

Hepatitis C and hepatitis B virus infections in the etiopathogenesis of pemphigus*

Gulsen Tukenmez Demirci¹
Ayse Tulin Mansur³
Ilknur Kivanc Altunay⁵

Ikbal Esen Aydingoz²
Guldehan Atis⁴

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Abstract: BACKGROUND: Previous studies have shown that some viral infections may be triggers for autoimmune diseases. The role of viral infections in the etiopathogenesis of pemphigus has also been investigated.

OBJECTIVES: To investigate the relationship between pemphigus and the hepatitis B and C virus infections.

METHODS: This retrospective study included 62 patients with pemphigus and 50 healthy controls of matching ages and genders. The control group included relatives who accompanied the orthopedic patients to the hospital but had no history of systemic and/or autoimmune diseases.

RESULTS: The group of patients with pemphigus was composed of 43 (69.3%) females and 19 (29.7%) males, and the mean age was 48.08 ± 15.38 . The hepatitis C virus antibody was negative in all of the patients. Hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), or both, were studied in 44 of the 62 patients. Two (4.3%) of these patients were positive for HBsAg and found to have HBV infection. Fourteen of them were HBsAb positive. Two (4%) of the 50 control subjects showed hepatitis C virus antibody positivity, while only 1 (2%) patient with pemphigus displayed HBsAg positivity. There was no statistically significant difference between the two groups for hepatitis B and C virus infections.

CONCLUSIONS: This study does not support an association between pemphigus and hepatitis B and/or C virus infections.

Keywords: Hepatitis B virus; Hepatitis antibodies; Pemphigus

INTRODUCTION

Pemphigus is a rare autoimmune disease of the skin and mucous membranes. Previous studies have shown that some viral infections may be triggers for autoimmune diseases in patients with genetic susceptibility to them.¹ The role of viral infections in the etiopathogenesis of pemphigus has also been investigated.² The role of HCV in the etiopathogenesis of secondary anti-phospholipid syndrome, Sjögren syndrome, autoimmune thrombocytopenic purpura and cryoglobulinemia, have been reported.^{3,4} Similarly, the mechanisms

involved in HBV infection have been proposed as a trigger in some autoimmune diseases such as diabetes mellitus type 1, polyarteritis nodosa and vitiligo.^{5,6,7} However, there are few studies that evaluate the relationship between pemphigus and HCV and HBV infections.⁸⁻¹¹ The purpose of this study is to investigate the frequency of HCV and HBV infections in our patients who had recently been diagnosed with pemphigus.

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¹ Baskent University Faculty of Medicine Istanbul Hospital - Istanbul, Turkey.

² Acibadem University Faculty of Medicine - Istanbul, Turkey.

³ Ahi Hetman Hospital - Mugla, Turkey.

⁴ Siyami Ersek Thoracic and Cardiovascular Training and Research Hospital - Istanbul, Turkey.

⁵ Sisli Etfal Training and Research Hospital - Istanbul, Turkey.

MATERIALS AND METHODS

Sixty-two patients with a new diagnosis of pemphigus were included in this retrospective study. In addition to clinical and histopathological findings, diagnosis of pemphigus had been confirmed through direct immunofluorescent microscopy. The control group was composed of 50 subjects of matching ages and genders, gathered from among the relatives of the orthopedic patients. The controls all had a negative history for systemic and/or autoimmune diseases and had provided verbal informed consent for the study. In our departments, all patients with pemphigus are screened for HBsAg, HBsAb and anti-HCV, using ELISA, before starting appropriate immunosuppressive therapy, since this treatment can exacerbate viral infections such as HBV and HCV infections. The control group was set up after the decision had been taken to conduct a retrospective study. This group was informed about viral hepatitis and the vaccination for HBV, and those who were found to be eligible for the study were included. The study used their patient records or face-to-face interviews to obtain their ages, genders, serologic test results, family history of HBV and HCV occurrences and the risk factors for HBV and HCV infections, such as blood transfusion, hemodialysis, past operations, transplantation, ear piercing, dental surgery and similar trauma histories. The serological test results of pemphigus patients were acquired from the database of our patients' records.

Statistical Analysis:

SPSS Statistics 17.0 for Windows was used for statistical analysis. The distribution of the data was tested using Kolmogorov-Smirnov and Anova tests. The independent test was used for the analysis of the data; $p < 0.05$ was considered to be significant.

RESULTS

The study group involved 62 pemphigus patients, including 43 women and 19 men (age range: 10-78 years, mean 48.08 ± 15.38) and 50 controls with 35 women and 15 men (age range 18-82 years, mean 48.56 ± 15.50). Of the 62 pemphigus patients, 57 (92%) had pemphigus vulgaris, 2 (3.2%) had pemphigus foliaceus, 2 (3.2%) had pemphigus vegetans and 1 (1.6%) had pemphigus erythematousus.

Anti-HCV Ab was negative in all of the pemphigus patients. Among this group, only one had a family member with HCV infection. In the control group, anti-HCV test results were found to be positive in 2 (4%) individuals who were also positive for HCV-RNA, confirming HCV infection. We did not find a statistically significant difference between the two groups for HCV infection ($p = 0.114$) (Table 1). In the assessment of risk factors, only one of the HCV-

positive controls declared a past surgery, but that had been more than three months before and was not interpreted as a risk factor.

