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GRISEOFULVIN THERAPY OF LICHEN PLANUS

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Abstract. Thirty-one patients who had lichen planus treated with griseofulvin were randomly selected for review from a group of patients with lichen planus seen at the Mayo Clinic between January 1976 and June 1980; two patients were excluded because of lack of adequate follow-up. Of the 11 patients with only oral lesions, 6 showed a marked improvement or complete remission. Of the 18 patients with lichen planus involving one or more sites with or without oral lesions, 15 had cutaneous lesions. Three of the 15 had improvement of their cutaneous lesions; however, 1 of the 3 continued to develop new lesions, although old ones were improving. In patients with recalcitrant, symptomatic oral lichen planus, a trial of griseofulvin would seem justified. Success in patients with cutaneous lichen planus is less likely; however, griseofulvin may afford relief in selected patients. This study indicates that further prospective studies are needed to clarify the efficacy of griseofulvin in lichen planus.

Key words: Dermatology; Griseofulvin; Lichen Planus; Mucous membranes; Pruritus; Skin

Lichen planus is a benign disorder of the skin and mucous membranes. Less frequently, the scalp and nails are involved. Although some progress has been made in elucidating the histologic and immunopathologic features and the tissue dynamics of this disease (4, 10), the cause remains unknown. The course is unpredictable, but spontaneous remission can usually be expected in 8 months to 4 years, with relapses in some 12–17% of patients (1, 6, 11).

Despite the benign nature of this disease and its usually favorable outcome, there is a subgroup of patients whose disease process is prolonged or disabling (or both) because of pruritus, pain, or cosmetic deformity. Hence, the search for an effective and safe treatment for this condition continues. In a disease with such an unpredictable course, evaluation of therapy is most difficult. Prompted by the optimistic reports of successful treatment of lichen planus with griseofulvin (2, 5, 7–9), we undertook a retrospective study of patients who had lichen planus treated with griseofulvin.

PATIENTS AND METHODS

Charts of 31 patients seen at the Mayo Clinic between January 1976 and June 1980 who had been treated with griseofulvin for lichen planus were reviewed. The patients were divided into two main groups (Tables I and II). Group 1 consisted of 11 patients who had oral lichen planus only. The clinical diagnosis was supported histologically in all of the 8 patients who had biopsy specimens taken. Group 2 consisted of 18 patients with cutaneous, scalp, or nail involvement with or without oral lichen planus. Thirteen patients of this group had biopsy specimens taken, and in 10, the clinical diagnosis was supported. Two additional specimens were suggestive of lichen planus, and 1 was interpreted as chronic dermatitis. All 18 patients were clinically judged by the physician as having lichen planus.

All of the patients received doses of griseofulvin greater than or equal to 500 mg per day of the microsize preparation orally, in divided doses, with the exception of 3 patients in group 2, in whom the dosage used was either not known or less than 500 mg per day. One patient was excluded from each group because of lack of follow-up.

Table I. *Patients with oral lichen planus only*

Case	Sex and age (yr)	Duration of disease	Duration of treatment (mo.)	Result[a]
1	F, 58	15 mo.	3/4	3+
2	F, 60	6 mo.	1 1/2	3+
3	F, 76	6 yr	4	3+
4	M, 63	9 mo.	4	2+
5	F, 76	8 yr	12[b]	2+
6	F, 41	5 yr	3	2+
7	M, 46	1 yr	3	1+
8	F, 47	1 1/2 mo.	1 1/2	1+
9	F, 69	4 mo.	5	1+
10	F, 47	12 yr	3	0
11	F, 66	1 yr	2	0

[a] Result: 3+ = complete remission, 2+ = marked improvement, 1+ = mild improvement, and 0 = no improvement.

[b] Beneficial results (2+) were seen in this patient after 3 months of treatment.

Table 11. *Patients with lichen planus of the skin, genitalia, nails or scalp, with or without oral lesions*

Case	Sex and age (yr)	Duration of disease	Duration of treatment (mo.)	Site[a] and results[b]				
				C	S	O	G	N
12	F, 61	10 yr	10	–	2+	3+	3+	1+
13	M, 10	2 mo.	1 1/2	3+	–	3+	–	–
14	M, 62	6 mo.	7	2+	3+	–	–	–
15	M, 27	1 mo.	1	2+	–	2+	NR	–
16[c]	F, 60	2 mo.	2	0	–	2+	–	–
17	F, 61	3 yr	3	–	–	0	3+	–
18	M, 62	1 mo.	1	1+	–	1+	–	–
19	F, 23	3 mo.	1	1+	–	0	–	–
20	F, 53	8 mo.	5	0	–	0	–	–
21	F, 59	4 mo.	1	0	–	0	–	–
22	F, 27	20 yr	1	0	0	0	–	–
23	M, 43	7 yr	4	0	–	0	–	–
24[d]	F, 58	2 yr	2	–	0	–	–	–
25	F, 60	54 yr	1 1/2	0	–	0	–	–
26	F, 29	5 mo.	1 1/2	0	–	0	–	–
27	M, 38	2 mo.	1	1–	–	NR	NR	–
28	F, 53	4 mo.	1 1/2	1–	–	NR	–	–
29[d]	M, 46	1 wk	1/2	1–	–	–	–	–
Total[e]				3/15	2/4	4/15	2/4	0/1

