Acta Clin Croat 2025; 64:388-394
doi: 10.20471/acc.2025.64.02.23

Case Report

CONCURRENT *CLOSTRIDIUM DIFFICILE* COLITIS AND CYTOMEGALOVIRUS INFECTION AS A CAUSE OF PERSISTENT DIARRHEA AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR NON-HODGKIN LYMPHOMA FOLLOWING BENDAMUSTINE-BASED CONDITIONING

Martina Sedinić Lacko[1], Zdravko Mitrović[1,3], Sandra Šestan Crnek[2], Ozren Jakšić[1,3], Željko Prka[1] and Vlatko Pejša[1,3]

[1]Division of Hematology, Department of Internal Medicine, Dubrava University Hospital, Zagreb, Croatia; [2]Center for Clinical Microbiology and Hospital Infections, Dubrava University Hospital, Zagreb, Croatia; [3]School of Medicine, University of Zagreb, Zagreb, Croatia

SUMMARY – Diarrhea usually appears early following autologous hematopoietic stem cell transplantation (ASCT) due to toxic mucosal damage and neutropenia. Infectious agents also cause diarrhea in the post-transplantation period, with *Clostridium difficile (C. difficile)* being most common. In contrast, cytomegalovirus (CMV) enterocolitis is extremely rare after ASCT. We report a case of a 55-year-old male who underwent ASCT for non-Hodgkin lymphoma that was complicated by severe persistent diarrhea resulting in significant hypovolemia and electrolyte imbalance. Prior to transplantation, the patient received rituximab in combination with chemotherapy (R-CHOP/R-DHAP) followed by a bendamustine-based conditioning regimen (BeEAM). After treatment with oral metronidazole, vancomycin and fidaxomicin, diarrhea persisted despite undetectable *C. difficile* toxin, with elevation of hepatic enzymes. Eventually, CMV infection was diagnosed by real-time polymerase chain reaction and treated with ganciclovir and valganciclovir. Due to hypogammaglobulinemia following previous rituximab treatment, CMV immunoglobulins were also administered. The patient's condition gradually improved with CMV DNA being undetectable in serum. This case shows that diarrhea may be caused by concurrent infection with *C. difficile* and CMV after ASCT. Bendamustine-induced colitis and prior rituximab treatment may have been additional risk factors in this patient. Therefore, more comprehensive workup of diarrhea is needed in ASCT recipients treated with these agents.

Key words: *Autologous hematopoietic stem cell transplantation; Cytomegalovirus; Clostridium difficile; Colitis; Bendamustine; Rituximab*

Introduction

Clostridium difficile infection (CDI) is the leading cause of nosocomial diarrhea and a well-known early complication of autologous stem cell transplantation

Correspondence to: *Zdravko Mitrović, MD*, Division of Hematology, Department of Medicine, Dubrava University Hospital, Av. G. Šuška 6, HR-10000 Zagreb, Croatia
E-mail: zdravko.mitrovic@mef.hr

Received May 6, 2019, accepted December 16, 2019

(ASCT). These patients may have a particularly high risk of developing CDI due to long hospital stay, administration of broad-spectrum antibiotics, underlying immunodeficiencies, and chemotherapy-related disruption of enteric mucosal barriers[1].

Cytomegalovirus (CMV) is a recognized cause of morbidity and mortality in immunocompromised patients. CMV reactivation occurs frequently after transplantation in patients who were seropositive before transplantation or who have seropositive donors[2]. Active CMV infection occurs in a significant number of allogeneic and less frequently in ASCT recipients[3]. Pneumonitis is the most common manifestation among transplant recipients, with enteritis being the second most common, occurring more often among older individuals. However, the incidence of CMV enterocolitis among hematopoietic stem cell recipients remains low and it is significantly lower in ASCT[2,3].

The BEAM (carmustine, etoposide, cytarabine, melphalan) conditioning regimen has been considered the gold standard for patients with lymphoma undergoing ASCT. However, due to carmustine shortage, BeEAM (carmustine replaced by bendamustine) is being increasingly used as an alternative conditioning regimen. On safety evaluation of this regimen, one of the frequently reported toxicities was colitis[4-7].

