Journal of Pakistan Association of Dermatologists. 2022;**32(2)**:430-434.

Case Report

Acrodermatitis continua of hallopeau evolving into generalized pustular psoriasis: A case series

Haken Tennizar Toena, Nita Damayanti Sulistianingrum, Yulia Eka Irmawati, Sunardi Radiono

Department of Dermatology & Venereology, University of Gadjah Mada. Yogyakarta.

Abstract Acrodermatitis continua of Hallopeau (ACH) is considered as a variant of localized pustular psoriasis which involved fingertip and nail. ACH is rarely reported to evolve into generalized pustular psoriasis (GPP). This paper report 3 cases of GPP which initially manifested as ACH. The aim of this report is to increase clinician awareness of localized pustular psoriasis history when met a case with GPP, and to review a concept of clinical course of ACH and it's relation with GPP. Three patients which have been diagnosed as ACH, came to the hospital with generalized manifestation of multiple pustules in underlying erythematous base. Based from clinical manifestation and histopathology examination, all of them was diagnosed as GPP. GPP was already known to have genetic predisposition, with mutation in gene IL36RN, CARD14, and APS13 have been documented in patient with GPP. The same genetic mutation in ACH was considered as the reason why this manifestation of localized pustular psoriasis could evolve into GPP. GPP could be preceded by manifestation of ACH. Clinician should ask for history of localized pustular psoriasis when met with a case of GPP.

Key words
Acrodermatitis continua of Hallopeau, generalized pustular psoriasis, localized pustular psoriasis.

Introduction

Pustular psoriasis is a clinical form of psoriasis which is characterized by the appearance of sterile pustules on an erythematous base. There are two forms of pustular psoriasis, i.e. localized pustular psoriasis and generalized pustular psoriasis (GPP).[1] Localized pustular psoriasis has two variants, namely palmoplantar pustular psoriasis which affects the palms and soles, and acrodermatitis continua of Hallopeau (ACH) which involves the distal parts of the fingers as well as nails.[2,3] Acrodermatitis continua of Hallopeau is a rare disease. Incidence and prevalence rate of this condition is unknown. It occurs mostly in middle-aged women.[4] At our center hospital in Yogyakarta, there were 6 documented cases of ACH in the last five years (2015-20).

The clinical manifestations of ACH change with the course of the disease. Lesion initially developed as pustules and erythema on the distal fingers and nails, then become hyperkeratotic lesions that can lead to onychodystrophy with bone involvement.[5] Acrodermatitis continua of Hallopeau which later progresses to widespread eruptions of pustules is rare, but has been reported in some studies.[2,6]

In this article, we report 3 cases of ACH which progressed to GPP lesions. Methotrexate was used for treatment, allowing clinical improvement for pustules eruption. However ACH lesions mostly persist.

Address for correspondence
Dr. Nita Damayanti, MD
Department of Dermatology and Venereology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Dr. Sardjito General Hospital, Yogyakarta, Indonesia
Ph: 062-8232919995
Email: nitadamayanti91@gmail.com

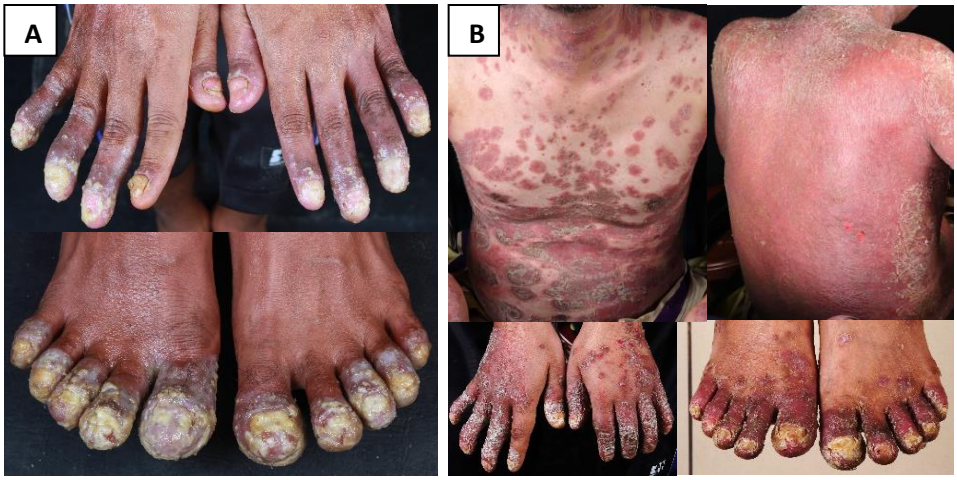

Figure 1 Lesions of ACH initially limited on fingers, toes, and nails (A). Later developed into widespread pustular eruption (B).

