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Patients with multiple myeloma infected with COVID-19 during autologous stem cell transplantation

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Abstract

Despite the global vaccination campaigns, certain patient groups remain highly vulnerable to SARS-CoV-2 and are at high risk for unfavorable COVID-19 outcomes. As previously shown by our group and a more recent report by Chang Su and coworkers, patients with multiple myeloma (MM) undergoing autologous stem cell transplantation (ASCT) represent one of such high-risk populations. This is due to the underlying disease-related immunodeficiency, suboptimal response to vaccines, heavy exposure to dexamethasone, and the use of high-dose melphalan prior to the ASCT procedure. Contracting SARS-CoV-2 and developing COVID-19 during the ASCT procedure remain high-risk events for these patients. It is then crucial to maintain and implement all appropriate strategies to prevent COVID-19 breakthroughs in this clinical setting. This might include targeted pre- and post-exposure prophylaxis with monoclonal antibodies, based on the circulation and prevalence of different SARS-CoV-2 variants/subvariants, and the prompt use of antivirals if, despite prophylaxis, MM patients develop COVID-19 during the transplantation procedure. We emphasize the importance of regularly monitoring MM patients for SARS-CoV-2 infection at all stages of the ASCT procedure. This is crucial to promptly implement measures to reduce the risk of unfavorable COVID-19 outcomes during the current post-pandemic phase.

Keywords Multiple myeloma, SARS-CoV-2, COVID-19, Autologous stem cell transplantation

Even though the Coronavirus disease-19 (COVID-19) pandemic has evolved into an epidemic, the circulation of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its variants remains a global health issue [1, 2]. Patients with hematologic malignancies were considered at higher risk for adverse outcomes if they contracted SARS-CoV-2 infection since the early stages of the pandemic. The higher rates of COVID-19-related morbidity and mortality in these patients were due to both to the immunobiologic traits of some hemopoietic tumors and the immunosuppressive action of specific treatments [3, 4]. B-cell non-Hodgkin lymphomas (NHL) and multiple myeloma (MM) are usually associated with disease-related impairments of the humoral immune response, which may increase the risk of SARS-CoV-2 infection and lead to unfavorable COVID-19 outcomes [5–8]. From the beginning of the pandemic, it was evident that being exposed to B-cell lymphodepleting anti-CD20 antibodies and undergoing high-dose chemotherapy and stem cell transplantation (SCT) were significant risk factors for contracting SARS-CoV-2 and experiencing poor outcomes from COVID-19 [9–12].

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While the global vaccination campaigns have reduced COVID-19-related morbidity and mortality in onco-hematological patients, a recent report from Su et al. emphasized that even in the post-pandemic era, patients with MM who undergo autologous SCT (ASCT) deserve special attention [13].

In the case of MM, COVID-19 vaccines may be less effective due to the suboptimal humoral and T-cell response typical of these patients, making them highly vulnerable also to breakthrough infections [14, 15]. In addition, exposure to dexamethasone and high-dose melphalan during ASCT represents additional risk factors for an unfavorable outcome if MM patients develop COVID-19 [16–18].

The two patients with MM described by Su et al. contracted SARS-CoV-2 in the community and underwent high-dose melphalan and ASCT during the viral incubation period [13]. The occurrence of additional viral infections and preexisting hypogammaglobulinemia were potential contributing factors to the fatal outcome in one of the patients [13]. However, the report from Su et al. emphasizes the need to maintain all necessary measures to prevent and manage the risk of contracting COVID-19 for patients with MM undergoing ASCT during the current post-pandemic phase [13, 19].

Strategies to achieve this can be diverse and tailored to the local epidemic situation, the vaccination status of the patients (including booster dosing), their social environment, and internal hospital procedures. First is important to underline that vaccine boosters can enhance the seroconversion rates and/or increase anti-SARS-CoV-2 antibody titers in patients with MM [20, 21]. Therefore, booster dosing is to be implemented in these patients in view of the ASCT procedure possibly by means of novel bivalent vaccines active on both the original strains and the new Omicron subvariants [22].

Social distancing before admission to the transplant ward and regular molecular testing for SARS-CoV-2 during the hospital stay could reduce, but not entirely eliminate, risks [13, 19, 21, 23]. Then, implementing pre- and post-exposure prophylaxis strategies with monoclonal antibodies in this specific group of patients should be given consideration.

In the case of MM patients undergoing ASCT, the use of post-exposure prophylaxis should take into account the possible effects of anti-SARS-CoV-2 monoclonal antibodies on the hematologic recovery times. In this regard, we have demonstrated that administering sotrovimab during the post-ASCT aplastic phase, to a MM patient who was heavily exposed to the B.1.1.529 Omicron variant, was safe, effective, and had no impact on hematopoietic recovery times [23]. A different study demonstrated the efficacy of sotrovimab when given as pre-exposure prophylaxis a week before conditioning in patients with hematopoietic malignancies undergoing allo-SCT and ASCT [24]. Interestingly, it was found that patients who underwent ASCT, mostly due to MM, had higher sotrovimab exposure compared to those who received allo-SCT [24]. However, while sotrovimab can be an option for post-and pre-exposure prophylaxis in MM patients who have been exposed to SARS-CoV-2 during or shortly after ASCT, its limited effectiveness against some viral variants represents a downside [25].

More consistent data are available as to the pre-exposure prophylaxis with Tixagevimab-cilgavimab (AZD7442), a combination of two human monoclonal antibodies that simultaneously targets distinct epitopes on the spike protein receptor binding domain of the SARS-CoV-2 virus. Studies have shown that Tixagevimab-cilgavimab, at the optimal dosing of 300/300 mg induces a sensible reduction in the risk of SARS-CoV-2 infection and of unfavorable outcomes of COVID-19 in subjects, including patients with MM, who underwent SCT [26–29]. While the emergence of Omicron subvariants, i.e. the BA.4/5, reduced the efficacy of Tixagevimab-cilgavimab, doubling the dosage of this antibody combination was suggested to increase its prophylactic activity [30, 31].

Should MM patients get infected during the ASCT procedure despite prophylactic measures, prompt initiation of antiviral therapy, with nirmatrelvir/ritonavir, molnupiravir, or remdesivir) is highly advisable [32, 33]. The choice of the antiviral should be primarily based on potential pharmacological interactions with other medications administered during transplant. In fact these antiviral agents continue to be effective on most currently circulating Omicron variants, including the most recently emerged subvariants of KP and JN types [33].

In conclusion, patients with multiple myeloma remain highly vulnerable to COVID-19, even after vaccination. This is especially true during ASCT, which is a critical frontline procedure for their disease. However, different options are available to protect these patients that need to be selected according to the ongoing epidemic situation and prevalence of specific viral variants. Current evidence clearly indicates that in the post-pandemic era, this specific patient population still requires intensive molecular monitoring for SARS-CoV-2 throughout all stages of the transplantation process. The continuous evolution of new Omicron subvariants with increased immune evasion capacity will pose further challenges in caring for patients with MM [34].

Author contributions

R.D.F., G.M., S.M., C.B. and A.P. conceived the manuscript, prepared the original draft and critically revised and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
N/A.

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