Thalidomide Therapy on A Case of Prurigo Nodularis

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Prurigo nodularis is a troublesome chronic dermatosis that showed unsatisfactory response to conventional therapies. Since thalidomide has been applied to the treatment of prurigo nodularis, although the action mechanism is still uncertain, many dermatologists have confirmed its effectiveness.

We treated a 54-year-old male patient who had prurigo nodularis affecting the whole body for 10 years with 100 to 300mg of thalidomide daily as the sole therapy for 4 months. The skin lesions were flattened leaving postinflammatory hyperpigmentation and the pruritus also subsided. Two years after stopping thalidomide, no recurrence was observed.

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Key Words: Prurigo nodularis, Thalidomide

Prurigo nodularis is a benign chronic dermatosis that is often difficult to treat successfully. The causes of prurigo nodularis are unknown but some consider it as a variant of lichen simplex chronicus[2]. Although many therapeutic modalities such as intralesional corticosteroid, benoxaprofen, PUVA and cryotherapy have been used[6,7], the results were not satisfactory and frequent relapses were common. Since Mattos reported the successful treatment of prurigo nodularis with thalidomide in 1973[1], the effectiveness has been confirmed by several authors[3-5]. Therefore, we decided to administer this medication to our patient who had been suffering from prurigo nodularis, which resisted various kinds of treatment for 10 years.

REPORT OF A CASE

A 54-year-old male patient was first seen at our hospital with a 10-year history of pruritic nodular skin lesions. The skin lesions had appeared on the lower back initially and gradually spread to become generalized. Prior to vising our hospital, he received a number of treatments including intralesional injection of triamcinolone, occlusive dressing therapy with potent corticosteroids, sedatives and cryotherapy which only had a temporary effect on the pruritus and the skin lesions. The patient was hospitalized for further evaluation and treatment. His physical examination disclosed no abnormal findings except for the numerous pea to bean sized, elevated, reddish to dark brownish, somewhat scaly, excoriated firm nodules on the trunk and extremities (Fig. 1.). At admission, complete blood cell count, urinalysis, renal and liver function tests were within normal limits. IgE PRIST level was slightly elevated up to 448 IU/ml (normal, below 250 IU/ml). To appraise his immunologic status, multitest CMI, peripheral T cell and B cell counts and T4/T8 level were checked and the results were all within normal limits. We also performed mental status examinations and MMPI which revealed no abnormalities. A Skin biopsy from a nodule on the lower leg showed marked hyperkeratosis, acanthosis, papillomatosis of the epidermis as well as perivascular inflammatory infiltrates in the upper parts of the dermis (Fig. 3.). The changes were considered consistent with prurigo nodularis. After we diagnosed it as prurigo nodularis clinically and histopathological-

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ly, administration of thalidomide at a dose of 100 mg twice daily was begun. During the thalidomide therapy, all topical and systemic medications were stopped. On the 7th day of therapy, the dosage was increased to 300 mg per day and some of the skin lesions became erythematous and edemtous, and some even started to ooze. By the 12th day, most of the skin lesions showed oozing and some were flattened with crust formation. At that time, we performed an immunoperoxidase stain of the oozing lesion which showed a strong positive reaction to UCHL 1 (pan-T cell marker) (Fig. 4.). By

