debarbieux S, Jullien D, Garnier L, Dalle S, Thomas L (2015) Acrodermatitis Continua of Hallopeau Treated Successfully with Ustekinumab and Acitretin after Failure of Tumour Necrosis Factor Blockade and Anakinra. Dermatology; 230: 97-100.
11. Puig L, Barco D, Vilarrasa E, Alomar A (2010) Treatment of acrodermatitis continua of Hallopeau with TNF-blocking agents: case report and review. Dermatology; 220: 154-158.
12. Thielen A-M, Barde C, Marazza G, Saurat J-H (2008) Long-term control with etanercept (Enbrel) of a severe acrodermatitis continua of Hallopeau refractory to infliximab (Remicade). Dermatology; 217: 137-139.
13. Adişen E, Oztaş M, Gürer MA (2007) Lack of efficacy of etanercept in acrodermatitis continua of Hallopeau. Int J Dermatol; 46: 1205-1207.
14. Weisshaar E, Diepgen TL (2007) Successful etanercept therapy in therapy refractory acrodermatitis continua suppurativa Hallopeau. J Dtsch Dermatol Ges; 5: 489-492.
15. Kazinski K, Joyce KM, Hodson D (2005) The successful use of etanercept in combination therapy for treatment of acrodermatitis continua of hallopeau. J Drugs Dermatol; 4: 360-364.
16. Bonish B, Rashid RM, Swan J (2006) Etanercept responsive acrodermatitis continua of Hallopeau: is a pattern developing? J Drugs Dermatol; 5: 903-904.
17. Silpa-arch N, Wongpraparut C (2011) A recalcitrant acrodermatitis continua of Hallopeau successfully treated with etanercept. J Med Assoc Thai; 94: 1154-1157.
18. Nikkels AF, Piérard GE (2006) Etanercept and recalcitrant acrodermatitis continua of Hallopeau. J Drugs Dermatol; 5: 705-706.
19. Rubio C, Martin MA, Sánchez DM, Vidaurrazaga C, Casado M (2009) Excellent and prolonged response to infliximab in a case of recalcitrant acrodermatitis continua of Hallopeau. J Eur Acad Dermatol Venereol; 23: 707-708.
20. Ahmad K, Rogers S (2006) Three years' experience with infliximab in recalcitrant psoriasis. Clin Exp Dermatol; 31: 630-633.
21. Ahmad K, Rogers S (2007) Two years of experience with etanercept in recalcitrant psoriasis. Br J Dermatol; 156: 1010-1014.
22. Mang R, Ruzicka T, Stege H (2004) Successful treatment of acrodermatitis continua of Hallopeau by the tumour necrosis factor-alpha inhibitor infliximab (Remicade). Br J Dermatol; 150: 379-380.
23. Okumo K, Ogura K, Okuyama R, Itoi E (2013) Two cases of acrodermatitis continua of Hallopeau associated with generalized arthritis. Acta Dermatovenerol Crot; 21: 265-267.
24. Kioka M, Yu A, Tanizaki H, Kokunai Y, Kurokawa T, Moriwaki S (2018) Acrodermatitis continua of Hallopeau successfully treated only with infliximab: a case report. J Cutan Immunol Allergy; 1: 73-76.
25. Georgakopoulos JR, Ighani A, Yeung J (2017) Short- and longterm management of an acute pustular psoriasis flare: a case report. J Cutan Med Surg; 21: 452-456.
26. Di Costanzo L, Napolitano M, Patruno C, Cantelli M, Balato N (2014) Acrodermatitis continua of Hallopeau (ACH): two cases successfully treated with adalimumab. J Dermatolog Treat; 25: 489-494.
27. Crowley EL, Maliyar K, Rodriguez-Bolanos F, O'Toole A, Gooderham MJ (2019) Acrodermatitis continua of Hallopeau successfully treated with adalimumab: A case report. SAGE Open Med Case Rep; 7: 2050313X19829620.
28. Sopkovich JA, Poulos GA, Wong HK (2012) Acrodermatitis continua of Hallopeau successfully treated with adalimumab. J Clin Aesthet Dermatol; 5: 60-62.
29. Ryan C, Collins P, Kirby B, Rogers S (2009) Treatment of acrodermatitis continua of Hallopeau with adalimumab. Br J Dermatol; 160: 203-205.
30. Lutz V, Lipsker D (2012) Acitretin- and Tumor Necrosis Factor Inhibitor–Resistant Acrodermatitis Continua of Hallopeau Responsive to the Interleukin 1 Receptor Antagonist Anakinra. Arch Dermatol; 148: 297-299.
31. Palacios-Álvarez I, Simal-Gómez G, Mas-Vidal A, Bernad-Alonso I (2018) Treatment of acrodermatitis continua of Hallopeau with ustekinumab as monotherapy after failure of anti-TNF agents. J Dtsch Dermatol Ges; 16: 611-613.

32. Smirnova LM, Vertieva EY, Olisova OY, Anpilogova EM (2019) Outcomes of various types of therapy in patients with treatment-resistant acrodermatitis continua of Hallopeau. Biologics; 13: 83-87.

