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O. Coşkun[1] · E. Yazici[1] · F. Şahiner[2] · A. Karakaş[1] · S. Kiliç[3] · M. Tekin[4] · C. Artuk[1] ·
L. Yamanel[5] · B. A. Beşirbellioğlu[1]

[1] Department of Infectious Diseases and Clinical Microbiology, Gulhane Military Medical Academy, Etlik/Ankara, Turkey

[2] Department of Medical Microbiology, Virology Unit, Gulhane Military Medical Academy, Ankara, Turkey

[3] Department of Public Health and Epidemiology, Gulhane Military Medical Academy, Ankara, Turkey

[4] Department of Anesthesiology and Reanimation, Gulhane Military Medical Academy, Ankara, Turkey

[5] Department of Intensive Care Unit, Gulhane Military Medical Academy, Ankara, Turkey

Cytomegalovirus and Epstein–Barr virus reactivation in the intensive care unit

Introduction

Cytomegalovirus (CMV) and Epstein–Barr virus (EBV) infections become more prevalent with advancing age and remain as a latent infection. Both viruses cause a self-limiting infection in immunocompetent patients and may become reactivated under various stress conditions that can suppress the immune system [5, 6, 14]. In recent years, some studies have been conducted to evaluate herpes virus reactivation in immunocompetent critically ill patients [5, 22].

Conditions, such as therapies administered in an intensive care setting, invasive interventions, sepsis, trauma, and prolonged hospitalizations, can suppress the immune system [14, 17]. Latent EBV and CMV infections can become reactivated due to immune suppression [16]. Viral reactivation must be taken into consideration for immunocompetent patients who develop unexplained fever and lymphomonocytosis and remain unresponsive to antibacterial therapies.

In the present study, reactivation of EBV and CMV in immunocompetent adult patients hospitalized in intensive care units (ICU) was investigated. In addition, risk factors for viral reactivation and association of certain laboratory parameters with reactivation were evaluated. Finally, the effects of viral re-activation on survival on day 28 were assessed.

Materials and methods

Study design and patients

This observational study was conducted on 60 consecutive adult patients who were hospitalized in the ICU of the Department of Internal Medicine and Anesthesiology and Reanimation Intensive Care Units, Gulhane Military Medical Academy Hospital, for more than 7 days between March 2013 and April 2014. All ethical and organizational permits were obtained before starting the study. The patients were included if (1) they were 18 years old or older, (2) they or their relatives (for unconscious patients) gave written consent, (3) they tested seropositive for anti-CMV IgG and anti-EBV IgG, and (4) they stayed for at least 7 days in the ICU. Patients were excluded if (1) they had malignancy, (2) they had received chemotherapy, (3) they were being treated with high-dose steroids, (4) they were being treated with immunosuppressive drugs, (5) they had neutropenia (absolute neutrophil count <1500/µl), and (6) those who had a positive viral load for CMV and EBV in plasma or blood at admission.

Reactivation of CMV or EBV was considered if patients had symptoms consistent with viral infections and had CMV or EBV viral load at ≥1000 copies/ml limit in the plasma or urine sample or both. Vital signs during clinical follow-up, the cause of admission, comorbid conditions (e. g., chronic renal failure, metabolic disorder, cardiovascular diseases, chronic pulmonary diseases), fever, hospital-acquired infections, history of blood transfusion, and their course in the intensive care unit (transfer, discharge, or death) were recorded. The blood biochemical parameters on the days of sample collection were recorded.

Sample collection and analysis

Complete blood and urine samples were collected at admission and on day 7 for quantitative detection of viral DNA and on days 14, 21, and 28 if hospitalization continued. For patients who were transferred to another center, or were discharged or died, the samples obtained during the hospitalization period were included in the study. The high-sensitivity C-reactive protein (hsCRP) levels of the patients were tested at admission. Serological markers (anti-CMV IgG, anti-EVB IgG) were studied by ELISA for both viruses.

