Multiple drugs

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Aspergillus super-infection, COVID-19, and urinary tract infection: case report

A 56-year-old woman developed COVID-19, urinary tract infection, and aspergillus super-infection following with rituximab, dexamethasone, etoposide, vincristine, methotrexate, and cytarabine [*routes and time to reaction onsets not stated; not all outcomes and dosages stated*].

The woman was hospitalised on 06 April 2020 to an emergency unit of Bergamo hospital in Italy. Twelve days later, she was shifted to the ICU of the same hospital for severe respiratory distress, developed secondary to COVID-19. The continuous positive airways pressure (CPAP) trial proved to be ineffective, and she required intubation with invasive mechanical ventilation. She also developed an aspergillus super-infection of the lower respiratory tract and a urinary tract infection, which completely resolved with an antimicrobial treatment. On 18 May 2020, the ventilatory support was weaned, and a CPAP course was carried out for 5 days. On 08 June 2020, she was shifted to the rehabilitation unit. On 12 June 2020, she was admitted to the COVID department for worsening dyspnoea and cough. Upon admission, she reported a low BP and a low partial artery CO_2 pressure. A low level of partial artery O_2 pressure was also detected, which eventually normalised with an oxygen supply. Diffuse and bilateral crackles were detected at the lungs bases. A laboratory analysis reported macrocytic hyperchromic anaemia, with an elevated CRP level. A serum protein electrophoresis revealed increased levels of β-globulins, α-1, α-2 globulins and decreased γ-globulins level. Flow cytometry detected low CD3-CD19+ B-cells in peripheral blood. The quantitative real time PCR failed to identify the SARS-CoV-2 nucleic acid. On 14 June 2020, she was transferred to the sub-ICU, and a repeat quantitative PCR performed in the bronco-alveolar lavage confirmed the COVID-19 infection. A CT scan reported reticular pattern interstitial abnormalities, diffuse traction bronchiectasis, sub pleural consolidations in the right lobe, and ground-glass opacities in the upper and lower right lobes. The clinical findings were associated with a significant increase in the thrombi formation and serum-induced C5b-9 deposition. The D-dimer levels, von Willebrand factor antigen, and plasma fibrinogen concentration were also elevated. According Anamnesis revealed that she was diagnosed with double-hit diffuse large B-cell lymphoma in April 2019, and according to the first-line protocol of the German Multicentre Study Group for adult acute lymphoblastic leukaemia, she had received 6 cycles of chemo-immunotherapy with dexamethasone, rituximab 375 mg/m^2, methotrexate, vincristine, cytarabine [cytarabine], and etopiside. The therapy also included two additional doses of rituximab 375mg/m^2, administered every 21 days following completion of the final cycle. The chemo-immunotherapy concluded on December 2019. Due to rituximab therapy, she had also undergone persistent and complete depletion of CD19+ B lymphocytes. Thus, antibody-producing plasma cells were not formed. Thus, it was confirmed that she was unable to establish an antiviral humoral response due to a severe immunosuppressed state associated with the chemo-immunotherapy, which led to unremitting COVID-19 infection, urinary tract infection, and an aspergillus super-infection of the respiratory tract.

The woman received a single IV infusion of off-label convalescent-anti-SARS-CoV-2-plasma on 16 June 2020, which was obtained from a patient who had completely recovered from COVID-19. The solution was infused in four hours and showed no fluid overload, cardiovascular instability or acute reactions. Ten days later, the immunoassay methods detected the presence of antiviral immunoglobulins and anti-nucleocapsid antigen (N) circulating IgG. The serum concentrations of anti-SARS-CoV-2 antibodies, which were initially unidentifiable, sharply increased on day 1 of infusion, and eventually decreased on day 7, day 14, and day 21 of infusion. The circulating anti-SARS-CoV-2 IgG were associated with the failure to identify antiviral IgM antibodies and the persistent depletion of CD3-CD19+ B-cell in peripheral blood. On 23 June, she was transferred to the low intensity case medicine unit. On 01 July, a qPCR was performed and it did not detect the SARS-CoV-2 RNA. Following infusion, an additional nasal swab test also failed to detect nucleic viral material. At the same time, her respiratory distress also improved, and the associated laboratory parameters also normalised. A CT scan performed 13 days post-infusion reported decrease in unmodified reticular abnormalities and bronchiectasis. The thrombi formation and serum-induced C5b-9 deposition also eventually normalised. On 08 July 2020, 22 days following antibody infusion, she was discharged with a good health condition with no chronic sequelae. Six months later, she was symptom-free and the diffuse interstitial lung involvement was significantly resolving. However, lymphocytopenia and hypogammaglobulinaemia showed no recovery. The flow cytometry continued to detect B-cell depletion in the circulation.

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