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Lichen planus and HCV infection in Turkish patients

Türk hastalarda liken planus ve hepatit C virus enfeksiyonu

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Background/aims: *A relation between hepatitis C virus (HCV) infection with lichen planus (LP) has been reported in the literature but remains controversial. To find out the prevalence of HVC infection among patients with LP.* ***Methods:*** *Forty-one cases of LP diagnosed at the Dermatology Clinic of our hospital between March 1995 and May 1996 were evaluated (22 men and 19 women; mean age 41.6 years). They were screened for the presence of HBsAg, anti HBs, and anti-HCV by ELISA and HCV-RNA by nested polymerase chain reaction (PCR). Blood donors registered in Ankara University îbni Sina Hospital Blood Bank were used as a control group.* ***Results:*** *Of the 41 LP patients, 2 (4.8%) had anti-HCV positivity together with HCV-RNA positivity. Twelve patients (29.2%) had anti-HBs and 3 patients (7.3%) had HBsAg positivity. In blood donors, anti-HCV positivity prevalence was 2.5%.* ***Conclusions:*** *The results of this study suggest that no relationship exists between hepatitis C virus infection and lichen planus among Turkish patients.*

Keywords: Lichen planus, hepatitis C infection, epidemiology, Turkey

Amaç: *Literatürde hepatit C virüsü (HCV) enfeksiyonu ile liken planus (LP) arasında bir ilişki olduğu bildirilmiştir fakat halen sonuçlar çelişkilidir. Türk LP hastalarında HCV enfeksiyonu sıklığını saptamak.* ***Yöntem:*** *Mart 1995 ile Mayıs 1996 tarihleri arasında hastanemizin Dermatoloji Kliniği'ne başvuran 41 liken planus hastası (22 erkek, 19 kadın; ortanca yaşları 41.6) değerlendirildi. Hastalarda HBsAg, anti-HBs, anti-HCV varlığı ELISA yöntemi ile ve HCV-RNA varlığı nested-PCR yöntemi ile araştırıldı. Kontrol grubu olarak Ankara Üniversitesi İbni Sina Hastanesi Kan Bankası'na kayıtlı olan kan donörleri kullanıldı.* ***Bulgular:*** *41 LP hastasının 2'sinde (% 4.8) anti-HCV ve HCV-RNA birlikte pozitif saptandı. 12 hastada (% 29.2) anti-HBs, 3 hastada (% 7.3) HBsAg pozitif saptandı. Kan donörlerinde anti-HCV pozitiflik sıklığı % 2.5 olarak bulundu.* ***Sonuç:*** *Bu çalışma sonucunda Türk hastalarda hepatit C virüsü enfeksiyonu ile liken planus arasında anlamlı bir ilişki saptanmamıştır.*

Anahtar kelimeler: Liken planus, hepatit C enfeksiyonu, epidemiyoloji, Türkiye

INTRODUCTION

Lichen planus (LP) is an inflammatory pruritic disease of the skin and the mucous membranes characterized by distinctive papulosquamous lesions with a predilection for the flexor surfaces and the trunk (1, 2). It may present as an acute self-limiting disorder or chronic recurrent disease that affects men and women between 30 to 60 years of age. Although the etiology of LP is not known, some reports have suggested an association of LP with diabetes mellitus (3), myasthenia gravis, thymoma (4) and with some drugs (1). Possibility of genetic predisposition and abnormal immune mechanisms are also thought to be important (5-8).

Recently many studies have drawn attention to the coexistence of LP with liver diseases including primary biliary cirrhosis (PBC) (9, 10) and chronic active hepatitis (CAH) (11-14). The association of LP with hepatotropic viruses has also been reported (12, 15-20, 21-24), but it is controversial. Some studies reported a relationship between hepatitis B virus (HBV) and LP (12, 15, 16). Hepatitis C virus (HCV) infection, which has many extrahepatic manifestations, has also been detected in patients with LP in some studies (17, 18, 20, 23-26). But there are many conflicting reports about the etiopathologic role of these viruses (25, 26), and it

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is suggested that the geographic origin of the patients could be an important factor of HCV prevalence in patients with LP. We designed this study to determine the prevalence of HCV infection in patients with LP in Turkey.

MATERIALS AND METHODS

Forty-one cases of LP diagnosed at the Dermatology Clinic of our hospital between March 1995 and May 1996 were enrolled in our study. All were diagnosed with usual clinical features and histopathologic findings of LP. Twenty-two of them were men and 19 were women, and their ages ranged from 9 to 74 years (average 41.6 years). Thirty-three patients presented with only cutaneous lesions, one had genital and buccal lesions and the remaining seven patients had buccal and cutaneous LP.

All patients were studied for their serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl-transpeptidase (GGT) and bilirubin by standard laboratory methods. Enzyme-linked immunosorbent assays (ELISA) were performed for HBV markers, including hepatitis B surface antigen and hepatitis B surface antibodies. Anti-HCV antibodies were searched by second generation ELISA (Abbott Diagnostic Systems). HCV RNA was tested by nested polymerase chain reaction (PCR) in all patients. As control group, representing a small sample of the normal population, we determined the percentage of anti-HCV positivity among 18, 360 blood donors applying to Ankara University Ibni Sina Hospital Blood Bank between 2000-2001. Anti-HCV status of blood donors had been determined by ELISA.

