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RESEARCH ARTICLE

EVALUATION OF CMV DNA ANTIGENEMIA STATUS IN PATIENTS WITH ALLOGENEIC BONE MARROW TRANSPLANT

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ABSTRACT

Purpose: The risk of cytomegalovirus (CMV) reactivation following allogeneic hematopoietic stem cell transplantation (ASCT) reaches 30-50%, and there are numerous diagnostic tests to detect CMV replication. The most common tests used in this group of patients include 65kDa phosphoprotein (pp65) antigenemia immunofluorescence assay and nucleic-acid-based quantitative CMV-DNA polymerase chain reaction (qPCR).
Material and Methods: In this study, patients who underwent ASCT and developed CMV positivity from 2009 to 2016 in our hospital were evaluated retrospectively. The study included samples of the same patient with antigenemia and CMV-DNA qPCR test for up to 48 hours. The study aimed to determine the factors affecting CMV DNA antigenemia and compare CMV DNA PCR and pp65 antigenemia immunofluorescence assay.
Results: The results of 138 specimens of 39 patients who underwent ASCT were evaluated. The mean value of CMV PCR, which was positive for both tests, was 57.887 copies/ml (70- 1.213.633 copies/ml) and a significant correlation was found between the two tests and the positive samples ($p = 0.018$). The ROC analysis showed that 322 copies/ml CMV viral load in plasma corresponds to ≥1 antigen-positive cells/200 thousand leukocytes (Sensitivity: 68.5%; Specificity: 31.5%). CMV infection was observed in 32 samples; CMV DNA cut-off values of the reference according to CMV DNA PCR and antigenemia results, compared to the development of CMV infection, presented a significant correlation ($p=0.004$).
Conclusion: Although there is a common agreement between antigenemia and CMV DNA PCR tests, one should keep in mind that the sensitivity of antigenemia test is low especially in the neutropenic period.

Keywords: Allogeneic Hematopoietic Stem Cell Transplantation (ASCT), CMV Antigenemia (pp65), CMV DNA qPCR, CMV Infection

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is the process of collecting stem cells from individuals or tissue-compatible individuals and transferring them to the recipient under appropriate conditions in order to restore the hematopoietic system. Hematopoietic

stem cell transplantation (HSCT) can be performed in various ways depending on the diagnosis and stage of the patient. It is mainly divided into two: allogeneic and autologous HSCT. Autologous stem cell transplantation (autologous SCT) is the infusion of healthy hematopoietic stem and progenitor cells taken from the patient's own cells into the patient. Allogeneic SCT, on the other hand, uses hematopoietic progenitor cells collected from a healthy person (not the patients themselves). There are several possible sources for the origin of these cells: 1-An identical twin (syngeneic, human leukocyte antigen [HLA] identical), 2-A sibling, relative, or unrelated donor (whose HLA may be identical, haploidentical, or incompatible), and finally 3-Umbilical cord blood (may be the same as HLA, haploidentical or incompatible) (1). ASCT is the transfer of HLA tissue from the compatible donor to the recipient after the preparation of stem cells (2). CMV reactivation or primary infection after ASCT is observed in 15-80% of patients and CMV infections are the most important cause of viral disease morbidity and mortality in this patient group (3,4). CMV seropositivity or post-transplant CMV reactivation adversely affects the ASCT results. In the past, most of the CMV reactivations and cases of pneumonia were seen in the early post-transplant period, but this rate was significantly decreased with preemptive therapies following routine ganciclovir prophylaxis or viral reactivation. However, recent years have seen an increased rate of late CMV reactivation and diseases. Late CMV disease is observed in between 4% and 15% of the cases and usually after 4 to 12 months (4). If the recipient and donor are seronegative, CMV disease occurs in less than 3% after transplantation, whereas if both are seropositive, CMV disease occurs in up to 30% of cases (5).

