Bullous Pemphigoid in a Patient with Systemic Sclerosis (Scleroderma)

To the Editor:

A 65-year-old Caucasian man with scleroderma presented for evaluation of 6 months of intense pruritus and recurrent cutaneous ulcerations. He began to develop ulcerated lesions on both the upper and lower extremities thought to be secondary to self-inflicted trauma from scratching areas of dry thickened scleroderma skin. Several times, these lesions became secondarily infected and required topical and systemic antibiotic therapy. It was noted that the ulcers seemed to respond to topical application of triamcinolone 0.1% cream.

Examination on presentation revealed diffuse cutaneous sclerosis with taut scaly skin over the dorsum of the hands, face, arms, trunk, and legs. Superimposed on areas of scleroderma skin were multiple papules, becoming confluent in some areas. The papules were erythematous with fine overlying scale and areas of lichenification. Well demarcated punched-out ulcerations were also present, particularly over the lower extremities (Figure 1). Mucous membranes and conjunctivae were normal. No bullae were present on examination, but he reported previously noting thin blisters on his legs.

H&E staining of the biopsy specimen from the right shoulder revealed acute spongiotic dermatitis with focal substitutive collagenosis, consistent with nonspecific eczematous change superimposed on scleroderma. Direct immunofluorescence performed on the biopsy specimen showed heavy linear deposition of IgG and C3 along the basement membrane zone (Figure 2), a finding that is diagnostic for bullous pemphigoid. He was given mycophenolate mofetil 1 g PO bid, and the prednisone was increased to 50 mg PO qam for 4 weeks before being reduced back to 40 mg PO qd. He responded to this therapy with improved pruritus, healed ulcerations, and resolution of papules. He currently is doing well with inactive pemphigoid skin disease, taking mycophenolate mofetil 1 g PO bid and prednisone 5 mg PO qod.

Although a case of a 73-year-old woman with generalized morphea who developed bullous pemphigoid after receiving whole-body UV-A-1 phototherapy is reported, the coexistent systemic sclerosis (scleroderma) with bullous pemphigoid is not described in the literature.

Figure 1. Bullous pemphigoid causing multiple ulcerations in the sclerotic skin on the extremity of a patient with scleroderma.

Figure 2. Direct immunofluorescence performed on the biopsy specimen showing heavy linear deposition of IgG and C3 along the basement membrane zone, a finding that is diagnostic for bullous pemphigoid.
Bullous pemphigoid is an autoimmune bullous skin disease affecting keratinocytes' adherence to each other and to the basement membrane. Autoimmune bullous diseases with blistering at the intraepidermal level are in the pemphigus group (pemphigus vulgaris, pemphigus foliaceus, and paraneoplastic pemphigus), while blistering occurring at the subepidermal level is classified as pemphigoid disease (bullous pemphigoid, gestational pemphigoid, and cicatricial pemphigoid). Bullous pemphigoid has primary cutaneous involvement, gestational pemphigoid (also known as herpes gestationis) has primary cutaneous involvement in pregnant women, while cicatricial pemphigoid has primary mucosal involvement.

Clinically, bullous pemphigoid presents with cutaneous lesions, with only rare mucosal involvement. Disease progression typically begins with urticarial plaques or papules, erythematous macules, or, as in our case, eczematous lesions, all of which are usually intensely pruritic. Tense clear blisters then develop over an erythematous base, which may manifest as an extensive bullous eruption.

Direct immunofluorescence findings are diagnostic for bullous pemphigoid. On biopsy of normal-appearing skin adjacent to a lesion, direct immunofluorescence reveals deposition of IgG and C3 along the epidermal basement membrane zone. Deposition of C3 is characteristically more intense than that of IgG. While direct immunofluorescence is 100% sensitive, indirect immunofluorescence is approximately 90% sensitive when salt-split human skin is used as a substrate for circulating bullous pemphigoid autoantibodies. These antibodies bind to the epidermal roof. Biopsy histology shows epidermal blistering with prominent polymorphonuclear and eosinophilic infiltrates. Bullous pemphigoid is triggered by autoantibody formation against the BP180 antigen, also known as Type XVII collagen. BP180 antigen is a key component of the epidermal hemidesmosomes, and is a transmembrane protein composed of a short non-collagenous ectodomain adjacent to the plasma membrane as well as a long collagenous endodomain that interacts with the basement membrane's anchoring proteins. Pathogenic autoantibodies in bullous pemphigoid recognize an immunodominant epitope in the ectodomain of BP180 antigen. Antibody activation against BP180 antigen leads to complement activation, resulting in neutrophil and eosinophil infiltration. Protease release from neutrophils is likely the critical step in subepidermal blister formation.