RESULTS

The features of patients are shown in (Table 1). Two of 41 patients (4.8%) with LP had anti-HCV antibodies by ELISA, and in both HCV RNA was detected by PCR, proving active viral replication. None of the 39 anti-HCV negative patients were HCV-RNA positive. Twelve patients (29.2%) were found to have anti-HBV antibodies in their serum. Three patients (7.3%) were HBsAg (+) and anti HBsAg (-). Abnormal transaminase levels were found in eight patients (19.5%); two of them were anti-HCV (+), and three were HBsAg (+) patients. Three other patients with mild elevated transaminases were found to have steatosis on ultrasound. Only one patient had a history of blood transfusion and he was HBsAg (+). The clinical and laboratory features of HBV and HCV patients are summarized in Table 2. The two patients with anti-HCV positivity and LP had chronic active hepatitis, and two of the three patients with HBV infection had CAH; one patient had cirrhosis. Among the 18, 360 blood donors seen at Ankara University Ibni Sina Hospital Blood Bank in one year, anti-HCV prevalence was found as 2.5%. HBsAg positivity among the 41 patients with LP was 7.3%.

Table 1. Features of LP patients

Patients	(n = 41)
Mean age	41.6 (9-75)
Sex (male/female)	22/19
Blood transfusions	1
Surgical operations	6
Abnormal transaminases	8
HBsAg(+)	3
Anti HBsAg .(+)	12
Anti HCV (+)	2
HCV RNA (+)	2

DISCUSSION

Lichen planus is a relatively common benign, chronic inflammatory disease of unknown etiology. It affects both the skin and the mucous membranes. Recently in many studies, both the cutaneous and mucosal forms of the disease have been related to chronic HCV infection. However,

Table 2. Clinical and laboratory findings of LP patients with elevated serum transaminases

Patient no	sex/age	clinica findings	serum ALT	HbsAg	AntiHBs	AntiHCV	HCV RNA
1	F/50	Cut./buccal	51IU/L	(-)	(+)	(-)	(-)
2	M/41	Cutan. LP	57IU/L	(+)	(-)	(-)	(-)
3	M/66	Cutan. LP	62IU/L	(-)	(+)	(-)	(-)
4	M/40	Cutan. LP	89IU/L	(+)	(-)	(-)	(-)
5	F/56	Cutan. LP	56IU/L	(-)	(-).	(+)	(+)
6	F/62	Cutan. LP	60IU/L	(-)	(-)	(+)	(+)
7	M/36	Cutan. LP	55IU/L	(+)	(-)	(-)	(-)
8	F/55	Cutan. LP	65 IU/L	(-)	(-)	(-)	(-)

data on this subject are controversial because of the high variability in results of different studies.

In our study we did not find an increased prevalence of HCV infection in patients with LP when compared to the blood donor population of our hospital. Our study thus confirms a previous study from Turkey on this subject (27). The rate of HBsAg positivity found in this study is unlikely to be different from the HBV incidence in this area, which has been reported to be 5.7% among blood donors in central Anatolia (28).

Liver abnormalities in LP were first suggested by the demonstration of coexistence of LP with PBC (9, 10). Results of a large multi-center cohort study involving 577 LP patients was then published by GISED (Grouppo Italiano Studi Epidemiologici in Deramatologia) in 1990, and it reported an association between LP and liver disease (12). They found that the risk of LP was two times higher in patients with liver disorders (with high transaminase levels or HBsAg positivity). In another study, Rebora et al. (14) reported that the prevalence of HCV antibodies was 14% in a series of 87 patients with LP. In another study from Italy, Mignogna et al. (29) found that 28.8% of oral LP patients were HCV positive, with a statistically significant difference compared to the control group. Recently, a study from Spain reported anti-HCV positivity of 8.9% in 101 patients with LP compared to 2.02% in the control group (30). Nagao et al. (31) from Japan found a 13.6% LP prevalence in 81 anti-HCV positive patients, whereas LP prevalence was 3.4% in 29 patients with chronic hepatitis B infection. There are many other trials (18-20, 21, 23, 32, 33, 34, 35, 36) supporting an association of LP with HCV infection. However, there are also studies showing no association between LP and HCV infection (25, 26, 27, 37, 38, 39). The reported frequency of anti-HCV antibodies in groups of oral LP and/or cutaneous LP patients varies from 4% to 65% (39, 40). As a general comment, it can be said that epidemiologic studies show a geographical difference in the distribution of HCV infection among LP patients, with higher prevalences in southern Europe (Spain, Italy), Germany and Japan, and lower prevalences in England and northern France (40, 41). This geographical variation may be a consequence of viral or host factors. With regard to the former, virological studies performed in countries with both higher and lower prevalence of HCV in LP patients have shown no significant differences in serum levels of HCV RNA or in HCV genotypes between HCV-infected patients with and without LP (36, 42-44). There are only a few studies investigating the role of host factors. In one such study performed by Carrozzo et al. (41) from Italy, major histocompatibility complex class II alleles were assessed in patients with HCV-related LP, and it was found that patients with pure oral LP and HCV infection possessed the HLA-DR6 allele more frequently than patients with pure oral LP but without HCV infection ($p=0.028$). However, this is only one study, the results of which need to be confirmed. Still, this study could serve as a clue in understanding the geographic variation in incidence of HCV infection in patients with LP around the world. Our study further supports the notion that the relation between these two diseases discloses a geographic variation for which host factors may be responsible.

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