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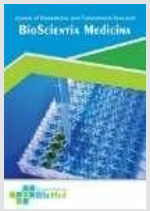

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A Methodical Approach to a 15-Year Diagnostic Enigma: Unmasking Acrodermatitis Continua of Hallopeau Through Dermoscopy, Histopathology, and Structured Therapeutic Sequencing

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A B S T R A C T

Background: Acrodermatitis continua of Hallopeau (ACH) is a rare, debilitating variant of pustular psoriasis. Its profound clinical mimicry of common infections, particularly onychomycosis, often leads to extensive diagnostic delays and ineffective treatments, causing significant patient morbidity. This report details a case with a 15-year history of misdiagnosis, illustrating a structured methodological approach to diagnosis and management. **Case presentation:** A 40-year-old Indonesian woman presented with a 15-year history of painful pustular lesions and severe onychodystrophy affecting seven digits, refractory to numerous antimicrobial therapies. The diagnostic process was systematically re-evaluated; dermoscopy revealed features inconsistent with onychomycosis (dotted vessels, hemorrhagic spots), prompting a definitive skin and nail matrix biopsy. Histopathology confirmed pustular psoriasis with pathognomonic Kogoj's spongiform pustules and Munro's microabscesses. Treatment was initiated with cyclosporine (3.3 mg/kg/day), leading to rapid remission. However, the development of gingival hyperplasia and hypertension necessitated a transition to weekly methotrexate (15 mg). The patient achieved and maintained clinical remission on this regimen. **Conclusion:** This case underscores the necessity of a high index of suspicion for ACH in chronic, treatment-resistant nail dystrophy. It demonstrates that a methodical application of dermoscopy and histopathology is indispensable for overcoming clinical mimicry. The main lesson is that structured diagnostic evaluation and sequenced therapy, responsive to adverse events, are crucial for achieving long-term remission and restoring quality of life.

1. Introduction

Acrodermatitis continua of Hallopeau (ACH), also known by synonyms including acrodermatitis perstans and dermatitis repens, represents a rare and challenging inflammatory dermatosis within the spectrum of pustular psoriasis.[1] It is defined by a chronic and often relentless course of sterile pustular eruptions that primarily target the distal phalanges of the fingers and toes. The inflammatory process typically originates near the nail apparatus, leading to significant pain, functional impairment, and severe nail abnormalities, including onychodystrophy, subungual hyperkeratosis, onycholysis, and in advanced cases, permanent nail loss (anonychia).[2] The persistent inflammation can extend beyond the cutaneous structures, potentially causing osteitis and osteolysis of the underlying distal phalanges, resulting in irreversible acral deformities.[3] Consequently, ACH carries a substantial burden of morbidity, profoundly impacting patients' quality of life through chronic pain, cosmetic disfigurement, and loss of hand function.

Epidemiological data on ACH are limited due to its rarity, primarily deriving from case series and retrospective cohort studies.[4] Existing evidence indicates a predilection for middle-aged adults, with a peak incidence occurring between the ages of 30 and 50. A notable sex disparity has been observed, with women being affected up to five times more frequently than men. Interestingly, the mean age of onset appears to vary between ethnic groups, with Caucasian cohorts reporting an onset between 48 and 54 years, whereas Asian populations tend to present earlier, at a mean age of approximately 38.5 years. This case, involving a 40-year-old Indonesian woman, aligns perfectly with the demographic profile observed in Asian patient groups.[5]

The etiology of ACH is multifactorial and not yet fully elucidated, though it is understood to arise from a complex interplay of genetic predisposition, immune dysregulation, and environmental triggers.[6] A significant proportion of cases are preceded by minor local trauma or infection at the site of onset, suggesting that these events can act as a Koebner-like phenomenon, initiating the inflammatory cascade in susceptible individuals.[7] On a molecular level, the pathophysiology of ACH is deeply rooted in the dysregulation of innate and adaptive immunity. Landmark genetic studies have identified mutations in several key genes as major drivers of pustular psoriasis phenotypes.[8] The most prominent among these is the IL36RN gene, which encodes the interleukin-36 receptor antagonist (IL-36Ra). Loss-of-function mutations in IL36RN lead to unopposed signaling by pro-inflammatory cytokines IL-36α, IL-36β, and IL-36γ, resulting in a massive influx of neutrophils into the epidermis and the formation of sterile pustules—the clinical hallmark of the disease. This condition is now classified as Deficiency of Interleukin-36 Receptor Antagonist (DITRA). Beyond IL36RN, mutations in other genes, including CARD14 (encoding a keratinocyte-specific scaffold protein that activates NF-κB signaling) and AP1S3 (involved in keratinocyte autophagy and stress responses), have also been implicated, further highlighting the central role of keratinocyte-driven inflammation in ACH pathogenesis.[9]