[a] C = cutaneous, S = scalp, O = oral, G = Genital, N = nails.
[b] Results: 3+ = complete remission, 2+ = marked improvement, 1+ = mild improvement, 0 = no improvement, 1– = worsened, – = no involvement recorded, and NR = result not recorded.
[c] Received dose of griseofulvin of 250 mg per day.
[d] Dose of griseofulvin not known.
[e] Fraction of patients with successful therapy (2+ or 3+ response).

RESULTS

Group 1. Of 11 patients with oral lesions only, 3 obtained complete remission and 3 improved markedly. Of these 6 patients who benefited from therapy, 4 had been unsuccessfully treated with topical agents alone and 3 continued topical treatment with griseofulvin. Improvement occurred between 3 weeks and 3 months of therapy. It should be noted that our patients, most of whom live far away, are often not seen more frequently than at 3-month intervals. Two other patients of group 1 are of particular interest. One had no change at 3 months, while the other had slight improvement at 5 months, but both had a definite transient period of improvement early in the course of treatment.

The duration of disease in the responsive group varied from as short as 6 months to as long as 8 years. In the responsive group, 2 patients had disease of short duration (less than 12 months) and 4 had protracted disease (greater than 12 months). The disease duration had no predictive value for response to treatment. The overall response rate, therefore, was 6 of 11 patients (54.5%). This response rate would seem to be noteworthy, particularly because the mucous membrane lesions have been considered to be especially recalcitrant to therapy and augur a prolonged course (1, 11). In addition, since 4 patients in the responsive group had protracted disease, their improvement after 3 weeks to 4 months of treatment is better than that expected from the natural history of the disease.

Group 2. All 18 patients had cutaneous, scalp, or nail involvement with or without oral lesions. Three of 15 patients experienced a significant improvement of their cutaneous lesions; however, one of these 3 continued to develop new lesions while receiving treatment, although the older lesions were resolving. All 3 of these responsive patients had disease of short duration (1, 2, and 6 months). Two patients had a slight improvement of their cutaneous lesions. Ten of 15 patients experienced no beneficial response of their cutaneous lesions, and 3 of these are of special interest. The first (case 29) had only a single lesion of lichen planus and was given griseofulvin for tinea pedis and tinea manuum. After 2 weeks of this therapy, widespread lichen planus developed. The other 2 patients (cases 27 and 28) became worse after 4 and 6 weeks of

griseofulvin therapy; however, it was impossible to determine whether the exacerbation of their disease was due to the drug or to the natural history of lichen planus.

In group 2, 15 of the 18 patients had oral lesions. Four patients obtained complete remission or marked improvement of the oral lesions. Of the remaining 11 patients, 2 had no specific comment recorded on the outcome of the oral lesions, one had slight improvement, and 8 had no improvement. Oral improvement was not as striking in group 2, but the oral lesions in this group tended to be less severe and to attract less clinical attention because of the other areas of involvement.

No conclusions could be drawn regarding scalp, nail, or genital involvement. Only 4 of our patients had scalp involvement. Of these 4, one showed an excellent response, one a good response, one had the drug therapy discontinued early because of drug rash, and one had no clinical change. One patient in our series had nail involvement and was only slightly improved by treatment. Four patients had gemital involvement; 2 obtained complete clearing, and 2 had no results recorded.

Griseofulvin was generally well tolerated. Side effects were a "rash" (2 patients), nausea and constipation (1 patient), and diarrhea (1 patient).

ILLUSTRATIVE CASES

Case 2. A 60-year-old white woman presented to the Mayo Clinic in August 1977 with complaints of sore mouth, tongue, and gingiva since February 1977. The condition had become progressively worse and was especially aggravated by spicy foods. Topical therapy in her home community with an "antibiotic" elixir and nystatin had been unsuccessful. Her general health was otherwise good.

Examination revealed reticular and papular white lesions on both the buccal mucosae and the gingiva. Both the tongue and the posterior buccal mucosa were affected by erosive lesions. The complete blood count and the chemistry group results were normal. Biopsy of the buccal mucosa revealed lichen planus with ulceration. Therapy was started with fluocinonide gel (five to six times each day) applied to the involved areas and with ultra-fine-particle griseofulvin orally (125 mg twice a day).

