

Sequential Therapy Using Cyclosporine and Acitretin for Treatment of Total Body Psoriasis

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Systemic sequential therapy using cyclosporine and acitretin is a novel strategy that can provide quick resolution and maintenance in refractory cases of psoriasis. We describe the case of a patient with a psoriatic flare over 98% of his body, despite methotrexate therapy. Implementing sequential therapy with cyclosporine and acitretin maximized the benefit of each treatment and allowed for rapid improvement with minimal risk of toxicity.

Cutis. 2004;74:185-188.

Case Report

A 23-year-old man with a 5-year history of psoriasis presented with a flare over 98% of his body. During the preceding 3 days, the patient experienced progressive tightening of the skin, followed by development of diffuse thick scale and bleeding fissures that left him bedridden because of pain. The patient had been treated with a weekly dose of methotrexate 12.5 mg for the previous 5 years; this treatment maintained stable improvement of his active psoriasis, which involved less than 5% total body surface area until the time of flare.

Results of a physical examination revealed no fever. The patient was confined to a wheelchair because he was unable to walk. Diffuse erythema and silvery scale covered 98% of his body surface area, with some sparing of the glans penis and

digits. His skin was tight and leatherlike with diffuse weeping of serous fluid and bleeding fissures caused by movement.

Results of laboratory tests revealed a metabolic panel and erythrocyte sedimentation rate within reference ranges and an elevated white blood cell count of 15,300 with normal differential count. Results of skin culture showed pan-sensitive *Staphylococcus aureus*, and a throat culture was positive for group C β -hemolytic *Streptococcus pyogenes*.

Initial supportive treatment consisted of fluid hydration, oral hydroxyzine 25 mg every 8 hours, oral acetaminophen/oxycodone hydrochloride as needed for pain, Eucerin[®] cream, and intravenous cefazolin 1 g every 8 hours. Baseline values for blood pressure; complete blood count; and serum levels of creatinine, blood urea nitrogen, magnesium, potassium, uric acid, and lipids were obtained before initiating treatment with cyclosporine 5 mg/kg per day administered as a twice daily dosage regimen. Methotrexate, which the patient had last taken 1 week before presenting with the psoriatic flare, was discontinued.

The patient was seen at 2 weeks and 1 month after cyclosporine treatment was started; blood pressure and laboratory values remained at baseline level. Treatment with oral cyclosporine led to a remarkable degree of clearing, with loss of erythema, thinning of confluent plaques, reduction in scale, and resolution of fissures. Photographs taken over the course of treatment showed progressive clearing of the lesions on the patient's back over 1 month (Figure 1). The lesions on the patient's arms rapidly improved within 2 weeks of the start of treatment, while those on the abdomen cleared later, at 1 month (Figure 2).

After 1 month of cyclosporine treatment, therapy with acitretin 25 mg/d was started; cyclosporine was continued at maximum dermatologic doses for an additional 2 months. After 3 months of high-dose cyclosporine, the skin lesions had nearly

Accepted for publication December 11, 2003.

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The opinions expressed are those of the authors and should not be construed as official or as representing those of the US Army or the US Department of Defense.

The authors report no conflict of interest.

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Figure 1. Severe psoriasis on the back prior to (A) and after 2 weeks (B) of treatment with oral cyclosporine. There was resolution after 1 month of treatment (C).

resolved. Cyclosporine was tapered at a rate of 1 mg/kg per day each month, while acitretin was continued at its initial dose.

The patient experienced a mild flare of psoriasis 4 months after initiation of oral sequential treatment and 1 month after cyclosporine was initially tapered to 4 mg/kg per day. Erythematous plaques developed on the patient's upper neck, chest, lower legs, and arms. The cyclosporine dosage was

increased to the original 5 mg/kg per day, and the acitretin dosage was increased to 50 mg/d to facilitate clearing before the cyclosporine dosage would be tapered.

