Long-term Control of Papular Dermatitis ("Dermal Hypersensitivity Reaction") With Mycophenolate Mofetil

In dermatology practice, patients frequently present with a recalcitrant eruption distinguished by the presence of edematous, urticarial, intensely pruritic papules. After analysis of patient biopsy specimens, the dermatopathologist will often report a "dermal hypersensitivity reaction" (DHR) characterized by an eosinophil-rich infiltrate. The only clinical differentials that correspond to this pathologic diagnosis are arthropod bite and drug eruption, neither of which is clinically relevant to the present case.

This skin biopsy finding of DHR was described by Fung as "a histopathologic pattern for which corresponding clinical phenotypes have not been established." Fung's description of DHR (which he termed urticarial papulosis) is clinically and histologically identical to what was termed papular dermatitis by Clark et al in 1998. Both studies comment on the difficulty of long-term control in affected patients.

This skin disease (herein referred to as "papular dermatitis") is not rare, and it is very challenging to treat. Affected patients rarely respond to topical therapy, and dependence on systemic steroids becomes a significant problem. The following case illustrates my experience with mycophenolate mofetil as a steroid-sparing agent for long-term control of papular dermatitis.

Report of a Case. A 69-year-old man presented with a progressively intense, pruritic eruption. The rash consisted of edematous, erythematous, papular papules and plaques. These lesions were concentrated symmetrically over the scalp, lower back, buttocks, and the extensor surfaces of the extremities. Initial treatments included tacrolimus ointment, clobetasol cream, acitretin, and oral doxepin, none of which relieved the extreme pruritus. Three courses of prednisone were required for relief, with significant rebound flares occurring after each steroid course. A generalized screening laboratory workup was performed, which showed no hematologic abnormalities. Hepatitis profile findings were negative.

Skin biopsy specimens revealed a superficial and deep perivascular and interstitial dermatitis with numerous eosinophils. These findings were read by the dermatopa-

Table. Clinical Characteristics of 2 Other Patients With Papular Dermatitis Treated With Mycophenolate Mofetil

<table>
<thead>
<tr>
<th>Age/ Sex</th>
<th>Duration of Papular Dermatitis Symptoms</th>
<th>Prior Therapies</th>
<th>Biopsy Confirmation of Papular Dermatitis</th>
<th>Dosage of Prednisone When Starting Mycophenolate Mofetil Therapy</th>
<th>Onset of Clinical Response to Mycophenolate Mofetil, wk</th>
<th>Length of Time Without Recurrence, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>33/F</td>
<td>6 mo</td>
<td>Clobetasol propionate ointment, tacrolimus ointment, fexofenadine, cetirizine, prednisone (up to 80 mg/d)</td>
<td>Yes, with negative DIF</td>
<td>20 mg/d</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>64/M</td>
<td>22 mo</td>
<td>Clobetasol propionate foam, tacrolimus ointment, hydrocortisone butyrate cream, doxycycline, permethrin, prednisone (5 tapering courses of 60-80 mg/d)</td>
<td>Yes, with negative DIF</td>
<td>Therapy begun within 1 week of finishing prednisone taper</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

Abbreviation: DIF, direct immunofluorescence.
tologist to represent a DHR. Direct immunofluorescence findings were negative.

Owing to the need for a steroid-sparing agent in this case, the patient was started on a treatment regimen of mycophenolate mofetil at a dose of 2 g/d. Within 6 weeks, he had experienced resolution of his symptoms. The patient reported no adverse effects or laboratory abnormalities while being treated with mycophenolate mofetil, and he did not require any further courses of prednisone during the subsequent 9 months of mycophenolate mofetil therapy. Mycophenolate mofetil has been used to treat other patients in a similar manner; details of 2 other cases are summarized in the Table.

Comment. Mycophenolate mofetil is an immunosuppressive agent that has been shown to have efficacy in the treatment of a wide array of inflammatory skin diseases including psoriasis and bullous disorders. It is rapidly gaining acceptance as a steroid-sparing agent with a favorable tolerability profile. The use of mycophenolate mofetil in a patient with papular dermatitis represents a novel approach to treat a dermatologic condition that has not been precisely defined as a clinical entity.

These cases suggest that mycophenolate mofetil may prove to be a viable steroid-sparing option for the management of papular dermatitis. It behaves like other steroid-sparing agents in that it is not effective as monotherapy. The onset of action is gradual, and thus mycophenolate mofetil should be administered while the patient’s symptoms are adequately controlled by systemic steroids. This approach to the management of papular dermatitis is similar to the standard management of blistering disorders. Furthermore, it should be noted that mycophenolate mofetil is one of many potential steroid-sparing agents that may be useful in treating this condition. Just as in the treatment of blistering dermatoses, other nonsteroidal immunosuppressive agents such as azathioprine, methotrexate, cyclosporine, and thalidomide may have efficacy in the management of papular dermatitis. Further study of similar patients will aid in defining the proper treatment parameters and clinical course of this enigmatic, but by no means rare, dermatologic condition.

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Financial Disclosure: None reported.

Acknowledgment: I thank Paul Chu, MD, for his valuable input regarding the pathologic findings in this case.


Figure 1. Immunoblot study of the molecular specificity of autoantibodies from patients with bullous systemic lupus erythematosus (BSLE). Extracts from human dermis were separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis under reducing conditions and electrophoretically transferred to a nitrocellulose membrane. Like the IgG from a reference patient with epidermolysis bullosa acquisita (EBA), IgG2 and to a lesser extent IgG1 and IgG3, but not IgG4, autoantibodies from a patient with BSLE (case 1) recognize a band at 290-kDa corresponding to type VII collagen. IgG4 from normal healthy serum (NHS) did not react with any specific protein. Migration positions of the molecular weight markers are depicted to the left.

Autoantibodies From Patients With BSLE Inducing Recruitment of Leukocytes to the Dermoepidermal Junction and Subepidermal Splits in Cryosections of Human Skin

Bullous systemic lupus erythematosus (BSLE) and epidermolysis bullosa acquisita (EBA) are subepidermal blistering diseases associated with autoimmunity against type VII collagen. The criteria for the diagnosis of BSLE include (1) a diagnosis of systemic lupus erythematosus (SLE), (2) a nonscarring vesiculobullous eruption, (3) subepidermal blisters with a neutrophil-rich infiltrate in the papillary dermis, (4) deposition of immunoreactants at the epidermal basement membrane, and (5) immunoglobulin deposits at or beneath the lamina densa seen by immunoelectron microscopy.

By immunofluorescence (IF) microscopy, autoantibodies binding to the dermal side of the salt-split skin have been demonstrated in patients with BSLE. Bullous SLE autoantibodies recognize the noncollagenous domain 1 of type VII collagen. Immunoreactant deposits in skin biopsy specimens of patients with BSLE were shown to recruit leukocytes and induce separation at the