CMV pp65 antigenemia immunofluorescence test (CMV antigenemia), CMV DNA quantitative real-time PCR test (CMV DNA qPCR), cell culture, histopathology, and serological tests are used for detection of CMV infection. The two tests most commonly used in the diagnosis and follow-up of CMV infection are CMV antigenemia test and CMV-DNA qPCR. The viral pp65 antigen is a structural late protein expressed in blood leukocytes at an early stage of the CMV replication cycle. Antigenemia is measured by the quantification of the positive leukocyte nucleus in an immunofluorescence assay for CMV matrix phosphoprotein pp65 in a cytospin preparation of 2x105 peripheral blood leukocytes. In neutropenic patients, false-negative results may occur; antigenemia test result depends on the presence of a sufficient number of polymorphonuclear leukocytes (6). For optimal results, samples should be studied within 6 hours (6). The other nucleic acid-based test is the detection of CMV DNA by PCR method, which quantitatively realizes the CMV DNA by the quantitative real-time PCR method in a more sensitive and quantitative manner (4). PCR generally targets a number of early and late antigen genes in large, well-conserved regions to detect CMV DNA. DNA can be removed from whole blood, leukocytes, plasma or any other tissue (tissue biopsy samples) or body fluids (urine, cerebrospinal fluid (CSF), bronchoalveolar lavage (BAL)) (7). Live cell presence is not required for measurement. In the presence of a mutation in the regions where the primers bind, false negative results may be obtained. The situation can be illuminated by using a primer suitable for another region in the virus genome. In such cases, CMV antigenemia is positive and CMV DNA PCR may be negative. Sequence analysis is the most accurate method to determine mutation (5). The sensitivity and specificity of the test were 55.4% and 95.5%, respectively, when the standard CMV DNA qPCR assay was used to detect antigenemia (8). PCR-based assays are more sensitive than antigenemia; however, high sensitivity leads to the detection of controversial low viral replications with clinical implications. Although the international CMV-DNA standard has been developed, differences between the qPCR tests employed make it difficult to achieve inter-laboratory standardization and also complicates decision making on clinically significant thresholds. In this study, the results of CMV antigenemia and plasma CMV-DNA qPCR in plasma leukocytes were compared in the patients who had ASCT at the Hematology Unit of Dokuz Eylul University Hospital. The correlation between the two methods was evaluated, and the viral load level corresponding to the antigenemia positivity was determined.

MATERIAL AND METHODS

This study included all patients with CMV pp65 antigenemia positivity in the Stem Cell Transplantation Unit of Dokuz Eylul University Hospital between June 2009 and October 2016. All patients with hematological malignancies who had a

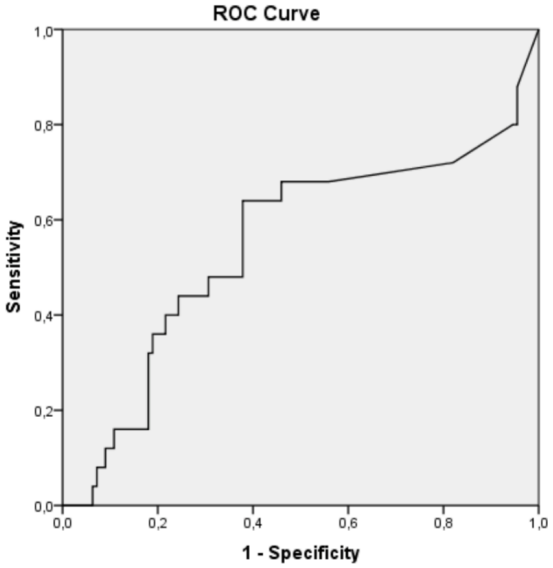

Figure 1. ROC Curve for CMV pp65 antigenemia assay

fully compatible relative donor and underwent ASCT were included in the study. Patients under 18 years of age, who had undergone autologous stem cell transplantation and without fully accessible medical data were excluded from the study. We noted the results of the antigenemia test and CMV DNA PCR test of the same patient. The laboratory values of the patients with CMV positivity were determined by any test. This value was taken as >1 positive cell/200,000 cells for pp65 antigenemia test and as >80 x 108 copies/ml and above for CMV DNA PCR test.

