LETTER TO THE EDITORS

A PROPOS LYELL’S SYNDROME TREATMENT

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Dear Sir,

The article by Cabral et al., published in Annals, vol. 17 (2), 2004, reports every other treatment of Lyell’s syndrome (corticosteroids, plasmapheresis, N-acetylcisteine, Pentoxifylline, cyclophosphamide, cyclosporin A, granulocyte colony-stimulating factor, hyperbaric oxygen therapy) but makes no mention of a therapy that in recent years has considerably enriched the literature on the subject.

We are referring to the use of elevated doses of IVIG in the immediate days after the onset of the disease, the rationale of which is the blockade, by the antibodies contained in the preparations of IVIG, of the apoptosis receptor (FAS or CD 95) present on the cell membrane of the keratinocytes and therefore in the competition with its ligand (FAS-L). This is, if not the only mechanism (a perforin-mediated way has been reported), the main pathogenetic mechanism that leads to the death of epithelial cells.

It may therefore be useful to recall some recent case history reports regarding the use of IVIG in Lyell’s syndrome, even if only to demonstrate that a lively debate rotates around this type of therapy (Table I).

As can be seen, not all results show an effective benefit induced by the therapy with IVIG. In the collected cases of Bachot et al. - one of the most numerous - actual mortality (32%) was higher than that expected (24%). Even if the majority of deaths occurred among elderly patients and with kidney failure, the conflicting results led some researchers to suggest that in the absence of any proven effectiveness of IVIG, the only valid therapy (Lyell’s syndrome is a self-limiting disease) is one of support.

It is probably more reasonable to consider a non-routine use of IVIG, also in view of the serious side effects that it is capable of causing, namely:

1) aseptic meningitis, with severe headache, especially in patients with a positive history of hemicranial attacks;

2) serious anaphylactic reactions in patients with IgA deficit in the presence of anti-IgA antibodies that form immunocomplexes with activation of the complement with the IgA contained in IVIG preparations;

3) syndrome caused by haematic hyperviscosity with cerebral ictus, myocardial infarctus, and jugular thrombosis especially in elderly patients or those with extensive vascular disease due to increased risk of thromboembolic episodes;

4) acute kidney failure due to osmotic suffering of the proximal tubule following the use of IVIG containing saccharose.

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High doses of IVIG are widely indicated in addition to its use in Lyell’s syndrome. However, the serious side effects (and also the particularly high costs) have induced some researchers to use low doses.

Kofler et al. (1997) successfully treated a case of acquired bullous epidermolysis resistant to therapy with low doses of IVIG. Toth et al. (1999) successfully treated a case of penicillin-induced pemphigus foliaceus resistant to low-dose IVIG therapy.

Recently we successfully used low doses of IVIG (gamma venin P 2.5 g 2 per day), in association with frozen

<table>
<thead>
<tr>
<th>Author and bibliographical ref.</th>
<th>Year</th>
<th>Number of cases</th>
<th>Days of therapy</th>
<th>Dosage (g/kg/d)</th>
<th>Deaths</th>
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</thead>
<tbody>
<tr>
<td>Viard et al. (2)</td>
<td>1998</td>
<td>10</td>
<td>4</td>
<td>0.20/0.75</td>
<td>-</td>
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<td>Morici et al. (5)</td>
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<td>5</td>
<td>3</td>
<td>1.52</td>
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<tr>
<td>Pognel et al. (4)</td>
<td>2001</td>
<td>1</td>
<td>5</td>
<td>0.75</td>
<td>-</td>
</tr>
<tr>
<td>Stella et al. (5)</td>
<td>2001</td>
<td>9</td>
<td>IVIG+methylprednisolone pulse therapy</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tritthart-Viumvat (6)</td>
<td>2002</td>
<td>8</td>
<td>4</td>
<td>0.5/0.75</td>
<td>-</td>
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<tr>
<td>Tricot et al. (7)</td>
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<td>16</td>
<td>4</td>
<td>1</td>
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<tr>
<td>Prins et al. (8)</td>
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<td>48</td>
<td>4</td>
<td>0.75</td>
<td>6</td>
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<tr>
<td>Bachot et al. (9)</td>
<td>2004</td>
<td>34</td>
<td>2</td>
<td>1</td>
<td>11(32%)</td>
</tr>
<tr>
<td>Al-Muttalib et al. (10)</td>
<td>2004</td>
<td>12</td>
<td>4.5</td>
<td>0.5-1</td>
<td>-</td>
</tr>
</tbody>
</table>

*Expected mortality (CUTIEN) 8.7 (24%)

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fresh plasma (4 units per day) as an adjuvant function to reduce the dosage of corticosteroids and immunosuppressors in a case of very extensive pemphigus vulgaris. We treated the last cases of SJS-Lyell that we have seen with low-dosage IVIG associated with frozen fresh plasma. The administration of frozen fresh plasma has three functions:

1) to provide fluids for reanimation due to the increase of volaemia caused by the increased protein content;
2) to provide a specific treatment for the elevated presence of immunoglobulins;
3) to reduce the dosage of IVIG or to replace its action after suspension. 

BIBLIOGRAPHY