Examination of Sera and Lesional Biopsy Specimens of Patients with Psoriasis for the Presence of HCV Antibodies and HCV RNA

PSORİAZİSTE SERUMDA VE LEZYONEL DERİDE HCV ANTİKOR VE HCV RNA VARLIĞININ ARAŞTIRILMASI

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Summary

Background: Hepatitis C virus (HCV) is the main cause of parenterally transmitted non-A, non-B viral hepatitis. HCV infection has been proposed to induce psoriasis through immunologic mechanisms.

Objective: The aim of this study was to evaluate the prevalence and the pathogenic role of HCV in patients with psoriasis.

Methods: Sixty three patients with psoriasis and a control group of 63 age and sex-matched patients with minor dermatological disorders were enrolled in the study. Anti-HCV antibody status were evaluated by ELISA. RT PCR was utilized to examine HCV RNA in sera and lesional cutaneous biopsy samples of HCV-infected patients.

Results: Anti-HCV antibodies were detected by ELISA in 5 of 63 psoriasis (7.9%) and 3 of 63 control patients (4.8%). The difference between psoriasis group and control group was not statistically significant (p=0.46). HCV RNA was detected in sera of 4 of 5 HCV-infected patients with psoriasis. None of these 4 patients had HCV RNA in lesional biopsy samples by RT PCR.

Conclusion: We conclude that HCV infection rate is not increased in patients with psoriasis and our data does not support an important pathogenic role for HCV in psoriasis.

Key Words: Psoriasis, HCV infection, Polymerase chain reaction

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Özet

Giriş: Hepatit C virüsü (HCV) kan yoluyla edinilen A ve B dışı hepatitlerin en sık etkenidir. HCV infeksiyonunun immünolojik mekanizmalar ile psoriazisi tetikleyebileceği ileri sürülmektedir.

Amaç: Bu çalışmada psoriazis hastalarında HCV'nün prevalansının ve virüsün olası patojenik rolünün belirlenmesi amaçlanmıştır.

Hastalar ve Yöntem: Çalışmaya ardışık 63 psoriazis hastası ve yaş ve cinsiyetleri uygun 63 kontrol hastası alınmıştır. Anti-HCV antikor pozitifliği ELISA ile değerlendirilmiş ve HCV pozitifliği saptanan olgularda revers transkriptaz polimeraz zincir reaksiyonu (RT PCR) ile serum ve lez-yonel dokuda HCV RNA varlığı araştırılmıştır.

Bulgular: ELISA ile 5 psoriazis hastasında (7.9%) ve 3 kontrol hastasında (4.8%) anti-HCV antikor pozitifliği saptanmış ve iki grup arasında istatistiksel olarak anlamlı fark bulunmamıştır (p=0.46). HCV infeksiyonu olan 5 psoriazis hastasının 4 ünde serumda HCV RNA varlığı gösterilmiş ancak bu 4 hastanın hiçbirinde RT PCR ile deri dokusunda HCV RNA varlığı saptanmamıştır.

Sonuç: Bulgularımız psoriaziste HCV infeksiyon prevalansının artmadığını göstermekte ve HCV'nün psoriazis olgularında patojenik rolü olduğu hipotezini desteklememektedir.

Anahtar Kelimeler: Psoriazis, HCV infeksiyonu, Polimeraz zincir reaksiyonu

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Hepatitis C virus (HCV) infection can be associated with disorders of various organs other than the liver, including the skin (1). Cryoglobulinemia associated vasculitis, poliarteritis nodosa, sporadic

porphyria cutanea tarda, urticaria, etythema multiforme, erythema nodosum, pruritus, mucosal and cutaneous lichen planus are the main dermatological disorders associated with HCV infection (1,2). In recent years there have been reports of increased prevalence of HCV infection in patients with psoriasis suggesting a pathogenic role for this virus in psoriasis (3-5).

The purpose of this study was to evaluate the prevalence of HCV infection in psoriasis patients.

Materials and Methods

Patients and Control Group

The present study includes 63 sequential patients with psoriasis, admitted to the Dermatology department of Kırıkkale University Faculty of Medicine between July 1998 and December 1999. For the purpose of discussion, psoriasis was classified clinically as severe (generalized psoriasis involving > 50% of body surface area, erythrodermic psoriasis, generalized pustular psoriasis and psoriatic arthritis), moderate (psoriasis involving 10-50% of body surface area) and mild (psoriasis involving < 10% of body surface area and palmoplantar pustular psoriasis). A control group of 63 age and sex-matched patients with minor dermatological disorders were selected among dermatological outpatients.

Our psoriasis and control groups comprised 27 males and 36 females. The age range for both groups were 5-84 (mean 37.36±2.29). The duration of psoriasis ranged from 1 month to 56 years (mean 44.92±11.57 months; median 18.00 months). Eighteen of 63 patients with psoriasis (28.6%) had mild disease, 26 (41.2%) had moderate disease (5 had guttate psoriasis) and 19 (30.2%) had severe disease (2 had psoriatic arthritis). None of the patients had erythrodermic or generalized pustular psoriasis.