Within 1 week, the soreness abated, and during the next 3 weeks the lesions slowly resolved. When seen 1 month after her initial visit, her mouth was clear of lesions. Correspondence with the patient 2 years later revealed that she was free of lesions or discomfort. She wrote that she was aware of an occasional "slight irritation", for which she applied fluocinonide gel, which quickly relieved her symptoms.

Case 3. A 76-year-old white woman was seen in October 1976 with a history of white lesions and ulcers in the oral cavity for 6 years. These were aggravated by acid foods and denture irritation. She denied having cutaneous lesions or oral or cutaneous blisters. The pattern of her problem was that she suffered from oral lesions for 2 to 3 months, then experienced remission for 1 to 2 weeks, after which her lesions promptly recurred. Past medical history was significant for diabetes mellitus treated with insulin (Lente, 20 units per day) as well as for hypertension, ischemic heart disease, and aortic insufficiency.

Examination revealed a lacy-white pattern on the buccal mucosae, more extensive on the right than on the left. A plaque also was noted on the right side of her tongue, and a 1-cm ulcer was seen on the left buccal sulcus. Her fingernails were ridged. Complete blood count, chemistry group results, and urinalysis were within normal limits, except for an elevation of blood glucose level to 414 mg/dl. Biopsy specimens of the right buccal mucosa and of the right side of her tongue were interpreted as suggestive of lichen planus. Immunofluorescence of the right buccal mucosa revealed cytoid bodies with IgM and C3. The clinical pattern and biopsy were consistent with the diagnosis of oral lichen planus, and a trial of ultra-fine-particle griseofulvin, 125 mg orally three times a day, without topical treatment, was begun. She was seen 3 months later, at which time she was 80% improved both objectively and subjectively. She was seen again in April 1977, 6 months after the initiation of griseofulvin therapy, at which time she had maintained the improvement, although she had stopped the use of griseofulvin because of the cost.

Case 13. A 10-year-old boy was seen in August 1979. Eight weeks previously, a small red-purple plaque had developed on his right flank, which a dermatologist in his home community had diagnosed as pityriasis rosea. Shortly thereafter, the child had a 2-day febrile illness. During the illness and afterward, the mother noted spreading of these red-purple papules, accompanied by severe pruritus. The child's previous medical history and family history were unremarkable.

Examination revealed mild obesity and red-to-violaceous plaques and papules, with prominent Wickmann's striae spread diffusely on his trunk, arms, and legs. A lacy-white reticulated pattern was noted on both buccal mucosae. Complete blood count and results of urinalysis were within normal limits. The patient was treated with 0.05% triamcinolone cream under wet dressings continuously for 4 days, with relief of pruritus but no change in the lesions. A course of ultra-fine-particle griseofulvin, 125 mg orally three times a day, was started, and 6 weeks later, the patient was in complete remission, with total resolution of the cutaneous and oral lesions.

Case 25. A 60-year-old white woman was seen in November 1975 with a history of intermittent lichen planus since the age of 6 years. Typical attacks lasted 1 to 6 months, and remissions were characteristically long, approximately 6 to 9 years. Her past history was remarkable for peptic ulcer disease and osteoporosis. Family history revealed that two sisters, two brothers, and one nephew also had lichen planus. Previous topical treatments and multiple courses of oral prednisone achieved temporary remissions.

Examination revealed characteristic flat-topped violaceous lesions on the arms, legs, and trunk. White reticulated lesions were noted on both buccal mucosae, more severe on the left than on the right. Complete blood count, urinalysis, and chemistry group results were all within normal limits. Griseofulvin therapy, 250 mg orally twice a day, was begun. When seen 5 weeks later, the patient had stopped taking the drug because she had not noted any benefit. She has been re-examined at our clinic and has experienced a waxing-and-waning course of lichen planus. When last seen in January 1979, she was still symptomatic from her lichen planus.

DISCUSSION

Previous reports have described rapid improvement in clinical lesions of lichen planus within 4 to 8 weeks of griseofulvin treatment (7–9). These previous studies have not strictly delineated their patients with oral versus other lesions, except to state that similar, moderate improvement was noted in the mucus membrane lesions (7). Our results are primising, but certainly not as dramatic. Impressive improvement of the nails in lichen planus has not been seen (3, 5), and our one patient with nail involvement was also only slightly improved.

The chance of complete remission or significant improvement in patients with protracted uncomfortable or unremitting oral lichen planus treated with griseofulvin appears to be about 50%. Improvement in oral lesions has been briefly alluded to before in an isolated case report (5). In cutaneous lichen planus, benefit from griseofulvin therapy appears to be much less likely, but a trial may be warranted when the disability and discomfort are great. We have no data regarding the duration of remission obtained by many of our patients. Prospective studies are needed to better assess the effectiveness of griseofulvin in the treatment of lichen planus. However, our present study provides some data that will be helpful in establishing the framework for such a future study.

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