The collected samples were stored at –80 °C until the day of analysis. The samples were thawed at room temperature, and quantitative DNA detection was conducted using the previously described real-time PCR method, general primers,

Table 1 Characteristics of patients and factors affecting reactivation of CMV/EBV in critically ill patients

Variables		No reactivation (n = 43) n (%)	Reactivation (n = 17) n (%)	p
Gender	Male	25 (58.1)	9 (52.9)	0.714[a]
	Female	43 (41.9)	8 (47.1)	
Age, ≥65 years		25 (58.1)	12 (70.6)	0.371[a]
MV support		26 (60.5)	14 (82.4)	0.105[a]
Blood transfusion		27 (62.8)	15 (88.2)	0.053[a]
HAI		21 (48.8)	12 (70.6)	0.127[a]
BSI		11 (25.6)	8 (47.1)	–
Pneumonia		6 (13.9)	4 (23.5)	–
UTI		4 (9.3)	0 (0.0)	–
Exitus		14 (32.6)	6 (35.3)	0.429[a]
Presence of CD		27 (62.8)	12 (70.6)	0.445[a]
No of CDs	1	13 (30.2)	3 (17.6)	
	≥2	14 (32.6)	9 (52.9)	
Diagnosis at admission				
Pneumonia		8 (18.6)	7 (41.1)	0.099[b]
Trauma		7 (16.2)	3 (17.6)	1.0[b]
MI		5 (11.6)	0 (0.0)	0.309[b]
COPD exacerbation		4 (9.3)	1 (5.8)	1.0[b]
Sepsis		3 (6.9)	1 (5.8)	1.0[b]
Gunshot		2 (4.6)	1 (5.8)	1.0[b]
Others		14 (32.5)	4 (23.5)	0.550[b]

MV Mechanical Ventilation, *HAI* Hospital-Acquired Infection, *BSI* Blood Stream Infection, *UTI* Urinary Tract Infection, *MI* Myocardial Infarction, *COPD* Chronic Obstructive Pulmonary Disease, *CD* Comorbid Diseases
[a] χ^2 test
[b] Fisher's exact test

Table 2 Survival rate of patients on day 28 with respect to their clinical characteristics

Characteristic		Survival rate at day 28 (%)	Log-rank	p
Fever (≥38.3 °C)	No	55.8	0.497	0.481
	Yes	66.0		
Anemia (Hb; <13 g/dl in men <12 g/dl in women)	No	45.0	0.962	0.327
	Yes	65.8		
Blood transfusion	No	58.8	0.001	0.987
	Yes	64.2		
Hospital-acquired infection	No	44.5	3.489	0.062
	Yes	72.7		
Mechanical ventilation support	No	87.2	4.539	0.033
	Yes	53.6		
CMV reactivation	No	63.7	0.762	0.383
	Yes	50.0		
EBV reactivation	No	62.5	0.033	0.856
	Yes	64.3		

Hb Hemoglobin

and specific probes [23, 24]. The authenticity of the sequences was tested using the BLAST feature of GenBank and synthesized using the MWG-Biotech (Germany) company.

Statistical analysis

The statistical analyses were performed using SPSS 22.0 (IBM Inc., USA) statistical software. The descriptive statistics represented by mean, standard deviation, median, minimum, maximum for continuous variables and frequency, and percentage for categorical variables. The one-sample Kolmogorov–Smirnov test was used to test to evaluate the distribution of continuous variables. The continuous variables were compared using the Mann–Whitney U test, and the categorical variables were compared using the χ^2 or Fisher's exact test. The Kaplan–Meier analysis with a log-rank test used to evaluate survival times between groups. A *p* values less than 0.05 were considered statistically significant.

Results

A total of 60 patients (34 men, age range 20–96 years, mean 63.3 ± 23.4 years) were included in the study. Mean APACHE II scores for patients was 25 at admission. Of these patients, 28 (46.7 %) were hospitalized in the medical ICU and 32 (53.3 %) were hospitalized in the anesthesiology ICU. CMV/EBV reactivation was found in 17 patients. CMV reactivation was detected in a total of 3 patients: 1 in blood and 2 in urine (8.3 %). EBV reactivation was detected in the plasma samples of 12 patients (23.3 %). EBV and CMV DNA were simultaneously detected in 2 patients. The patients' characteristics are shown in ▪ **Table 1**.

CMV DNA analysis showed a positive result in 4 patients with CMV reactivation on day 7 of hospitalization and in 1 patient on day 14 of hospitalization. All 14 patients with EBV reactivation were positive on day 7.

The concurrent complete blood count did not show lymphocytosis or monocytosis in those patients with EBV and CMV reactivation. Fever was present during the follow-up period in 37 patients

Abstract · Zusammenfassung

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Cytomegalovirus and Epstein–Barr virus reactivation in the intensive care unit

Abstract

Aim. The purpose of this work was to evaluate the reactivation of cytomegalovirus (CMV) and Epstein–Barr virus (EBV) in immunocompetent patients in the intensive care unit (ICU) and to identify risk factors associated with reactivation.

