Successful Treatment With Etanercept of von Zumbusch Pustular Psoriasis in a Patient With Human Immunodeficiency Virus

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

Treatment of von Zumbusch pustular psoriasis is a formidable task, especially when confounded by concomitant human immunodeficiency virus (HIV) infection. To our knowledge, this is the first report of successful use of a biologic agent to treat a patient with both von Zumbusch pustular psoriasis and HIV. Given the propensity of HIV to both trigger and exacerbate psoriasis and the potentially severe complications associated with the acute, von Zumbusch variant, we believe this report provides precedence for dermatologists to consider anti–tumor necrosis factor α (anti–TNF-α) agents as a part of the armamentarium in the treatment of these patients.

REPORT OF A CASE

A 32-year-old man with a history of HIV, psoriasis, and psoriatic arthritis presented with increased joint pain, widespread pruritic pustules, erythema, and intermittent fever with leukocytosis of 2 weeks’ duration (Figure 1 and Figure 2). The patient had an 11-year history of HIV infection (CD4 cell count, 435/µL; nadir, 200/µL; viral load, <75/µL). He was prescribed lamivudine plus zidovudine, tenofovir disoproxil fumarate, and atazanavir sulfate and had taken no new medications within 6 months prior to presentation. The topical regimen of clobetasol propionate ointment, the superpotent corticosteroid he had been using twice daily to control his plaque psoriasis, failed to alleviate the eruption. In addition, his arthritis became so severe that he was unable to accomplish activities of daily living without assistance. Findings from a biopsy

Figure 1. Patient at presentation, prior to treatment, showing widespread patches of erythema with overlying pustules affecting 90% of his body surface.

Figure 2. Closeup of the patient at presentation showing numerous pinpoint pustules over a background of erythema.
The sample of lesional skin demonstrated psoriasiform epidermal hyperplasia with intraepidermal pustules, pustules in the cornified layer, parakeratosis, and a superficial and midperivascular lymphocytic infiltrate most consistent with a diagnosis of pustular psoriasis.

**CLINICAL CHALLENGE**

Von Zumbusch pustular psoriasis is a severe, acutely generalized form of psoriasis associated with systemic complications such as leukocytosis, fever, arthropathy, congestive heart failure, and infection.1 Although in many patients the etiology is unknown, common triggers include withdrawal of systemic steroids, infections, drugs, and hypocalcemia.2 It is notoriously recalcitrant to treatment and may be life threatening.3 Current therapeutic modalities such as acitretin, cyclosporine, methotrexate, and phototherapy, or a combination of these, are often insufficient to achieve lasting remissions.4 In the recent literature, there have been several reports4-9 of successful treatment of generalized pustular psoriasis with anti–TNF-α agents (Table 1). Use of immunomodulatory medications in HIV patients, however, is tempered by concerns of increasing the risk of opportunistic infections, sepsis, and progression to AIDS.10 To our knowledge, there are no reports in the literature regarding use of biologic agents in HIV patients with generalized pustular psoriasis.

A MEDLINE search produced 2 case reports,11,12 1 case series,13 and 1 clinical trial14 pertaining to the use of etanercept, and 3 case reports15-17 documenting the use of infliximab in HIV patients (Table 2). Although the available data are limited, it has been speculated that administration of biologic agents that block TNF-α in HIV patients does not adversely affect morbidity and mortality.10 Owing to the severity of disease and concomitant disabling arthritis that our patient was experiencing, we initiated therapy with etanercept at a dosage of 50 mg subcutaneously weekly after obtaining a negative purified protein derivative (PPD) test and a normal chest radiograph. Within 4 weeks, the patient achieved com-

### Table 1. Reports of Anti–TNF-α Therapy in Patients With Pustular Psoriasis

<table>
<thead>
<tr>
<th>Source</th>
<th>Patients, No.</th>
<th>Regimen</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trent and Kerbel,1 2004</td>
<td>4</td>
<td>Infliximab</td>
<td>All improved within 24 h; however, all reverted to plaque psoriasis for which 3 required systemic medications</td>
</tr>
<tr>
<td>Weisenseel and Prinz,4 2006</td>
<td>1</td>
<td>Infliximab + etanercept</td>
<td>Rapid improvement; maintenance of remission with etanercept</td>
</tr>
<tr>
<td>Benoit et al,5 2004</td>
<td>1</td>
<td>Infliximab</td>
<td>Rapid improvement, resolution within 72 h; patient was prescribed acitretin for maintenance</td>
</tr>
<tr>
<td>Newland et al,6 2002</td>
<td>1</td>
<td>Infliximab</td>
<td>Rapid improvement, resolution by day 4</td>
</tr>
<tr>
<td>Elewski,7 2002</td>
<td>2</td>
<td>Infliximab</td>
<td>Patient 1: Improvement within 2 wk, clearance by 4 wk; patient 2: clearance within days</td>
</tr>
<tr>
<td>Lewis et al,8 2004</td>
<td>1</td>
<td>Infliximab</td>
<td>Rapid response</td>
</tr>
<tr>
<td>Schmick and Grabbe,9 2004</td>
<td>1</td>
<td>Infliximab</td>
<td>Total clearance within 48 h, relapse requiring second dose 1 wk later followed by 3-mo remission</td>
</tr>
</tbody>
</table>

Abbreviation: TNF-α, tumor necrosis factor α.

