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DOI: [10.1159/000161124](https://doi.org/10.1159/000161124)**Thalidomide-Related Headache**Alice Phan^a, Pascal Favrole^b, Sonia Alamowitch^b, Olivier Chosidow^aDepartments of ^aDermatology and Allergy and ^bNeurology, 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.

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Table 1. General characteristics of the patients

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

References

- 1 Franks ME, Macpherson GR, Figg WD: Thalidomide. *Lancet* 2004;363:1802–1811.
- 2 Garcia-Albea E, Cabrera F, Tejero J, Jimenez-Jimenez FJ: Typical migraine and thalidomide. *Med Clin (Barc)* 1993;100:557.
- 3 Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. *Cephalalgia* 1988;8(suppl 7):1–96.

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