Long-Term Colchicine for Recalcitrant Palmoplantar Pustulosis: Treatment Outcome in 3 Patients

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Palmoplantar pustulosis (PPP) is a chronic, relapsing, pustular eruption affecting the palms and soles for which treatment is often difficult and frustrating. Short-term colchicine has been used to treat PPP with variable response. We report on the successful treatment of 3 patients with severe, therapy-resistant, chronic PPP. We observed significant reduction in the frequency of pustular eruptions and the number of pustules with maximum tolerable doses of colchicine treatment for up to 12 months.

Treatment of palmoplantar pustulosis (PPP) is often difficult and frustrating. Many different topical and systemic therapeutic modalities have been used with varying degrees of success. Colchicine has been used with favorable results for a variety of neutrophilic dermatologic conditions, including psoriasis, generalized pustular psoriasis, and psoriatic arthropathy.[1-4] Short-term colchicine was found to be highly effective in PPP in one study,[5] although this was not confirmed in subsequent placebo-controlled studies.[6-8] We report the long-term effect of colchicine in 3 patients with chronic recalcitrant PPP.

Case Reports

Patient 1—A 31-year-old Chinese man had recurrent attacks of sterile pustules on the palms and soles for 4 years (Figure 1). He failed to respond to treatment with tetracycline, 500 mg twice daily, and potent topical corticosteroids. Etretinate and psoralen plus ultraviolet A (Re-PUVA) therapy were partially effective. He was maintained on low-dose etretinate for 4 years with poor disease control; higher doses produced side effects. Colchicine treatment was started with a dose of 0.5 mg twice daily for 2 weeks and increased to 1 mg twice daily. During the 12-month treatment period, there was significant reduction in the number of pustules at the peak of each attack compared with earlier etretinate or PUVA therapy. No side effects were noted.

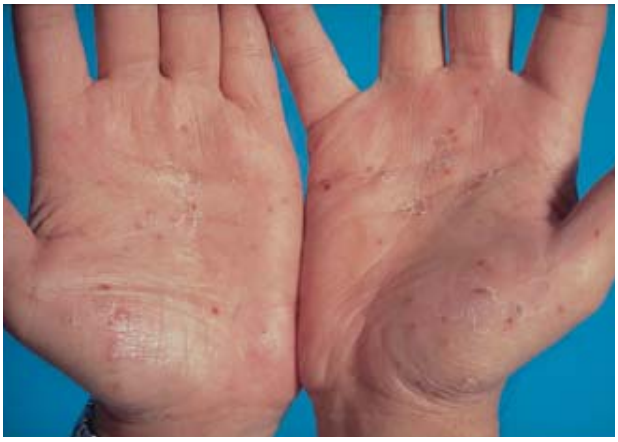

Figure 1. Palmoplantar pustulosis in patient 1. Groups of pustules in different stages of evolution.

Patient 2—A 49-year-old Chinese man had a 6-year history of sterile PPP and nail dystrophy. No improvement was obtained with a 3-year treatment of high-potency steroid creams, etretinate, PUVA, Re-PUVA, or methotrexate. Colchicine 0.5 mg twice daily was begun and increased to tolerance over an 8-week period. During the ensuing 12 months of treatment with colchicine 1 mg twice daily, a marked reduction was noted in the frequency and duration of pustular eruptions, as well as

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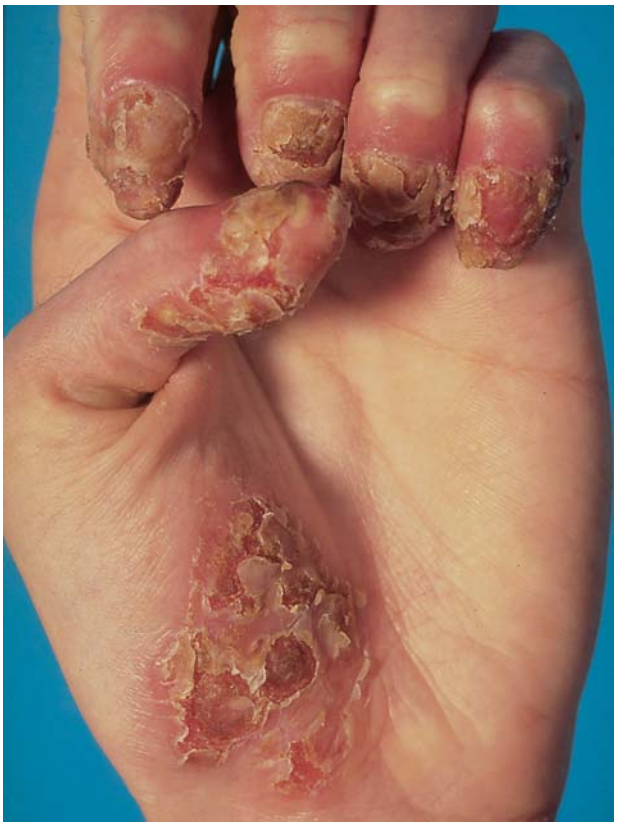

