A 66-year-old male suffered from painful pustular eruptions of acrodermatitis continua of Hallopeau on bilateral thumbs for about 2 years, with associated nail dystrophy and markedly disabled manual skills. Initial treatment with topical corticosteroids, tars and calcipotriol failed to improve the acral lesions. Dapsone therapy began at a dose of 200 mg/day, which cleared the acral lesions within two weeks of therapy. However, new lesions relapsed when the dose was tapered to 150 mg/day. Increasing dapsone back to 200 mg/day was followed by another clearance of the acral pustules. During a total course of 6-week therapy, no dapsone-related side effects were noted. The patient remained symptom-free and nail growth was noted at the follow-up visit 3 months after the medications were discontinued. (Dermatol Sinica 21: 165-170, 2003)

Key words: Acrodermatitis continua of Hallopeau (ACH), Dapsone, Psoriasis
INTRODUCTION

Acrodermatitis continua of Hallopeau (ACH) is a rare, sterile pustular eruption of the distal phalanges with frequent involvement of the nail beds. Associated nail dystrophy and skin atrophic changes are commonly seen. The main histopathologic feature is characterized by spongiform pustules with aggregates of neutrophils between the degenerated keratinocytes. ACH was considered by many to be a variant of pustular psoriasis because of similar histologic features. However, it is individualized by its unique clinical course and resistance to standard anti-psoriatic therapies.

Dapsone (4-4’ diaminodiphenyl sulfone), regarded as a strong anti-inflammatory agent targeting on neutrophils, has been successfully used in more and more dermatosis associated with infiltration of neutrophils. It was also reported to be able to break the relentless course of refractory ACH. We present a patient with ACH refractory to numerous treatments responded to dapsone therapy.

CASE REPORT

A 66-year-old male had painful eruption of pustulations with scaling, tender swelling over bilateral thumbs for about 2 years. He has been treated at a surgical clinic as paronychia regularly. Various treatments, including several courses of antibiotics, non-steroidal anti-inflammatory drugs, as well as systemic steroids were tried but failed to relieve his sufferings. He was referred to our clinic for further management.

Fig. 1
Painful pustules erupted on the acral portion of thumbs. Continuous postulations on the nail bed resulted in onychodystrophy.

Fig. 2
(A) Pustules coalesced to form lakes of pus. (B) Complete clearance of pustules was achieved within 2 weeks of dapsone therapy. (C) No relapses were noted for 3 months without medications.
Physical examinations revealed pustules within areas of erythema and scaling over the acral portion of bilateral thumbs. Some pustules coalesced to form lakes of pus (Fig. 1 & Fig. 2A). Nail beds were involved and both thumb-nails showed onychodystrophy. Tenderness, hyperaesthesia with markedly reduced manual skills were also noted.

Pus cultures from the pustules revealed negative findings. Histologic sections from the affected nail bed showed numbers of spongiiform pustules with aggregates of neutrophils between the degenerated keratinocytes (Fig. 3). Roentgenograms of the thumbs demonstrated mild acroosteolysis, but no abnormal changes of the joints.

Initial treatment with topical steroids and polytar emollients failed to improve the acral lesions. Calcipotriol ointment was then applied twice daily on the acral lesions for two weeks without noticeable efficacy. After a careful screening for hemoglobin level, methemoglobin level, G6PD deficiency and liver functions, dapsone therapy with 200 mg/day was begun.

The disease responded promptly with complete suppression of the formation of new pustules within 2 weeks of therapy (Fig. 2B & Fig. 4A). The attempt to taper dapsone to 150 mg/day was frustrated by eruption of new pustules within days (Fig. 4B). Increase the dose of dapsone back to 200 mg/day produced another clearance of pustules.

Dapsone therapy was continued for 6 weeks. Periodic blood checks were done and no

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**Fig. 3**
Histopathology showed spongiform pustules with aggregates of neutrophils between degenerative keratinocytes. (H & E, x400)

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**Fig. 4**
(A) Acral pustulations responded to dapsone 200mg/day with complete clearance of pustules in 2 weeks. (B) New pustules erupted when dapsone was tapered to 150mg/day. (C) Nail re-growth at the site of lunula was noted at a 3-month follow-up visit.
Dapsone-related side effects were noted. Local tenderness and erythema resolved gradually and the patient was satisfied to restore his manual function. Moreover, the patient remained lesion-free even after dapsone was discontinued. At a follow up visit 3 months later, new nails were noted at the site of lunula (Fig. 2C & Fig 4C).