Prednisone has been a mainstay of treatment, with rapid effects seen at 0.5–1 mg/kg PO qd. Antibiotic therapy can also have effective antinflammatory effects as part of a steroid-sparing strategy. Newer data suggest that mycophenolate mofetil 1 g PO bid may be exceedingly useful in limiting steroid usage while inducing prompt and persistent remission of bullous pemphigoid.

Diagnosis of blistering skin disease like bullous pemphigoid can be overlooked in patients with scleroderma because significant pruritus and ulcerations are commonly part of the scleroderma skin process. Our case demonstrates that bullous pemphigoid should be considered when evaluating scleroderma patients with diffuse papules, lichenified lesions, blistering, or ulcerations. It also illustrates the unique concurrence of 2 rare autoimmune diseases.

We describe a case of bullous pemphigoid in a man with systemic sclerosis (scleroderma) skin disease, who when diagnosed correctly responded to appropriate therapy. This report may serve as a reminder of the need to consider bullous pemphigoid in patients with systemic sclerosis.

NOELLE S. SHERBER, MD, Johns Hopkins University School of Medicine; FREDRICK M. WIGLEY, MD, Departments of Rheumatology and Medicine; GRANT J. ANHALT, MD, Departments of Dermatology and Pathology, Johns Hopkins Medical Institutions, Baltimore, Maryland, USA.

Address reprint requests to Dr. F. Wigley. E-mail: fwig@jhmi.edu

REFERENCES

Intestinal Flora and Psoriatic Arthritis

To the Editor:

The editorial comment on “Psoriatic Disease” and the importance of the gut reminded us of a noteworthy patient. A 52-year-old white woman had no psoriasis or psoriatic arthritis. She was hit by another car from the left while driving. In the emergency room computed tomography of the abdomen raised concern over splenic rupture. She was admitted and observed.

On the second hospital day our patient developed a Streptococcus faecalis positive bladder infection. By the fourth hospital day she had developed psoriasis and psoriatic arthritis.

Our observations support Dr. Scarpa’s suggestion that the bowel is important possibly as a site for streptococcal immune activation. In the same issue of The Journal, Madland, et al reported improved global assessment after patients with psoriatic arthritis ingested seal oil. Could Madland, et al speculate on the influence of seal or fish oil on the bacteriological content of the stool? They refer to a report showing the benefit of fish oil in patients with inflammatory bowel disease. Data suggest that fish oil can alter intestinal microflora in mice. Could this explain the positive effect of seal oil in their patients?

FRANK B. VASEY, MD, Professor; JOHN D. CARTER, MD, Assistant Professor; Department of Internal Medicine, Division of Rheumatology, University of South Florida, Tampa, FL, USA.

Email: jdcarter@hsf.usf.edu

REFERENCES

Hypothyroidism and Antithyroperoxidase Antibodies in the Pathogenesis of Autoimmune Associated Congenital Heart Block

To the Editor:

Neonatal lupus (NL) is a model of passively acquired autoimmunity, in which disease in an offspring likely represents insult to fetal tissue follow-
Antithyroid antibodies in patients with primary SS (Sjögren’s syndrome), mothers of children with NL

IJEOMA ILOH, MD, MPH, ANCA DINU ASKANASE, MD, MPH, IJEOMA ILOH, MS, JILL P. BUYON, MD, Department of Medicine, Division of Rheumatology, Hospital for Joint Diseases, New York University School of Medicine, New York, NY 10016, USA. E-mail: jill.buyon@nyumc.org

Patients and serum samples were obtained through the Research Registry for Neonatal Lupus, funded by US National Institutes of Health contract no. AR4-2271 to J.P. Buyon.

