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CASE REPORT

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SARS-CoV-2 infection in hematological patients during allogenic stem cell transplantation: A double case report

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Abstract

Despite severe immunosuppression due to conditioning chemotherapy for acute myeloid leukemia, COVID-19 did not lead to clinical deterioration or death, thus raising the question of the impact of immunosuppressive treatment on clinical course evolution.

KEYWORDS

Aplasia, acute myeloid leukemia, SARS-CoV-2

1 | INTRODUCTION

We report two cases of SARS-CoV-2 infection in severely immunosuppressed patients due to conditioning chemotherapy for allogenic hematological stem cell transplantation for acute myeloid leukemia. Clinical course evolution was favorable for both patients despite their concurrent aplasia, raising the question of the impact of immunosuppression in infected patients.[1-5]

The first patient, a 64-year-old man with AML, secondary to essential thrombocythemia (ET), was admitted to hospital in the beginning of the COVID crisis for allogeneic stem cell transplantation (aHSCT) from an antigen mismatched unrelated donor. Conditioning consisted of Fludarabine 30mg/m^2/d with Aracytine 1 g/m^2/d and Amsacrine 100 mg/m^2/d, from D-14 to D-11, followed by Busulfan 1mg/kg/6h from D-7 to D-5, cyclophosphamide 60mg/kg/d from D-4 toD-3, and finally antithymoglobulin (ATG) 2.5 mg/kg/d from D-3 to D-2. The immunosuppressive prophylaxis consisted of mycophenolate mofetil and cyclosporine. Apart from his ET, the patient had no significant medical history. Six days before the programmed aHSCT, while the patient was already in profound aplasia, a nasopharyngeal swab was performed. This was motivated by an inward outbreak of COVID-19. On D-5, PCR results were found to be positive for SARS-CoV-2 infection. At that time, the patient showed no symptoms of COVID-19 disease, and his chest CT scan was negative. A hydroxychloroquine treatment, administered according to the Belgian recommendations at the time (400 mg twice daily on day 1 and then 200 mg twice daily from day 2–5), was initiated 4 days before HSCT. Shortly after, antibiotic therapy was started for febrile neutropenia and documented sepsis with Klebsiella pneumoniae. Twelve days later, the patient received larger spectrum antibiotics due to a new episode of febrile neutropenia and a transient saturation lowering to 93%. A chest CT scan showed unspecific right basal condensations and ground-glass opacities in the upper right lobe, corresponding to a severity score of 1 for pulmonary

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SARS-CoV-2 infections. A second and third nasopharyngeal swab were performed 13 and 15 days after the first one. Both were negative. At that point, the patient was still in aplasia, with a total white blood cell (WBC) count of 80/microliter. No respiratory failure occurred at resolution of leukopenia. The patient was released on D + 25 post-HSCT, but his AML soon relapsed and he passed away.

The second patient, a 58-year-old female with AML in first complete remission, was also admitted to undergo allogeneic HSCT with a matched unrelated donor 10/10 following RIC (Fludarabine 30 mg/m²/d from D-6 to D-2, Busulfan 1 mg/kg/6 h from D-4 to D-3, and ATG 2.5 mg/kg/d from D-2 to D-1) and immunosuppression by mycophenolate mofetil and Tacrolimus. Her medical history primarily involved stage 2 chronic obstructive pulmonary disease. Three days before the programmed HSCT, PCR results from a nasopharyngeal swab turned out positive for SARS-CoV-2 infection. Again, symptoms associated with COVID-19 disease were absent, and the chest CT scan was negative. The same hydroxychloroquine treatment as our first patient's was started. Systematic dosing of troponin showed a significant elevation, and the patient was transferred to the ICU for cardiac monitoring the day before the programmed HSCT. The ECG remained normal, and troponin levels decreased spontaneously. Transthoracic cardiac ultrasound showed no abnormalities, and particularly no signs of myopericarditis. The patient developed left lateral chest pain while in the ICU, without any ECG alterations, but compatible with left upper-lobe Pseudomonas Aeruginosa pneumonia, which eventually led to septic shock. Neurological deterioration, of unknown origin, led to intubation. The lumbar puncture (with SARS-CoV-2 PCR), the electroencephalogram, and cerebral magnetic resonance were all negative, thus pleading against COVID-associated encephalopathy. Extubation was possible 7 days after intubation with complete neurological recovery. A bronchoalveolar lavage (BAL) and two further nasopharyngeal swabs were performed 8, 12, and 16 days after the first nasopharyngeal swab. All PCR results were negative. Unfortunately, the patient eventually died from complications of her hematological disease.

The available data on SARS-CoV-2 infection in patients undergoing chemotherapy for AML are scarce. Yet, a growing number of articles concerning concurrent HM and SARS-CoV-2 infections are being released.[6-10] To our knowledge, only three case reports regarding adult AML patients infected by the new form of coronavirus while undergoing chemotherapy have been published so far.[1-3] A strict comparison between our two patients and the ones mentioned in the previously cited publications is impossible due to the lack of information about their immunosuppressive treatment. However, our patients' positive clinical evolution concerning their SARS-CoV-2 infection has to be stressed. Remarkably enough, both patients survived without developing respiratory insufficiency or the most severe complication of the SARS-CoV-2 infection, ARDS (acute respiratory distress syndrome). ARDS is attributed to the cytokine release syndrome (CRS), a direct consequence of the virus-induced immune system activation, and its effect on the alveolar epithelial cells. Elevated levels of certain proinflammatory cytokines, like IL-6, are associated with more severe disease outcome, as is lymphopenia and particularly a lack of CD8+ T cells. It is still unclear what the exact cause of lymphopenia in SARS-CoV-2 infected patients is, and whether there is a direct relation to the virus-induced CRS and the vicious circle that develops due to T-cell loss and subsequent lack of immune system control.[11,12] Can we therefore suggest that severely immunosuppressed patients, as the ones described above, are protected against severe forms of the disease? This hypothesis, as well as the hypothesis that severe immunosuppression could positively alter the clinical course and outcome of that disease, have also been suggested by some authors,[1,13] and not only in patients suffering from hematological diseases. Indeed, clinicians of solid organ transplant (SOT) recipients faced the same uncertainties concerning their patients' clinical outcome when infected with this recently discovered coronavirus. Publications on the matter also suggest that immunosuppression hinders the cytokine release storm observed in SARS-CoV-2 infection, thus diminishing the severity of the viral pneumonia.[14-16]

However, not all SARS-CoV-2 infections in SOT recipients or patients undergoing intensive treatment for AML show favorable outcomes, and so far, it seems that the clinical evolution in these patients is definitely associated with more severe disease and worse outcome than other less fragile groups.[6-9,17-20]

In conclusion, infection by the new form of coronavirus while suffering from a HM is often associated with poor clinical outcome. Yet, these case reports highlight that concurrent SARS-CoV-2 infections and intensive treatment for a HM, and particularly AML, should not systematically be associated with poor clinical evolution in clinicians' minds. Clinical outcome variability may reside in the difference in immunosuppression type. Further research and case publications will hopefully answer the numerous questions raised in this field.

CONFLICT OF INTEREST

We declare no conflict of interest.

AUTHOR CONTRIBUTIONS

AVU: served as main author. CS: served as supervising author. SW, NM, AL and J-CS: participated in the writing of the paper.

ETHICAL APPROVAL

This case report was submitted to the ethics committee of the Institut Jules Bordet, which granted their approval for publication on 21 September 2020.

DATA AVAILABILITY STATEMENT

Not applicable as no datasets were generated or analyzed for this article.

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