Materials and methods. In this observational prospective study, 60 adult immunocompetent patients who stayed at least 7 days in an ICU were evaluated. During hospitalization, the viral load was monitored at admission and on day 7 with polymerase chain reaction to detect viral reactivation and weekly thereafter on days 14, 21, and 28 if hospitalization continued.

Results. The mean age of patients was 63.3 years (±23.4 years) and 34 (56.7 %) of them were male. Mean APACHE II scores for patients was 25 at admission. Of these patients, 28 were hospitalized in the internal ICU and 32 were hospitalized in the anesthesiology ICU. CMV/EBV reactivation was found in 17 individuals (12 for EBV, 3 for CMV, and 2 for both). The median high-sensitive C-reactive protein value in patients with CMV reactivation was significantly higher than in those patients without CMV reactivation ($p = 0.037$). EBV reactivation was statistically higher in patients with mechanical ventilation compared to patients without mechanical ventilation ($p = 0.023$). EBV reactivation in patients with fever was found to be statistically higher than in the patients without fever ($p = 0.035$).

Conclusion. There is a need for extended studies with a larger number of patients from specific groups to better understand the reactivation frequency and identify risk factors. EBV and CMV reactivation should be taken into consideration in critically ill patients with fever, without specific symptoms and unresponsive to the treatment.

Keywords

Immunosuppression · Fever · Mortality · C-reactive protein · Mechanical ventilation

Reaktivierung des Zytomegalovirus und des Epstein-Barr-Virus auf der Intensivstation

Zusammenfassung

Ziel. Ziel dieser Arbeit war es, die Reaktivierung des Zytomegalovirus (CMV) und des Epstein-Barr-Virus (EBV) bei immunkompetenten Patienten auf der Intensivstation (ICU) zu beurteilen und mit der Reaktivierung assoziierte Risikofaktoren zu identifizieren.

Material und Methoden. In dieser prospektiven Beobachtungsstudie wurden 60 erwachsene immunkompetente Patienten untersucht, die mindestens 7 Tage auf der Intensivstation waren. Während des Krankenhausaufenthalts wurde bei Aufnahme sowie an Tag 7 die Viruslast mittels Polymerase-Kettenreaktion (PCR) überprüft, um eine virale Reaktivierung festzustellen, und anschließend an Tag 14, 21 und 28, wenn der Krankenhausaufenthalt andauerte.

Ergebnisse. Das mittlere Patientenalter betrug 63,3 Jahre (±23,4 Jahre) und 34 (56,7 %) waren männlich. Bei Aufnahme lag der mittlere APACHE-II-Score der Patienten bei 25. Von diesen Patienten waren 28 auf der internistischen Intensivstation und 32 auf der anästhesiologischen Intensivstation. Eine Reaktivierung von CMV/EBV wurde bei 17 Patienten festgestellt (12 bei EBV, 3 bei CMV und 2 bei beiden). Der mediane Wert des hochsensitiven C-reaktiven Proteins bei Patienten mit CMV-Reaktivierung war signifikant höher als bei Patienten ohne CMV-Reaktivierung ($p = 0,037$). Eine EBV-Reaktivierung war statistisch höher bei Patienten mit maschineller Beatmung als bei Patienten ohne maschinelle Beatmung ($p = 0,023$). Die EBV-Reaktivierung bei Patienten mit Fieber war statistisch höher als bei Patienten ohne Fieber ($p = 0,035$).

Schlussfolgerung. Erweiterte Studien von spezifischen Gruppen mit einer größeren Anzahl von Patienten sind erforderlich, um die Reaktivierungshäufigkeit besser verstehen und Risikofaktoren identifizieren zu können. Eine EBV- und CMV-Reaktivierung sollte kritisch in Betracht gezogen werden bei Patienten mit Fieber, ohne spezifische Symptome und bei Nichtansprechen auf die Behandlung.

Schlüsselwörter

Immunsuppression · Fieber · Mortalität · C-reaktives Protein · Maschinelle Beatmung

(61.7 %). In addition, 51 cases (85 %) had anemia and 42 cases (70 %) had a history of blood transfusion. In all, 33 patients (55 %) developed hospital-acquired infections. The origin of the infection was blood stream in 19 patients, respiratory tract in 10 patients, and urinary tract in 4 patients (◘ Table 1).