In total, 138 specimens of 39 patients with CMV positivity were retrospectively reviewed. Demographic characteristics, clinical status, diagnosis, laboratory values of transplantation, time of engraftment, amount of CD34 infused product, transplant preparation regimens, GVHD development status, CMV infection status, pp65 at the time of CMV infection and concurrent CMV DNA levels, CMV immunization, the immunosuppressive therapy of the donor, GM data of the recipient's CMV infection, BK virus status, white blood cell, neutrophil, lymphocyte and CRP values were evaluated retrospectively and all data were recorded in the SPSS Statistics V22.0 program. The data about the patients were obtained by scanning the patient's ID and patient numbers from the electronic medical record system (HEMCIS) of the hematology department.

CINAKit Argene® (France) Rapid Antigenemia test was used as a method of detection of CMV Antigenemia, and the internal matrix phosphoprotein (protein kinase) of peripheral blood leukocytes from cytomegalovirus (CMV) was determined by indirect immunofluorescence method of 65-68 kD (pp65). Artus® CMV QS-RGQ KIT - QIAGEN (Germany) PCR method was used to determine the CMV DNA level.

Statistical Analysis

In our study, descriptive statistics were used to interpret the available data. The data were evaluated with the package program Statistical Package for the Social Sciences (SPSS) (version 22.0 SPSS Inc, Chicago, IL, USA). The variables yielded by counting were summarized by means of percentage distribution as well as mean and standard deviation. Pearson and Spearman correlation tests were used for dependent group analysis of the variables. ROC analysis was also performed to determine the viral load corresponding to CMV antigenemia positivity. The level of significance was set at $p < 0.05$.

Ethical considerations

The study was approved by Dokuz Eylul University Faculty of Medicine Ethics Committee for Non-Invasive Clinical Studies on 18/01/2018 with the decision number 2018/02-38.

RESULTS

In our study, 138 of the 39 patients with CMV antigenemia and concomitant CMV DNA qPCR positivity were evaluated retrospectively. The female/male ratio of cases was 1.05/1 and the median age was 38 years (range: 18-64). CMV infection developed in 23.2% of the patients and survival rate was 28.2% during follow up period.

Of the 39 patients examined, 20 (51%) had acute myeloid leukemia (AML), 12 (30%) had acute lymphoid leukemia (ALL), 4 (10%) had myelodysplastic syndrome (MDS), 1 (3%) had biphenotypic leukemia, 1 (3%) had lymphoblastic lymphoma, 1 (3%) had non-Hodgkin's lymphoma (NHL). Evaluated according to the diagnostic CMV episodes, there were 50 episodes with AML (36.2%), 45 episodes with ALL (32.6%), 21 episodes with MDS (15.2%), 9 episodes with biphenotypic leukemia (6.5%), 7 episodes with lymphoblastic lymphoma (5.1%) and 6 episodes with NHL (4.3%).

The conditioning regimens of patients before AHSCT included Busulfan plus cyclophosphamide in 35 patients (90%), Busulfan plus Fludarabin in 1 patient (2.5%), RIC (Reduced intensity conditioning, Fludarabin plus Melfalan) in 1 patient (2.5%), TBI plus

Table 1. Patient and donor CMV conditions at the transplantation

Patient / donor CMV status in transplant	Samples	
	N	%
Positive / Positive	98	%71
Positive / Negative	3	%2,2
Negative / Positive	16	%11,6
Negative / Negative	16	%11,6
Not Reached	5	%3,6