The primary diagnostic challenge of ACH lies in its remarkable ability to mimic other more common conditions, particularly chronic nail infections such as onychomycosis and bacterial paronychia. The clinical presentation of yellowish, brittle, and dystrophic nails with subungual debris is virtually indistinguishable from that of a fungal nail infection at first glance.[10] This clinical overlap frequently leads to an initial misdiagnosis of onychomycosis, often resulting in months or even years of ineffective and inappropriate antifungal therapy, while the underlying inflammatory disease progresses unchecked. The failure to respond to standard antifungal treatments, coupled with the presence of pustulation, should serve as a critical red flag for clinicians, prompting consideration of alternative diagnoses.

While case reports of ACH exist, few have methodically documented the step-by-step refutation of a long-standing misdiagnosis using modern tools, nor have they detailed the therapeutic sequencing in response to adverse events. This report, therefore, aims to provide a valuable real-world evidence framework for the diagnosis and management of refractory acral pustulosis. By presenting a detailed longitudinal account structured in accordance with the CARE (CAse REport) guidelines, we offer a structured educational model that elevates the purpose from simply "showing a case" to "providing a transparent and reproducible diagnostic and therapeutic pathway" for clinicians faced with this diagnostic enigma.

2. Case Presentation

A 40-year-old Indonesian woman, a housewife from a rural community, was referred to the tertiary care Dermatology and Venereology clinic of Prof. Dr. I.G.N.G. Ngoerah General Hospital. Her chief complaint was a 15-year history of painful, brittle, and pus-discharging fingernails that had rendered her unable to perform daily household chores. The patient's journey was one of significant physical and

emotional distress. She described her experience: "*For fifteen years, it felt like I was cursed. It started small, on one finger, and I thought it was just a simple infection. Doctors kept giving me creams and pills for fungus, but it never got better; it only spread. The pain was constant, a throbbing that never left. Simple things like washing dishes, cooking for my family, or even combing my hair became agonizing. I became ashamed of my hands and would hide them in public. I felt hopeless and started to believe I would have to live with this pain and disfigurement forever. When the new treatment started working, it was like a miracle. For the first time in over a decade, I saw a normal nail growing. I cannot express the relief; it was like getting my life back.*"

The condition began insidiously 15 years prior (circa 2008), following a minor cut to her left index finger while preparing food. Initially, a tender pustule developed, which she treated with over-the-counter antibiotic ointments without success. Over the next two years, the lesion evolved into a chronic cycle of erythema, pustulation, and crusting, with progressive thickening and yellowing of the nail plate. Between 2010 and 2020, the process relentlessly and symmetrically progressed to involve six other digits. She described a fluctuating but unremitting clinical course characterized by a constant, low-grade throbbing pain in the affected fingertips. This pain was severely exacerbated by contact with water and detergents, profoundly impairing her daily activities. Periodically, she observed a visible collection of yellowish-white pus under the nail fold (a "lake of pus"), which would sometimes discharge spontaneously, providing transient relief. She denied any history of similar lesions on her toes or other parts of her body and reported no associated joint pain, stiffness, or systemic symptoms such as fever or malaise.

The patient had navigated a complex diagnostic odyssey, consulting multiple general physicians and dermatologists. She was consistently diagnosed with chronic onychomycosis with secondary bacterial superinfection. Her treatment history was extensive and marked by a uniform lack of response, as detailed in Table 1. Her past medical history was significant for controlled hypertension, managed with amlodipine 5 mg daily. She denied any history of diabetes mellitus, other autoimmune diseases, or systemic conditions. There was no family history of psoriasis or similar skin disorders. She was a non-smoker and did not consume alcohol.