The median hsCRP level was 116.03 mg/l (min: 10 mg/l, max: 306 mg/l) on the initial evaluation of the patients. The median lymphocyte and monocyte ratio were 8.2 % (min: 7 %, max: 14.1 %) and 7.6 % (min: 1 %, max: 11.1 %) in patients with CMV reactivation, respectively ($p = 0.370$ and $p = 0.640$). The median lymphocyte and monocyte ratios were 9.15 % (min: 1.6 %, max: 24.5 %) and 6.95 % (min: 1 %, max: 17.1 %) in patients with EBV reactivation, respectively ($p = 0.341$ and $p = 0.889$).

Of the 60 patients, 20 died. The survival rate was 72.6 % in men and 50.4 % in women (log-rank: 1.231, $p = 0.267$). There was no significant difference in terms of the survival rate between the patients aged 65 years and older and those younger than 65 years (54.9 % vs. 77.5 %, log-rank: 1.652, $p = 0.199$).

There was also no statistically significant difference in terms of survival between the patients with and without fever, anemia, blood transfusion, and hospital-acquired infection except mechanical ventilation. There was no statistically significant difference in terms of survival between the patients with CMV reactivation and those with EBV reactivation (◘ Table 2). We found no statistically significant relationship between EBV reactivation and presence of fever.

CMV reactivation was observed in 4.8 % of the patients without comorbid conditions, 12.5 % of the patients with one comorbid condition, and 18.2 % of the patients with two comorbid conditions ($p = 0.362$).

The median hsCRP was higher in patients with CMV (179 mg/l vs. 101 mg/l, $p = 0.037$) and EVB reactivation (155 mg/l vs. 105 mg/l, $p = 0.09$). The presence of EBV reactivation was significantly higher in patients with fever (32.4 % vs 8.7 %, $p = 0.035$). There was no significant difference for EBV reactivation between groups according to presence of anemia (22.2 % vs 23.5 %, $p = 1.00$), blood transfusion (28.6 % vs 11.0 %, $p = 0.192$), hospital-acquired infections (30.3 % vs 14.8 %, $p = 0.158$), or comorbid conditions (12.5 % vs 19 %, $p = 0.395$). However the presence of EBV reactivation was significantly higher in patients with mechanical ventilation (32.5 % vs 5.0 %, $p = 0.023$).

Discussion

Viral infections can be often overlooked, due to a lack of specific clinical findings and diagnostic difficulties, in patients hospitalized in intensive care units. Due to the fact that ICU patients exhibit a severe clinical course, therapies and invasive interventions performed in the ICUs setting often place the patient in a stressful condition which can result in the reactivation of latent virus infection [14, 17]. CMV reactivation has increasingly become an important concern in immunocompetent critically ill patients. The rate of CMV reactivation was reported to range between 0 and 35 % in immunocompetent critically ill patients [14]. One study that evaluated CMV reactivation in immunocompetent ICU patients hospitalized due to sepsis reported a positive correlation between CMV reactivation and the duration of stay in the ICU and the duration of mechanical ventilation [13]. Heininger et al. [10] suggested CMV infection prolonged the length of hospital stay and increased mortality rates. Another study found CMV reactivation in 17 % of immunocompetent patients with unexplained fever that lasted for more than 3 days and they re-

ported higher mortality in these patients compared with the control group [13]. On the other hand, Lutz von Müller et al. [27] evaluated 25 immunocompetent patients with septic shock and reported that CMV reactivation had no significant influence on mortality.

The rate of CMV reactivation may vary from one center to another as well as in different patient groups. In the present study, CMV reactivation was detected in 8.3 % of patients in a 28-day follow-up period. Reactivation had no significant influence on survival. It is highly probable that many other factors such as the diagnosis at admission, immune system status, therapies administered, and comorbid conditions also have an influence on CMV reactivation. The lack of a standardized laboratory method and the use of different methods may have also affected the current results. Furthermore, the low number of patients may be the cause of nonsignificant correlation between mortality and CMV reactivation. Long-term studies with a higher number of patients are required in order to establish the impact of CMV reactivation on mortality. Mortality can be associated with EBV reactivation but also with the risk factors associated with EBV infection. Mortality varies according to the specific patient group, follow-up periods, and severity of disorders.

