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Evaluation of HBV, HCV, and HIV seroprevalence in patients with plasma cell disorders

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Abstract

Hepatitis B (HBV) and hepatitis C (HCV) viruses are hepatotropic and lymphotropic viruses that can proliferate either in lymphocytes and monocytes or hepatocytes.

The aim of this study was to evaluate the seroprevalence of HBV, HCV, and human immunodeficiency virus (HIV) in patients with plasma cell disorders. We also aimed to compare patients with plasma cell disorders and chronic lymphocytic leukemia (CLL) in terms of HBV, HCV, and HIV seropositivity.

This is a retrospective study. The patients who had patient file in the Multiple Myeloma Outpatient Unit of our hospital and were followed in our outpatient unit between January 1, 2012 and September 15, 2019, with diagnoses of either of the plasma cell disorders were included in the study. In addition, 272 CLL patients who were admitted to the Leukemia Outpatient Unit of our hospital were also enrolled in the study. The 2 disease groups were compared in terms of HBV, HCV, and HIV seropositivity.

A statistically significant relationship was found between disease groups according to hepatitis B surface antigen ($P < .05$). Hepatitis B positivity were found to be more common in CLL patients. There was also a statistically significant relationship between the disease groups in terms of hepatitis B e antigen positivity ($P = .001$).

We found that hepatitis B surface antigen positivity rate in CLL patients was higher than in patients with plasma cell disorders. Seroprevalence of HBV, HCV, and HIV was found to be very low in patients with plasma cell disorders.

Abbreviations: Anti- HIV = HIV antibody, Anti-Delta = delta antibody, Anti-HBc IgG = immunoglobulin G antibody to hepatitis B core antigen, Anti-HBc IgM = immunoglobulin M antibody to hepatitis B core antigen, Anti-HBe = hepatitis B e antibody, Anti-HBs = hepatitis B surface antibody, Anti-HCV = HCV antibody, CLL = chronic lymphocytic leukemia, HBe Ag = hepatitis B e antigen, HBs Ag = hepatitis B surface antigen, HBV = hepatitis B virus, HCV = hepatitis C virus, HIV = human immunodeficiency virus, MM = multiple myeloma.

Keywords: hepatitis B virus, hepatitis C virus, human immunodeficiency virus, plasma cell disorders

1. Introduction

Hepatitis B (HBV) and hepatitis C (HCV) viruses are hepatotropic and lymphotropic viruses that can proliferate either in lymphocytes and monocytes or hepatocytes.[1,2] Agnello et al suggested that Type II cryoglobulinemia and HCV infection were strongly associated.[3] Human immunodeficiency virus (HIV) may cause the cancer development by causing impaired cellular immunity.[4] HBV, HCV, and HIV are viruses that could proliferate in lymphoid tissues. These viruses are also known to be involved in the etiology of various malignancies. Plasma cell disorders are a group of diseases characterized by the proliferation of 1 or more clones of differentiated B lymphocytes. Immunologically homogenous immunoglobulin production, known as paraprotein or monoclona protein, is a common finding in this disease group.[5]

Plasma cell disorders include a range of diseases ranging from solitary plasmacytoma and life-threatening multiple myeloma (MM) to monoclonal gammopathy of undetermined significance.[6] The aim of this study was to evaluate the seroprevalence of HBV, HCV, and HIV in patients with plasma cell disorders. We also aimed to compare patients with plasma cell disorders and chronic lymphocytic leukemia (CLL) to determine the relationship between these diseases in terms of HBV, HCV, and HIV seropositivity.

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The data and the analysis of the data could be shared during the review process.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

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2. Methods

The study was a retrospective study. Approval was obtained from the Ethics Committee of Health Sciences University Ankara Dr Abdurrahman Yurtaslan Oncology Training and Research Hospital (Approval date: October 16, 2019 and decision no: 2019-10/423).

The patients who had patient files in the Multiple Myeloma Outpatient Unit of our hospital and who were followed in our outpatient unit between January 1, 2012 and September 15, 2019, with diagnosis of either of plasma cell disorders were included in the study. Two hundred seventy-two CLL patients who were admitted to the Leukemia Outpatient Unit of our hospital were also included in the study. Data were obtained from patients with plasma cell disorders followed in the Multiple Myeloma Outpatient Unit of our tertiary hospital and from the CLL patients who had patient files in our Leukemia Outpatient Unit. The test results which were reachable were analyzed for frequencies. And the patients whose serological test results were not known were not included for the frequency analyses in each subgroups demonstrated in the table. The patients with unknown serological tests were not included in frequency analyses.

Patients with multiple myeloma, smoldering myeloma, monoclonal gammopathy of undetermined significance, polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes syndrome and/or Waldenström macroglobulinemia had been followed in the multiple myeloma outpatient unit. Castleman disease without polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes were routinely followed in the lymphoma outpatient unit of our clinic in previous years. (Not in multiple myeloma outpatient unit). The diagnoses and other results of the patients were obtained from patient records.