Table 2. Distribution of pp65 and CMV DNA PCR results

	Pp 65 positive N (%)	Pp 65 negative N (%)	Total N (%)
CMV DNA			
Positive ≥80 copies / ml	42 (30.4%)	62 (45%)	112 (75.4%)
Positive < 80 copies / ml	7 (5.1%)	19 (13.9%)	26 (19%)
CMV DNA negative	0	8 (5.6%)	8 (5.6 %)
Total N (%)	49 (35.5%)	89 (64.5%)	138 (100%)

ATG plus Fludarabin in 1 patient (2.5%), in 1 patient (2.5%) TBI plus Etoposide, and preparatory regimens of the 138 CMV samples examined included 116 samples (84.1%) of Busulfan plus Cyclophosphamide, 12 samples (8.8%) of Busulfan plus Fludarabine, 6 samples of (4.4%) RIC, 3 samples of (2.2%) TBI plus ATG plus Fludarabin, and 1 sample (0.8%) of TBI plus Etoposide was built. (While the first sentence expresses the preparation regimens through the patient, the second sentence describes the ratio of the preparation regimens through examples.).

The average amount of CD34+ cells infused was 5.9 x106/kg (2-12x106/kg) and the mean neutrophil engraftment period was 12 days (10-22 days), whereas the mean platelet engraftment period was 15.7 days (10-30 days). CMV antigenemia positivity was more common in patients with early neutrophil engraftment (p=0.028).

When CMV Ig M and Ig G status of the patients at the time of transplantation were examined, CMV Ig G was found to be positive in 68% and negative in 23%, whereas the CMV status could not be reached in 9% of cases. The donor CMV status was Ig G negative in 17% and Ig G positive in 83%. Patient and donor CMV conditions during transplantation are presented in Table 1.

All patients received prophylaxis for the treatment of viral infections, including prophylaxis for the treatment of bacterial, fungal and pneumocystis carini infections. CMV infection was detected in 23.2% (n: 32) of all CMV positive samples. Of the 7 patients with clinically diagnosed CMV infection, 6 had gastrointestinal tract (GIS) involvement and 1 had CMV pneumonia. All the patients were treated with antiviral treatment with IV ganciclovir and three patients were treated with oral valganciclovir. Seven patients had undergone preemptive antiviral treatment due to CMV infection. Cidofovir treatment was started for 1 patient because of resistance to ganciclovir.

While acute graft versus host disease (GVHD) cases were detected in 42.8 % of the patients with CMV infection, skin GVHD, skin and lung GVHD were found in 19.5%, skin and lung GVHD were present in 10.2%, skin and hepatic GVHD were present in 7.2%, and in 20.3% of patients with CMV infection there was no GVHD. As immunosuppressive treatment, 54.4% of the patients received prednisolone and cyclosporine, 19.2% received cyclosporine, 10.3% received prednisolone, 9.5% received combination with prednisolone, cyclosporine and MMF, and 6.6% received combination with prednisolone and tacrolimus. One patient was treated with photophoresis and 2 had mesenchymal stem cell therapy. Of the patients with GVHD, 46.2% had GVHD grade 2 (n: 48), 31.8% had grade 3 (n: 33), 20% had grade 4 (n: 21), and 2% had grade 1 (n: 2). In addition, there was no correlation between the grade of GVHD and CMV infection (p = 0.12).

Regarding the CMV status, cases were positive after transplantation median on the 112th day (10-720 days). White blood cell count, neutrophil and lymphocyte levels were examined in this period).

Table 3. Comparison of CMV DNA PCR results and Antigenemia results with respect to CMV DNA cut-off values in the references.