Methods

Blood samples were drawn from patients and stored at -20ºC until tested. Anti-HCV antibodies (UBI HCV EIA 4.0; Organon Teknika; Netherlands) were detected by ELISA. Transaminases were assayed by AST-ALT reagents (Sigma diagnostics) in Hitachi 717 automatic analyzer (Boehringer; Germany). In HCV positive cases, RT PCR was performed to amplify HCV RNA in serum and in routinely processed paraffin-embedded lesional biopsy samples as described previously. A 251 bp long target sequence selected from the highly conserved 5' non-coding region of the HCV genome was amplified by using MasterAmp RT-PCR kit (Epicenter Technologies). Paraffin-embedded liver biopsy specimen of a patient with positive serum HCV RNA was used as positive control.

Statistical Analysis

The results were statistically analyzed by PC using SPSS 6.0 program. In comparison of groups, categorical data have been tested by using chi-square test. Mann Whitney U test has been utilized to compare numerical data. A p value of £ 0.05 was considered significant.

Results

Serum values of psoriasis patients for AST and ALT ranged between 10-121 (mean 36.01±3.03) and 11-206 (mean 36.12±3.88) respectively. Anti-HCV antibodies were detected by ELISA in 5 of 63

Table 1. Characteristics of anti-HCV positive psoriasis patients (N=5)

Patient no	Sex/age	Duration of psoriasis	Clinical severity	ALT/ AST	Route of HCV transmission	HCV RNA in serum	HCV RNA in lesion
1	M/65	chronic	moderate	78/64	Blood transfusion?	+	-
2	M/43	2 years	moderate	15/18	Unknown	+	-
3	F/33	6 months	mild	16/12	Unknown	-	NP
4	F/17	2 months	moderate	126/104	Unknown	+	-
5	F/84	chronic	moderate	54/62	Unknown	+	-

The clinical, laboratory and molecular biologic features of anti-HCV positive psoriasis patients (M: male; F: female; ALT: serum alanine transaminase; AST: serum aspartate transaminase; +: positive; -: negative; NP: not performed).

Table 2. Prevalence of hepatitis markers in patient and control groups

Patient and control groups	Anti-HCV (+)	
	#	(%)
Psoriasis (n=63)	5	(7.9)
Control group (n=63)	3	(4.8)
General population		(1)

The comparison of patient and control group for prevalence of anti-HCV antibodies (# : number of patients; %: percentage of affected patients; anti-HCV: hepatitis C virus antibodies; (+): positive).

psoriasis (7.9%) and 3 of 63 control (4.8%) patients. The difference between the two groups was not statistically significant (p=0.46). The HCV prevalence of both groups were higher than the reported HCV prevalence of 1% in general Turkish population (6). The clinical and laboratory characteristics of anti-HCV positive psoriasis patients are presented in Table 1 and comparison of groups are shown in Table 2.

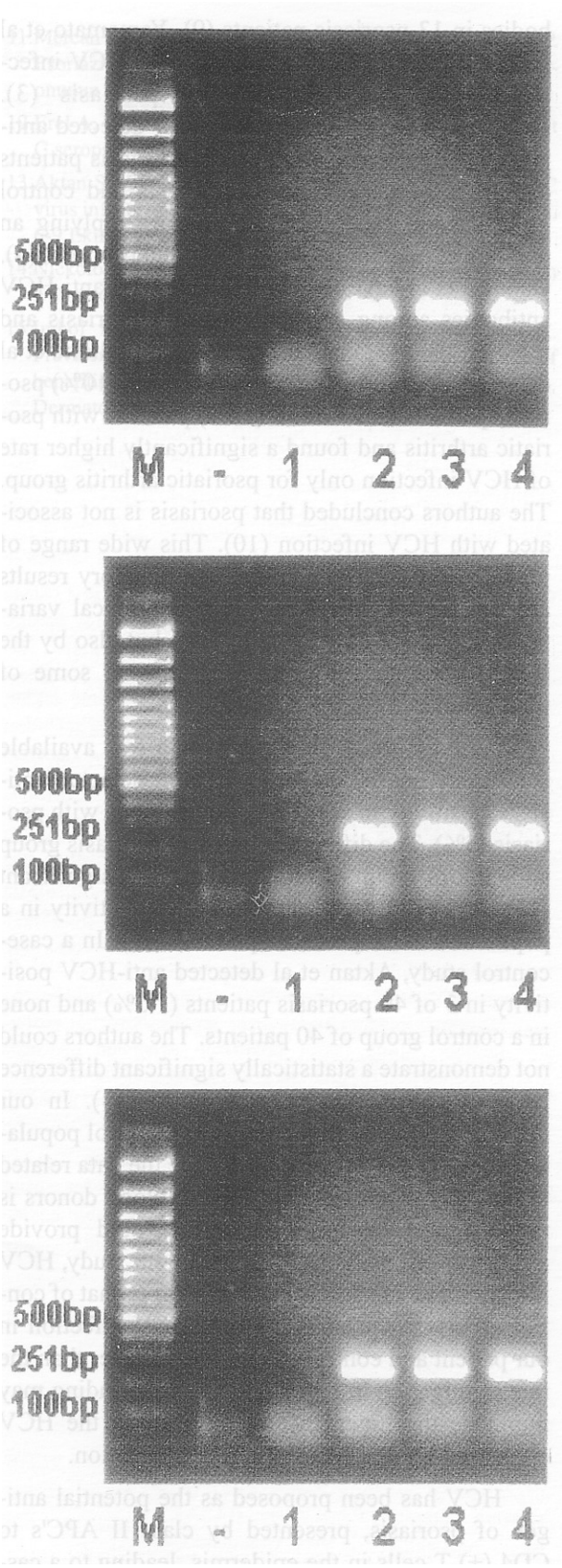
When the anti-HCV positive and negative psoriasis patients were compared, there was no statistically significant difference between the two groups in terms of age (u=103.5; p=0.29), gender (p=0.89), duration of disease (u=122.5; p=0.56), serum ALT (u=111.5; p=0.39) and AST (u=112.5; p=0.40) levels. Anti-HCV positivity did not correlate with severity of psoriasis (p=0.15).