Four patients tested positive for CMV DNA on day 7 following admission and one patient tested positive on day 14. Kalil et al. [15] reported an increased rate of reactivation in ICU admissions longer than 5 days. Another study [18] evaluated 120 patients in an ICU who were seropositive for CMV and reported that reactivation occurred between days 3 and 7 following admission. Frantzeskaki et al. [7] evaluated immunocompetent patients on mechanical ventilation and reported that reactivation occurred in a mean 7 days following admission; however, the comparison with the control group was not statistically different. The difference between the patients, in terms of the timing of reactivation, is considered to be related to the clinical conditions of the patients, the extent of

immunosuppression, comorbid disorders, and prolonged hospitalization.

Various studies have reported that mechanical ventilation is a risk factor in immunocompetent ICU patients and has a significant effect on reactivation [4, 21, 29]. Although CMV reactivation in ICU patients has been associated with worse outcome [20], another study conducted on immunocompetent critical patients on mechanical ventilation found 13.8 % rate of CMV reactivation but it was not associated with poor clinical outcome [7]. In the present study, no significant relationship between mechanical ventilation and CMV reactivation was found. This finding may be associated with the clinical conditions of the patients, organ failure, the presence of sepsis, and the duration of mechanical ventilation. There are studies reporting a significantly higher rate of CMV reactivation in patients with severe sepsis [10, 15]. Considering the role of sepsis in suppressing the immune system, the evaluation of CMV reactivation status only in immunocompetent ICU patients with sepsis or hospital-acquired infections would produce more reliable results.

Although no significant relationship has been reported between CMV reactivation and hemoglobin levels [13], various studies have reported that blood transfusion could be a risk factor for the development of CMV infection [4, 7, 18]. The seroprevalence of CMV vary between countries and prevalence increases with age [3, 9]. Seroprevalence is even higher in countries with low socioeconomic status [12]. In a study conducted in the United States, the seroprevalence of CMV was reported to be 36 % in children aged between 6–16 years and 91 % in adults aged above 80 years [3]. In a study conducted in Turkey, the rate of CMV seropositivity was found to be 82.1 % in the 1–6 year age group, 92 % in the 7–14 year age group, and 97.8 % in the 15–49 year age group [1]. Routine screening for CMV is not conducted on donated blood due to the high prevalence in the population and the latent infection status. It is probable, but of a minimal chance, that blood transfusions can cause CMV reactivation in immunocompetent patients, due to the fact that patients older

than the population average are followed in the ICU and seropositivity for CMV increases with age. A meta-analysis found that the use of leukocyte-reduced blood products could prevent CMV infections associated with transfusions [26]. Although leukocyte-reduced blood products may appear as a viable measure in seronegative patients, this would completely eliminate the risk of transmission.

In a study conducted by Jaber et al. [13], patients with hospital-acquired infections were found to have significantly higher rates of CMV reactivation. In the present study, there was no significant difference between the patients with or without hospital-acquired infections in terms of CMV reactivation. Hospital-acquired infections are caused by the conditions in the hospital and ICU, the adherence of hospital staff to infection control measures, and patient-specific clinical features. This may vary according to underlying disorders and associated risk factors.

Frantzeskaki et al. [7] found a relationship between CMV reactivation and CRP and IL-10 levels in immunocompetent ICU patients and suggested that reactivation could be related to the severity of inflammation. Elevated CRP levels, in addition to being a nonspecific acute phase reactant, may suggest reactivation in such high-risk patients.

There is controversy over the delivery of a therapy, since the effect of reactivation on mortality is unclear in immunocompetent patients. Given the side effects of antiviral medications, antiviral therapy planning must be based on clinical observation and patient-specific risk factors [14].

There are a very limited number of studies on EBV reactivation, although many have addressed the reactivation of CMV and other herpes viruses in ICU patients. Despite the well-established role of EBV in immunocompromised patients, recent studies on different groups have found that the virus could also become reactivated in immunocompetent patients. EBV reactivation was reported in patients under stressed conditions who were not followed in ICU [5, 22].

EBV infections are widespread throughout the world. The rate of seropositivity

was found to be around 90 % in the adult population [11]. Zeytinoglu et al. [30] reported that EBV VCA IgG antibodies, the indicator of a past infection, are found in 67.9 % of subjects in the first 4 years of life and this ratio increases to 84.4 % in the first 30 years of life, with the incidence increasing with age.