Table 1. Summary of Previous Ineffective Therapies (2009-2024)

A 15-year history of treatments for a misdiagnosed case of Acrodermatitis Continua of Hallopeau.

DRUG / AGENT	DOSAGE	DURATION	PRESCRIBER (SPECIALTY)	REPORTED OUTCOME / REASON FOR DISCONTINUATION
Topical Miconazole 2% Cream	Applied Twice Daily	> 2 years (intermittently)	General Practitioner	No improvement in nail dystrophy or pustulation.
Topical Gentamicin Ointment	Applied Twice Daily	> 3 years (intermittently)	General Practitioner	No effect on pustulation or pain.
Oral Cotrimoxazole	480 mg Twice Daily	10 weeks	General Practitioner	Discontinued due to lack of efficacy.
Oral Ciprofloxacin	500 mg Twice Daily	3 weeks	General Practitioner	No effect on lesions.
Oral Fluconazole	150 mg Daily	5 months	Dermatologist	No improvement in nail appearance or symptoms.
Topical Chloramphenicol Cream	Applied Twice Daily	6 months	General Practitioner	No improvement noted by the patient.
Itraconazole (Pulse Therapy)	200 mg Twice Daily (1 wk/mo)	3 months	Dermatologist	Discontinued due to lack of efficacy.

On physical examination, her vital signs were stable, with a blood pressure of 115/80 mmHg. Her height was 158 cm and her weight was 92 kg, with a body mass index (BMI) of 36.9 kg/m², corresponding to Grade II Obesity. Dermatological examination revealed involvement of digits I, II, III, IV, and V of the right hand and digits I and II of the left hand. The distal phalanges displayed confluent, erythematous, and slightly atrophic plaques with overlying yellowish-brown crusts and scattered sterile pustules. There was severe nail involvement in all seven digits, characterized by marked onychodystrophy, onycholysis, yellowish-white discoloration (dyschromia), and significant subungual hyperkeratosis. A classic "lake of pus" was visible beneath the proximal nail fold of the right third digit. The surrounding skin appeared shiny and mildly atrophic, with tenderness to palpation over all affected fingertips. A timeline of key clinical events is presented in Figure 1.

Figure 1. Timeline of key clinical events (2008 - 2025). This figure chronologically outlines the patient's 15-year journey from symptom onset through multiple misdiagnoses and failed treatments to the definitive diagnosis and successful management at our institution.

The initial working diagnosis for over a decade had been chronic onychomycosis with bacterial superinfection, based on the clinical appearance of dystrophic, discolored nails. However, this diagnosis was challenged by several key factors: the absolute lack of response to multiple appropriate courses of systemic antifungal and antibacterial agents, the presence of sterile pustules on Gram stain, and the inconsistent microbiological findings, which were more suggestive of contamination or colonization (*Aspergillus sp.*, *Acinetobacter baumannii*) than true infection. Given this history, the differential diagnosis was systematically broadened to include inflammatory dermatoses. The leading possibilities considered were: (1) Acrodermatitis Continua of Hallopeau (Pustular Psoriasis): This became the leading hypothesis due to the classic presentation of sterile pustules localized to the acral sites, severe nail dystrophy, and the history of a traumatic trigger; (2) Reactive Arthritis (formerly Reiter's Syndrome): Considered due to the potential for nail changes and pustular lesions (keratoderma blenorrhagicum), but was deemed less likely due to the absence of the classic triad of arthritis, urethritis, and conjunctivitis; (3) Pustular Bacterid of Andrews: This entity involves sterile pustules on palms and soles, often linked to a distant focal infection. It was considered less likely due to the strict confinement of lesions to the distal digits and nail apparatus.

