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...
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. Although in many patients the etiology is unknown, common triggers include withdrawal of systemic steroids, infections, drugs, and hypocalcemia. It is notoriously recalcitrant to treatment and may be life threatening. Current therapeutic modalities such as acitretin, cyclosporine, methotrexate, and phototherapy, or a combination of these, are often insufficient to achieve lasting remissions. In the recent literature, there have been several reports 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. To our knowledge, there are no reports in the literature regarding use of biologic agents in HIV patients with generalized pustular psoriasis.

**SOLUTION**

A MEDLINE search produced 2 case reports, 1 case series, and 1 clinical trial pertaining to the use of etanercept, and 3 case reports 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. 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 complete remission within 24 hours of initiating therapy with etanercept. Further, repeat tuberculosis skin testing was negative and CD4 cell counts increased with no change in antiviral medications or viral load.

**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 Kerdel, 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, 2006</td>
<td>1</td>
<td>Infliximab + etanercept</td>
<td>Rapid improvement; maintenance of remission with etanercept</td>
</tr>
<tr>
<td>Benoit et al, 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, 2002</td>
<td>1</td>
<td>Infliximab</td>
<td>Rapid improvement, resolution by day 4</td>
</tr>
<tr>
<td>Elewski, 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, 2004</td>
<td>1</td>
<td>Infliximab</td>
<td>Rapid response</td>
</tr>
<tr>
<td>Schmick and Grabbe, 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, 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, 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, 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, INF-γ, or HIV-1 RNA levels; no serious adverse events attributed to etanercept</td>
</tr>
<tr>
<td>Wallis et al, 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, 2003</td>
<td>1</td>
<td>Reiter syndrome unresponsive to NSAIDs</td>
<td>Infliximab</td>
<td>All complaints resolved in 6 mo of treatment with no change in antiviral medications or viral load</td>
</tr>
<tr>
<td>Bartke et al, 2004</td>
<td>1</td>
<td>Severe psoriasis and psoriatic arthritis</td>
<td>Infliximab</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>Sellam et al, 2007</td>
<td>2</td>
<td>Psoriatic arthritis in patients prescribed HAART and methotrexate</td>
<td>Infliximab</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; INF, interferon; NSAIDs, nonsteroidal anti-inflammatory drugs; TNF-α, tumor necrosis factor α.
complete remission of his skin lesions, resolution of his fevers and joint pain, and normalization of his white blood cell count (Figure 3).

As of his most recent follow-up visit, 20 weeks after the initiation of therapy, the patient remained entirely free of pustular lesions and arthritic symptoms but had developed some recurrence of his plaque psoriasis. His CD4 cell count had increased to 633/µL, the viral load remained undetectable, and he had negative findings from a repeated PPD test. Furthermore, he had experienced no infections requiring antibiotic administration during the 20-week treatment period. With maintained remission of his generalized pustular psoriasis and psoriatic arthritis, the patient refused additional topical corticosteroid treatment of his plaque lesions and continued to be prescribed etanercept alone. Although his acute flare of generalized pustular psoriasis, its associated systemic symptoms, and his debilitating psoriatic arthritis improved dramatically with etanercept, 50 mg subcutaneously weekly, we suspect that additional treatment with a higher dose of etanercept, concomitant methotrexate, or another biologic agent will be needed to fully control his plaque psoriasis.

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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: Smith. Analysis and interpretation of data: Mikhail, Weinberg, 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-


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 JPG 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).