Palmoplantar pustulosis (PPP) is a chronic inflammatory disease characterized by recurrent pustules on the palms and soles. Its etiology is unknown, and its relationship to psoriasis is not clear. Treatment of PPP can be challenging. Several immunomodulatory drugs have been used with moderate results. Herein, we report 2 cases of PPP that achieved complete remission with leflunomide.

**REPORT OF A CASE**

**CASE 1**

In 1995, a 30-year-old woman presented with a 6-day history of fever and pruritic pustules on her left hand. Physical examination revealed confluent pustules surrounded by erythema on the dorsal aspect of the left hand, palm, and wrist (Figure 1). There were no lesions in other locations. Her medical history was otherwise unremarkable.

A complete laboratory blood cell count showed a slightly low white blood cell count (3600/µL [reference range, 4500-10 800/µL]; to convert to ×10⁹/L, multiply by 0.001). Findings from biochemical tests were within reference range. Cultures of the pustules were negative for organisms. Findings from skin biopsy specimens showed an intraepidermal pustule with mild acantholysis and moderate mononuclear infiltrate in dermis. A diagnosis of localized pustulosis was made.

The patient was initially treated with topical and oral antibiotics with poor response. After a month, oral retinoids and topical steroids were added to her treatment, but the patient experienced new flares. Seven months after the onset of the process, she complained about arthralgias and chest and back pain. Imaging studies (radiography, computed axial tomography) revealed sacroileitis. A diagnosis of incomplete SAPHO syndrome (sacroileitis, acne, pustulosis, hyperostosis, osteitis) was made. Therapy was begun with methotrexate, 7.5 mg/wk, and the dosage was subsequently increased to 10 mg/wk. Two months later there was no improvement, so oral cyclosporine was added to her drug regimen but was poorly tolerated because of headache. During the following 4 years the patient subsequently failed treatment with sulfone, prednisone, colchicine, sulfasalazine, and numerous nonsteroidal anti-inflammatory drugs (NSAIDs).

**CASE 2**

A 36-year-old woman presented with a 1-year history of pustules on her left palm, with poor response to treatment with topical steroids. Her medical history was significant for allergic rhinitis. She worked as a maid, and the hand lesions affected her daily activities.

On physical examination there was a 4 × 3-cm erythematous, desquamative plaque with pustules limited to the left palm (Figure 2). There was no nail involvement. Findings from skin biopsy specimens showed pustules. Fungal and bacterial cultures were negative for organisms. A diagnosis of localized pustulosis was made.

She was sequentially treated with topical steroids, oral and topical antifungals and antibiotics, dapsone, and sulfadiazine, with no response. Fourteen months after the onset of disease, she developed seconegative polyarthritis. Treatment with methotrexate, 10 mg/wk, was begun and subsequently increased to 20 mg/wk during the following year. The patient showed mild improvement of joint symptoms, with persistence of the erythematous desquamative plaque that made her unable to work.

Figure 1. Patient 1 prior to treatment. The dorsum of the hand has multiple confluent pustules surrounded by erythema and inflammation.
THERAPEUTIC CHALLENGE

Treatment of localized palmar pustulosis is challenging and often unsuccessful. Therapeutic options include a variety of topical and systemic immunosuppressants (corticosteroids, UV light, cyclosporine, methotrexate, colchicine, retinoids). Therapeutic limitations include variable efficacy, limited access to the medications, and the potential for systemic toxic effects. Our patients were treated unsuccessfully for 5 and 2 years, respectively, and their skin disease affected their quality of life. A safe and effective therapy was needed.

SOLUTION

Leflunomide (Arava; Sanofi-Aventis US, Bridgewater, New Jersey) is an immunomodulatory drug that was approved in 1998 for the treatment of rheumatoid arthritis. Recent studies have shown improvement of psoriatic arthritis and psoriatic lesions. The concomitant arthritis and the failure of other treatments caused us to initiate treatment with leflunomide at a dosage of 100 mg/d orally (loading dose for 3 days) followed by 20-mg daily doses.

Patient 1 continued therapy with NSAIDs. After 1 month of treatment with leflunomide, she achieved complete remission of her skin lesions (Figure 3). One year later, she developed high blood pressure; therefore, the dosage of leflunomide was lowered to 20 mg per 48 hours. During the following 5 years, she remained asymptomatic, with neither flares of pustules nor joint symptoms. To date, 2 years have elapsed without any treatment, and she has not experienced a rebound of skin lesions.

In patient 2, leflunomide was given with methotrexate, 20 mg/wk. No flares of pustules occurred. After 3 months, only mild erythema was observed. Seven months after the initiation of therapy, she remained entirely free of pustular lesions and arthritic symptoms (Figure 4).

The dosage of methotrexate was lowered to 15 mg/wk. After 2 years of follow-up with maintenance of therapy, she had not experienced any adverse effect or skin pustules.

COMMENT

Palmoplantar pustulosis is a chronic inflammatory skin condition characterized by crops of sterile pustules that erupt repeatedly over months or years. In some patients, the association with psoriasis elsewhere on the body is striking, but others may show palmoplantar pustules in the absence of other cutaneous changes. Many different treatments have been used for PPP, but none is generally accepted as being reliably effective.

Figure 2. Patient 2 prior to treatment. The left palm has erythematous desquamative plaque with pustules.

Figure 3. Patient 1 after 1 month of treatment with leflunomide, showing complete remission of the skin lesions on the dorsum of her hand.

Figure 4. Patient 2 after 7 months of treatment with leflunomide, showing minimal erythema of the palm.
Psoriasis and psoriatic arthritis are seen as autoreactive inflammatory disorders, driven by an ongoing chronic helper T cell (Th1) response in the skin. In vitro activities of A77 1726, the active metabolite of leflunomide, include the modulation of cytokine production in T cells and neutrophils, suppression of immunoglobulin synthesis in B cells, and reduction of mononuclear cellular adhesion, suggesting a therapeutic potential in a broad range of inflammatory and autoimmune disorders.\(^{11}\)

Leflunomide has been reported as effective in 2 cases of SAPHO syndrome\(^{12}\) and 1 case of severe recalcitrant pustular psoriasis and psoriatic arthritis.\(^{13}\) In 2004, a multinational, double-blind, placebo-controlled clinical trial evaluated the efficacy and safety of leflunomide in patients with psoriatic arthritis and plaque-type psoriasis.\(^{8,13}\) Guttate, pustular, or erythrodermic forms of psoriasis were excluded. Leflunomide was well tolerated, convenient, and effective in moderating joint and skin symptoms and improving quality of life. Diarrhea was the most common adverse event in the leflunomide group (24% vs 13% for placebo). No serious liver toxic effects or infections occurred.

In conclusion, we describe 2 cases of recalcitrant localized pustulosis that failed to respond to several topical and systemic treatments yet achieved complete reversion with leflunomide. The oral administration, safety, and cost benefit of leflunomide may provide an important treatment option for recalcitrant localized pustulosis, especially in those cases with concomitant arthritis. Further studies are needed to evaluate the efficacy and duration of treatment.

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REFERENCES


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