Efficacy of Thalidomide in the Treatment of Prurigo Nodularis

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Prurigo nodularis (PN) is a chronic and intensely pruritic dermatosis characterized by lichenified and excoriated papules and nodules. Although thalidomide has shown promise in the treatment of refractory PN, its safety and efficacy for this indication has not been firmly established.

MATERIALS AND METHODS

The aim of this retrospective study was to determine the efficacy, and identify any adverse side-effects, of thalidomide treatment for PN. We included all patients referred to two hospitals in Lorraine, France (CHU Nancy and CHR Metz-Thionville) between November 2001 and December 2008 for the treatment of PN. Efficacy in each case was classified as: (*i*) successful treatment (disappearance of the pruritus and reduction of nodules); (*ii*) slight improvement (reduction of the nodules, i.e. number and/or flattening, no disappearance of itching); or (*iii*) unsuccessful. Any side-effects arising during treatment were recorded.

RESULTS

Among a total of 116 patients with PN, 13 (3 men, 10 women; mean age 49.7 years) were treated with thalidomide (Table I). None of them had any underlying disease responsible for the PN. Each of these patients had responded poorly to previous treatments. The daily dose of thalidomide ranged from 50 to 100 mg, except for one patient (No. 12) who received 200 mg daily for 1 month and 150 mg daily for 2 months. The duration of treatment ranged from 3 to 142 months. Seven patients (54%) showed complete improvement after a mean duration of treatment of 3 months, with four of these continuing on maintenance treatment at the time of last follow-up. Four patients (31%) showed slight improvement, and the treatment was judged to be unsuccessful in two patients (15%). Thalidomide treatment had to be discontinued in four patients (31%) because of peripheral neuropathy (two patients, paraesthesia and abnormal electromyogram while treated with 100 mg/day of thalidomide), renal toxicity, or symptoms of sedation and dizziness. One patient abandoned the treatment.

DISCUSSION

Until recently, the thalidomide dose used to treat PN was most often between 100 and 300 mg daily (1, 2). Herranz et al. (3) used 100 mg daily to treat an HIV-positive patient with PN, who responded after 6 weeks of treatment with a dramatic improvement in lesions and disappearance of the pruritus. More recently, Lan et al. (4) treated six patients with thalidomide at a dosage ranging between 50 and 100 mg daily, and observed a rapid and marked improvement of the lesions in 66% of their patients, and remission in the remainder. Doherty & Hsu (5) reported good efficacy for at least a month-long thalidomide regimen of 100 mg daily, observing a slight-to-moderate improvement in PN symptoms in approximately 60% of patients, resolution of lesions in

Table I. *Patient characteristics and details of thalidomide treatment*

Case no.	Age/Sex	First-line treatment	Disease duration, years	Thalidomide duration, mo. Dose, mg/day			Clinical response	Side-effects	Evolution
				50 mg	100 mg	≥150 mg			
1	57/F	TC, AH, UV	15	2	1		Slight improvement	Sedation	Stopped due to SE
2	59/F	TC, UV	5	18			Successful after 2 mo.	No	Lesion free
3	38/F	TC, UV, SC	3	23[a]			Successful after 2 mo.	No	MD = 50 mg ×2/week
4	37/F	UV, SC	4	12			Successful after 6 mo.	No	MD = 50 mg/day
5	47/M	TC, UV	15	4	8		Slight improvement	Neuropathy	Stopped due to SE
6	41/M	TC	3	4	20		Successful after 3 mo.	Neuropathy	Stopped due to SE
7	60/M	TC, AH	3	20	9		Slight improvement	Renal toxicity[b]	Stopped due to TE
8	68/M	TC, UV	8		4		Unsuccessful	No	Stopped
9	39/F	TC, UV	20	4	7		Slight improvement	No	Stopped
10	61/F	TC, UV	2	2	3		Unsuccessful	No	Stopped
11	62/F	TC, UV, AH	17	102	4		Successful after 4 mo.	No	MD = 50 mg/day
12	65/F	TC, UV	6	119	20	3	Successful after 1 mo.	No	MD = 50 mg/day
13	64/F	TC, UV, SC	12	25	2		Successful after 2 mo.	No	MD = 50 mg ×2/week

[a]Then 50 mg every second day for 80 months. [b]Haematuria and/or proteinuria.
F: female; M: male; PN: prurigo nodularis; TC: topical corticosteroid; AH: antihistaminic treatment; SC: systemic corticosteroid; UV: phototherapy; SE: side-effect; LF: lesion-free; MD: maintenance dose.

8%, and no apparent benefit in 30%. Finally, Orlando et al. (6) treated a patient with 50–100 mg thalidomide daily, seeing marked improvement after 1 month and remission after 6 months of treatment. In the current study, we confirmed that a low dose of thalidomide is sufficient to treat PN, with 84% of patients showing a moderate-to-good response and only 16% experiencing no apparent benefit. If the initiating daily dose was more than 50 mg, no relapse was observed after tapering the daily dose to at least 50 mg/day of thalidomide.

The major side-effect of thalidomide is neurotoxicity, which occurs most frequently at daily doses above 100 mg. Wulff et al. (7) reported that, for patients receiving daily doses of thalidomide between 150 and 400 mg, 100% developed peripheral neuropathy as evidenced by electrophysiology, with 86% of patients reporting clinical symptoms such as paraesthesia. Aronson et al. (8) found electrophysiological evidence of peripheral neuropathy in 60% of patients receiving between 100 and 300 mg thalidomide daily. Doherty & Hsu (5) reported a 24% incidence of peripheral neuropathy in patients treated for a variety of diseases with a maximum of 100 mg thalidomide daily, while neither Lan et al. (4) nor Orlando et al. (6) found any evidence of this side-effect in patients they treated with the same dosage. In comparison, we found symptoms of peripheral neuropathy in 15.4% of our patients after 8 and 20 months of thalidomide at 100 mg/day.

In conclusion, this study has shown thalidomide to be a useful treatment for refractory PN. Although a dosage below 100 mg daily appears to be optimal for avoiding side-effects, physicians should nonetheless carefully monitor potential symptoms during treatment with this drug.

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