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LTC LEONARD C. SPERLING, MC, USA, and CPT(P) WILLIAM L. HEIMER II, MC, USA Washington, D.C.

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Brief communications

Treatment of pemphigus and linear IgA dermatosis with nicotinamide and tetracycline: A review of 13 cases

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Pemphigus usually requires long-term therapy with oral corticosteroids, which can cause significant morbidity.[1, 2] Several immunomodulating drugs, such as cyclophosphamide, azathioprine, and gold have proved beneficial as steroid-sparing agents.[3, 4] However, these agents also have limited long-term utility because of their potential to induce renal and hepatic dysfunction and bone marrow suppression.

Nicotinamide in combination with tetracycline has been reported to be effective for bullous pemphigoid (BP) and linear IgA bullous dermatosis (LABD).[5, 6] This regimen has the advantage of lower toxicity compared with corticosteroids and immunosuppressant regimens. We have treated 11 cases of pemphigus and two cases of LABD with nicotinamide and tetracycline and report our experience.

MATERIAL AND METHODS

Eleven patients with pemphigus (six with pemphigus vulgaris [PV], three with pemphigus foliaceus [PF], two with pemphigus erythematosus [PE]) and two patients with LABD were treated with nicotinamide, 1.5 gm/day, and tetracycline, 2 gm/day, with or without oral corticosteroids as summarized in Table I. The clinical diagnosis was confirmed in all cases by routine histopathology and immunofluorescence studies.

Therapeutic responses were graded by the degree of clinical improvement after 8 weeks of treatment. Responses were recorded as follows: complete response (CR) = total clearing of lesions; partial response (PR) = clearing of more than 50% of lesions; and no response (NR) = clearing less than 50% of lesions or worsening of the disease.

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A complete blood cell count as well as levels of serum electrolytes, glucose, serum glutamic oxaloacetic transferase, serum glutamic pyruvate transferase, γ-glutamyl transferase, and bilirubin were determined on all patients before beginning therapy, after 4 to 8 weeks of treatment, and periodically thereafter. In four patients pemphigus autoantibodies were determined by indirect immunofluorescence on monkey esophagus at the time of diagnosis and after at least 8 weeks of treatment.

RESULTS

The therapeutic responses of the patients are summarized in Table I. When evaluated as a group, 7 of 13 patients experienced CR. Four patients had PR, and two patients failed to respond. Of the six patients with PV, three had CR, two had PR, and one had NR. Only two patients with PV were able to be treated with nicotinamide and tetracycline alone; the four other patients required a mean daily dose of 8 mg of prednisone to control disease activity. Patient 3 was also treated with 150 mg of azathioprine per day. The follow-up period for these patients ranged from 6 to 13 months (mean 9 months).

Of the five patients with superficial pemphigus, two had CR, two had PR, and one patient did not respond. Only one patient (patient 10) required a mean daily dose of 7.5 mg of prednisone for 10 months. For the last 5 months his disease has been controlled with tetracycline and nicotinamide alone. The follow-up period for these patients ranges from 11 to 41 months (mean 22 months).

Three of four patients had a significant reduction in pemphigus antibody titers during treatment. Patients 1 and 2 had a twofold decrease. Patient 10 had an initial titer of 1:2560 that became negative during treatment.

Both patients with LABD achieved rapid and complete clearing. However, patient 12 discontinued therapy after 2 months because of persistent headaches. He has subsequently remained clear

Table I. History and therapeutic response of patients treated with nicotinamide and tetracycline for autoimmune bullous diseases

Patient	Age (yr)/ Sex	Diagnosis	Concurrent treatment	Response*	Follow-up period (mo)
1	34/M	PV	Topical steroids	CR	8
2	47/F	PV	Prednisone, 5 mg q.o.d.-30 mg q.d.	PR	6
3	71/F	PV	Prednisone, 5 mg/day Azathioprine, 150 mg/day	PR	10
4	81/M	PV	Topical steroids	CR	9
5	57/F	PV, oral	Prednisone, 2.5 mg/day	CR	14
6	41/F	PV, oral	Prednisone, 10 mg/day	NR	
7	60/F	PF	None	CR	24
8	51/M	PF	Topical steroids	CR	41
9	50/M	PF	Topical steroids	PR	11
10	28/F	PE	Prednisone, 7.5-0 mg/day	PR	13
11	73/M	PE	None	NR	
12	70/M	LABD	Antihistamines, topical steroids	CR	2 mo w/ medication, 11 mo clear
13	69/F	LABD	Topical steroids	CR	19

LABD, Linear IgA bullous dermatosis; *PE*, pemphigus erythematosus; *PF*, pemphigus foliaceus; *PV*, pemphigus vulgaris.
*Responses graded as: CR = complete response (all lesions resolved) after 8 weeks of nicotinamide/tetracycline; PR = partial response (>50% of lesions resolved) after 8 weeks of nicotinamide/tetracycline; NR = no response (<50% of lesions resolved) or worsening of disease after 8 weeks of nicotinamide/tetracycline.

with topical steroid therapy for approximately 1 year. Patient 13 (previously reported in Peoples and Fivenson[5]) has remained clear for more than 2 years with nicotinamide and tetracycline therapy.

Eight of the 13 patients reported no adverse effects. There were no abnormalities in any patient's serum chemical or hematologic findings. Four patients experienced nausea, abdominal discomfort, and mild diarrhea. Gastrointestinal symptoms were relieved in three patients when minocycline, 100 mg twice a day, was substituted for tetracycline and in the fourth patient when the dose of tetracycline was reduced to 1.5 gm/day. Patient 10 developed a generalized morbilliform eruption that was believed to be caused by tetracycline but was able to tolerate minocycline, 100 mg twice a day. Patient 12 experienced headaches with nicotinamide and tetracycline, as well as with nicotinamide and minocycline.

DISCUSSION

Although this is an uncontrolled study with a limited follow-up period, the preliminary results appear promising. Six of 11 patients with pemphigus and two patients with LABD were able to be controlled with nicotinamide and tetracycline as their only oral agents. We should emphasize that

of six patients with PV. The role of these agents in PV appears to be that of a steroid-sparing adjuvant, rather than a steroid alternative. The combination of nicotinamide and tetracycline was found to be an effective alternative to steroids in superficial pemphigus (PE and PF) and LABD in six of seven patients.

The primary advantage nicotinamide and tetracycline offer over corticosteroids and immunosuppressive agents is a broader safety profile. The most common side effect in our patients was gastrointestinal upset. In higher doses, nicotinamide has been reported to produce flushing, pruritus, headache, vomiting, and a flu-like syndrome.[7-9] Acanthosis nigricans, ichthyosiform skin changes, and hepatotoxicity have also been reported.[8, 10, 11] The side effects of tetracycline are well known and have been reviewed elsewhere.[12, 13]

Because this study is uncontrolled, it is possible that a selection bias towards patients with a tendency toward milder disease or spontaneous remission may have occurred. However, the fact that several of our patients (7, 8, 10, and 13) had recurrences when nicotinamide and tetracycline were discontinued argues against this explanation for the therapeutic results.

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