BRIEF ARTICLES

Treatment of Pityriasis Rubra Pilaris with Adalimumab: A Case Report

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ABSTRACT

Pityriasis Rubra Pilaris (PRP) is a rare inflammatory dermatosis of unknown etiology and variable presentation. Common clinical features include hyperkeratotic follicular papules, palmoplantar hyperkeratosis and well-demarcated red-orange scaly plaques interspersed with islands of unaffected skin. A limited body of anecdotal evidence predominantly supports the use of systemic retinoids and/or methotrexate in treating the disease. In a subset of these patients, there has been a documented role for biologic tumor necrosis factor (TNF) inhibitors, especially in patients who have failed retinoid or antimetabolite therapy. We present a case of a woman whose PRP responded favorably to adalimumab, highlighting the role of TNF inhibitors and the need for their continued exploration in the treatment of PRP.

CASE REPORT

A 65-year-old woman with a history of hypertension, hypercholesterolemia, and successfully excised melanoma presented with an “itchy rash”. The rash had begun several months earlier and had now progressed to involve most of the body. The patient endorsed moderate pruritus. Physical exam revealed generalized erythematous and scaly plaques with follicular keratosis of the trunk, abdomen, extremities, face, and scalp. Marked scaling and fissuring of the feet and hands were noted. The groin and antecubital fossae were spared. Topical emollients had yielded no improvement. She was also treated with ultraviolet phototherapy without success.

Biopsy samples taken from the back and temple demonstrated chronic spongiotic and psoriasiform dermatitis. The epidermis was acanthotic with foci of mild intercellular edema, scattered parakeratotic foci, and perivascular mononuclear infiltrate. Flow cytometry with peripheral smear was negative, excluding possible cutaneous T cell lymphoma. The histologic findings, combined with the clinical picture, favored a diagnosis of pitryriasis rubra pilaris.

The patient was started on adalimumab 40 mg every two weeks and noted marked improvement of erythema, scale, and pruritus at her first follow-up visit. She continued on adalimumab, and her lesions had completely resolved by her last visit save for a few remaining areas of mild follicular hyperkeratosis.

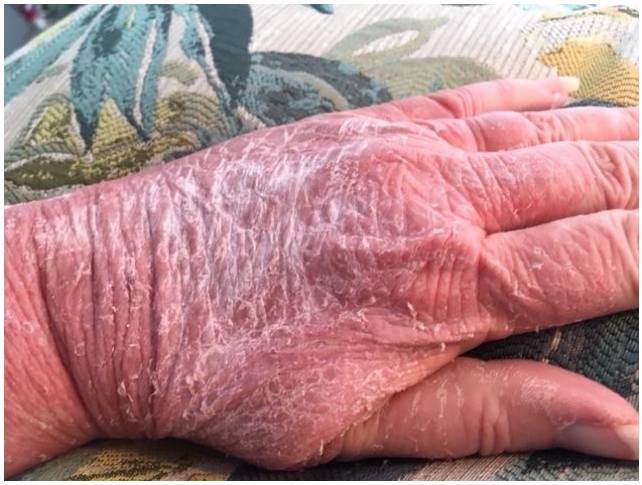

Figure 1. Notable erythema and scaling of the dorsum of the hand prior to treatment.

Figure 2. Marked resolution of disease following adalimumab.

DISCUSSION

Like other rare diseases, PRP's low incidence—as low as 1 in 400,000 according to some estimates—poses a challenge in the development of effective and widely accepted treatment recommendations, as large controlled trials are difficult to conduct. Augmenting this low incidence, the poorly understood etiology and pathophysiology of the disease has resulted in treatment algorithms based largely on anecdotal evidence such as case series and case reports. In light of this, we hope reporting of our case will contribute to the ever-growing body of literature supporting adalimumab and other TNF inhibiting agents in the treatment of PRP.

While mild cases of PRP can be responsive to topical agents, extensive disease like our patient's necessitates systemic therapy. Based on the current literature, the most utilized treatment is systemic retinoid therapy[1], most commonly isotretinoin 1-1.5 mg/kg/day. For those patients who are not candidates for retinoids, 10-25 mg of methotrexate weekly has demonstrated efficacy as well.[2] Though potentially effective, both systemic retinoids and methotrexate are associated with notable adverse effects, ranging from mild xerosis to teratogenicity, hepatotoxicity, and myelosuppression.

Given the limitations of the above mentioned first line therapies for PRP, other classes of medication are often necessary. Though the pathogenesis of PRP is not fully understood, immunologic and inflammatory factors likely contribute on a cellular and biomolecular level. TNF-alpha is a proinflammatory cytokine known to play a role in many inflammatory disorders such as psoriasis, Crohn's disease, ulcerative colitis, and rheumatoid arthritis. Similarly, it has been demonstrated that TNF-alpha levels are upregulated in areas of skin affected by PRP.[3] It follows, therefore, that TNF inhibitors could produce a beneficial effect in treating the disease. Indeed, over the last ten years there have been a growing number of reports of TNF inhibitors demonstrating success in treating refractory patients or those intolerant of retinoids or antimetabolites. Agents that have met success include etanercept[4], infliximab[5], and—as in our case—adalimumab[6,7,8,910], with some patients showing complete resolution. Adalimumab is a recombinant human monoclonal antibody with high affinity for TNF-alpha, thereby combating some of the inflammatory

processes underlying the disease. Systemic review of the role of anti-TNF agents in PRP has demonstrated marked clinical response within three to eight weeks in those patients who received adalimumab monotherapy.[11]

While potentially beneficial for patients, TNF inhibitors are not without risks of their own. Adverse effects include injection site reactions, headaches, and increased creatine kinase. Downregulation of immune surveillance is also an undesired concomitant effect of TNF inhibitors' anti-inflammatory properties. This leaves patients more susceptible to a variety of infections, as well as some malignancies. Weighing these effects is of particular importance in our patient's case given her history of melanoma, as there are accumulating reports that anti-TNF agents may be associated with the development or recurrence of latent malignancies, specifically malignant melanoma.[12]

Our case adds to the continually expanding body of evidence advocating anti-TNF agents in the treatment of PRP. While their therapeutic effects must certainly be weighed against their risks, these medications are often well tolerated by patients, and clinicians should continue to consider and further explore their use for appropriate candidates.

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