Solar urticaria treated with intravenous immunoglobulins

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Background: Solar urticaria (SU) is a rare idiopathic photodermatosis induced immediately after sun exposure. This disorder may considerably restrict normal daily life and management is extremely difficult when treatment with oral H1 antihistamines and sun avoidance are ineffective.

Objective: We sought to report the effectiveness of intravenous immunoglobulins (IVIG) in severe SU.

Methods: We performed a retrospective multicentric study via the mailing of a questionnaire to the French photodermatology units to analyze all cases of patients with SU who were treated with IVIG.

Results: Seven patients (5 women) with a mean age of 40 years (range 32-55 years) and a mean disease duration of 5 years (range 2-10 years) received IVIG. The administration schedule differed from one patient to another: 1.4 to 2.5 g/kg were infused over 2 to 5 days. Five of 7 patients obtained a complete remission. The number of courses necessary to obtain clinical remission varied from 1 to 3 courses. Complete remission was maintained during 4 to more than 12 months but antihistamines were still required. In one case, psoralen plus ultraviolet A photochemotherapy was administered.

Limitations: Retrospective study design, limited number of patients, and variations in the IVIG administration schedule could limit the interpretation of the results.

Conclusion: Our case series suggests a beneficial effect of IVIG in severe SU but additional prospective trials including a larger number of patients are needed to demonstrate the effectiveness of IVIG and to specify the optimal modalities of their administration in this disease. (J Am Acad Dermatol 2011;65:336-40.)

Key words: intravenous immunoglobulins; solar urticaria.

Solar urticaria (SU) is a rare idiopathic photodermatosis induced after sun exposure. The incidence of SU is suggested to account for 0.4% of all cases of urticaria. Most commonly SU appears during the third decade and preponderantly in women. The symptoms are characterized by pruritus with erythema and wheals, developing on exposed areas usually within minutes, and lasting for minutes to hours when sun irradiation is discontinued. Although all sun-exposed areas can be involved, SU lesions are most frequently located on the V area of the neck and on the arms. Headache, dizziness, wheezing, nausea, and systemic collapse may occur when large areas of the body are exposed to sunlight for a long period of time. SU is a chronic...
Solar urticaria is a rare idiopathic photodermatosis. Its management is extremely difficult when treatment with antihistamines and sun avoidance are ineffective.

Seven patients with severe solar urticaria received intravenous immunoglobulins. Complete remission was achieved in 5 cases. In one patient, psoralen plus ultraviolet A was administered.

Our case series suggests a beneficial effect of intravenous immunoglobulins in severe solar urticaria but additional prospective trials are needed to demonstrate the effectiveness of intravenous immunoglobulins.
Patients 2 and 3 who were previously unable to work returned to their employment. As far as the patients who did not improve with IVIG are concerned, patient 5 declined further infusion after a single course and was not followed up. Patient 4 received 3 courses of 2 g/kg of IVIG repeated every 2 months without clinical improvement and without any modification of the MUD. He did not benefit either from plasmapheresis prescribed later. Regarding the side effects observed during IVIG administration, minor symptoms occurred such as transient headache (patients 2 and 5) and eczema (patient 2). Patient 6 experienced meningeal syndrome during the IVIG infusion and finally received 70% of the 2-g/kg initial planned dosage.

DISCUSSION

The pathogenesis of SU is still obscure. SU lesions are most frequently triggered by UVA or visible light and less commonly by UVB.4 It is hypothesized that a provocative allergen derived from a chromophore localized in the skin is produced after an appropriate wavelength radiation, allowing recognition by specific IgE. The histamine-releasing activity could be secondary to the cross-linking of these IgE on mast cell receptors.9,10

First-intention treatment of SU including H1-blocking antihistamines and sun avoidance may be sufficient in the majority of cases. Repeated phototherapeutic exposure with an UV artificial source could represent another therapeutic option when antihistamines are ineffective. Different types of desensitization phototherapy have been used such as broadband UVB, narrowband UVB, psoralen plus UVA, or UVA alone. The starting dose should be inferior to the MUD to avoid flare or syncope.4 In very debilitating SU, systemic treatments have been
tested such as plasmapheresis, extracorporeal photochimiotherapy, or cyclosporine. IVIG are increasingly used to treat dysfunctional immune dermatosis. Studies performed on patients with chronic urticaria or delayed pressure urticaria showed 20% to 50% of complete response. Sporadic cases of refractory SU successfully treated with IVIG have been previously reported, including 3 of our patients. Our report shows that of 7 patients affected with severe SU who have been treated with IVIG in France, 5 experienced a considerable improvement after 1 to 3 courses (71% complete remission rate) and remission has been maintained for more than 1 year in 60% of the responsive patients. A single infusion of IVIG afforded two patients a dramatic response. In two cases, IVIG were ineffective. The first patient did not respond to additional IVIG infusions, and the second one did not experience any improvement after a single course but did not receive any further treatment.