In this paper, we report a case of CDI and CMV infection as early ASCT complications following conditioning with BeEAM. In addition, a review of previously reported cases of concurrent CDI and CMV enterocolitis published in medical literature is presented.

Case Report

A 55-year-old male diagnosed with advanced stage mantle cell non-Hodgkin lymphoma (NHL) received chemotherapy consisting of alternating R-DHAP (dexamethasone, cytarabine, cisplatin + rituximab) and R-CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone + rituximab) for a total of six cycles, after which he achieved complete remission and underwent ASCT. Prior to conditioning regimen with BeEAM (bendamustine at a dose of 160 mg/m^2), the patient was in good general condition without any signs of infection. On day +4 after the transplant, the patient developed neutropenic fever with abdominal pain. Empirical antimicrobial treatment with cefepime, metronidazole and vancomycin was initiated, and later due to prolonged fever changed to levofloxacin, meropenem and linezolid. Oseltamivir was added after influenza A virus had been detected by polymerase chain reaction (PCR) in nasopharyngeal secretions. On day +11, white blood cell count recovered, however, the patient developed abdominal cramps with severe diarrhea (more than 20 stools *per* day) and persistent fever. *Clostridium difficile* toxins A and B were detected by chromatographic immunoassay in the stool and metronidazole *per os* was initiated. Computed tomography (CT) scans showed distal and rectosigmoid colon thickening with diverticulosis, as well as jejunum thickening, indicating severe diffuse enterocolitis (Fig. 1). Laboratory tests also revealed hepatic injury through increased hepatic enzymes. The patient developed hemodynamic instability due to significant dehydration, severe electrolyte imbalance (hypokalemia, hyponatremia, hypocalcemia, hypomagnesemia and hypophosphatemia) and

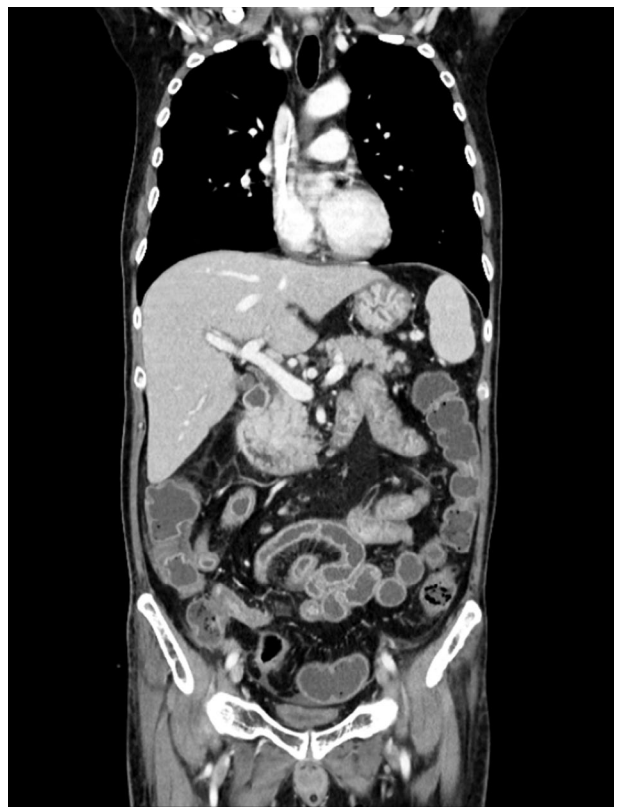

Fig. 1. Computed tomography scan showing jejunum and colon thickening.