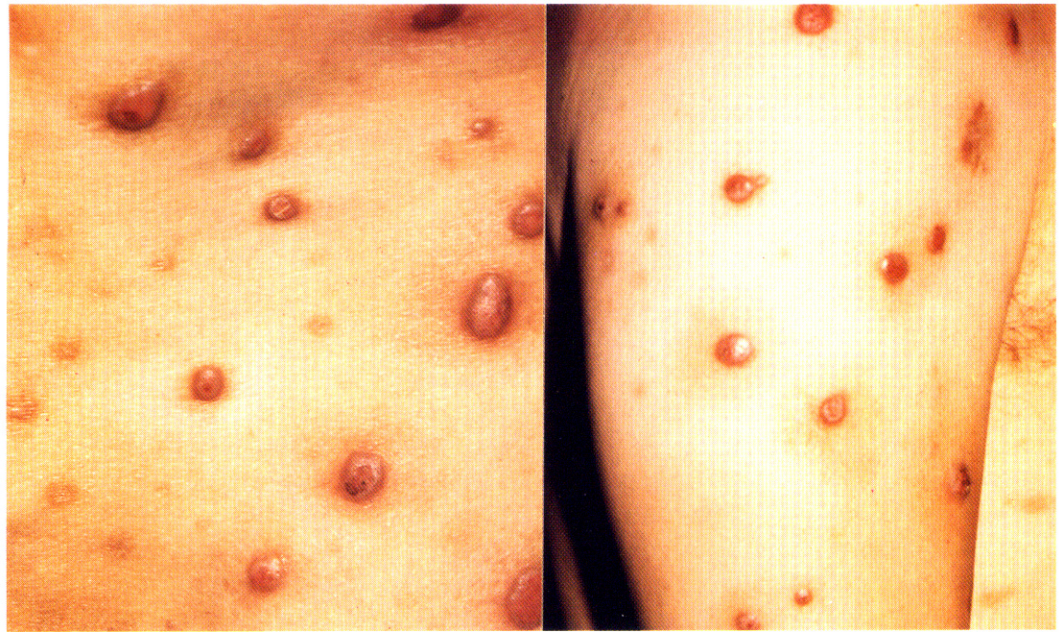

Fig. 1. Before treatment: Numerous pea to bean sized, excoriated, firm nodules on the lower back (Lt) and upper arm (Rt).

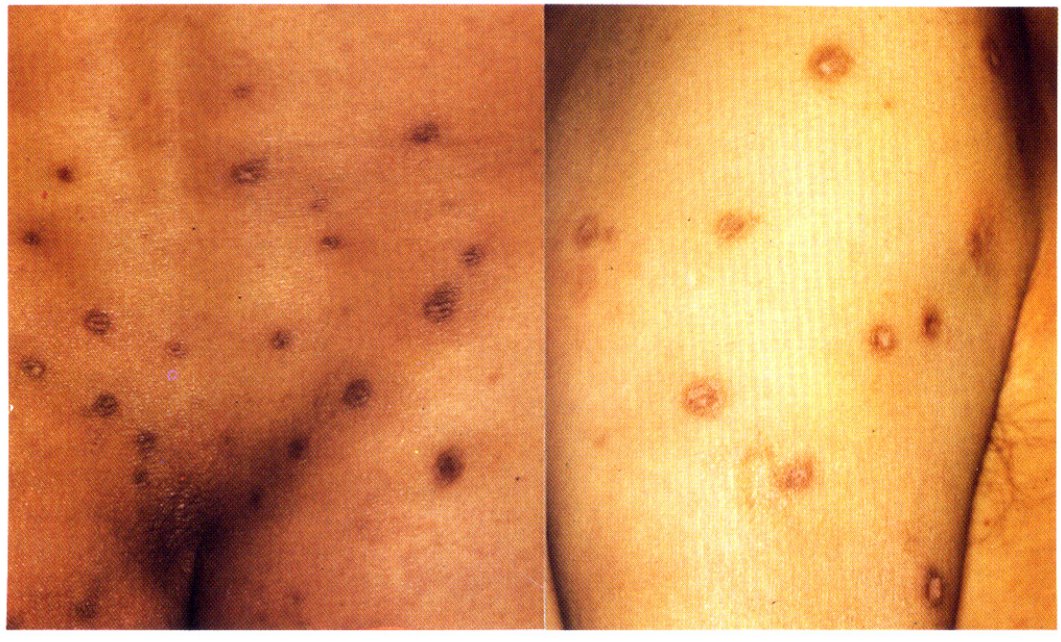

Fig. 2. One hundred twentieth day after stopping thalidomide: Completely flattened nodules leaving postinflammatory hyperpigmentations.

the 30th day, he didn't complain of pruitus any more. During the course of the therapy, laboratory values were unchanged and no serious side effects were observed. As the marked clinical improvement was noted, the dosage was tappered gradually. By the 127th day, as all the skin lesions were completely flattened leaving only postinflammatory hypopigmentation with hyperpigmented halo, we stopped the thalidomide. During the next 24 months of the follow up period with no additional medication, the skin lesions and pruritus did not recur.