We could only evaluate HBV screening in 44 of the 62 pemphigus patients because of temporary technical problems. Fourteen (31.8%) of the patients were HBsAb positive and 2 (4.3%) were HBsAg positive, denoting HBV infection. We did not find any of the risk factors in the two pemphigus patients with Hepatitis B infection (Table 2). In the control group, 14 (28%) individuals were HBsAb positive and 1 (2%) was HBsAg positive. There were no statistically significant differences between the two groups for HBsAb and HBsAg positivity ($p = 0.848$, $p = 0.526$, respectively) (See Table 1). We did not encounter any of the risk factors in the patients and controls with positive serology for HBV.

DISCUSSION

Pemphigus is an autoimmune disease characterized by painful oral mucosa erosions and fragile bullock skin lesions. The IgG-type antibodies targeting the keratinocytic antigens, desmoglein 1 and desmoglein 3, play a major role in the etiopathogenesis of the disease, by inducing acantholysis.¹²

Although there is some conflicting evidence, the hypothesis that some infections trigger autoimmune disease in genetically predisposed individuals is still up to date. The association of cryoglobulinemia and Sjögren syndrome with chronic HCV infections is well-known. Furthermore, the antinuclear, anti-smooth muscle, anticardiolipin and antithyroid antibody positivity accompanying these infections, support this view.⁴

The exact pathogenetic mechanism involved in HCV and autoimmunity is not known. However, this microorganism has been incriminated in the elimination of tolerance that is protected from autoimmunity.¹³ In addition, the activation of B lymphocytes resulting from HCV residence on these cells has been seen as responsible for autoimmunity.¹⁴

Some studies have investigated the association of HCV with autoimmune diseases. Agmon-Levin et al. found that the frequency of HCV infection in 1,322 patients with various autoimmune diseases was significantly higher (8.7%), compared with the control group (0.4%). In this study, the prevalence of HCV was found to be 14% among the pemphigus vulgaris patients, and the authors emphasized a new association between HCV and pemphigus.⁸ The prevalence of HBV infection in anti-HCV-positive pemphigus foliaceus patients was also found to be considerable.¹⁰ Sagi et al. found that the frequency of HBV, HCV, *H. pylori*, *T. gondii*, *T. pallidum* and CMV was significantly higher than in the control group in pemphigus and

TABLE 1: The comparison of HBsAg, Anti HBsAg and Anti-HCV test results and the existence of risk factors for hepatitis virus infections between the pemphigus group and the control group

		Pemphigus patients		Control group		P		
		n	%	n	%			
Anti-HCV	Positive:	0	0	Positive:	2	4	0.114	
	Negative:	62	100	Negative:	48	96		
HBsAg	Positive:	2	4.56	Positive:	1	2	0.526	
	Negative:	42	95.44	Negative:	49	98		
AntiHBsAg	Positive:	14	31.8	Positive:	14	28	0.848	
	Negative:	30	68.2	Negative:	36	72		
Risk Factors	Abnormality in hepatic function tests	Yes:	2	3.2	Yes:	3	6	0.932
		No:	60	96.8	No:	47	94	
	Hepatitis B and/or C virus infection in family members	Yes:	1	1.6	Yes:	0	0	0.159
		No:	61	98.4	No:	50	100	
	Past operation (operations done under local or general anesthesia)	Yes:	14	22.6	Yes:	10	20	0.960
		No:	48	77.4	No:	40	80	
	Ear piercing	Yes:	11	17,75	Yes:	13	26	0.294
		No:	51	82,25	No:	37	76	
	Blood transfusion	Yes:	2	3.2	Yes:	1	2	0,381
		No:	60	96.8	No:	49	98	
	Hemodialysis	Yes:	0	0	Yes:	0	0	1
		No:	62	100	No:	50	100	
Transplantation	Yes:	0	0	Yes:	0	0	1	
	No:	62	100	No:	50	100		
Blood transfusion or past operation in the last 3 months	Yes:	0	0	Yes:	0	0	1	
	No:	62	100	No:	50	100		

TABLE 2: There were no risk factors in the two pemphigus patients with Hepatitis B infection

		Patient 1	Patient 2
Risk factors	Hepatitis B infection in family members	Absent	Absent
	Past operation (operations done under local or general anesthesia)	Absent	Absent
	Ear piercing	Absent	Absent
	Blood transfusion	Absent	Absent
	Hemodialysis	Absent	Absent
	Transplantation	Absent	Absent
	Blood transfusion or past operation in the last 3 months	Absent	Absent

bullous pemphigoid patients.⁹ In accordance with these results, a pemphigus case has been reported after a hepatitis B vaccination.¹¹ However, there are also opposing results: Rosa et al. did not find any association between HCV infection and pemphigus in 126 patients with fogo selvage, in their study group.¹⁰ In terms of our findings, although the prevalence of HCV infection was 4% in the control group, none of our 62 pemphigus patients had HCV infection. Nevertheless, the prevalence of HBV infection in our pemphigus patients was 4.3%, while it was 2 % in the control group. There was no statistically significant difference between the two groups for HBV and HCV infections. According to the surveys, 1% of the Turkish population has been found to be infected by HCV, and

2.7% by HBV.¹⁵ The results are also slightly different from the general population. We believe that the results obtained may have been caused by the small numbers in our study groups. If the number of patients and controls were higher, the prevalence of these viral infections would probably be closer to the prevalence within the general population.

CONCLUSION

The controversy surrounding the role of viral infections in the etiopathogenesis of autoimmune diseases still exists today. However, the findings of our study do not support any association between pemphigus and HBV and/or HCV infections. □

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MAILING ADDRESS:

*Gulsen Tukenmez Demirci
Başkent Üniversitesi İstanbul Sağlık Uygulama
Ve Araştırma Hastanesi
Mahir İz Cad. No 43 34662
Altunizade/İstanbul. Turkey
E-mail: gulsentukenmez@yahoo.com*

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