Multiple microbiological tests had yielded conflicting or unhelpful results, as described in the timeline. Gram stains of pus consistently showed numerous leukocytes but no bacteria, supporting the sterile nature of the pustules. A complete blood count showed a white blood cell count of 8.85 x 10^9/L with neutrophilia (75.9%). Inflammatory markers were mildly elevated, with an Erythrocyte Sedimentation Rate (ESR) of 28 mm/hr (Normal <20 mm/hr) and a C-reactive protein (CRP) of 8.2 mg/L (Normal <5 mg/L). Dermoscopic examination (DermLite DL4, 10x magnification, polarized mode) of the nail plate and hyponychium was pivotal. It revealed prominent whitish-yellowish hyperkeratotic scaling, interspersed with regularly distributed dotted vessels and small, dark red hemorrhagic spots (figure 2). Crucially, no dermoscopic features typically associated with onychomycosis, such as the 'ruin' appearance or longitudinal striae, were observed. These findings strongly favored an inflammatory psoriasiform process. A 4-mm punch biopsy from the perilesional skin of the right index finger and a nail matrix biopsy were performed. The findings were definitive. The epidermis showed psoriasiform hyperplasia, acanthosis, and a thinned granular layer. The stratum corneum displayed parakeratosis. The pathognomonic findings were large intraepidermal neutrophilic aggregates forming spongiform pustules of Kogoj and smaller collections forming Munro's microabscesses. The superficial dermis contained dilated, tortuous blood vessels with a moderate perivascular lymphocytic infiltrate. These features confirmed the diagnosis of pustular psoriasis. Based on the synthesis of the long-term clinical history, failure of antimicrobial therapies, characteristic dermoscopic findings, and definitive histopathological evidence, a final diagnosis of Acrodermatitis Continua of Hallopeau was established.

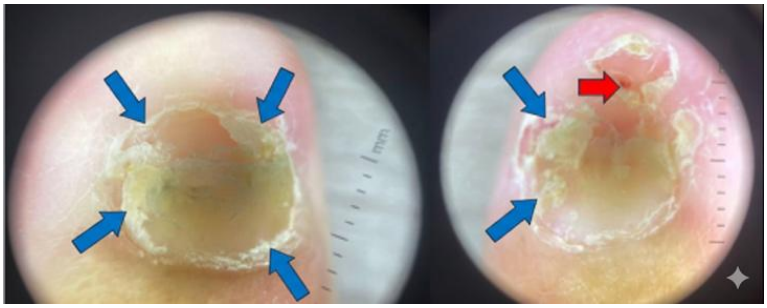

Figure 2. Dermoscopy examination of digit I of the left hand. Left figure: Whitish-yellowish hyperkeratosis/scaling is observed (blue arrow). Right figure: A hemorrhagic spot is observed (red arrow).

Table 2. Summary of Clinical and Diagnostic Findings

A multi-faceted approach to diagnosing Acrodermatitis Continua of Hallopeau.

DIAGNOSTIC DOMAIN	FINDING / TEST PERFORMED	KEY OBSERVATIONS	DIAGNOSTIC SIGNIFICANCE / INTERPRETATION
Clinical Examination	Physical Appearance	Severe onychodystrophy, sterile pustules, "lake of pus," erythematous plaques on 7 distal digits.	Suggestive of severe inflammatory process; atypical for simple onychomycosis.
Microbiology	Fungal/Bacterial Cultures & Gram Stain	Inconsistent cultures (contaminants); Gram stain showed numerous leukocytes but NO bacteria.	Strong evidence AGAINST an active infectious etiology. Supported sterile nature of pustules.
Laboratory Analysis	Blood Work (CBC, ESR, CRP)	Neutrophilia (75.9%), mildly elevated ESR (28 mm/hr) and CRP (8.2 mg/L).	Consistent with a systemic inflammatory state, not specific but supported a non-infectious process.
Specialized Imaging	Dermoscopy	Regularly distributed dotted vessels, hemorrhagic spots, whitish-yellow scaling. NO signs of onychomycosis.	Pivotal finding. Ruled out onychomycosis and strongly suggested a psoriasiform process.
Histopathology	Skin & Nail Matrix Punch Biopsy	Spongiform pustules of Kogoj, Munro's microabscesses, psoriasiform hyperplasia, parakeratosis.	Definitive & Pathognomonic for Pustular Psoriasis. Confirmed final diagnosis.