hypoalbuminemia. Consequently, the patient was temporarily transferred to the intensive care unit. Despite broad spectrum antimicrobial treatment and subsequent introduction of vancomycin *per os* followed by fidaxomicin for *C. difficile* colitis, fever and diarrhea remained persistent (10 to 20 stools *per* day). *C. difficile* toxins were negative and toxigenic *C. difficile* was negative by PCR. Follow up CT scans showed no improvement while *Acinetobacter baumannii* and vancomycin resistant *Enterococcus faecium* were isolated from the stool. His perianal region was severely irritated by frequent stools, thus further deteriorating his condition. Finally, following the lack of response, real-time PCR for CMV was done and CMV DNA with 6740 IU/mL was detected. However, rectosigmoidoscopy with histologic evaluation revealed nonspecific inflammatory changes without CMV inclusions. CMV serology test was IgG positive and IgM negative. Considering the clinical presentation and CMV viremia, systemic CMV infection with colitis and hepatitis was suspected and dose-adjusted ganciclovir was introduced, followed by valganciclovir. Due to severe hypogammaglobulinemia (2.6 g/L; normal range: 8.9-16.8 g/L), CMV immunoglobulins (CMV-IG; Cytotect®) were also administered at a dose of 100 U/kg weekly for two applications. The patient's condition gradually improved with significantly decreased number of stools. An improvement of hepatic enzymes and normalization of inflammatory marker levels were also observed, further confirming suspected CMV colitis and hepatitis. Follow up real-time PCR for CMV was negative. The patient was dismissed from the hospital in an improved general condition. However, he still suffered from persistent moderate diarrhea (five to ten stools *per* day), probably due to chemotherapy-associated colitis. Two months later, the patient had normal stool frequency and consistency with slightly elevated liver enzymes and the rituximab maintenance treatment was continued.

Discussion

Infectious diarrhea is an extensively described complication of ASCT with *C. difficile* being one of the most common infectious agents, with the incidence ranging from 3.8% to 6.9%[1,8]. The recommended treatment includes metronidazole for mild and moderate infection, and oral vancomycin for patients with severe or complicated infection. Recently, fidaxomicin has been introduced as a novel agent that provides sustained cure rates compared with vancomycin and metronidazole[9,10]. The administration of vancomycin and fidaxomicin in our patient did not lead to significant improvement in clinical outcome even though *C. difficile* toxin was no longer detectable. Therefore, other causes of diarrhea were suspected.

In an ASCT setting, CMV end-organ disease is rare occurrence, with the gastrointestinal (GI) tract being a rarely affected end-organ. According to Wingard *et al.*, CMV disease occurs in only 2% of ASCT recipients, while only 0.4% of them develop CMV enteritis[3]. Furthermore, van Burik *et al.* report on the incidence of CMV enteritis in ASCT recipients of only 0.2%[2]. According to Marchesi *et al.*, a pre-transplant seropositivity, a diagnosis of NHL and higher median age at transplant were associated with the risk of developing a clinically relevant CMV infection[11]. The gold standard for detection of CMV in GI mucosal biopsies is CMV-specific immunohistochemistry (IHC). Hematoxylin and eosin (H&E) staining may show typical viral inclusions ('owl eye appearance' inclusions) being highly specific for CMV, but the method is not sensitive compared to IHC and tissue PCR[12]. In our patient, CMV inclusions were not found, however, CMV DNA was detected by real-time PCR. Positive CMV by PCR from peripheral blood confirms CMV infection, yet it is not diagnostic for CMV colitis[12]. Nevertheless, in the context of clinical signs and symptoms, it is highly suggestive of CMV tissue invasive disease. The treatment of CMV infection includes ganciclovir and valganciclovir[13], whereas foscarnet can be used for ganciclovir-resistant cases[14]. In addition, CMV-IG may be used in transplant recipients as adjunctive treatment. This strategy improved the survival rate in different groups of transplant patients with CMV pneumonitis[15-18]. In contrast, data on HSCT recipients with CMV enteritis are scarce. A study by Alexander *et al.* included patients with enteritis in addition to those with pneumonitis and these authors report lower mortality rates compared to antiviral monotherapy[19]. Due to severe hypogammaglobulinemia in our patient, we administered CMV-IG in addition to ganciclovir.