**DISCUSSION**

Acrodermatitis continua of Hallopeau (ACH) was originally described by Hallopeau in 1890 as a sterile pustular eruption of the distal phalanges. Initially, crops of pustules erupt within areas of erythema on the acral portion of affected digits. The pustules then tend to coalesce and form polycyclic lakes of pus. Drying of the necrotic tissue results in crusts and scales that, when peeled away, reveal fresh formation of pustules beneath. Skin atrophy and underlying soft tissue sclerosis are commonly seen as the process goes on. The situation can be surprisingly painful and disabling. Paronychial involvement always occurs early. Continuous painful pustulation of the nail bed and nail matrix leads to destruction of nail plate and severe onychodystrophy.

The pathologic study of the spongiform pustule seen in ACH reveals that it is located in the uppermost portion of the Malpighian layer, where neutrophils aggregate intercellularly in a multilocular pustule in which the sponge-like network is composed of degenerated and flattened keratinocytes. These pathologic changes are characteristic and similar to those in the spongiform pustule of Kogoj shared by all forms of pustular psoriasis. Because of similar histologic features, ACH was considered by many to be a variant of pustular psoriasis.

However, the unique clinical features described above well distinguish ACH from the others. Besides, the treatment of ACH has been notoriously disappointing and shown to be poor-responsive to conventional treatments of psoriasis. In review of literature, topical treatment of ACH does not produce satisfying results. Efficacy of topical steroids is poor, even applied with occlusive dressing. Topical tars, calcipotriene ointment, tretinoin cream, and some antimetabolites including fluorouracil cream (5 %), have been utilized with variable results in a limited number of cases, but a long-term and large-series evaluation of these medications is lacking. Systemic regimens, such as etretinate (50-70 mg / day), acitretin (0.5 mg / kg, daily), cyclosporin A (3-5 mg / kg / day) and methotrexate (10-25 mg / week), as well as oral psoralen-UVA have been tried and reported with success on some cases. But various results were obtained on other reports. Besides, systemic side effects often discourage the treatment and rapid recurrence always occurs when medications were tapered. Up to date, no definite therapeutic guideline was established.

Dapsone, with remarkable anti-inflammatory capabilities besides its antibacterial properties, was first and then widely used in treating patients with dermatitis herpetiformis since the early 1950s, and was under more and more therapeutic trials nowadays in a multitude of diseases. These dermatoses for which dapsone therapy has been reportedly effective share a unifying feature with granulocytes as the predominant infiltrating cells. Hence, dapsone therapy could be considered when a pathologic lesion is characterized by abnormal neutrophilic infiltration and is unassociated with an infectious agent. Considering the prominent neutrophilic involvement in ACH, dapsone constitutes a reasonable therapeutic option.

But before therapy with dapsone, a careful clinical evaluation including drug history, complete blood cell count, and liver functions should be obtained. G6PD deficiency should be screened. During the period of therapy, periodic blood checks, especially complete blood cell count, hemoglobin and methemoglobin levels, are indispensable to prevent the possible adverse effects produced by dapsone. Among them are hemolysis, methemoglobinemia and agraulocytosis. In our presented case, a thorough pretest and follow-up checks were all within normal range.
Our experience with dapsone was satisfying. It cleared the acropustulosis in 2 weeks and produced a prompt and successful response lasting for 3 months. Today, numerous studies have attempted to determine how dapsone exerts its anti-inflammatory effect. Several potential mechanisms have been established. In vitro studies have demonstrated that dapsone inhibits human neutrophilic chemotaxis through G protein signal transduction system and interferes with neutrophil chemotactic migration through suppression of integrin-mediated adhesion function to the epidermis.\textsuperscript{2, 11-13} This suppresses neutrophil recruitment and accounts for the lack of influx of neutrophils into the dermis in treated patients. Moreover, dapsone is shown capable of inhibiting the myeloperoxidase-H\textsubscript{2}O\textsubscript{2}-halide cytotoxic system of neutrophils\textsuperscript{2, 14} and the zymosan-mediated human neutrophil respiratory burst.\textsuperscript{13} This accounts for the suppressive effect of dapsone on cytotoxic enzymes at sites of injury.

Therefore, we propose that through the above mechanisms, dapsone successfully suppresses abnormal neutrophil infiltration and protects tissue from neutrophil-mediated injuries, as we have observed in ACH as well as other neutrophilic dermatoses treated with dapsone. Dapsone appears to predominantly affect the effector mechanisms, while having an influence on the initial pathogenic process, which explains why dapsone is effective in treating a variety of dermatologic diseases that have different causes.

In conclusion, most therapies for ACH have been attempted with only partial remissions and rapid recurrences upon treatment interruption or dose reduction. Here, we presented a patient with refractory ACH responded promptly to dapsone therapy. Oral dapsone provides a fast, effective treatment option for ACH, with capability to produce a remission.

REFERENCES


12. Booth SA, Moody CE, Dahl MV, \textit{et al.}: Dapsone suppresses integrin-mediated neu-