Upon establishing the definitive diagnosis, the patient was initiated on systemic immunosuppressive therapy (Table 3). The initial treatment consisted of oral cyclosporine at a dose of 100 mg three times daily (total 300 mg/day, approximately 3.3 mg/kg/day), selected for its rapid onset of action in severe pustular psoriasis, and was augmented with topical desoximetasone 0.25% cream applied under occlusion at night. This regimen yielded a dramatic clinical improvement by the 93-day follow-up, at which point the formation of new pustules had ceased, erythema and pain had significantly subsided, and early signs of healthy new nail growth were evident. However, at the 133-day follow-up, the patient developed progressive gingival hyperplasia and her blood pressure had risen to 143/96 mmHg, both well-documented adverse effects of cyclosporine. Due to these complications, a decision was made to transition her to long-term maintenance therapy. She was started on oral methotrexate (MTX) at a weekly dose of 15 mg, a standard starting dose for moderate-to-severe psoriasis, which was preceded by a 2.5 mg test dose and supplemented with weekly folic acid. Six months after transitioning to methotrexate, the patient was in sustained clinical remission with no evidence of active pustulation and over 50% healthy regrowth of the nail plates. Her gingival hyperplasia had completely resolved, her blood pressure had normalized, and she reported a profound improvement in her quality of life, now able to perform all daily activities without pain.

3. Discussion

This case of a 40-year-old woman with Acrodermatitis continua of Hallopeau poignantly illustrates the immense diagnostic and therapeutic challenges posed by this rare disease. The 15-year odyssey from initial symptoms to definitive diagnosis highlights a critical educational point: the imperative for clinicians to look beyond common infectious etiologies in cases of chronic, treatment-refractory nail dystrophy.[11] This discussion will critically analyze the intricate pathophysiology of ACH, integrating the patient's specific clinical features; deconstruct the methodical diagnostic process that overcame the clinical mimicry; rationalize the evidence-based therapeutic sequencing; and address the limitations and generalizability of this report.

Table 3. Treatment, Outcome, and Follow-up

A sequenced therapeutic strategy for Acrodermatitis Continua of Hallopeau.

TREATMENT PHASE & AGENT(S)	DOSAGE & RATIONALE	FOLLOW-UP PERIOD	CLINICAL OUTCOME & OBSERVATIONS	STATUS / ACTION
Induction Therapy Oral Cyclosporine + Topical Desoximetasone	300 mg/day (3.3 mg/kg/day) Rationale: Rapid onset for severe pustular disease control.	Day 1 to Day 93	Dramatic clinical improvement. Cessation of new pustules, significant reduction in erythema and pain. Early signs of healthy nail regrowth observed.	Successful Induction
Adverse Event Monitoring Continued Cyclosporine	300 mg/day (3.3 mg/kg/day) Rationale: Continued therapy while assessing new symptoms.	Day 94 to Day 133	Patient developed progressive gingival hyperplasia. Blood pressure increased to 143/96 mmHg. Both are known side effects of cyclosporine.	Adverse Events Noted
Maintenance Therapy Oral Methotrexate + Folic Acid	15 mg/week (MTX), 5 mg/week (Folic Acid) Rationale: Transition to a safer long-term agent.	6-Month Follow-up	Sustained clinical remission. No active pustulation. >50% healthy nail regrowth. Complete resolution of gingival hyperplasia and normalization of blood pressure. Profound QoL improvement.	Stable Remission

Figure 3. The pathophysiological nexus of ACH.

ACH is fundamentally a disease of profound immune dysregulation, where a latent genetic susceptibility primes the cutaneous immune system for an aberrant, neutrophil-dominant inflammatory response (Figure 3).[12] This response is often initiated by non-specific environmental insults, such as the minor trauma reported by our patient, acting as a potent Koebner phenomenon. The resulting pathophysiology is not a linear process but a complex, self-amplifying feedback loop meticulously orchestrated between resident skin cells, primarily keratinocytes, and components of both the innate and adaptive immune systems, particularly neutrophils and Th17 lymphocytes.[13]