There are a limited number of studies regarding EBV reactivation in immunocompetent ICU patients. The rates of reactivation may vary from one center to another as well as in different patient groups. Libert et al. [17] evaluated reactivation status by measuring blood EBV DNA levels in immunocompetent patients who stayed longer than 5 days in the ICU and reported viral reactivation in 61 out of the 86 patients (70.9 %) who were tested positive for EBV. In a multicenter study that evaluated viral reactivation in patients with sepsis, 53.2 % of the patients were found to be seropositive in blood EBV DNA analysis [28]. One study in Germany on patients who were hospitalized in an ICU due to pneumonia reported EBV DNA in the bronchoalveolar lavage fluid in 48 of the 135 patients (35.6 %) [8]. This finding is affected by many factors, including patient-specific factors and disease characteristics, the therapies administered, and length of hospitalization. In addition, differences in diagnostic methods and laboratory kits used may have influenced these rates.

In terms of survival, no significant difference was found between the patients with or without EBV reactivation. In their study, Libert et al. [17] reported higher mortality rate in the reactivation group, whereas in a multicenter study conducted by Walton et al. [28], the 90-day mortality rate in EBV DNA-positive patients was lower compared with EBV DNA-negative patients. As indicated in the study by Sousa et al. [25], the detection of viremia, even in healthy individuals, complicates establishing a relationship between the EBV viral load and disease severity. Mortality can be associated with EBV reactivation but also with the risk factors associated with EBV infection. EBV reactivation in critically ill patients is not sufficient to explain the relationship between reactivation and mortality, due to the latent infection status

of EBV and the detection of the virus in various tissue samples from healthy subjects.

In all patients, EBV reactivation was detected in plasma samples obtained on day 7 of hospitalization. Similarly, Libert et al. [17] reported a mean 7.5 days for reactivation. Prolonged hospitalization in the ICU can be suggested to increase the frequency of EBV reactivation [28]. On the other hand, in another study [8], no significant difference was found in terms of the length of stay in the ICU when EBV DNA-positive patients were compared with EBV DNA-negative patients. Although the primary diagnosis of the patient, disease severity, the therapies administered, the presence of hospital-acquired infections, comorbid conditions, and interventions performed, all have an influence on the occurrence of reactivation in critically ill patients, we found no association between those risk factors and viral reactivation attributable to relatively small sample size in this study.

ICU patients can develop fever due to both infectious and noninfectious causes. It would be appropriate to consider viral reactivations only after excluding the primary causes of the fever. In the present study, the rate of EBV reactivation during the 28-day follow-up period was significantly higher in patients with fever when compared with those without fever ($p = 0.035$).

Mechanical ventilator support was found to have significantly increased the rate of EBV reactivation ($p = 0.023$). There was no significant difference between these patients in terms of survival during the 28-day follow-up period. Those studies in the literature which evaluated the relationship between the mechanical ventilation support and viral reactivation have often focused on the herpes simplex virus and CMV [4, 13, 15, 19, 27]. There are also studies reporting an association between EBV reactivation and presence and the duration of mechanical ventilation support in immunocompetent patients [8, 17]. Based on these findings, mechanical ventilation can be a risk factor for EBV reactivation. It would be appropriate to perform longer follow-up in order to clarify its association with survival.

Although the present study did not find any relationship between inflammatory marker hsCRP levels and reactivation, the studies that evaluated this parameter in patients with a high Sequential Organ Failure Assessment (SOFA) score, together with other inflammatory mediators (i. e., interleukin-6, procalcitonin, IL-10, and tumor necrosis factor), have reported significant differences [8, 17, 28]. Comparative studies, evaluated together with ICU scoring systems, could provide more reliable information regarding the relationship between reactivation and disease severity.

As in other studies, the present study found no relationship between EBV reactivation and blood transfusion and the presence of anemia [17, 25, 28]. Routine screening for EBV is not performed in donor blood due to the high prevalence in the population and latent infection status. The use of leukocyte-depleted blood products significantly reduced EBV and CMV transmission [2]. The prevalence of EBV in the population must be taken into consideration while prescribing transfusion in immunocompetent patients.