	CMV DNA copy / ml < 2x 10^2 (n:75)	CMV DNA copy / ml ≥ 2x 10^2 (n:63)
CMV Antigenemia Positive	15 (20 %)	34 (54%)
CMV Antigenemia Negative	44 (58.6 %)	9 (14.3%)
Insufficient cell	6 (8%)	2 (3.2%)
Unseen	10 (13.4%)	18 (28.5%)
	Sensivity 97.7 % and Specificity 94 %	

There was no statistically significant difference between the post-transplant lymphocyte value and the CMV DNA titers (p = 0.07). However, when the lymphocyte count was grouped as <500/mm3 and >500/mm3, the difference was significant in the patient group with a lymphocyte value <500/mm3 and positivity was found to be higher (p = 0.017). It was found that this situation was due to the lack of cell counts in patients with lymphopenia and in the absence of a sufficient number of cells for measure pp65 antigenemia test. As the lymphocyte count increased, antigenemia positivity was found to be higher and there was a statistically significant difference between the values of lymphocytes and CMV antigenemia (p = 0.038).

White blood cell count and neutrophil values were correlated with CMV DNA (p = 0.003, p = 0.002). Neutrophil values <1000/mm3, 1000-2000/mm3, >2000/mm3 were also correlated with CMV DNA qPCR, and as the neutrophil value increased, the CMV DNA qPCR titres increased as well (p = 0.027). There was also a statistical relationship between neutrophil value and CMV antigen (p = 0.034). Again, when the neutrophil values were examined with <1000mm3 and >1000/ mm3 as CMV antigenemia, the statistical relationship was found significant (p = 0.005). CMV antigenemia positivity was high in patients with neutrophil values >1000/ mm3.

Significance was determined between neutrophil engraftment and CMV antigenemia, and it was observed that those with late neutrophil engraftment were more positive, while those with CMV clinical infection were observed to be in the late neutrophil engraftment group (p = 0.028, p = 0.0001).

There was a significant difference between the platelet engraftment and CMV antigenemia and CMV DNA qPCR positivity; a higher positivity was detected in those with late platelet engraftment, and late platelet engraftment was observed in patients with CMV clinical infection (p = 0.025, p = 0.001).

The stem cell source used in all of our patients was peripheral CD 34 positive stem cells and no significant difference was found between the amount of infused CD34-positive stem cells and CMV antigenemia and CMV DNA positivity (p = 0.07, p= 0.2).

CMV antigenemia values ranged from 0 to 20 in 37 samples (26.8%) and 20 to 100 in 8 samples (5.8%), CMV antigenemia result was >100 in 4 samples (3%), and in 65 samples (47.1%) CMV antigenemia was negative although CMV DNA result was positive. A cell deficiency was observed in 31 samples (22.5%).

It was observed that 38 of the 49 samples with positive CMV antigenemia were detected within the first 100 days after transplantation.

In eight of the samples (5.8%), CMV pp65 antigenemia and CMV DNA qPCR were negative, while in 49 (35.5 %) both tests were positive. The number of CMV antigenemia negative/ CMV DNA qPCR positive samples was 81 (58.7%), whereas there was no positive antigenemia/ CMV DNA qPCR negative sample. The mean value of the CMV DNA was 49.887 copies/ml (70-1.213.633 p/ml). A significant correlation was found between the two tests and positive samples (p= 0.018). ROC analysis showed that 322 copies/ml CMV viral load in plasma corresponded to ≥1 antigen-positive cell/200 thousand leukocytes (Sensitivity: 68.5 %, Specificity: 31.5%) (Table 2, Figure-1). The samples with CMV DNA qPCR positive and pp65 antigenemia negative were attributed to false negative results of the CMV antigenemia test due to the patients being leukopenic. Again, the absence of CMV DNA negative and antigenemia positive samples can be explained by the fact that the CMV DNA qPCR test is more sensitive.

