Immunosuppressants

S

Various toxicities: case report

An 8-year-old boy developed COVID-19-pneumonia, *Staphylococcus epidermidis, Candida parapsilosis,* BK virus and cytomegalovirus infections following immunosuppressive treatment with antithymocyte globulin, busulfan, ciclosporin, cyclophosphamide, fludarabine and mycophenolate mofetil [*dosages, routes and time to reactions onsets not stated*].

The boy, with immune-dysregulation polyendocrinopathy X-linked (IPEX) syndrome underwent haploidentical, related bone marrow haematopoietic stem cell transplant (HSCT). His conditioning regimen included busulfan, fludarabine and antithymocyte globulin [antithymoglobulin]. Post-transplant, he received cyclophosphamide. Additionally, he received graft versus host disease prophylaxis including mycophenolate mofetil and ciclosporin. He contracted SARS-CoV-2 during the periengraftment period. On day 21 post-transplant, lack of engraftment and fever were noted. Thus, a sedated bone marrow aspiration was planned; however, prior to sedation he tested positive for COVID-19 pneumonia through nucleic acid amplification test. He was then hospitalised. Subsequently, he developed respiratory distress, and a chest CT showed bilateral ground-glass opacities. Laboratory investigations showed inflammatory parameters including ferritin 14167 ng/mL, procalcitonin 0.68 ng/mL, LDH 626 U/L, CRP 10.8 mg/dL and D-dimer 18.31 µg/mL.

The boy then received non-invasive ventilation, and was treated with 10 day course of remdesivir. His calculated H-score was found to be 209. Due to probability of cytokine release syndrome, he received 2 doses of tocilizumab and one unit of convalescent-anti-SARS-CoV-2-plasma [convalescent plasma] were given. After receiving first dose of remdesivir and tocilizumab, his inflammatory parameters were as follows: ferritin 14272 ng/mL, procalcitonin 1.04 ng/mL, LDH 780 U/L, CRP 11.8 mg/dL and D-dimer 17.11 µg/mL. On day+32 post-transplant, he was found to have severe hypotension, acute hypoxemia and mildly increased right ventricle systolic pressure indicating cytokine release syndrome, which required mechanical ventilation and nitric oxide. A comprehensive evaluation for superimposed infections showed *Staphylococcus epidermidis*, *Candida parapsilosis*, BK virus and *cytomegalovirus* infections. On day 42 post-transplant, his inflammatory parameters were as follows: ferritin 28884 ng/mL, procalcitonin 2.99 ng/mL, LDH 1093 U/L, CRP 2.2 mg/dL and D-dimer 9.33 µg/mL. On further evaluation, he was found to have primary graft failure and immune rejection. In preparation for a second haploidentical related $CD34^{+}$ selected peripheral haematopoietic stem cell infusion, conditioning with fludarabine for 3 days was initiated on day+39 post-transplant. Also, salvage therapy with a second unit of convalescent-anti-SARS-CoV-2-plasma, and a third dose of tocilizumab was given on day+41. However, despite all efforts, he died on day+42 post-transplant. The combination of graft failure, COVID-19 pneumonia with multiorgan failure and opportunistic infections contributed to his death.

Alicea Marrero MM, et al. Posthematopoietic stem cell transplant COVID-19 infection in a pediatric patient with IPEX syndrome. Pediatric Blood and Cancer 68: e28578, No. 1, Jan 2021. Available from: URL: http://doi.org/10.1002/pbc.28578

803536965