In a multicenter study that evaluated EBV reactivation in patients with sepsis, viral infections were reported to be more frequent in the presence of secondary fungal infections and opportunistic bacterial infections [28]. Considering the fact that the risk of hospital-acquired infections increases with prolonged hospitalization, patients must be followed for a longer period in order to establish a relationship between viral reactivation and hospital-acquired infections.

There are some limitations of this study. First, the small sample size may have affected our results. Therefore, our results should be interpreted with caution. Second, we did not have immunosuppressed patients. Diagnosis of CMV and EBV infection in such critically ill but immunocompetent cases is an area of controversy and there are no uniform guidelines available. There is still a diagnostic dilemma between active infection and disease. Qualitative determination of viral DNA by PCR cannot distinguish between latent and active viral DNA replication, thereby decreasing the specificity of the test. It

is important for predicting disease risk to differentiate low vs. high level of viral replication. In clinical practice, to consider this diagnosis a quantitative determination of viral load must be done and have compatible clinical manifestations.

Conclusion

Viral reactivation must be considered in immunocompetent critically ill patients who develop refractory fever despite appropriate antibiotic therapy when the source of infection cannot be determined and cultures fail to show any bacterial growth.

Corresponding address

A. Karakaş, M.D. (Associate Professor)
Department of Infectious Diseases and Clinical Microbiology, Gulhane Military Medical Academy
Etlik/Ankara, Turkey
akarakas@gata.edu.tr

## Compliance with ethical guidelines

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Buchbesprechung

R. Larsen, unter Mitarbeit von T. Fink und T. Müller-Wolff

Anästhesie und Intensivmedizin für die Fachpflege

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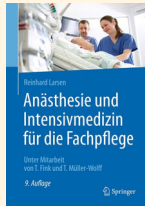
In der bewährten Struktur der Aufteilung in einen anästhesiologischen und intensivmedizinischen Abschnitt, präsentiert sich dieses Standardwerk in der 9. Auflage, und ist seit über 30 Jahren auf dem Markt. Die Inhalte der einzelnen Kapitel wurden sinnvoll überarbeitet, gekürzt oder ergänzt. So ist beispielsweise ein eigenes Kapitel zum Themenkomplex der Herz-Kreislauf-Funktionsstörungen platziert worden. Die vorgenommene „Verjüngung" einiger Kapitel spiegelt die Aktualisierung wieder und erhöht dem besseren Lese- und Informationsfluss. Allerdings sind diesem Vorgehen auch wenige Erklärungen und Abbildungen zum Opfer gefallen (z.B. Abbildung der ProSeal-Larynxmaske). Dies ist verschmerzbar, da die neue Gliederung gezieltes und schnelles Recherchieren problemlos zulässt.

Auch in dieser Auflage wurden zahlreiche pflegerelevante Themenbereiche, wie beispielsweise Körperpflege, Übergabe, Überwachung, Atemtherapie, Beatmung, NIV, mit der Unterstützung von Experten aus der Intensivpflege, praxisnah und evidenzbasiert be- bzw. überarbeitet. Ein entsprechender Praxisbezug wird dadurch deutlich unterstützt.

Aktuelle Leitlinien (u.a. Lagerungstherapien, Frühmobilisation, Delirmanagement, Prolongiertes Weaning) wurden bei den einzelnen Kapitel berücksichtigt und miteinbezogen. Beim Thema Dekubitus wäre ein Hinweis auf die Einteilung nach EPUAP hilfreich gewesen, um die derzeit gültige Einteilung nach Kategorien gerecht zu werden.

Die aktuellen ERC-Leitlinien ergänzen den grafischen Aufbau der einzelnen Kapitel. So werden zum Beispiel das Atemwegsmanagement und die kardiopulmonale Reanimation sehr gut dargestellt.

Für weiterführende Informationen und vertiefende Wissensquellen dienen am Ende jedes Kapitels die Verweise auf Nachschlagewerke und aktuelle Websites.

Die 9. Auflage ist Dank der inhaltlichen und grafischen Überarbeitung weiter als Standardwerk für die Fachpflege sehr zu empfehlen. Die Aktualisierung ist fast durchgängig gelungen. Auch wenn das Format und Gewicht (eBook Ausführung erwerbbar) eine arbeitsplatznahe Anwendung eher schwierig macht, ist das Buch ein bewährter Begleiter bei fachlichen Fragen.

Lutz Krüger
Kursleitung I+A
Lehrer für Pflegeberufe
Klinikum Landkreis Erding