Age, hepatitis B surface antigen (HBs Ag) positivity, hepatitis B surface antibody (Anti-HBs) positivity, immunoglobulin M antibody to hepatitis B core antigen(Anti-HBc IgM) positivity, immunoglobulin G antibody to hepatitis B core antigen (Anti-HBc IgG) positivity, hepatitis B e antigen (HBe Ag) positivity, hepatitis B e antibody (Anti-HBe) positivity, delta antibody (Anti-Delta) positivity, HIV antibody (Anti-HIV) positivity, and HCV genotype of the patients were recorded.

These data have been compared between patients with plasma cell disorders and patients with CLL. Two hundred thirty-one patients with plasma cell disorders and 272 patients with CLL (as the control group) were included in the study. Patients aged 18 years or older and diagnosed with any of the plasma cell disorders or CLL were included in the study. Patients under 18 years of age were excluded from the study. Patients who were not diagnosed with neither of the plasma cell disorders nor with CLL were excluded from the study.

2.1. Statistical analysis

SPSS (IBM SPSS Statistics 24) was used to analyze the data. Frequency tables and descriptive statistics were used to interpret the findings. Descriptive data were presented as categorical frequency distribution and percentage (%), while the measured ones were presented as mean ± standard deviation (SD) and median (maximum, smallest values).

"Cross tabulation and Pearson's χ^2-test " were used analyze the relationship between the qualitative variables. "Mann–Whitney *U* test" (Z-table value) statistics were used to compare two independent groups with normal distribution. $P < .05$ was considered statistically significant.

3. Results

Two hundred thirty-one patients with plasma cell disorders and 272 CLL patients were included in the study. In all of these patients, HBV, HCV, and HIV seroprevalence rates were recorded. One hundred (43.3%) of the patients with plasma cell disorders were female and 131 (56.7%) were male. One hundred four (38.2%) of the CLL patients were female and 168 (61.8%) were male. There was no statistically significant relationship between the 2 disease groups in terms of gender ($P > .05$) (Table 1).

The mean age of patients with plasma cell disorders was 59.93 ± 10.41 (years) and the mean age of patients with CLL was 64.37 ± 11.77 years old. A statistically significant difference was found between the 2 disease groups in terms of age (Z = -5.010; $P = .000$) (Table 1).

The ages of CLL patients were statistically significantly higher than the ages of patients with plasma cell disorders.

There was a statistically significant relationship between disease groups in terms of HBs Ag positivity ($P < .05$).

It was determined that 218 patients (97.8%) with plasma cell disorders and 218 patients (92.8%) with CLL were HBs Ag negative. On the other hand, 17 patients (7.2%) with CLL were HBs Ag positive. It was determined that HBs Ag positivity was more common in CLL patients (Table 2). Besides, there was no statistically significant relationship between disease groups in terms of Anti-HBs, Anti-HBc IgM and Anti-HBc IgG positivity ($P > .05$) (Table 2).

Anti-HBs were positive in 78 patients (36.3%) with plasma cell disorders and Anti-HBs were positive in 69 patients (31.1%) with CLL. There was no statistically significant relationship between the disease groups ($P > .05$) in terms of Anti-HBs positivity (Table 2). Anti-HBc IgG was positive in 74 patients (42.0%) with plasma cell disorders and Anti-HBc IgG were positive in 50 patients (34.7%) with CLL. But there was also no statistically significant relationship between the disease groups in terms of Anti-HBc IgG positivity ($P > .05$) (Table 2).

Table 1

Evaluation of the relationships of some features according to groups.

	Group			Statistical analysis* Possibility
Variable	**PCD (n = 231)**	**CLL (n = 272)**	**Total (n = 503)**	
Gender				
Female	100 (43.3%)	104 (38.2%)	204 (40.6%)	$\chi^2 = 1.324$
Male	131 (56.7%)	168 (61.8%)	299 (59.4%)	$P = .250$
Age (yr)	60.0 [29.0–91.0]	66.0 [21.0–86.0]	63.0 [21.0–91.0]	Z = -5.010; $P = .000$

* χ^2-cross tables are used to analyze the relations of 2 qualitative variables. "Mann–Whitney *U* test" (Z-table value) statistics were used to compare two independent groups with normal distribution.

Table 2

Evaluation of groups in terms of viral seropositivity.