One month later, the psoriatic flare had resolved with cyclosporine 5 mg/kg per day. Acitretin was continued at 50 mg/d, and the high-dose cyclosporine was tapered 1 month later at a rate of 1 mg/kg per day each month. Acitretin was continued as maintenance therapy (50 mg/d) to prevent recurrence.

Comment

This case report describes the treatment of refractory psoriasis using the novel therapeutic strategy known as *oral sequential therapy*. The traditional approach to treating psoriasis involves monotherapy, which is continued as long as the therapeutic response remains satisfactory. When the medication ceases to be effective, the treatment approach is



Figure 2. Severe psoriasis on the abdomen and arm prior to (A) and after 2 weeks (B) of treatment with oral cyclosporine. The psoriasis on the trunk cleared after 1 month of treatment (C).

changed. Sequential therapy focuses on maximizing the benefits of each medication to provide rapid clearing of psoriasis, as well as long-term maintenance.¹ In this case, the oral sequential therapy regimen included the use of cyclosporine and acitretin.

Cyclosporine was approved for the treatment of psoriasis by the US Food and Drug Administration in June 1997.² The dermatologic dose was established at 4 mg/kg daily, although 5 mg/kg daily is an internationally recognized dosage. Cyclosporine effects rapid clearing of psoriatic lesions, and it is typically well tolerated. Results of a randomized double-blind control trial in 1991 showed that cyclosporine 5 mg/kg per day provided an effective clearing of psoriasis with lower toxicity than seen with the agent used at higher doses.³ A study

reviewing the hospital records of patients with psoriasis treated with cyclosporine concluded that cyclosporine was unsuitable for long-term monotherapy because the adverse effects of the medication increased with duration of use.⁴ The more serious adverse effects of hypertension and decreased renal function were found to occur more often in older patients and those with pre-existing hypertension and high serum creatinine levels.⁴ Consensus guidelines have outlined the appropriate use of cyclosporine and the recommended monitoring for adverse effects.⁵

Acitretin, a retinoid, is not used for rapid clearing of psoriasis, but it is a relatively safe and effective medication for long-term maintenance therapy. The most common dose-related adverse

effects include cheilitis (>75% of patients), skin peeling or alopecia (50%–75%), and dry skin or rhinitis (25%–50%).⁶⁻⁸ In one study, acitretin was shown to increase serum triglyceride levels in 66% of patients and total cholesterol values in 33%.⁸ These lipid changes can be managed with changes in diet, decreases in the dosage of acitretin, and use of lipid-lowering agents.⁹ Hepatotoxicity, although possible with this medication, is usually transient and reversible when the medication dose is decreased or the agent is discontinued.⁸

Acitretin and cyclosporine have very few adverse effects in common.^{10,11} The rapid psoriatic clearing seen with cyclosporine and the lower adverse effect profile of acitretin as used for maintenance therapy support the use of these agents in combination. Because of the potential adverse effects of each medication, it is important to monitor laboratory test results and blood pressure on a regular basis. Blood pressure; complete blood count; and serum levels of creatinine, blood urea nitrogen, magnesium, potassium, uric acid, and lipids should be obtained before initiating treatment with cyclosporine and monitored every 2 weeks for 3 months. If blood pressure and laboratory results remain stable, monthly monitoring may be adequate thereafter.¹² Serum aminotransferases and fasting serum lipid levels should be assessed prior to treatment with acitretin and monitored every 1 to 2 weeks until the lipid response to the drug is established in 4 to 8 weeks. After that time, these values should be monitored as clinically indicated.¹²

In this case, implementing sequential therapy maximized the benefit of each treatment—allowing for rapid improvement without toxicity. Although new biologic therapies targeting activated T cells have become a major focus of psoriasis treatment,¹³ cyclosporine, acitretin, and methotrexate are cost-effective mainstays of treatment. This case illustrates the efficacy and safety of using cyclosporine in combination with acitretin for refractory psoriasis. Although skillful management during

the transition phase is essential, this new paradigm in psoriasis therapy can result in a successful patient outcome.

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