Case 1 A 39-year-old male came with multiple pustules on erythematous base on almost his entire body. He got a fever accompanied with itch, burn sensation, also pain in his fingers. Pustules appeared on fingers and toes, then quickly widespreads to the body and face in the last 4 days.

Based on his medical history, he was a regular patient with a diagnosis of ACH since the last 2 years. Lesions involved all of the distal fingers and nails, with multiple scattered pustules on an erythematous base, leading to onycholysis and dactylitis **(Figure 1)**. There was no previous history of plaque-type psoriasis. ACH was improved after being treated with cyclosporine 1x100 mg for 9 months, then changed to methotrexate due to an increase in renal function. A generalized pustular eruption reaction occurred after 1 month of continuous methotrexate therapy. After being given methotrexate injection, GPP lesions resolved but ACH persisted.

Case 2 A 60-year-old male came with the chief complaint of scaly skin with widespread pustules eruption in the last 3 weeks. He's been diagnosed as ACH since 2018, with no history of plaque psoriasis. Methotrexate has been given for his treatment since 2018, but he stopped consuming it because he felt that his complaints were improving. Examination showed multiple clustered pustules with erythematous base and desquamation. The fingernails appeared as yellowish hyperkeratotic plaques and some of the fingernails were loss **(Figure 2)**.

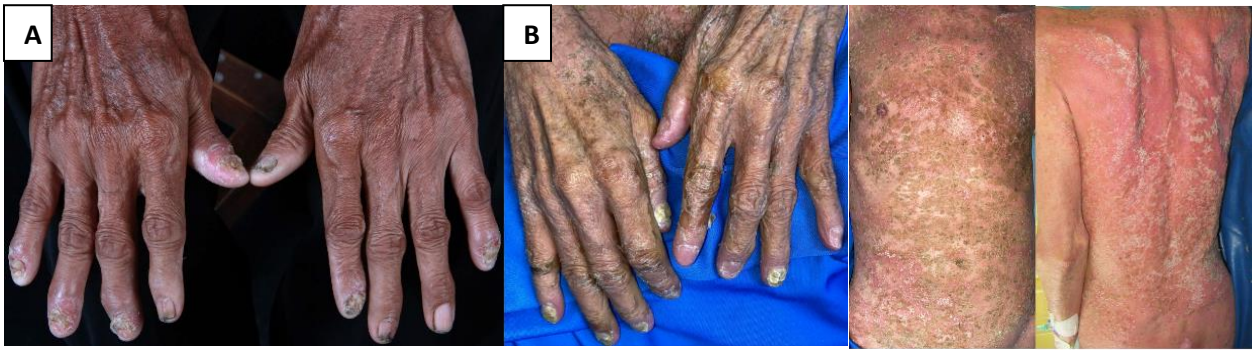

Figure 2 Lesions of ACH on fingers and nails (A). Later developed into widespread pustular eruption and desquamation (B).

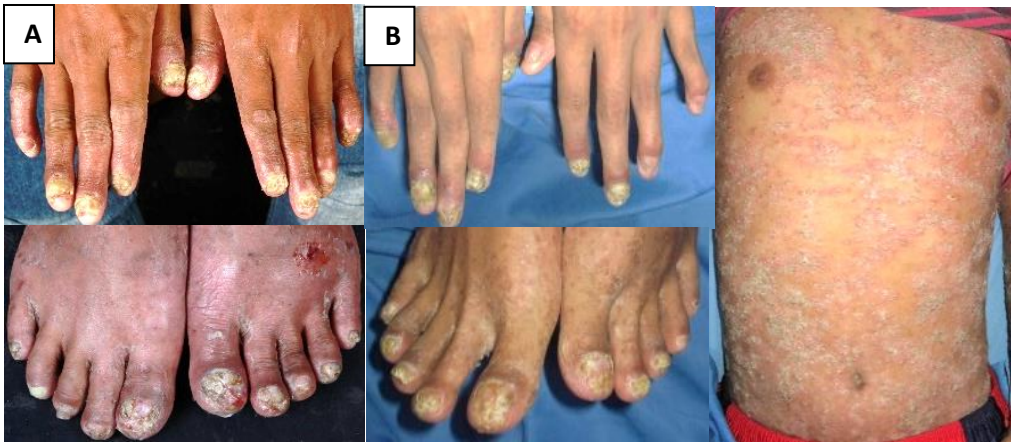

Figure 3 Lesions of ACH on fingers, toes, and nails (A). Later developed into widespread pustular eruption (B).