For the purpose of this article, we searched PubMed, combining the terms cytomegalovirus colitis

Table 1. Case reports of concurrent Clostridium difficile and cytomegalovirus enterocolitis published in medical literature

Reference	Age	Gender	Underlying condition	Immune system function	First pathogen diagnosed	C. *difficile* treatment	CMV treatment	CMV-IG administration	Outcome
Kottaridis *et al.*[20]	59	M	ALCL	Immunocompromised	*C. difficile*	Metronidazole and vancomycin	Ganciclovir	No	Recovery
Nichols *et al.*[21]	52	M	Lung transplant	Immunocompromised	*C. difficile*	Metronidazole	Ganciclovir	Yes	Death
Riva *et al.*[22]	39	M	ALL	Immunocompromised	CMV	Metronidazole	Foscarnet	No	Recovery
Veroux *et al.*[23]	42	F	Renal transplant	Immunocompromised	CMV	Metronidazole and vancomycin	Ganciclovir	No	Death
Alkhatib *et al.*[24]	81	M	Pneumonia	Immunocompetent	*C. difficile*	Metronidazole and vancomycin	Ganciclovir	No	Recovery
Dahman *et al.*[25]	73	F	Renal transplant	Immunocompromised	*C. difficile*	Metronidazole and vancomycin	Ganciclovir	No	Recovery
Florescu *et al.*[26]	35	M	Pancreatic transplant	Immunocompromised	CMV	Metronidazole	Valganciclovir and ganciclovir	No	Recovery
	55	F	Renal transplant	Immunocompromised	*C. difficile*	Metronidazole and vancomycin	Valganciclovir and ganciclovir	No	Recovery
Kurtz, Morgan[27]	78	F	GERD	Immunocompetent	*C. difficile*	Metronidazole, vancomycin and fidaxomicin	Ganciclovir and valganciclovir	No	Recovery
Antonio *et al.*[28]	37	F	Morbid obesity	Immunocompetent	*C. difficile*	Metronidazole and vancomycin	Ganciclovir and foscarnet	No	Recovery
John *et al.*[29]	63	M	Squamous cell carcinoma	Immunocompromised	*C. difficile*	Metronidazole, vancomycin and fidaxomicin	Valganciclovir	No	Recovery
Dumitru et *al.*[30]	53	M	Duodenal ulcer	Immunocompetent	*C. difficile*	Metronidazole, vancomycin and rifaximin	Ganciclovir and fecal transplantation	No	Recovery
Hung *et al.*[31]	85	M	Septic shock	Immunocompromised	*C. difficile*	Metronidazole and vancomycin	Ganciclovir	No	Recovery
Papaconstantinou *et al.*[32]	17	M	Refractory UC	Immunocompetent	*C. difficile*	Metronidazole and vancomycin	Ganciclovir	No	Recovery
Harano *et al.*[33]	60	F	NR	Immunocompetent	*C. difficile*	Metronidazole	NR	No	Recovery
Chao *et al.*[34]	63	F	NR	Immunocompetent	*C. difficile*	Metronidazole, vancomycin and fecal microbiota transplant	Ganciclovir and valganciclovir	No	Recovery
Present report	55	M	MCL	Immunocompromised	*C. difficil*e	Vancomycin and fidaxomicin	Ganciclovir and valganciclovir	Yes	Recovery

M = male; F= female; ALCL = anaplastic large cell lymphoma; ALL = acute lymphoblastic leukemia; GERD = gastroesophageal reflux disease; UC = ulcerative colitis; NS = nonsignificant; MCL = mantle cell lymphoma; *C. difficile* = *Clostridium difficile*; CMV = cytomegalovirus; CMV-IG = cytomegalovirus immunoglobulin; NR = not reported

and *Clostridium difficile*, and the search resulted in 61 articles. The criteria for exclusion were non-English language articles and articles that are not presenting concurrent CDI and CMV infection. We reviewed a total of 15 articles and compared underlying conditions, immune system function, treatment, and outcome (Table 1)[20-34]. Concurrent occurrence of two pathogens with similar clinical manifestations, especially when one of the pathogens occurs rarely, created a significant diagnostic problem in most of the reported cases. Most of the patients were immunocompromised and presented with several risk factors for both infections, such as solid organ transplantation and immunosuppressive therapy in seven patients, or hematologic malignancies in two patients. A possible explanation is that the infection might predispose a patient to develop the second infection affecting the same organ[26]. Similar to our patient, a case of CMV enterocolitis masked by CDI after ASCT for NHL has been reported by Kottaridis *et al.*[20]. However, our patient had additional risk factors for enterocolitis, such as prior rituximab treatment and bendamustine-based conditioning.