Figure 2. Palmoplantar pustulosis in patient 3. Acral pustule formation on the palm and fingers with destruction of the nail plates.

the number of pustules at each attack. The patient tolerated the treatment well with no side effects.

Patient 3—A 20-year-old Chinese man presented with a 7-year history of generalized pustular psoriasis and severe recurrent attacks of sterile PPP affecting the palms, fingers, and nails (Figure 2). Although his truncal pustulosis cleared while he was on etretinate therapy, the patient continued to experience frequent palmoplantar flares for 6 years, with destruction of the nail plates, despite the addition of PUVA therapy. The addition of colchicine, 0.5 mg twice daily, resulted in significant improvement in his palmoplantar disease, which allowed him to resume work. He could not tolerate higher doses of colchicine because of diarrhea.

Comment

PPP is a chronic skin disease characterized by relapses and remissions of bilateral and symmetrical yellow sterile pustules, erythema, and scaly plaques on the palms and soles.[9] Most patients (75%) with PPP continue to have pustular lesions 5 years after their first examinations.[10] Various forms of systemic treatment, including PUVA, etretinate, methotrexate, and cyclosporine, have been used for this highly refractory condition,[11-13] although adverse effects restrict their use, and treatment withdrawal often leads to rapid relapses.

The mode of action of colchicine is unknown, although its anti-inflammatory and microtubule disruptive effects on polymorphonuclear leukocytes have been observed in vitro and in vivo (Table).[14-21] These factors might account for the beneficial effects of colchicine on PPP and other neutrophil-rich dermatoses. The therapeutic effects of colchicine in psoriasis, however, have been mixed. In dosages ranging from 0.4 to 2 mg daily, colchicine has been used with variable results in plaque psoriasis, generalized pustular psoriasis, and psoriatic arthropathy.[2-4] Some studies show that higher doses of colchicine appear to be more effective than lower doses. With regard to PPP,

In Vitro and In Vivo Effects of Colchicine[14-21]

Reduces adherence and migration of neutrophils
Inhibits expression of adhesion molecules
Inhibits interleukin 1 activity
Decreases lysozymal enzyme release by neutrophils
Inhibits cyclooxygenase and lipooxygenase pathways
Prevents polymerization of tubulin dimers to microtubules in neutrophils
Inhibits HLA-DR expression
Increases superoxide scavenging activity of neutrophils

Takigawa et al[5] reported partial or complete disease remission in 90% of 32 Japanese patients in an uncontrolled study, after 2 to 8 weeks of oral colchicine (1–2 mg daily). Eight patients relapsed during a 3-month follow-up period.

The therapeutic efficacy of colchicine in controlled studies involving small numbers of patients was not conclusive.[6-8] Mann[6] observed no significant improvement between colchicine and placebo in 9 patients with PPP who were treated with 0.5 mg twice daily for 6 weeks. English et al[7] concluded that colchicine was ineffective in 10 patients with PPP treated with 0.5 mg twice daily for 3 months. The duration of disease, severity, and frequency of attacks were not mentioned in these 2 small studies. However, a Danish study[8] showed improvement in 10 of 27 patients treated with 1.5 mg daily of colchicine for 4 weeks. Therefore, differences in disease severity, length, and doses of treatment among patients with chronic recurrent PPP may account for different response rates. There are currently no available data on the exact therapeutic role of long-term continuous colchicine therapy in persistent PPP.

We started our patients with recalcitrant PPP on colchicine 1 mg daily and increased to 2 mg daily after 2 weeks. Dosages were reduced if patients developed diarrhea. Patients were then instructed to take the highest tolerable dose as maintenance. Although colchicine did not completely clear all the pustules in our patients, our findings indicate that long-term colchicine therapy is effective in the prophylaxis and treatment of persistent and recalcitrant PPP.

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