By PCR, HCV RNA was detected in sera of 4 of 5 HCV-infected psoriasis patients. None of these 4 patients had HCV RNA demonstrable by RT PCR in lesional samples.

Discussion

Psoriasis is an inflammatory skin disease of unknown etiology. Many observations indicate that T cells play an important role in the pathogenesis of the disease. Infections have been implicated in the etiology of psoriasis (7) and T-cell activating antigens could be derived from distant or local viral infections (8).

There have been a few studies assessing the prevalence of HCV infection among psoriasis patients. Burrows et al failed to detect anti-HCV anti-



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bodies in 13 psoriasis patients (9). Yamamato et al have reported 8 (10.1%) patients with HCV infection among 79 patients with psoriasis (3). Kanazawa et al in a controlled study detected anti-HCV positivity in 9 of 27 (33%) psoriasis patients and the difference between psoriasis and control groups were statistically significant, implying an etiological relation between HCV and psoriasis (4). Chouela et al have found 9 patients with anti-HCV antibodies among 118 patients with psoriasis and reported the prevalence as 7.6% (5). Taglione et al detected anti-HCV antibodies in 5 of 50 (10%) psoriasis patients and 6 of 50 (12%) patients with psoriatic arthritis and found a significantly higher rate of HCV infection only for psoriatic arthritis group. The authors concluded that psoriasis is not associated with HCV infection (10). This wide range of prevalence (0% to 33%) and contradictory results are caused not only by wide geographical variations in the rate of HCV infection, but also by the lack of case-specific control groups in some of these studies.

As for Turkey, the results of a few available studies are conflicting. Mercan et al detected anti-HCV positivity in sera of 3 of 60 patients with psoriasis (5%). The difference between psoriasis group and control group of blood donors was significant (11). Erel et al found no anti-HCV positivity in a population of 50 psoriasis patients (12). In a case-control study, Aktan et al detected anti-HCV positivity in 3 of 40 psoriasis patients (7.5%) and none in a control group of 40 patients. The authors could not demonstrate a statistically significant difference between patient and control group (13). In our opinion, the use of blood donors as control population may cause statistical bias since the data related to the HCV prevalence in Turkish blood donors is rather old. Case-control studies would provide more accurate statistical results. In our study, HCV infection rate in psoriasis was similar to that of control group. However the rate of HCV infection in our patient and control groups were higher than the rate of infection in blood donors. This finding may implicate the urgent need for updating the HCV epidemiology in general Turkish population.

HCV has been proposed as the potential antigen of psoriasis, presented by class II APC's to CD4 (+) T cells in the epidermis, leading to a cascade of events resulting in epidermal proliferation (7). It has been suggested that actively replicating HCV in cutaneous tissue could act as a superantigen and induce self reactive T-cell clones, resulting in psoriatic lesions (14). Alternatively, HCV immune complexes have been reported to result in the development of psoriasis at sites of cutaneous deposition (4). Despite these proposals, the pathogenic role of HCV in the development of psoriasis is obscure. Studies investigating the presence and replication of HCV within the lesions could provide objective evidence for a direct causal relationship (15). Previously Yamamato et al could demonstrate HCV mRNA in lesional tissue of 2 psoriasis patients by RT PCR. The authors suggested that HCV infection may cause immunologic abnormalities that may trigger psoriasis (3). In our study, HCV RNA was absent in lesional skin of 4 HCV-infected psoriasis patients, indicating that the virus could not be a potential antigen or superantigen in psoriasis. However, the results of the present study can not rule out the possibility that HCV infection could lead to the development of psoriasis by a postinfectious breakdown of self tolerance or as a result of antigenic mimicry (7).

In conclusion, HCV infection rate is not significantly increased in psoriasis patients and our data does not support a direct causal role for HCV in pathogenesis of psoriasis. We believe that the virus may be an innocent bystander in psoriasis patients with HCV infection. Further virological studies in HCV-infected patients with psoriasis will resolve the present controversies.

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