The anti-CD20 monoclonal antibody rituximab is used in the treatment of B-cell malignancies. It reduces the number and function of normal B cells, thereby lowering the immunoglobulin levels and consequently facilitating the CMV reactivation after HSCT[35,36].

There are serious concerns about safety of bendamustine-based conditioning prior to ASCT[5,6,37]. Recently, we have reported a retrospective analysis comparing a cohort of ASCT patients receiving either BEAM or BeEAM conditioning regimen, showing that patients receiving bendamustine were significantly more likely to require ICU management, develop acute kidney injury, develop febrile neutropenia, and had a significantly higher 100-day mortality[37]. Considering the toxicity of bendamustine, another important issue in our patient was the chemotherapy-induced mucosal damage. It has been shown that bendamustine-based conditioning regimen may be associated with digestive toxicity, including enterocolitis in a significant proportion of patients[5-7]. Garciaz *et al.* report on grade III-IV enterocolitis in 17% of the patients treated with BeEAM[6]. The incidence of grade I-IV colitis was 32% in the BeEAM group, as reported by Chantepie *et al.*[5], while Saleh *et al.* report on grade III or greater diarrhea in even 44% of the BeEAM patients[7]. Persistence of diarrhea in our patient even after *C. difficile* and CMV resolution supports this hypothesis.

To our knowledge, this is the first case report of concurrent *C. difficile* and CMV colitis in a transplant recipient treated with bendamustine-conditioning regimen and prior rituximab treatment. In contrast to the previously presented cases, our patient was successfully treated with fidaxomicin and CMV-IG in addition to standard antiviral treatment. Whether this treatment should become standard in this group of patients, remains to be elucidated in prospective trials.

Conclusion

C. difficile infection is a common early complication of hematopoietic stem cell transplant. Hematopoietic stem cell transplant recipients represent a high-risk population due to chemotherapy induced mucosal damage, neutropenia, and immunosuppression. This case shows that patients with persistent diarrhea after vigorous treatment for *C. difficile* should be also evaluated for CMV infection. Previous rituximab treatment and bendamustine-based conditioning in this patient may have been additional contributing factors.

References

1. Alonso CD, Treadway SB, Hanna DB, *et al.* Epidemiology and outcomes of *Clostridium difficile* infections in hematopoietic stem cell transplant recipients. Clin Infect Dis. 2012;54:1053-63. doi: 10.1093/cid/cir1035.
2. van Burik JA, Lawatsch EJ, DeFor TE, *et al.* Cytomegalovirus enteritis among hematopoietic stem cell transplant recipients. Biol Blood Marrow Transplant. 2001;7:674-9.
3. Wingard JR, Piantadosi S, Burns WH, *et al.* Cytomegalovirus infections in bone marrow transplant recipients given intensive cytoreductive therapy. Rev Infect Dis. 1990;12 Suppl 7:S793-804. doi: 10.1053/bbmt.2001.v7.pm11787530.
4. Visani G, Malerba L, Stefani PM, *et al.* BeEAM (bendamustine, etoposide, cytarabine, melphalan) before autologous stem cell transplantation is safe and effective for resistant/relapsed lymphoma patients. Blood. 2011;118:3419-25. doi: 10.1182/blood-2011-04-351924.
5. Chantepie SP, Garciaz S, Tchernonog E, *et al.* Bendamustine-based conditioning prior to autologous stem cell transplan-

