Correspondence and Opinions

Thalidomide-Related Headache

Alice Phan\textsuperscript{a}, Pascal Favrole\textsuperscript{b}, Sonia Alamowitch\textsuperscript{b}, Olivier Chosidow\textsuperscript{a}
Departments of \textsuperscript{a}Dermatology and Allergy and \textsuperscript{b}Neurology, Hôpital Tenon, Université Paris 6 Pierre-et-Marie-Curie, Paris, France

Key Words
Thalidomide • Headache • Migraine

Thalidomide is an alternative treatment for cancer and inflammatory diseases, e.g. recalcitrant aphthosis, cutaneous lupus erythematosus or myeloma [1]. Among side effects, teratogenicity and peripheral neuropathy are well documented but series on thalidomide-related headache have never been reported [2].

All patients treated by thalidomide by one of us (O.C.) from 2001 to 2007 were reviewed. Among 40 patients, 7 (17%) had suffered from chronic headache. All were reevaluated by a neurologist to characterize headache (according to the criteria of the International Headache Society [3]) and to establish causality relationships (table 1).

Three patients who had a personal history of migraine observed a change in intensity, frequency and duration of headache, after a mean time of 3 months (range 1–4 months) after the start of thalidomide treatment. Regarding the 4 remaining patients, headache occurred after a mean time of 7 months (range 1–14.5 months). In most cases, it was tension-type headache; only 1 patient suffered from migraine with visual aura. Neuroimaging was performed in all patients to exclude symptomatic forms of headache (neurolupus, thrombosis, …) and was normal. A dose reduction was performed in 6 patients, with a partial (5 cases) or complete (1 case) improvement of headache. Treatment continuation was then possible in 3 of the 5 partially improved patients. Thalidomide was interrupted in 4 cases (2 for complete remission of the underlying disease and 2 for unbearable headache), without relapse of the headache after a mean follow-up of 8 months. One patient was rechallenged with thalidomide and reexperienced headache.

Our cases suggest that thalidomide may induce headache (compatible chronology, improvement after discontinuation, positive rechallenge) which can limit its use. Its management should be based on dose adjustment or temporary interruption of the drug, as analgesics are not sufficient in most cases. There seems to exist an individual dose-dependent effect. If maintenance of the therapy is necessary, the minimal effective dose should be given.

Acknowledgments
We thank Anne Cohen for logistic assistance, the patients who kindly accepted to participate in the survey and the doctors who referred the patients. O.C. received a research grant from Pharmion.

Table 1. General characteristics of the patients

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age years</th>
<th>Indication for thalidomide</th>
<th>Duration from start of thalidomide treatment to onset of headache, months</th>
<th>Daily dose when headache occurred mg</th>
<th>Headache type</th>
<th>Personal history of migraine</th>
<th>Intensity</th>
<th>Other adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>F 31</td>
<td>cutaneous lupus erythematosus</td>
<td>3</td>
<td>100</td>
<td>migraine with aura</td>
<td>yes</td>
<td>mild</td>
<td>arethasia of the heel</td>
<td></td>
</tr>
<tr>
<td>F 52</td>
<td>recurrent erythema multiform</td>
<td>1</td>
<td>25</td>
<td>tension-type headache</td>
<td>yes</td>
<td>moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F 40</td>
<td>cutaneous lupus erythematosus</td>
<td>14.5</td>
<td>10</td>
<td>tension-type headache</td>
<td>no</td>
<td>mild</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F 58</td>
<td>recurrent aphthous stomatitis</td>
<td>4</td>
<td>50</td>
<td>migraine without aura</td>
<td>yes</td>
<td>severe</td>
<td>somnolence, constipation</td>
<td></td>
</tr>
<tr>
<td>M 33</td>
<td>cutaneous lupus erythematosus</td>
<td>11</td>
<td>25</td>
<td>migraine without aura</td>
<td>yes</td>
<td>moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F 35</td>
<td>cutaneous lupus erythematosus</td>
<td>1</td>
<td>50</td>
<td>tension-type headache</td>
<td>no</td>
<td>severe</td>
<td>somnolence, amenorrhea</td>
<td></td>
</tr>
<tr>
<td>F 44</td>
<td>sarcoidosis</td>
<td>1</td>
<td>100</td>
<td>migraine without aura</td>
<td>yes</td>
<td>severe</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References

Prof. Olivier Chosidow
Université Paris 6 Pierre-et-Marie-Curie
Department of Dermatology and Allergy, Hôpital Tenon (AP-HP)
4, rue de la Chine, FR–75020 Paris (France)
Tel. +33 1 56 01 76 70, Fax +33 1 56 01 64 58
E-Mail olivier.chosidow@tnn.aphp.fr