33. Miller AC, Holland TE, Cohen DJ (2021) Treatment of acrodermatitis continua of hallopeau with ixekizumab. J Dermatolog Treat; 32: 117-119.

34. Bardazzi F, Altobrando AD, Lacava R (2020) Brodalumab in the treatment of recalcitrant acrodermatitis continua of Hallopeau. Dermatol Ther; 33: e14301.

35. Caputo F, Parro S, Zoli G (2011) Adalimumab for a co-existing clinical condition of Crohn's disease and acrodermatitis continua of Hallopeau. J Crohns Colitis; 5: 649.

36. Conti A, Ciardo S, Mandel VD, Bigi L, Pellacani G (2016) Speckled variance optical coherence tomography for the assessment of nail involvement in acrodermatitis continua of Hallopeau: a case study. J Int Med Res; 44: 119-123.

37. Inoue S, Watanabe R, Ishitsuka Y, et al. (2021) Successful Treatment of Acrodermatitis Continua of Hallopeau with an Anti-IL-17A Agent. Indian J Dermatol; 66: 225.

38. Milani-Nejad N, Kaffenberger J (2019) Treatment of recalcitrant acrodermatitis continua of Hallopeau with brodalumab. J Drugs Dermatol; 18: 1047.

39. Múeller RB, Ogilvie A, Schwarz S, Kern P, Schett G, Sticherling M (2009) Adalimumab treatment of a patient with psoriasis suppurativa Hallopeau associated osteoarthropathy. Clin Exp Rheumatol; 27: 887.

40. Megna M, Fabbrocini G, Costa C, Ferrillo M (2020) A case of pediatric acrodermatitis continua of Hallopeau successfully treated with adalimumab biosimilar. Dermatol Ther; 33: e13327.

41. Samotij D, Gawron E, Szczęch J, Ostańska E, Reich A (2021) Acrodermatitis Continua of Hallopeau Evolving into Generalized Pustular Psoriasis Following COVID-19 A Case Report of a Successful Treatment with Infliximab in Combination with Acitretin. Biologics; 15: 107-113.

42. Tobin AM, Kirby B (2005) Successful treatment of recalcitrant acrodermatitis continua of Hallopeau with adalimumab and acitretin. Br J Dermatol; 153: 445-446.

43. Cymerman RM, Cohen DE (2016) Treatment of acrodermatitis continua of Hallopeau with ustekinumab as monotherapy. JAMA Dermatol; 152: 346-348.

44. Baron JA (2017) Acrodermatitis of Hallopeau and erosive oral mucositis successfully treated with secukinumab. JAAD Case Rep; 3: 215-218.

45. Galluzzo M, D'Adamio S, Teoli M, Bianchi L, Talamonti M (2019) Biologic therapy for acrodermatitis continua of Hallopeau: successful treatment with secukinumab and review of the literature. Dermatol Ther; 32: e12899.

46. Balestri R, Rech G, Tasin L, Rizzoli L, Girardelli CR (2018) Acrodermatitis continua of Hallopeau successfully treated with secukinumab. J Dermatolog Treat; 29: 3-5.

47. Muggli D, Maul J-T, Anzengruber F, Fopp MW, Navarini AA (2017) Secukinumab for Acrodermatitis continua of hallopeau. JAMA Dermatol; 153: 336-337.

48. Battista T, Guerrasio G, Fata Salvatores GD, Peduto T, Fabbrocini G, Guida AD (2022) Acrodermatitis continua of Hallopeau successfully treated with ixekizumab: A case report. Dermatol Ther; 35: e15383.

49. Pilz AC, Roenneberg S, Biedermann T, Eyerich K (2018) Ixekizumab for acrodermatitis continua. J Dtsch Dermatol Ges; 16: 907-910.

50. Langer N, Wilsmann-Theis D, Kromer C, Mohr J, Mössner R (2021) Successful therapy of acrodermatitis continua of Hallopeau with IL-23 blockers -two new cases. J Dtsch Dermatol Ges; 19: 1504-1507.

51. Passante M, Dastoli S, Nisticò SP, Bennardo L, Patruno C (2020) Effectiveness of brodalumab in acrodermatitis continua of Hallopeau: a case report. Dermatol Ther; 33: e13170.

52. Setta-Kaffetzi N, Navarini AA, Patel VM, et al. (2013) Rare Pathogenic Variants in IL36RN Underlie a Spectrum of Psoriasis-Associated Pustular Phenotypes. J Invest Dermatol; 133: 1366-1369.

53. Twelves S, Mostafa A, Dand N, et al. (2019) Clinical and genetic differences between pustular psoriasis subtypes. J Allergy Clin Immunol; 143: 1021-1026.

54. Yun-Liu Chen, Zhao-Yang Wang, Lin Ma, Zi-Gang Xu (2020) Three cases of IL36RN-associated pustulosis: An evolution of acrodermatitis continua of Hallopeau to generalized pustular psoriasis. Indian J Dermatol Leprol; 86: 562-565.