tation (ASCT): results of a French multicenter study of 474 patients from Lymphoma Study Association (LYSA) centers. Am J Hematol. 2018;93:729-35. doi: 10.1002/ajh.25077.
6. Garciaz S, Coso D, Schiano de Collela JM, *et al*. Bendamustine-based conditioning for non-Hodgkin lymphoma autologous transplantation: an increasing risk of renal toxicity. Bone Marrow Transplant. 2016;51:319-21. doi: 10.1038/bmt.2015.257.
7. Saleh K, Danu A, Koscielny S, *et al*. A retrospective, matched paired analysis comparing bendamustine containing BeEAM *versus* BEAM conditioning regimen: results from a single center experience. Leuk Lymphoma. 2017;22:1-8. doi: 10.1080/10428194.2017.1403019.
8. Zacharioudakis IM, Ziakas PD, Mylonakis E. *Clostridium difficile* infection in the hematopoietic unit: a meta-analysis of published studies. Biol Blood Marrow Transplant. 2014;20:1650-4. doi: 10.1016/j.bbmt.2014.06.001.
9. Rineh A, Kelso MJ, Vatansever F, *et al*. *Clostridium difficile* infection: molecular pathogenesis and novel therapeutics. Expert Rev Anti Infect Ther. 2014;12:131-50. doi: 10.1586/14787210.2014.866515.
10. Cornely OA, Nathwani D, Ivanescu C, *et al*. Clinical efficacy of fidaxomicin compared with vancomycin and metronidazole in *Clostridium difficile* infections: a meta-analysis and indirect treatment comparison. J Antimicrob Chemother. 2014;69:2892-900. doi: 10.1093/jac/dku261.
11. Marchesi F, Pimpinelli F, Gumenyuk S, *et al*. Cytomegalovirus reactivation after autologous stem cell transplantation in myeloma and lymphoma patients: a single-center study. World J Transplant. 2015;5:129-36. doi: 10.5500/wjt.v5.i3.129.
12. Yerushalmy-Feler A, Padlipsky J, Cohen S. Diagnosis and management of CMV colitis. Curr Infect Dis Rep. 2019;21:5. doi: 10.1007/s11908-019-0664-y.
13. Kotton CN. CMV: prevention, diagnosis and therapy. Am J Transplant. 2013;13 Suppl 3:24-40. doi: 10.1111/ajt.12006.
14. Wagstaff AJ, Bryson HM. Foscarnet. A reappraisal of its antiviral activity, pharmacokinetic properties and therapeutic use in immunocompromised patients with viral infections. Drugs. 1994;48:199. doi: 10.2165/00003495-199448020-00007.
15. Ljungman P, Engelhard D, Link H, *et al*. Treatment of interstitial pneumonitis due to cytomegalovirus with ganciclovir and intravenous immune globulin: experience of European Bone Marrow Transplant Group. Clin Infect Dis. 1992;14:831-5. doi: 10.1093/clinids/14.4.83.
16. Emanuel D, Cunningham I, Jules-Elysee K, *et al*. Cytomegalovirus pneumonia after bone marrow transplantation successfully treated with the combination of ganciclovir and high-dose intravenous immune globulin. Ann Intern Med. 1988;109:777-82. doi: 10.7326/0003-4819-109-10-777.
17. Reed EC, Bowden RA, Dandliker PS, *et al*. Treatment of cytomegalovirus pneumonia with ganciclovir and intravenous cytomegalovirus immunoglobulin in patients with bone marrow transplants. Ann Intern Med. 1988;109:783-8. doi: 10.7326/0003-4819-109-10-783.
18. Schmidt GM, Kovacs A, Zaia JA, *et al*. Ganciclovir/immunoglobulin combination therapy for the treatment of human cytomegalovirus-associated interstitial pneumonia in bone marrow allograft recipients. Transplantation. 1988;46:905-7. PMID: 2849818.
19. Alexander BT, Hladnik LM, Augustin KM, *et al*. Use of cytomegalovirus intravenous immune globulin for the adjunctive treatment of cytomegalovirus in hematopoietic stem cell transplant recipients. Pharmacotherapy. 2010;30:554-61. doi: 10.1592/phco.30.6.554.
20. Kottaridis PD, Peggs K, Devereux S, *et al*. Simultaneous occurrence of *Clostridium difficile* and cytomegalovirus colitis in a recipient of autologous stem cell transplantation. Haematologica. 2000;85:1116-7. PMID: 11025618.
21. Nichols L, Strollo DC, Kusne S. Legionellosis in a lung transplant recipient obscured by cytomegalovirus infection and *Clostridium difficile* colitis. Transpl Infect Dis. 2002;4:41-5. doi: 10.1034/j.1399-3062.2002.t01-1-01001.x.
22. Riva G, Luppi M, Potenza L, *et al*. Cytomegalovirus and *Clostridium difficile* co-infection in severe ulcero-hemorrhagic colitis during induction chemotherapy for acute lymphoblastic leukemia. Haematologica. 2005;90:ECR01. PMID: 15653455.
23. Veroux M, Puzzo L, Corona D, *et al*. Cytomegalovirus and *Clostridium difficile* ischemic colitis in a renal transplant recipient: a lethal complication of anti-rejection therapy? Urol Int. 2007;79:177-9. doi: 10.1159/000106334.
24. Alkhatib AA, Tietze CC, Peterson KA, *et al*. Cytomegalovirus clostridium colitis disease in an immunocompetent patient. South Med J. 2009;102:775-6. doi: 10.1097/SMJ.0b013e3181a9030a.
25. Dahman M, Krell R, Brayman K, *et al*. Simultaneous *Clostridium difficile*-associated colitis and late-onset intestinal cytomegalovirus disease in a renal transplant recipient. Ann Transplant. 2010;15:72. PMID: 21183880.
26. Florescu DF, Mindru C, Chambers HE, *et al*. *Clostridium difficile* and cytomegalovirus colitis co-infection: search for the hidden 'bug'. Transpl Infect Dis. 2011;13:411-5. doi: 10.1111/j.1399-3062.2011.00605.x.
27. Kurtz M, Morgan M. Concomitant *Clostridium difficile* colitis and cytomegalovirus colitis in an immunocompetent elderly female. BMJ Case Rep. 2012;2012. doi: 10.1136/bcr-2012-007273.
28. Antonio AC, Maccari JG, Seabra A, *et al*. *Clostridium difficile* and cytomegalovirus colitis coinfection after bariatric surgery: case

