

# Lichen Planus is Not Associated with Hepatitis C Virus Infection in Patients from North West England

SIMON C. TUCKER<sup>1</sup> and IAN H. COULSON<sup>2</sup>

<sup>1</sup>Section of Dermatology, University of Manchester, Hope Hospital, Salford and <sup>2</sup>Department of Dermatology, Burnley General Hospital, Lancashire, UK

**It has been suggested that infection with hepatitis C virus may be associated with the development of lichen planus and that geographical area may be an important factor affecting the relative risk. The present 2-centre, prospective, epidemiological study investigates this possible association in north west England. A total of 45 patients with classical and/or erosive mucous membrane lichen planus and 32 controls were tested for seropositivity to hepatitis C virus. None of the patients with lichen planus and only 1 of the control patients had serological evidence of infection with hepatitis C. Whilst there may be an important association between these 2 diseases in other countries, this study suggests that this does not appear to be the case in north west England and, furthermore, provides no evidence to advise routine investigation to exclude hepatitis C in patients with lichen planus in this region. Key words: lichen planus; hepatitis C; epidemiology; UK.**

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S. C. Tucker, Section of Dermatology, University of Manchester, Hope Hospital, Stott Lane, Salford, M6 8HD, UK. E-mail: stucker@fs1.ho.man.ac.uk

In 1991 reports began to emerge of the coexistence of lichen planus (LP) and hepatitis C virus (HCV) infection, and over the past 7 years many cases of this association have been described (1–11). It is acknowledged that this may be a fortuitous association (12–14), but other authorities believe that there now exists sufficient evidence to propose a causal role for HCV in LP (15, 16).

There appears to be wide international variation in this proposed link between the 2 conditions. In a study from Japan 37.8% of 45 patients with lichen planus had serological evidence of HCV infection (17). Italy, Spain and Germany are other countries in which surprisingly high levels of HCV infection have been described in patients with LP (16, 18, 19). On the other hand, a study from France found that only 3.8% of 52 patients with LP also had HCV, which was not significantly higher than among their controls (20). This may be partly explained by varying levels of HCV endemicity between different geographical areas. The predominantly urban north west of England has major problems with illicit intravenous drug abuse, constituting a significant risk factor for the development of HCV. Despite this, the level of endemic HCV infection in the region is low. This case-control study was conducted to investigate whether our patients with LP demonstrated a significant association with HCV.

## MATERIAL AND METHODS

Between October 1996 and August 1998, 45 consecutive patients (21 males, 24 females) with newly diagnosed or chronic classical and/or erosive mucous membrane lichen planus were identified in our departments and enrolled in the study. Diagnosis was based on both

clinical and histopathological findings. If a drug-induced lichenoid eruption was suspected, the patient was excluded, otherwise all lichen planus cases were included. The average age of patients was 51.2 years (range 24–76 years). Thirty-two patients had classical cutaneous LP. Four of these also had non-erosive oral lesions. Thirteen patients had erosive oral (9 patients) or vulval (4 patients) lichen planus.

From September 1997 to January 1998, 32 randomly selected patients (18 males, 14 females; age range 18–87 years; mean 51.6 years) admitted to our dermatology ward with dermatoses other than LP, and with no history of preceding LP, were identified and enrolled in the study and served as controls.

All the patients were asked about possible risk factors for HCV or liver disease, including previous history of blood transfusions, intravenous drug abuse and their weekly alcohol intake. Sera were tested for the presence of HCV antibodies using a second-generation enzyme-linked immunosorbent assay (ELISA-2; Sanofi Pasteur Diagnostics, Marnes La Coquette, France). Positive ELISA results (ratio >1) were confirmed using a third generation recombinant immunoblot assay (RIBA; Chiron Corporation, Emeryville, CA, USA). By way of screening tests for liver disease, blood was also sent for evaluation of serum levels of alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin (BR) and gamma glutamyltransferase (GGT). The modified  $\chi^2$  test was used for statistical comparison of the 2 groups, where relevant. The study was approved by both the Salford and the Burnley and Pendle Research Ethics Committees and all patients gave written, informed consent.

## RESULTS

Table I lists the demographic and risk factors for HCV infection, and the biochemical and virological characteristics of all the patients (LP and controls) included in the study.

None of the 45 patients with LP had anti-HCV antibodies by ELISA-2, compared with 1 of the 32 controls. That patient's result was confirmed by RIBA. One or more liver function test (LFT) abnormalities were found in 10 (22.2%) of the LP patients and 10 (31.3%) of the controls. This difference was not statistically significant. These abnormalities were felt to reflect excessive alcohol consumption or undiagnosed Gilbert's syndrome in all cases.

## DISCUSSION

The key finding from this study is that none of our patients with LP had concomitant infection with HCV. This is in vivid contrast with results from similar studies conducted in Japan, Italy, Spain, and Germany (16–19), and our results suggest no evidence for an aetiopathogenetic role for HCV in LP in this country. Furthermore, and in support of our observations, a recent study from London found no cases of HCV infection among 55 British patients with oral (LP) (21). In addition, the same group had previously found no significant association between liver dysfunction and oral LP in 180 patients (22).

In the face of such contrasting international results, the authors feel that the relevance, if any, of co-existent HCV

Table I. Characteristics of lichen planus patients and controls

Variable	LP (n=45)	Controls (n=32)
Mean age (years)	51.2	51.6
(range)	(24–76)	(18–87)
Sex (male/female)	21/24	18/14
Weekly alcohol consumption (units)	11.9	56.7 (n=9)
Blood transfusions	5	3
Intravenous drug abusers	0	0
Abnormal LFT levels	10	10
ALT mean (IU/l)	36.3	28.3
ALP mean (IU/l)	75.9	88.6
BR mean ( $\mu\text{mol/l}$ )	11.7	8.8
GGT mean (IU/l)	49.9	51.8
Anti-HCV positive	0	1

LFT: liver function tests; ALT: alanine aminotransferase; ALP: alkaline phosphatase; BR: total bilirubin; GGT: gamma glutamyltransferase.

infection in LP remains a mystery. We do not feel that differing geographic endemic levels of HCV provide an adequate explanation for these conflicting observations because the prevalence of HCV antibodies is reasonably constant worldwide, ranging from 0.3% to 1.5% (23). We feel that it is likely that other, probably host-related, factors may also be important. Such factors might include host immune dysregulation or concomitant immunomodulatory infections.

The situation is further complicated by the heterogeneous nature of the response to interferon therapy in LP patients infected with HCV. Initial reports described improvement or disappearance of LP in HCV patients treated with interferon (4). Since then, however, several cases have been detailed in which LP was aggravated by interferon, and in 1 patient LP even appeared for the first time during anti-viral treatment (24–26).

Although this study does not resolve the issue of the aetiology of LP, it does provide evidence against a link between LP and HCV, certainly in this region. We believe these results should be of interest to the practising dermatologist, since they argue against the need for the expense and inconvenience of routine venous blood sampling of LP patients to rule out HCV.

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