The highest CMV DNA value was found to be 1.213.633 copies/ml. This sample belongs to a patient with GIS CMV infection. The CMV DNA level was found to be > 80 copies/ml in 10^4 samples. ROC curve analysis was performed on CMV DNA levels of 138 samples according to the CMV infection development status, and as a result, when CMV DNA was <2x10^2 cut-off, the sensitivity was found to be

97.7% and the specificity was 94%, and in 75 of the samples, the CMV DNA copy was < $2x10^2$ copies/ml., in 63 of the samples, the result was >$2x10^2$ copies/ml. CMV infection was observed in 32 samples, CMV DNA cutoff values were compared with CMV DNA qPCR results, and antigenemia results were compared with respect to CMV infection (p = 0.004) (Table 3).

DISCUSSION

In stem cell transplant recipients, approximately 50-90% of them develop CMV infection in the post-transplant period in relation to recipient and donor's CMV status before transplantation, and 30%- 50% of them are symptomatic (9, 10, 11). CMV infection is an important cause of mortality and morbidity in ASCT patients in hematology stem cell transplantation clinics. CMV positivity may progress CMV disease with organ involvement such as pneumonia, gastroenteritis, retinitis, and central nervous system involvement. CMV seropositivity and CMV infection are more common in the first 100 days of post-transplantation period. In these patients, CMV pp65 antigenemia assay and CMV DNA qPCR tests can be used in the diagnosis of CMV infection. Currently, CMV DNA qPCR is preferred to a higher extent for pre-emptive treatment. In the study of Landolfo et al., post-ASCT CMV infection was found to be around 32-70% (12). CMV infection was detected in 23.2% (n: 32) of 138 samples from 39 patients who underwent ASCT with CMV positivity in our clinic, and it was found to be slightly lower compared to the literature (13).

In the literature, CMV positivity was shown to be more frequent in the first 3-4 months after transplantation, and CMV positivity was found in 112 days after transplantation in our study. It was observed that 38 of the 49 samples with positive CMV antigenemia were detected within the first 100 days after transplantation.

In a study conducted to determine the frequency of CMV infections and risk factors after day 100 (14), CMV disease was detected in 17.8% of patients and on median 169 (96-784) days, while mortality was 46% in this group. In the study, it was found that the risk increased in cases of antigen positivity, GVHD presence, low CD4 positive lymphocyte count, lymphocyte count <100/mm3 and CMV positivity before the 100th day. In our results, CMV positivity was detected on the median 112th day after the transplant, 80% of our patients had GVHD, and 51.3% had grade 3-4 GVHD. However, there was no correlation between GVHD degree and CMV detection. CMV DNA positivity rate was found to be significantly higher in the patient group with lymphocyte value <500/mm3.

Immunosuppression is important in the pathogenesis of CMV infection in patients with ASCT and the factors that affect it include age, HLA compliance, stem cell source, administered conditioning regimen (ATG, history of RT) as well as steroid treatment (12). In addition, the serological status of the recipient is an important risk factor, too (13). In our study, no relation was found between the preparation regimes and CMV status; however, there was a statistically significant correlation between age and CMV DNA qPCR positivity (p = 0.029), yet no correlation was found between CMV antigenemia and age. CMV copy positivity was more common in patients under 40 years of age (p = 0.014).

The donor serology is one of the most important criteria for CMV risk. According to the risk ratio,, those with Donor (D) positivity (+) and Recipient (A) negativity (-) have the highest risk, while D+ A+, D-A+ indicates a decreasing risk level. The presence of viremia has been demonstrated to be a risk factor for CMV disease. It has been shown that high viral load constitutes the greatest risk for CMV considering the donor and recipient serological status, high viral load and viremia (15). When the CMV status of our patients was examined at the time of transplant, 71% was D + A +, 11.6% had DA-, 11.6% had D-A + and 2.2% had D + A. In the study conducted by Schulenburg et al., D + A +, 24.3% DA and D-A + 19% were detected in 42% of the donor and donor CMV cases (16).

We know that CMV DNA qPCR positivity is considered to be a more sensitive test than CMV antigenemia in neutropenic patients. In our study, the neutrophil value <1000/ mm3, 1000 – 2000/ mm3, >2000/ mm3 were also correlated with CMV DNA, CMV DNA titres increased as the neutrophil value increased. There was also a statistical relationship between the neutrophil value and the CMV antigen. Also, CMV antigenemia positivity was high in the patient group with a neutrophil value >1000/ mm3.