Histopathological examination of the epidermal area showed acanthosis, hypogranulosis, and spongiosis as well as intraepidermal pustules containing dense neutrophils. There is a lymphohistiocytic infiltrate in the dermis. He was given methotrexate injection and showed clinical improvement, but his ACH lesions especially in nails mostly persisted.

Case 3 A 20-year-old male, has been diagnosed with ACH since 2015 with clinical signs of yellowish hyperkeratotic crusts on the distal fingers and dactylitis on all fingers and toes. He's been treated with methotrexate but never came back for check up after feeling his complaints improved. There was no history of plaque psoriasis in this patient.

He came back with complaints of widespread pustules eruption, started initially from lower limbs. Physical examination showed multiple scattered erythematous patches with a lake of pustules on almost his entire body **(Figure 3)**. Investigation with histopathology showed histopathological features suitable for pustular psoriasis. Lesions of GPP resolved after methotrexate injection, but ACH lesions mostly persisted.

Discussion

The term acrodermatitis continua of Hallopeau was first described by Henri Hallopeau in 1890 as a sterile pustular eruption in the distal phalanges.[3,7] This disorder is considered as a localized form of pustular psoriasis because of its histopathological characteristics similar to the other pustular psoriasis.[8] ACH patients generally do not develop manifestations of plaque-type psoriasis, as was the case with our patients reported in this case.[6]

Several factors are said to be the etiology of this disease, including traumatic, infection, and inflammatory conditions. Most of the ACH case reports stated that the patient had a history of minor trauma or infection that preceded the clinical manifestations of the disease in the same area.[5] Trauma factors were also a trigger for ACH in our cases, where 2 of 3 patients had a history of trauma to the fingers before the onset of ACH lesions at the same finger.

Acrodermatitis continua of Hallopeau tends to begins at the tips of fingers and rarely starts from the toes.[6] The clinical characteristics may vary according to the stage of disease. Acute episodes are characterized by small pustules that leave a shiny and erythematous area when ruptured. These lesions usually form a lake of pustules appearance. As these lesions extends proximally, the affected area shows an

erythematous or keratotic surface with crusts and fissures with newly formed pustules beneath. Pustulation of the nail bed and nail matrix is usually present and often results in nail plate destruction or severe onychodystrophy. This occur in a chronic cases, where complete destruction of the nail matrix eventually lead to loss of nail plate. Distal phalanges becomes thinner and the skin becomes very atrophic. In addition, phalangeal osteitis can occur which causes involvement of the interphalangeal joints and osteolysis.[3]

The development of GPP which initiated by the manifestation of ACH is a rare case, but has been reported several times.[4,9,10] Generalized pustular psoriasis is generally preceded by a history of plaque-type psoriasis.[1,2] In recent years, various studies have demonstrated a genetic involvement as a cause of pustular psoriasis.[6] Genetic studies in GPP patients have reported mutations in the gene encoding the IL-36 receptor antagonist (IL36RN), the gene encoding the keratinocyte adaptor protein (CARD14), and the subunit adaptor protein 1 complex (AP1S3).[2,11] This mutation is also found in other pustular psoriasis conditions. A study by Twelves *et al*. in 2019 showed that mutations in the IL36RN gene were found to be more common in cases of ACH and GPP than palmoplantar pustular psoriasis variants.[12] A study from Lebanon reported the case of a man with ACH who had a mutation in IL36RN, with his sister suffering GPP with the same gene mutation.[11] These studies suggest that ACH is most likely a local variant of GPP.

In the vast majority of cases, GPP is idiopathic. However, various precipitating factors such as drugs, infection, and pregnancy have been reported to trigger the onset of GPP.[13,14] The trigger for the development of GPP lesions in these patients is still unknown. Ranugha in 2013 reported a case of GPP lesions which initially started as ACH that previously treated with acitretin and methotrexate. GPP lesions occurred after the patient stopped the drugs because he felt it didn't show any response.[10] A similar withdrawal reaction may occur in patient case 1 in which switching cyclosporine to MTX was the trigger for GPP.