### Table II: Intravenous immunoglobulin administration modalities and outcome in patients with solar urticaria

<table>
<thead>
<tr>
<th>Patient</th>
<th>IVIG modalities administration</th>
<th>MUD before IVIG in J/cm² (action spectrum)</th>
<th>MUD after IVIG in J/cm² (action spectrum)</th>
<th>Clinical outcome</th>
<th>Treatment after IVIG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sandoglobuline 2 g/kg (over 5 d) 3 courses: months 1, 3, 5</td>
<td>0.025 (UVA)</td>
<td>27 (UVA)</td>
<td>Complete remission; no relapse 1 y after third course</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>2</td>
<td>Tegeline 2.5 g/kg (over 3 d) 3 courses: months 1, 5, 12</td>
<td>1 (UVA)</td>
<td>15.6 (UVA)</td>
<td>Complete remission; no relapse 1 y after third course</td>
<td>Antihistamines, PUVA after first course</td>
</tr>
<tr>
<td>3</td>
<td>Tegeline 2 g/kg (over 4 d) 1 course</td>
<td>0.9 (UVA)</td>
<td>13 (UVA)</td>
<td>Complete remission; no relapse after 1 y</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>4</td>
<td>Sandoglobuline 2 g/kg (over 2 d) 3 courses: months 1, 2, 4</td>
<td>0.02 (UVA)</td>
<td>0.03 (UVA)</td>
<td>Unchanged</td>
<td>Plasmapheresis (inefficient), antihistamines</td>
</tr>
<tr>
<td>5</td>
<td>Tegeline 2 g/kg (over 3 d) 1 course</td>
<td>0.01 (UVB)</td>
<td>0.01 (UVB)</td>
<td>Unchanged after 1 mo; declined further infusion</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td>6</td>
<td>Tegeline 1.4 g/kg (over 3 d) 1 course</td>
<td>0.3 (UVA)</td>
<td>0.5 (polyC)</td>
<td>Complete remission; no relapse after 6 mo</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>7</td>
<td>Tegeline 2 g/kg (over 3 d) 1 course</td>
<td>2 (UVA)</td>
<td>20 (UVA)</td>
<td>Complete remission; no relapse after 4 mo</td>
<td>Antihistamines</td>
</tr>
</tbody>
</table>

IVIG, Intravenous immunoglobulin; MUD, minimal urticarial dose; polyC, polychromatic solar spectrum including 95% ultraviolet A and 5% ultraviolet B; PUVA, psoralen plus ultraviolet A; UV, ultraviolet.

**Fig 2.** Polychromatic solar spectrum minimal urticarial dose (MUD) evaluations in patient 2 before and after treatment. **A,** Before intravenous immunoglobulin (IVIG) treatment, MUD value was decreased to 0.1 J/cm² with important urticarial reaction spreading out test area. **B,** One day after first course of IVIG, MUD value dramatically increased to 1.6 J/cm² with minimal urticarial reaction.
IVIG were usually well tolerated except in one patient who presented aseptic meningitis. The mechanisms of the action of IVIG in SU are not fully identified. The immunomodulatory activities of IVIG in SU could be similar to that in autoantibody IgG-mediated idiopathic thrombocytopenic purpura treated with IVIG and be based on a functional blockade of immunoglobulin Fc receptors secondary to saturation of Fc receptors by anti-idiotypic antibodies contained in IVIG. In SU, immunoglobulin Fc saturation could avoid the fixation of the autoreactive IgE, specific for the provocative photoallergen, on mastocytes and prevent a consequent histamine release.

The retrospective character of our series, the questionnaire-based study, the variations in the schedule of IVIG administration, and the small number of patients included in this study do not allow to draw out definitive conclusions regarding the effectiveness of IVIG in SU. Moreover, IVIG are expensive (average price €50/g). Nevertheless, the use of IVIG in SU can be considered when antihistamines are ineffective and quality of life is impaired. Additional prospective trials involving larger number of patient are required to demonstrate the effectiveness of IVIG in SU and to specify the optimal modalities of administration for this disease.

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REFERENCES