Einsele et al. found an unfavorable prognostic factor for CMV infection in lymphopenia after bone marrow transplantation (17). There was no significant difference between post-engraftment lymphocyte and CMV DNA titres in our study, but CMV DNA positivity

rate was found higher in patients with a lymphocyte value <500/mm3.

In our patient population, CMV infections were observed more frequently in patients with late neutrophil and platelet engraftment. The reason for this can be the delay of engraftment in our patients due to CMV infection.

Gökahmetoğlu et al. investigated the presence of CMV in 450 samples from 54 bone marrow recipients with CMV antigenemia test and CMV DNA qPCR methods. The researchers found positive results in 5.2% of the samples, the antigenemia test alone in 6%, and the CMV DNA qPCR test alone in 9.3% (18). In our study, both tests were positive in 35.5% of the samples, the CMV antigenemia test alone was found in 5.7% and CMV DNA qPCR test alone was found in 38.4% of the samples.

In another study in which 415 peripheral blood samples were obtained from 42 patients with AHSCT every week until the 100th day after transplantation, the presence of CMV DNA was investigated by the real-time PCR method. It was stated that 51% of the patients had viral reactivation. It was also reported that the CMV DNA qPCR testing may be useful in monitoring CMV reactivation and response to the antiviral therapy in BMT receptors (19). In our study, it was observed that 38 of the 49 samples with positive CMV antigenemia were detected within the first 100 days after transplantation.

In a study by Schulenburg et al. (16), the CMV DNA qPCR method was employed to determine the CMV infection and CMV antigenemia. In our cases, CMV DNA qPCR results and antigenemia results were compared in terms of CMV DNA cutoff values according to the CMV DNA cutoff values. In our study, there was a significant correlation between CMV DNA qPCR and CMV antigenemia in CMV detection.

In a study conducted on the stem cell transplant receivers in Turkey, which compared the results of CMV pp65 antigenemia test with two different PCR test results, the value of viremia corresponding to antigenemia positivity (≥1 positive cell/200,000 cells) was found 1543.5 copies/ml in one test and 423 copies/ml in the other (18). A cutoff value of 423 copies/ml was determined in the study of Çolak et al., and sensitivity and specificity were found to be 70.7% and 79.5%, respectively (20). In a study conducted in solid organ transplant patients in our university, ROC analysis was performed based on pp65 antigenemia positive (≥1 positive cell/200.000 cell), and the CMV DNA threshold value corresponding to antigenemia positivity in solid organ transplant recipients was found to be 205 copies/ml (sensitivity: 91.7%, specificity: 90.3%) (21). In a study by Breda et al., the cutoff value in which CMV antigenemia could be separated as positive and negative was 1067.5 copies/ml, which was reported with 100% sensitivity and 71% specificity (22). In our study, the mean value of CMV DNA qPCR of 49 samples in both tests was 57.887 copies/ml (70- 1.213.633 copies/ml) and a significant correlation was found between the two tests and positive samples ($p = 0.018$). In ROC analysis, 322 copies/ml CMV viral load in plasma corresponds to ≥1 antigen-positive cell/200 thousand leukocytes (sensitivity: 68.5%, specificity: 31.5%).

CONCLUSION

As a result, in this study, in the group that received stem cell transplantation and CMV pp65 antigenemia test, the CMV DNA qPCR test value, corresponding to 1 positive cell/200,000 cells, was determined as 322 copies/ml. Although these results may vary slightly depending on the clinic and patient population, it has been shown that there is concordance between the CMV pp65 antigenemia test and the CMV DNA qPCR test in the clinical follow-up of patients with CMV infection, and it is thought that it will be helpful in the follow-up of patients.

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