In contrast to GPP, ACH is more difficult to treat.[15] In all our cases, methotrexate therapy has shown clinical improvement for generalized pustular lesions, but ACH lesions haven't shown any remission. The absence of standard therapeutic guidelines for ACH and the limited selection of therapeutic agents in the clinical setting contribute to the prognosis of this disease.

Conclusion

We report three rare cases of ACH which progressed into GPP. This suggests that GPP may be initiated by localized pustular psoriasis manifestations such as ACH. The presence of similar genetic mutations, especially in the IL36RN gene, makes these two disease entities related. Clinicians should suspect a history of localized pustular psoriasis when dealing with cases of GPP.

References

1. Johan R, Hamzah RA. Gejala Klinis dan Terapi Psoriasis Pustulosa Generalisata tipe von Zumbuch. *Cermin Dunia Kedokt*. 2016;**43(2)**:117-22.
2. Gudjonsson JE, Elder JT. Psoriasis. In: Kang S, Amagai M, Bruckner A, editors. *Fitzpatrick's Dermatology. 9th ed*. New York: McGraw-Hill Education; 2019. p. 457–97.
3. Megasasi Y, Brahmanti H, Kumala YD, Manggala G. Acrodermatitis Continua of Hallopeau yang memberi respons baik terhadap terapi kombinasi salep klobetasol propionat 0,05% dan dapson. *Media Dermato-Venereologica Indones*. 2018; **45(1)**:18-24.

4. Alorainy M, Alshaya M, Ayesh M, Alsaif F, Al-rikabi A. Acrodermatitis Continua of Hallopeau with Bone Resorption in an 8-Year-Old Patient : A Case Report. *Case Rep Dermatol*. 2017;**9**:259-64.
5. Smith MP, Ly K, Thibodeaux Q, Bhutani T, Liao W, Beck KM. Acrodermatitis continua of Hallopeau : clinical perspectives. *Psoriasis Target Ther*. 2019;**9**:65-72.
6. Burden AD, Kirby B. Psoriasis and Related Disorders. In: Griffiths CEM, Barker J, Bleiker T, Chalmers R, Creamer D, editors. *Rook's Textbook of Dermatology. 9th ed*. Chichester: Wiley Blackwell; 2016. p. 35.1-35.48.
7. Kioka M, Yu A, Tanizaki H, Kokunai Y. Acrodermatitis continua of Hallopeau successfully treated only with infliximab : A case report. *J Cutan Immunol Allergy*. 2018;**1**:73-6.
8. Sadlier M. Acrodermatitis continua of Hallopeau and geographic tongue are variants of pustular psoriasis. *JAAD Case Reports*. 2018;**4(3)**:277.
9. Kim KH, Kim HL, Suh HY, Jeon JW, Ahn JY, Park MY, *et al*. A Case of Acrodermatitis Continua Accompanying with Osteolysis and Atrophy of the Distal Phalanx That Evoluted into Generalized Pustular Psoriasis. *Ann Dermatol*. 2016;**28(6)**:794–5.
10. Ranugha PSS, Kumari R, Thappa DM. Acrodermatitis Continua of Hallopeau Evolving into Generalised Pustular Psoriasis. *Indian J Dermatol*. 2013;**58(2)**:161–2.
11. Abbas O, Itani S, Ghosn S, Kibbi AG, Fidawi G, Farooq M, *et al*. Acrodermatitis Continua of Hallopeau Is a Clinical Phenotype of DITRA : Evidence that it is a variant of pustular psoriasis. *Dermatology*. 2013;**226**:28–31.
12. Twelves S, Mostafa A, Dand N, Burri E, Farkas K, Wilson R, *et al*. Clinical and genetic differences between pustular psoriasis subtypes. *J Allergy Clin Immunol*. 2019;**143(3)**:1021-7.
13. Hoegler KM, John AM, Handler MZ, Schwartz RA. Generalized pustular psoriasis: a review and update on treatment. *J Eur Acad Dermatology Venereol*. 2018;**32(10)**:1645-51.
14. Ly K, Beck KM, Smith M, Thibodeaux Q, Bhutani T. Diagnosis and screening of patients with generalized pustular psoriasis. *Psoriasis Target Ther*. 2019;**9**:37-42.
15. Crowley EL, Maliyar K, Rodriguez-bolanos F, Toole AO, Gooderham MJ. Acrodermatitis continua of Hallopeau successfully treated with adalimumab : A case report. *SAGE Open Med Case Reports*. 2019;**7**:1-4.