efits deriving from the use of safer, non-steroidal anti-inflammatory agents. In this double-blind controlled trial the outcome of sequential therapy with the NSAID nimesulide and the H1-antagonist ketotifen was substantially equivalent to that obtained with a 7-week taper of prednisone, with almost complete resolution of the disease at the end of both treatments. The response to the steroid was more prompt, with a sharp decrease of mean number of recurrences within the first 2 weeks; on the contrary, nimesulide + ketotifen therapy led to a slower but more continuous decline of disease activity. Unfortunately, because of the high number of patients lost to follow-up, too few data were available for proper statistical analyses of post-treatment outcome. Nevertheless, we believe that the results obtained support the possibility that the preliminary administration of a non-steroidal agent is able to lower the response threshold of DPU to antihistamines. Future follow-up studies will verify this hypothesis.

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Lichen Planus and Hepatitis C Virus Infection: A Clinical and Virologic Study

Sir,
The possible link between hepatitis C virus (HCV) infection and lichen planus (LP) has been raised in some series which have shown a high prevalence of HCV markers in patients with lichen planus (1 – 4). Some evidence shows that the HCV genotype may be one of the factors influencing the severity and outcome of liver disease (5). In a French study, it has been found that all of the HCV genotypes common in patients with chronic HCV of this country could be detected in HCV-infected LP patients (6). We have evaluated here whether some clinical features and humoral immunologic abnormalities of LP patients are associated with specific HCV genotypes.

MATERIAL AND METHODS

The study included 13 consecutive patients (9 females, 4 males; mean age 63.9, range 29 – 78 years) with LP and HCV infection diagnosed at the Department of Dermatology of Hospital Universitario de la Princesa, Madrid, between December 1991 and March 1994. The diagnosis of LP was assessed by (i) clinical changes typical of LP and (ii) histopathologic examination of cutaneous and/or mucosal lesions. A group of 130 patients diagnosed as chronic hepatitis associated with HCV infection were selected as controls. The results were analysed using the chi-square test. Routine liver profile, immunoglobulins G, A and M, the antinuclear, smooth muscle, antimitochondrial, antiparietal cell, liver-kidney microsome, antithyroid autoantibodies and HCV antibodies were performed as described in our previous report (1). Nested polymerase chain reaction (PCR) was performed to detect HCV RNA using primers from the highly conserved 5′ non-coding region of the HCV genome (7). Titrations of positive RNA were performed using semiquantitative PCR, by Amplicor HCV Monitor (Roche Diagnostic Systems, Branchburg, NJ). The method described by Stuyver et al. (8) was used for genotyping, which is now available as Inno-Lipa HCV II (Innogenetics N.V., Germany).

RESULTS

The clinical and laboratory features of patients with LP associated with the presence of HCV-RNA are summarized in Table I. Of the 13 patients with LP and HCV infection, 9 (69%) were infected with HCV genotype 1b, 3 (23%) with genotype 1a and 1 (8%) with genotype 2a/2c. The localization and duration of HCV-related LP patients was the same irrespective of the genotype of infecting HCV. In eight cases, LP was diagnosed at the same time as HCV infection and in five patients the diagnosis of LP was made 7 to 22 years after evidence of liver disease had been detected.

No significant differences existed between patients of both groups as to HCV-1 and HCV-2 types and subtypes, whilst HCV-3a was found in 10 and HCV 4c/4d in 5 patients with chronic C hepatitis. Patients with LP and HCV infection had abnormal transaminase levels and increased polyclonal gammaglobulin levels were observed in eight patients. Only two patients (15%) had serum antinuclear antibodies at a significant titer ($>1/40$) and antithyroid antibodies were found in two (15%), both being antithyroglobulin. These immunologic abnormalities were observed in patients infected with the serotypes 1 and 2.

DISCUSSION

In this series of 13 HCV-positive consecutive patients with LP, HCV RNA has been detected, reflecting an active replication of the virus. The HCV RNA levels in serum were high in 12 of these patients and the HCV genotype associated to LP was

Table I. *Clinical and laboratory findings of LP associated with HCV infection in patients from Spain*

Pat. no.	Sex/age	Clinical findings	Duration of LP	HCVAb ELISA	HCV RNA (cop/ml)	HCV genotypes
1	M/51	Buccal reticular striae and cutaneous LP	20 months	+	8.4×10^5	lb
2	F/71	Buccal erosive LP	>5 years	+	1.4×10^5	2a/2c
3	F/61	Buccal erosive LP	>5 years	+	1.0×10^6	1b
4	M/78	Buccal erosive LP	>5 years	+	8.0×10^5	1b
5	M/29	Buccal reticular striae	>5 years	+	1.3×10^3	1b
6	F/69	Cutaneous LP	6 months	+	6.3×10^5	1b
7	M/71	Buccal and genital erosive LP	>4 years	+	1.8×10^6	1b
8	F/72	Buccal reticular striae and cutaneous LP	8 months	+	5.5×10^4	1b
9	F/71	Cutaneous LP	4 months	+	6.9×10^5	1a
10	F/45	Buccal reticular striae and cutaneous LP	2 years	+	7.9×10^5	1a
11	F/71	Buccal erosive LP and cutaneous LP	>3 years	+	5.0×10^5	1b
12	F/64	Buccal reticular striae and cutaneous LP	>3 years	+	2.3×10^5	1a
13	F/78	Buccal reticular striae and cutaneous LP	>3 years	+	7.3×10^5	1b

F, Female; M, Male; LP, Lichen Planus; HCV, Hepatitis C Virus.

mostly 1b, which is the most frequent in our geographic area. No correlation existed between the erosive mucosal LP lesions and the high HCV RNA levels. Nagao et al. (9) determined that no significant differences existed in HCV genotype between chronic hepatitis C patients with and without oral LP lesions, suggesting that oral LP pathogenesis was a result of host rather than viral factors.

In our study, the occurrence of serum antinuclear and antithyroid antibodies was detected in 54% of HCV-positive patients with LP, which seems to be a nonspecific finding possibly related to HCV-induced immunologic alterations favouring the synthesis of autoantibodies by B lymphocytes.

The pathogenic mechanisms of HCV in LP are unknown, but several observations suggest that HCV probably acts as a major triggering factor for the development of the clinical changes in some cases of LP: (i) In our geographical area the prevalence of positive HCV RNA (16%) in LP patients was significantly higher than that found in control dermatological patients (2.4%) (1) and also in that of volunteer blood donors (0.45%) (10). (ii) In 5 out of 13 HCV-positive patients, the clinical manifestations of hepatitis were noted before the onset of LP and in the remaining patients the LP was diagnosed at the same time as the HCV infection. However, our study demonstrated that the clinical changes of LP are not a consequence of a specific HCV genotype, because HCV genotypes present in patients with chronic hepatitis C can be detected in cases with LP and HCV infection.

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