report. Arg Bras Cir Dig. 2013;26 Suppl 1:85-7. doi: 10.1590/S0102-67202013000600019.

29. John SG, Dominguez C, Chandiramani V, *et al*. A rare case intractable diarrhea secondary to *Clostridium difficile* and cytomegalovirus coinfection. Am J Case Rep. 2013;14:498-501. doi: 10.12659/AJCR.889700.
30. Dumitru IM, Dumitru E, Resul G, *et al*. Concomitant CMV and *Clostridium difficile* colitis in an immunocompetent patient treated with ganciclovir and fecal transplantation. J Gastrointestin Liver Dis. 2014;23:221-2. PMID: 24949617.
31. Hung YP, Lin HJ, Wu CJ, *et al*. Vancomycin-resistant *Clostridium innocuum* bacteremia following oral vancomycin for *Clostridium difficile* infection. Anaerobe. 2014;30:24-6. doi: 10.1016/j.anaerobe.2014.07.009.
32. Papaconstantinou I, Zampeli E, Dellaportas D, *et al*. Synchronous cytomegalovirus and *Clostridium difficile* infection of the pouch: a trigger for chronic pouchitis? Clin J Gastroenterol. 2014;7:132-5. doi: 10.1007/s12328-014-0458-6.
33. Harano Y, Kotajima L, Arioka H. Case of cytomegalovirus colitis in an immunocompetent patient: a rare cause of abdominal pain and diarrhea in the elderly. Int J Gen Med. 2015;8:97-100. doi: 10.2147/IJGM.S63771.
34. Chao HC, Yu WL. Treatment failure of fecal microbiota transplant for pseudomembranous colitis due to coexistent cytomegalovirus colitis. J Microbiol Immunol Infect. 2016;49:617-8. doi: 10.1016/j.jmii.2015.05.021.
35. Vieira CA, Agarwal A, Book BK, *et al*. Rituximab for reduction of anti-HLA antibodies in patients awaiting renal transplantation: 1. Safety, pharmacodynamics, and pharmacokinetics. Transplantation. 2004;77:542-8. doi: 10.1097/01.TP.0000112934.12622.2B.
36. Lee MY, Chiou TJ, Hsiao LT, *et al*. Rituximab therapy increased post-transplant cytomegalovirus complications in non-Hodgkin's lymphoma patients receiving autologous hematopoietic stem cell transplantation. Ann Hematol. 2008;87:285-9. doi: 10.1007/s00277-007-0397-0.
37. Lucijanic M, Prka Z, Jaksic O, *et al*. Bendamustine-based conditioning prior to autologous stem cell transplantation is associated with high rate of febrile neutropenia and higher mortality. Am J Hematol. 2019;94:E42-E43. doi: 10.1002/ajh.25340.