At the very heart of this dysregulation, especially in severe pustular phenotypes like ACH, lies the Interleukin-36 (IL-36) signaling pathway. For decades, keratinocytes were viewed merely as structural components of the epidermis. It is now unequivocally clear that they are critical sentinels of the innate immune system, capable of initiating and propagating robust inflammatory responses.[14] Upon sensing danger signals, such as those from trauma or microbes, keratinocytes release a triad of pro-inflammatory agonist cytokines: IL-36α, IL-36β, and IL-36γ. These cytokines bind to the IL-36 receptor (IL-36R), which is highly expressed on keratinocytes themselves as well as on other immune cells like dendritic cells and macrophages. This binding triggers a powerful intracellular signaling cascade, leading to the activation of key transcription factors such as NF-κB and AP-1. The result is a massive upregulation of a broad spectrum of inflammatory mediators, including other cytokines (TNF-α, IL-6), and, most crucially, potent neutrophil-attracting chemokines like CXCL1, CXCL2, and CXCL8 (IL-8).[15]

In healthy skin, this potentially explosive pathway is held in exquisite balance by a constitutively expressed brake: the IL-36 receptor antagonist (IL-36Ra), encoded by the IL36RN gene. IL-36Ra binds to the same IL-36R with high affinity but fails to elicit a downstream signal, effectively acting as a competitive inhibitor that prevents the agonist cytokines from docking. A significant subset of patients with generalized pustular psoriasis and ACH carry loss-of-function mutations in the IL36RN gene.[16] This genetic defect leads to a deficiency of functional IL-36Ra, essentially removing the brakes from the system. Consequently, any minor trigger that induces IL-36 production can lead to an unchecked, explosive inflammatory response. This results in the massive chemoattraction and subsequent infiltration of neutrophils into the epidermis, a hallmark of the disease. These neutrophils migrate through the intercellular spaces of the epidermis, which, under the influence of inflammatory mediators, begin to break down, culminating in the formation of the sterile, macroscopic pustules seen clinically and the pathognomonic spongiform pustules of Kogoj observed on histopathology—a feature definitively identified in our patient's biopsy. While the genetic status of our patient was not determined, her severe, unremitting, and trauma-induced pustular phenotype is highly suggestive of an underlying dysregulation within this critical pathway.

Further genetic insights have revealed that the IL-36 axis is not the sole driver. Gain-of-function mutations in the CARD14 gene, which codes for a scaffold protein essential for NF-κB activation in keratinocytes, can also lead to a pustular phenotype by causing constitutive activation of this central inflammatory pathway. Similarly, mutations in AP1S3, a gene involved in cellular autophagy, have been implicated. Defective autophagy leads to an accumulation of cellular stress and the activation of innate immune sensors, again resulting in an overproduction of inflammatory mediators.[17]

This initial, powerful innate immune activation is then seamlessly amplified and perpetuated by the adaptive immune system, primarily through the IL-23/Th17 axis, which is now understood to be central to all forms of psoriasis. Antigen-presenting cells in the skin, such as dermal dendritic cells, activated by the initial innate signals, produce copious amounts of IL-23. This cytokine acts on a specific subset of T-helper cells, driving their differentiation and

expansion into Th17 cells. These Th17 cells, in turn, become prolific factories for IL-17 and IL-22. IL-17 is a master cytokine that acts directly on keratinocytes, inducing them to hyperproliferate (leading to the acanthosis and scaling seen clinically) and, critically, to produce even more neutrophil-attracting chemokines, thus creating the vicious, self-sustaining feedback loop that defines the chronic nature of ACH. IL-22 further contributes to the epidermal hyperplasia. This intricate and relentless interplay between innate and adaptive immunity, driven by genetic predisposition and centered on the keratinocyte, perfectly explains the chronic, unremitting nature of the inflammation seen in this patient.

A critical and often overlooked factor in the pathogenesis and clinical severity of psoriasis is the role of systemic comorbidities, particularly obesity. Our patient presented with Grade II Obesity (BMI 36.9 kg/m^2), a condition that must be considered not as an incidental finding but as an active contributor to her disease state. Adipose tissue is not a passive energy reservoir but a highly active endocrine and metabolic organ. In obesity, particularly visceral adiposity, adipocytes become dysfunctional and hypertrophic, leading to a state of chronic, low-grade systemic inflammation often termed "meta-inflammation."

