Infliximab for the Treatment of Adult-Onset Pityriasis Rubra Pilaris

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REPORT OF CASES

CASE 1

A 77-year-old man presented in June 2002 with a 2-month history of a progressive eruption that initially involved his scalp and progressed to his face, neck, trunk, and extremities. This eruption was associated with chills. His medical history was remarkable for congestive heart failure, hypertension, a mitral valve repair, and gout. His medications included warfarin sodium, digoxin, losartan potassium, hydrochlorothiazide, and terazosin hydrochloride. He had also been taking prednisone and cephalexin prescribed by his primary care physician for his skin condition. Physical examination revealed erythematous, scaly plaques and papules on his scalp, face, neck, upper trunk, and proximal extremities (Figure 1). He had ectropion of both lower eyelids, keratoderma of the palms and soles, and significant pitting edema of the lower extremities. A biopsy specimen was obtained and revealed parakeratosis, moderate acanthosis, and a mild superficial perivascular lymphocytic infiltrate, consistent with pityriasis rubra pilaris (PRP).

Initial therapy consisted of acitretin, 25 mg twice daily, topical 0.1% triamcinolone acetonide ointment, and oral antihistamines. Prednisone therapy was tapered, and cephalexin therapy was discontinued. The patient was admitted to the hospital for intensive therapy with twice-daily whirlpool baths and to monitor his hemodynamic status. Lower extremity edema improved with hospitalization. His skin eruption improved only slightly. Acitretin therapy was continued as an outpatient; however, the skin eruption failed to improve. After 4 months of acitretin monotherapy, cyclosporine A was added at a daily dose of 3 mg/kg in October 2002. After 2 months of the combination therapy of acitretin with cyclosporine A, the patient's skin eruption worsened, with increased total body skin area involvement and increased pruritus.

CASE 2

A 53-year-old man presented in November 2003 with a 6-month history of pruritic lesions that initially involved his left shoulder, then spread to involve his chest and face and subsequently his trunk and legs. He complained of chills. Physical examination revealed erythematous, scaly patches and plaques that involved approximately 99% of his skin surface. Several 1- to 1.5-cm “islands of sparing” were present. He had keratoderma of the palms and soles as well. His medical history was remarkable for hypertension. His family history was significant for a brother with PRP who responded to treatment with acitretin monotherapy. His medications included lisinopril, aspirin, and hydroxyzine hydrochloride. He had been using tacrolimus ointment, which was prescribed by his primary care physician for the skin eruption. A biopsy specimen was obtained and revealed parakeratosis, acanthosis, and focal follicular plugging, consistent with PRP.

Initial therapy consisted of acitretin, 50 mg once daily, emollients, and oral antihistamines. After 2 months of this...
therapy, the patient had some improvement of his palms and soles only. The rest of his eruption failed to improve.

THERAPEUTIC CHALLENGE

Pityriasis rubra pilaris is an uncommon, idiopathic, papulosquamous disorder that often progresses to erythroderma and causes a disabling keratoderma. No single therapy is universally effective, and some cases are resistant to multiple therapies. Systemic retinoids,1-3 methotrexate,3,4 immunosuppressive agents (azathioprine and cyclosporine A),5,6 and phototherapy3,7-9 have been used with variable success.

SOLUTION

In case 1, the patient was admitted to the hospital again in December 2002. He was given infliximab at a dose of 5 mg/kg. Therapy with cyclosporine A was discontinued; acitretin therapy was maintained at a dose of 25 mg twice daily. Two weeks after infliximab was administered, the patient had marked improvement of his skin disease, with decreased erythema, pruritus, and total body skin area involvement (Figure 2). Given the response to infliximab, the patient received 4 subsequent doses of infliximab at weeks 4, 8, 14, and 22 after the initial dose with continuing improvement. The dose of acitretin was tapered as well without flare of the skin lesions. The patient remains 98% clear 1 year after the first infliximab dose. He is presently taking acitretin, 25 mg 3 times weekly.

In case 2, infliximab was administered at a dose of 5 mg/kg, and a subsequent dose of 5 mg/kg was administered 2 weeks later. The patient was also maintained on acitretin therapy. Two weeks after the first dose of infliximab, the patient had markedly less erythema, pruritus, and desquamation. Overall, he showed a 50% improvement after the infliximab infusion. He is presently taking acitretin, 50 mg once daily.

COMMENT

Therapy for PRP is largely based on anecdotal reports owing to the rarity of cases, lack of controlled trials, and the idiopathic nature of the disorder. In addition, some cases of PRP spontaneously resolve without therapy, and so evaluation of the success of any therapy is problematic. Multiple therapies have been tried: high-dose vitamin A (retinol),1,2 synthetic retinoids,3,4 methotrexate,3,4 azathioprine,5 cyclosporine A,3,6 stanozolol,10 phototherapy,3,7-9 and extracorporeal photochemotherapy.11 Systemic retinoids and methotrexate are the most frequently used therapies for PRP. Another more common papulosquamous disorder, plaque psoriasis, responds to these agents as well. Given the clinical overlap and therapeutic response overlap between psoriasis and PRP, and given recent evidence that infliximab is efficacious in treating psoriasis,12,13 we decided to administer infliximab to our patients with PRP. The response in both patients was rapid and significant. It is highly likely that infliximab was responsible for the clinical response in the 2 patients.

Infliximab is a chimeric monoclonal antibody that binds to the proinflammatory cytokine tumor necrosis factor α. Initially developed for the treatment of Crohn disease, this medication has been reported to be effective in treating a number of inflammatory dermatoses in addition to psoriasis, including hidradenitis suppurativa,14 pyoderma gangrenosum,15 and cutaneous sarcoidosis,16 among others.

With the excellent responses our patients had to infliximab, we hypothesize that tumor necrosis factor α may play a pathophysiological role in PRP. Controlled studies with tumor necrosis factor α inhibitors (infliximab, etanercept, adalimumab, and thalidomide) for PRP would be informative. In conclusion, we recommend infliximab as an alternative agent for treating adult-onset PRP.

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REFERENCES

Clinicians, local and regional societies, residents, and fellows are invited to submit cases of challenges in management and therapeutics to this section. Cases should follow the established pattern. Submit 4 double-spaced copies of the manuscript with right margins nonjustified and 4 sets of the illustrations. Photomicrographs and illustrations must be clear and submitted as positive color transparencies (35-mm slides) or black-and-white prints. Do not submit color prints unless accompanied by original transparencies. Material should be accompanied by the required copyright transfer statement, as noted in “Instructions for Authors.” Material for this section should be submitted to George J. Hruza, MD, Laser and Dermatologic Surgery Center, 14377 Woodlake Dr, Suite 111, Town and Country, MO 63017 (cuttingedge@lasersurgeryusa.com).

Missing Footnote Symbols. In Table 3 of the article titled “Skin Markers of Occult Spinal Dysraphism in Children,” in the September 2004 issue of the ARCHIVES (2004; 140:1109-1115), the single-dagger footnote symbol should have appeared with the Group 3 lesions Hemangiomma, PWS [port-wine stain], Hypertrichosis, and Pigmentary nevus to indicate that each of these lesions was considered an isolated lesion.