DISCUSSION

Our therapeutic trial of thalidomide in prurigo nodularis, which lasted 10 years, confirmed the

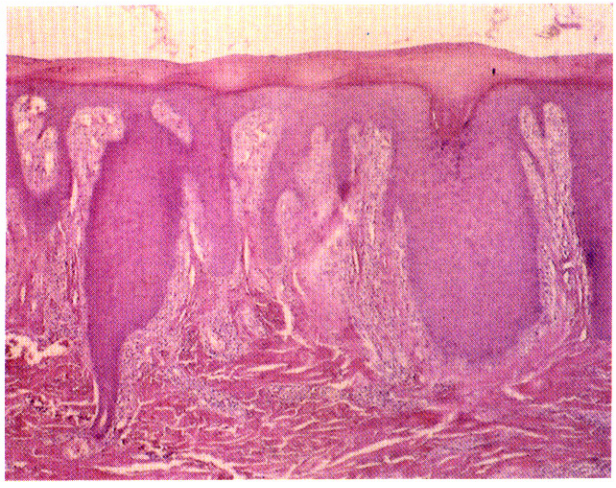

Fig. 3. Before treatment: Marked hyperkeratosis, acanthosis and elongation of rete ridges with conspicuous papillomatosis and inflammatory infiltrates in the dermis (H&E stain, ×40).

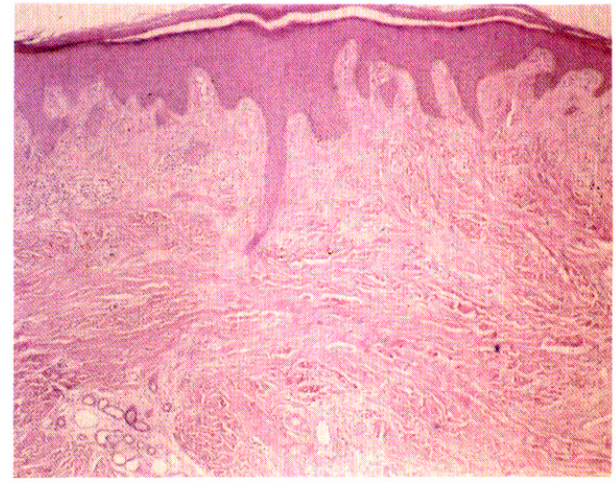

Fig. 5. Eightyfourth day of treatment: Diminished rete ridge elongation and dermal inflammatory infiltrates (H&E stain, ×40).