This state is driven by the overproduction of a variety of pro-inflammatory cytokines known as adipokines, which are released into the systemic circulation. These include tumor necrosis factor-alpha (TNF-α), leptin, and IL-6. TNF-α is a cornerstone cytokine in psoriasis, and its systemic overproduction in an obese state creates a pervasive pro-inflammatory environment that significantly lowers the threshold for cutaneous inflammation.[18] Leptin, another key adipokine, also exerts pro-inflammatory effects and can further drive the Th1/Th17 immune responses implicated in psoriasis. This systemic inflammatory milieu likely played a crucial role in our patient's disease in two ways: first, it probably lowered the threshold for the initial Koebner response to trauma, allowing a minor cut to spiral into a 15-year disease process; second, it almost certainly contributed to the severity and refractory nature of her ACH over the subsequent years. The systemic inflammation originating from adipose tissue synergizes powerfully with the genetically primed local immune response in the skin, creating a more intense, widespread, and difficult-to-control disease phenotype. This profound connection highlights the absolute necessity of a holistic patient assessment and firmly suggests that lifestyle interventions, including weight management, should be considered an essential ancillary component of the long-term therapeutic strategy in such patients.

The staggering 15-year diagnostic delay in this case was a direct consequence of the profound and notorious clinical overlap between ACH and chronic onychomycosis. Both conditions can present with a strikingly similar constellation of features, including onycholysis (separation of the nail plate from the bed), significant subungual hyperkeratosis (accumulation of debris under the nail), and yellowish-brown discoloration. This mimicry makes reliance on clinical morphology alone a recipe for diagnostic error and prolonged patient suffering. Our experience powerfully demonstrates the indispensable value of integrating two key diagnostic techniques into the evaluation of any refractory or atypical nail disorder.

First, dermoscopy served as the initial, pivotal, and most crucial step in challenging and ultimately dismantling the long-standing but incorrect diagnosis of onychomycosis. The dermoscopic patterns of fungal nail infection are well-characterized and include features such as a jagged, "ruin-like" proximal border of the onycholytic area and distinctive longitudinal whitish-yellow striae. Absolutely none of these features were present in our patient. Instead, dermoscopy revealed a completely different set of clues pointing towards an inflammatory, psoriasiform process. We observed a pattern of regularly distributed dotted vessels, a hallmark finding in psoriasis that corresponds to the dilated, tortuous, and elongated papillary dermal capillaries that rise closer to the epidermal surface. Furthermore, the presence of small

hemorrhagic spots, representing micro-trauma to these fragile vessels, and a diffuse pattern of whitish-yellow scaling further solidified the suspicion of an inflammatory, rather than infectious, etiology. Dermoscopy is a rapid, non-invasive, and cost-effective tool that, in this case, provided immediate and powerful evidence to redirect the entire diagnostic pathway, saving the patient from further ineffective treatments.

Second, while dermoscopy reoriented the diagnosis, histopathology provided the definitive, irrefutable evidence required to establish it. A 4-mm punch biopsy from the perilesional skin and nail matrix confirmed the diagnosis unequivocally. The microscopic findings painted a classic picture of pustular psoriasis: psoriasiform epidermal hyperplasia, parakeratosis, hypogranulosis, and dilated papillary dermal vessels. However, the discovery of the two pathognomonic features sealed the diagnosis. The first was the presence of spongiform pustules of Kogoj, which represent the microscopic journey of neutrophils as they migrate through the epidermis and accumulate in the upper spinous layer, creating distinctive sponge-like cavities filled with inflammatory cells. The second was the identification of Munro's microabscesses, which are smaller collections of neutrophils found within the parakeratotic stratum corneum. These findings are the gold standard for diagnosing pustular psoriasis. The biopsy not only confirmed ACH but also definitively ruled out onychomycosis (by the absence of fungal elements on a PAS stain) and other inflammatory mimics. This case powerfully advocates for a low threshold for performing a biopsy in any case of atypical or treatment-resistant nail dystrophy.

The treatment of ACH is challenging due to the lack of high-quality evidence from randomized controlled trials; current strategies are therefore extrapolated from established guidelines for other forms of severe and pustular psoriasis. The therapeutic journey of our patient reflects a standard, evidence-based, and methodical approach: first, induce rapid remission with a fast-acting systemic agent, and second, transition to a safer, more sustainable long-term maintenance therapy while actively monitoring for and responding to adverse events.