Variable	Group			Statistical analysis* Possibility
	PCD	CLL	Total	
HBs Ag				
Negative	218 (97.8%)	218 (92.8%)	436 (95.2%)	$\chi^2=5.191$
Positive	5 (2.2%)	17 (7.2%)	22 (4.8%)	$P=.023$
Anti-HBs				
Negative	137 (63.7%)	153 (68.9%)	290 (66.4%)	$\chi^2=1.322$
Positive	78 (36.3%)	69 (31.1%)	147 (33.6%)	$P=.250$
Anti-HBc IgM				
Negative	153 (100.0%)	124 (100.0%)	277 (100.0%)	#
Anti-HBc IgG				
Negative	102 (58.0%)	94 (65.3%)	196 (61.3%)	$\chi^2=1.790$
Positive	74 (42.0%)	50 (34.7%)	124 (38.7%)	$P=.181$
HBe Ag				
Negative	141 (100.0%)	82 (92.1%)	223 (97.0%)	$P=.001$
Positive	–	7 (7.9%)	7 (3.0%)	
Anti-HBe				
Negative	119 (85.0%)	76 (84.4%)	195 (84.8%)	$\chi^2=0.013$
Positive	21 (15.0%)	14 (15.6%)	35 (15.2%)	$P=.909$
Anti-Delta				
Negative	14 (100.0%)	23 (100.0%)	37 (100.0%)	#
Anti-HCV				
Negative	220 (98.7%)	233 (98.7%)	453 (98.7%)	$P=.630$
Positive	3 (1.3%)	3 (1.3%)	6 (1.3%)	
Anti-HIV				
Negative	219 (100.0%)	230 (100.0%)	449 (100.0%)	#

* "χ^2-cross tables" were used to evaluate the relationships between the qualitative variables.
CLL = chronic lymphocytic leukaemia, PCD = plasma cell disorders.

However, there was a statistically significant relationship between the disease groups in terms of HBe Ag positivity ($P=.001$). One hundred forty-one patients (100.0%) with plasma cell disorders were HBe Ag negative and seven (7.9%) patients with CLL were HBe Ag positive. It was determined that HBe Ag negative patients were predominantly patients who had either of the plasma cell disorders. On the other hand, all HBe Ag positive patients had CLL (Table 2).

Twenty-one patients (15.0%) with plasma cell disorders were found to be Anti-HBe Ag positive and 14 patients with CLL (15.6%) were found to be Anti-HBe Ag positive. On the contrary, there was no statistically significant relationship between the disease groups in terms of Anti-HBe Ag positivity ($P>.05$) (Table 2).

Two hundred twenty patients (98.7%) with plasma cell disorders were found to be Anti-HCV negative and three patients with CLL (1.3%) were Anti-HCV positive. There was no statistically significant relationship between disease groups in terms of Anti-HCV negativity ($P>.05$) (Table 2).

4. Discussion

MM, which is among plasma cell disorders, constitutes approximately 10% of all hematologic malignancies.[7] It is a malignant plasma cell disease and results from malignant transformation of post-germinal central plasma cells.[8] Clinically, it is a disease that frequently occurs with hypercalcemia, renal dysfunction, anemia and bone fractures.[9] In the etiology of MM, it was reported that there are other potential risk factors such as immunosuppression and environmental factors besides aging and genetic predisposition.[10,11] Alexander DD et al. did not suggest general specific factors in the etiology of MM.[12] HIV-infected patients or patients with acquired immunodeficiency syndrome (AIDS) would be at risk of developing MM.[13,14]

People with hepatitis virus infection were suggested to have a higher risk of MM.[15,16] In contrast, we found that HBs Ag positivity rate in CLL was higher than in plasma cell disorders.

MM and chronic HCV infection were suggested to have a relationship between them.[17–19] The relationship between HCV infection and MM is controversial. The relationship between chronic HCV infection, including non-Hodgkin lymphoma, Hodgkin lymphoma , and MM has long been debated. In many published studies, the prevalence of HCV infection in MM has been shown to be higher than in healthy control populations.[20,21] In a cohort study by Duberg et al, there was a significant increase in the risk of MM in patients with HCV infection for more than 15 years.[22] In contrast, positive correlation was not identified in the studies conducted by Franceschi et al, Abe et al, Giordano et al, Anderson et al.[23–26]

Waldenström macroglobulinemia refers to a monoclonal gammopathy of the IgM type, usually associated with plasmacytoid lymphoma. The association of Waldenström macroglobulinemia with HCV has been reported.[27]

On the other hand, we also found no difference between CLL and plasma cell disorders in terms of HCV seropositivity.

Limited and variable results have been reported in terms of the incidence of HBV and/or HCV infections in CLL patients.[17,28] In a study, it was reported that HBV or HCV infections do not play an important role in the pathogenesis or course of CLL.[29] We included CLL patients as the control group because HBV or HCV infections were known as not to play an important role in the pathogenesis of CLL. We found HBs Ag positivity statistically higher in CLL patients.

In conclusion, we suggest that hepatitis B and hepatitis C viruses may not play a role in the etiology of plasma cell disorders. In our study seropositivity of hepatitis is lower in patients with plasma cell disorders. So that we can assume that plasma cell disorders may not be related with hepatitis. Further studies comparing either type of the plasma cell disorders one by one with healthy control groups would give more accurate estimations.

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Author contributions

Duygu Mert was the designer, coordinator, data collector and corresponding author. Alparslan Merdin was the other designer and data collector of study. The other authors were data collectors and supevisors. Duygu Mert is the main author of the study.

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