### Table 2. Reports of Anti–TNF-α Therapy in Patients With HIV

<table>
<thead>
<tr>
<th>Source</th>
<th>Patients, No.</th>
<th>Indication</th>
<th>Agent</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aboulafia et al,10 2000</td>
<td>1</td>
<td>Recalcitrant plaque psoriasis and psoriatic arthritis</td>
<td>Etanercept</td>
<td>Dramatic improvement in 3 mo; no change in viral parameters; developed polymicrobial infections requiring discontinuation at 4 mo</td>
</tr>
<tr>
<td>Kaur et al,11 2007</td>
<td>1</td>
<td>Recalcitrant rheumatoid arthritis</td>
<td>Etanercept</td>
<td>Disease activity decreased from 28 to less than 5 joints</td>
</tr>
<tr>
<td>Sha et al,12 2002</td>
<td>11</td>
<td>To study effects on cytokines induced by IL-2 therapy in patients prescribed HAART</td>
<td>Etanercept</td>
<td>Single dose resulted in decreased IL-6 and CRP; no change in IL-4, IL-10, IL-12, IFN-γ, or HIV-1 RNA levels; no serious adverse events attributed to etanercept</td>
</tr>
<tr>
<td>Wallis et al,13 2004</td>
<td>16</td>
<td>To determine safety in patients with HIV-associated tuberculosis</td>
<td>Etanercept</td>
<td>Patients had a 25% increase in CD4 cell counts by week 4 with no change in HIV RNA levels</td>
</tr>
<tr>
<td>Gaylis,14 2003</td>
<td>1</td>
<td>Reiter syndrome unresponsive to NSAIDs</td>
<td>Etanercept</td>
<td>Improvement of skin lesions and joint pain within 2 days of therapy; CD4 cell count increased with no change in antiviral medications or viral load</td>
</tr>
<tr>
<td>Bartke et al,15 2004</td>
<td>1</td>
<td>Severe psoriasis and psoriatic arthritis</td>
<td>Etanercept</td>
<td>Single dose resulted in decreased IL-6 and CRP; no change in IL-4, IL-10, IL-12, IFN-γ, or HIV-1 RNA levels; no serious adverse events attributed to etanercept</td>
</tr>
<tr>
<td>Sellam et al,16 2007</td>
<td>2</td>
<td>Psoriatic arthritis in patients prescribed HAART and methotrexate</td>
<td>Etanercept</td>
<td>Dramatic improvement; good tolerance and stable viral load and CD4 cell counts at 50 wk; no opportunistic infections reported; alteration in antiviral regimen was needed</td>
</tr>
</tbody>
</table>

Abbreviations: CRP, C-reactive protein; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; IL, interleukin; IFN, interferon; NSAIDs, nonsteroidal anti-inflammatory drugs; TNF-α, tumor necrosis factor α.
Dysregulation of the proinflammatory cytokine TNF-α is common to both von Zumbusch pustular psoriasis and HIV infection. The integral role of TNF-α in the pathogenesis of psoriasis and psoriatic arthritis is evidenced by the elevated levels detected in lesional skin and synovium, as well as by the therapeutic efficacy of biologic anti-TNF-α agents. Von Zumbusch pustular psoriasis is a hyperinflammatory, generalized form of psoriasis characterized by the appearance of widespread erythematous pustules with systemic involvement. Tumor necrosis factor α has been implicated in the pathogenesis through its role in the stimulation of granulocyte overactivation and tissue invasion that results in the formation of generalized erythematous pustules. There are few reports in the literature, however, documenting the use of anti-TNF-α agents in von Zumbusch pustular psoriasis.

In terms of HIV, studies have shown that TNF-α stimulates viral replication in vitro and may also contribute to development of aphthous ulcers, fatigue, lipodystrophy, fever, and dementia. These data have led several researchers to suggest that HIV treatment should include blockade of TNF-α, making it an attractive target in HIV patients with severe and generalized pustular psoriasis.

We describe an HIV patient with von Zumbusch pustular psoriasis and severe psoriatic arthritis who had a dramatic response to etanercept, 50 mg subcutaneously weekly. This is the first report, to our knowledge, of successful treatment of a patient with both HIV and von Zumbusch pustular psoriasis using an anti-TNF-α agent. Given the propensity of HIV infection to both trigger and exacerbate psoriasis and the potentially severe complications associated with the acute, von Zumbusch variant, anti-TNF-α agents should be used cautiously as part of our armamentarium in the treatment of these patients.

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Author Contributions: Drs Mikhail, Weinberg, and Smith have reviewed the manuscript and take full responsibility for the accuracy of the data. Study concept and design: Weinberg and Smith. Acquisition of data: Mikhail, Weinstein, and Smith. Drafting of the manuscript: Mikhail. Critical revision of the manuscript for important intellectual content: Weinberg and Smith. Administrative, technical, and material support: Mikhail and Smith. Study supervision: Weinberg and Smith.

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REFERENCES

3. Umezawa Y, Ozawa A, Kawasima T, et al. Therapeutic guidelines for the treat-


**Submissions**

Clinicians, residents, and fellows are invited to submit cases of challenges in management and therapeutics to this section. Cases should follow the established pattern. Manuscripts should be prepared double-spaced with right margins nonjustified. Pages should be numbered consecutively with the title page separated from the text (see Instructions for Authors [http://archderm.ama-assn.org/misc/ifora.dtl] for information about preparation of the title page). Clinical photographs, photomicrographs, and illustrations must be sharply focused and submitted as separate JPEG files with each file numbered with the figure number. Material must be accompanied by the required copyright transfer statement (see authorship form [http://archderm.ama-assn.org/misc/auinst_crit.pdf]). Preliminary inquiries regarding submissions for this feature may be submitted to George J. Hruza, MD (ghruza@aol.com). Manuscripts should be submitted via our online manuscript submission and review system (http://manuscripts.archdermatol.com).