Cyclosporine was chosen as the initial induction agent for its well-established ability to induce rapid and profound immunosuppression.[19] As a calcineurin inhibitor, it acts by blocking the transcription of Interleukin-2 (IL-2) and other key cytokines, which are essential for T-cell activation and proliferation. By effectively shutting down this central step in the adaptive immune cascade, cyclosporine can bring severe, acute flares of pustular psoriasis under control quickly and reliably, as demonstrated by our patient's excellent clinical response within the first three months. However, the utility of cyclosporine is significantly limited by its potential for serious long-term toxicities, most notably nephrotoxicity, hypertension, and an increased risk of malignancy. The development of both gingival hyperplasia and an elevation in blood pressure in our patient after just 15 weeks of therapy perfectly exemplified the unfavorable side-effect profile that precludes its use for long-term maintenance.

This necessitated a planned transition to methotrexate (MTX), a cornerstone of long-term psoriasis management for decades. As a folic acid antagonist, MTX exerts its therapeutic effects through multiple mechanisms, including the inhibition of DNA synthesis in rapidly proliferating cells like keratinocytes and activated lymphocytes, thereby slowing the hyperproliferation characteristic of psoriasis. Furthermore, it has potent anti-inflammatory effects, partly through the promotion of adenosine release. MTX is recommended as a first-line systemic agent for moderate-to-severe psoriasis due to its well-established efficacy, convenient oral administration, and a safety profile that, while requiring regular monitoring of blood counts and liver function, is generally considered more favorable for long-term use than cyclosporine.[20] The successful transition and sustained clinical remission on MTX in our patient represent an ideal therapeutic outcome, achieving excellent disease control while minimizing

treatment-related toxicity. For patients who fail or cannot tolerate conventional systemic agents like methotrexate, the next therapeutic echelon involves highly targeted biologic therapies. These agents, which block specific cytokines like TNF-α, IL-17 (secukinumab), or IL-23 (guselkumab), have shown significant efficacy in case reports of ACH and represent a promising future for managing refractory disease.

This report, while detailed, has several inherent limitations that must be acknowledged for scientific transparency. First, as a single case report, it represents the lowest level in the hierarchy of evidence, and its findings cannot be generalized to the broader population of patients with ACH. Second, the historical data spanning the first decade of the illness rely on patient recall, which introduces a potential for recall bias. Third, although the clinical phenotype was highly suggestive, genetic testing for mutations in IL36RN, CARD14, or AP1S3 was not performed due to resource limitations. Such testing would have provided a more complete pathophysiological picture but was not essential for the clinical diagnosis or management.

While the specific outcomes of this single case cannot be generalized, the diagnostic process and therapeutic strategy serve as a highly instructive and generalizable model. This report provides a clear framework for clinicians faced with similar undifferentiated cases of acral nail dystrophy: maintain a high index of suspicion for inflammatory mimics, utilize dermoscopy as a key decision-making tool, proceed to biopsy for confirmation, and employ a sequenced therapeutic approach. Future research should focus on establishing larger patient registries for rare diseases like ACH to better understand their natural history and to conduct trials for newer targeted biologic therapies that may offer improved safety and efficacy.

4. Conclusion

This case provides Class V evidence demonstrating that in patients with chronic, treatment-refractory nail dystrophy mimicking onychomycosis, a structured diagnostic approach using dermoscopy and histopathology is essential for accurate diagnosis. For fifteen years, this patient's condition was concealed behind a misdiagnosis, underscoring the protean nature of rare inflammatory skin diseases. This report illustrates that a methodical re-evaluation, prompted by a history of treatment failure, is paramount. The therapeutic sequence of rapid induction with cyclosporine followed by methotrexate maintenance appears to be an effective strategy, though conclusions on efficacy are limited by the nature of a single-case observation. Ultimately, this case reaffirms that a systematic application of modern diagnostic tools, guided by a deep understanding of the disease's pathophysiology, can unravel even the most prolonged diagnostic dilemmas, leading to profound clinical remission and the restoration of a patient's quality of life.

5. References

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