Sažetak

ISTODOBNI *C. DIFFICILE* KOLITIS I CITOMEGALOVIRUSNA INFEKCIJA KAO UZROK USTRAJNOG PROLJEVA KOD BOLESNIKA S NE-HODGKINOVIM LIMFOMOM NAKON KONDICIONIRANJA BAZIRANOG NA BENDAMUSTINU I AUTOLOGNE TRANSPLANTACIJE KRVOTVORNIH MATIČNIH STANICA

M. Sedinić, Z. Mitrović, S. Šestan Crnek, O. Jakšić, Ž. Prka i *V. Pejša*

Proljev je česta komplikacija autologne transplantacije krvotvornih matičnih stanica (ATKMS), uzrokovan je različitim infektivnim uzročnicima, a potpomognut toksičnim oštećenjem crijevne sluznice i neutropenijom. *Clostridium difficile (C. difficile)* jedan je od najčešćih uzročnika proljeva, dok se citomegalovirusni (CMV) enterokolitis vrlo rijetko opisuje nakon ATKMS. Prikazujemo slučaj 55-godišnjeg muškarca s razvojem teškog ustrajnog proljeva sa značajnom hipovolemijom i poremećajem elektrolita nakon ATKMS zbog ne-Hodgkinovog limfoma. Prije transplantacije bolesnik je liječen rituksimabom u kombinaciji s kemoterapijom (R-CHOP/R-DHAP), a u sklopu kondicioniranja dobio je bendamustin kao dio protokola BeEAM. Nakon liječenja dokazane *C. difficile* infekcije metronidazolom *per os*, vankomicinom i fidaksomicinom proljev je i dalje ustrajao unatoč negativnom toksinu *C. difficile* u stolici. Bolesnik je bio febrilan uz povišene jetrene enzime. Naposljetku, lančanom reakcijom polimerazom u stvarnom vremenu dokazana je infekcija CMV koja je liječena ganciklovirom i valganciklovirom. Zbog hipogamaglobulinemije nakon prethodnog liječenja rituksimabom primijenjeni su i CMV-specifični imunoglobulini. Bolesnikovo stanje se postupno popravilo, a CMV DNA u serumu je postala nedetektabilna. Ovaj slučaj pokazuje da proljev nakon ATKMS može biti uzrokovan usporednom infekcijom *C. difficile* i CMV-om. Oštećenje stijenke crijeva kemoterapijom koja je sadržavala bendamustin (BeEAM) kao i prethodna primjena rituksimaba vjerojatno su predstavljali dodatni rizični čimbenik. Stoga pojava proljeva kod takvih bolesnika zahtijeva sveobuhvatniju obradu.

Ključne riječi: *Autologna transplantacija krvotvornih matičnih stanica; Citomegalovirus; Clostridium difficile; Kolitis; Bendamustin; Rituksimab*