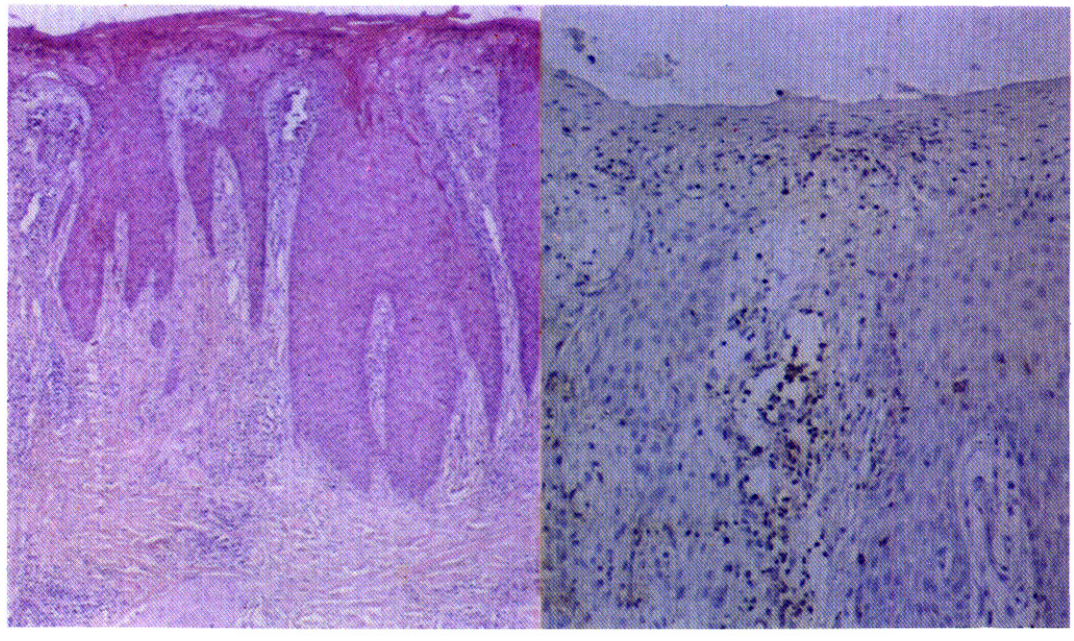

Fig. 4. Twelfth day of treatment: A. Crust formation, exocytosis and spongiotic vesicles in the epidermis and patchy inflammatory infiltrates in the upper dermis (H&E stain, ×40), B. Strong positive reaction to pan-T cell markers (PAP stain, ×100).

results of others[1,3,5]. Our case showed resolution of pruritus in 4 weeks and involution of nodular skin lesions in 3 months. Reports of Mattos[1], Sheskin[5] and Winkelmann et al[4]. showed that the resolution of pruritus occurred in 8 to 60 days and nodular skin lesions in 2 to 9 months. They used 200 to 400 mg of thalidomide daily and some of them believe that 200 mg of thalidomide daily may be adequate to treat prurigo nodularis, but it is not apparent whether a lower maintenance dosage might be equally effective. We did not observe any significant side effects during the course of the treatment, although a few cases of polyneuritis associated with long-term thalidomide therapy have been reported previously[8].

Thalidomide is a derivative of glutamic acid. Chemically, it is related to bemegride and glutethimide, though its pharmacologic properties are different[9]. This drug has a calming effect on the central nervous system, reducing the voluntary activity of laboratory animals and promoting sleep. It has a sedative effect, but acts differently from barbiturates, and is counteracted by central nervous system stimulants. The action mechanism of thalidomide in prurigo nodularis is not completely explained by the central sedative effect because this does not explain why other sedatives have not been effective. On the other hand, some consider that there may be direct peripheral action on the proliferated neural tissue in the lesions of prurigo nodularis[8]. This action could be similar to that causing damage to peripheral nerves and induces polyneuritis, which is one of the chronic toxicities of thalidomide.

Aside from those points, Winkelmann et al.[4] strongly suggested that a certain change in immunoreactivity was related to the mechanism of thalidomide. For example, the increased T cells in their patients during treatment could represent an active enhancement of T cell response and IgE values were also decreased in proportion to the involution of the nodular skin lesions. Other evidence supporting the effects of thalidomide on the immune system are a suppression of graft-versus host reaction in animal experiments documented by Field et al.[10], depressed antibody formation by Gusdon and Cohen[11] and a decrease in IgA concentration in leprosy by thalidomide treatment by Sagher[12]. In our case, even though we couldn't perform sufficient immunologic studies, the results suggest the immunologic mechanism of thalidomide. One piece of evidence is individual nodular skin lesions showing oozing and edematous change in the early stage of treatment, and the other is that the majority of the infiltrated cells in the oozing lesions were T cells.

In summary, thalidomide is effective in prurigo nodularis but requires careful monitoring of laboratory values and neurologic signs for thalidomide neuropathy during therapy. As the action mechanism of thalidomide is still uncertain, a prospective study of the immunologic status of patients with prurigo nodularis may present further clues.

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