REFERENCES


Table 1. Antithyroid antibodies in patients with primary SS (Sjögren’s syndrome), mothers of children with NL (neonatal lupus), and mothers of children with CHB (congenital heart block).

<table>
<thead>
<tr>
<th>Patients</th>
<th>Anti-TPO Antibodies, No. Positive (%)</th>
<th>Anti-TG Antibodies, No. Positive (%)</th>
<th>Hypothyroidism, No. Positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary SS, N = 137*</td>
<td>35 (25.5)*</td>
<td>24 (17.5)*</td>
<td>20 (14.6)*</td>
</tr>
<tr>
<td>NL mothers, N = 69</td>
<td>15 (21.7)</td>
<td>23 (33.3)</td>
<td>9 (13.0)</td>
</tr>
<tr>
<td>CHB mothers, N = 54</td>
<td>14 (25.9)</td>
<td>20 (37.0)</td>
<td>5 (9.3)</td>
</tr>
<tr>
<td>p values (NL/CHB mothers vs primary SS patients)</td>
<td>NS</td>
<td>&lt; 0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Cohort of patients with primary SS*. TPO: thyroperoxidase, TG: thyroglobulin.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2006. All rights reserved.
Book review

Fibromyalgia and Other Central Pain Syndromes

Daniel J. Wallace and Daniel J. Clauw. Philadelphia: Lippincott Williams & Wilkins, 2005. 432 pages, price $79.95 US.

This is an excellent and comprehensive outline of current knowledge and understanding of fibromyalgia and other central pain syndromes. There are 43 contributors, most of them leading experts and investigators in this area.

The discussions deal with various features of fibromyalgia including myofascial pain, sleep abnormalities, and psychological factors. Other related syndromes such as chronic fatigue syndrome, functional bowel disease, and genitourinary associations are discussed. A number of chapters deal with underlying biological disturbances. Other topics include approaches to management as well as disability.

Overall, this is an outstanding up to date outline of current knowledge and understanding of fibromyalgia and other central pain syndromes that we commonly encounter in rheumatological practice.

W.J. Reynolds, MD, FRCP. Rheumatologist, University Health Network, Associate Professor of Medicine, University of Toronto, Toronto, Ontario, Canada.

Correction


Table 1, which summarizes the present and previously described cases, was omitted from the report; it is presented below. We regret the error.

Table 1. Summary of cases of osteonecrosis after intraarticular injection of corticosteroids.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient Age &amp; Gender</th>
<th>Drug</th>
<th>Dose, mg × No. (total)</th>
<th>Injection Site</th>
<th>Period*, mo</th>
<th>ON</th>
<th>Histology</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>42 F</td>
<td>Triamcinolone</td>
<td>40 × 2 (80)</td>
<td>Bilateral shoulder</td>
<td>6</td>
<td>Bilateral hips</td>
<td>Biopsy (ON)</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>78 F (RA**)</td>
<td>Triamcinolone</td>
<td>40 × 8 (740)**</td>
<td>Shoulder, knee, ankle</td>
<td>5</td>
<td>Bilateral hips</td>
<td>Done (L FH:ON)</td>
<td>L THA</td>
</tr>
<tr>
<td>7</td>
<td>67 F</td>
<td>Triamcinolone</td>
<td>40 × 6 (408)****</td>
<td>Bilateral knee</td>
<td>13</td>
<td>Bilateral femoral condyles &amp; tibial plateau</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Present report</td>
<td>50 F</td>
<td>Methylprednisolone</td>
<td>80 × 1 (80)</td>
<td>L hip</td>
<td>3</td>
<td>L hip</td>
<td>Done (ON)</td>
<td>Rapid collapse &amp; THA</td>
</tr>
</tbody>
</table>

* From the first corticosteroid injection until the radiographic confirmation of osteonecrosis. ** History of seronegative rheumatoid arthritis. *** Oral prednisone (420 mg) was also taken. **** Oral prednisone (168 mg) was also taken. No.: Number of injections; ON: osteonecrosis; L: left; THA: total hip arthroplasty; FH: femoral head; NA: not available.