Immunosuppressants

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Severe acute respiratory syndrome coronavirus-2 infection: case report

A male patient [*age at the onset not stated*] developed severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection associated pneumonia during immunosuppressive therapy with tacrolimus, prednisolone and mycophenolic acid. Additionally, hydrocortisone contributed to SARS-CoV-2 infection associated pneumonia [*duration of treatments to reaction onsets not stated*; *not all dosages and routes stated*].

The male patient had undergone combined kidney-pancreas transplant previously. He had been receiving maintenance immunosuppressive therapy with tacrolimus aiming at a trough level of 4.6 mg/mL, mycophenolic acid and prednisolone. He developed symptoms of gastroenteritis and Coronavirus disease-2019 (COVID-19) pneumonia. A SARS-CoV-2 PCR obtained 10 days following symptom onset, showed positive results. He also showed very high tacrolimus level due to diarrhoea. Therefore, tacrolimus was temporarily stopped. Further, 21 days following the symptom onset, he had a gradual decrease of pancreas and kidney graft function. He was therefore transferred to the transplant centre.

The patient's immunosuppressive therapy was switched to IV hydrocortisone 200 mg/day due to prolonged convalescence and progressive COVID-19 pneumonia as noted on CT. Immune monitoring was started. He had increased creatinine levels and proteinuria. A kidney allograft biopsy revealed moderate interstitial mononuclear cell infiltrate and tubular damage. Acute kidney and pancreas graft failure was noted. Also, SARS-CoV-2 RNA transcripts were observed upon reverse transcription (RT)-PCR and in-situ hybridisation. Analysis of immune status revealed a profound decrease of circulating immune cells. He continued to receive hydrocortisone monotherapy. Over the following 7 days, a continuous normalisation of clinical symptoms and laboratory parameters were observed. Further, monitoring of cellular immunity revealed a slight increase in the frequencies of certain activated differentiated effector T cell subsets. Therefore, tacrolimus was re-introduced. Analysis revealed a rising magnitude of SARS-CoV-2 reactive T-cells despite T-cell lymphopenia. Subsequently, he had acute deterioration of the vigilance along with convulsive seizure and diarrhoea over the following 4 days. Laboratory investigations revealed the constellation of microangiopathic haemolysis and thrombopenia, suggesting thrombotic microangiopathy. MRI revealed meningoencephalitis and RT-PCR of the CSF showed positivity for SARS-CoV-2-RNA consistent with progression of SARS-CoV-2 pneumonia. Tacrolimus was withdrawn again. Subsequent immune monitoring of SARS-CoV-2 reactive CD4+ T-cells showed a strong antiviral response with slightly increased frequencies. His immunosuppressive regimen remained unchanged and hydrocortisone infusion in combination with off-label hydroxychloroquine for 4.5 days were continued. Over the following 5 days, clinical improvement of neurological symptoms and diarrhoea along with a stable level of SARS-CoV-2 reactive T cells and low, but stable levels of unspecific bulk T-cell subsets were observed. Complete resolution of SARS CoV-2-associated symptoms were observed on day 18, and he was discharged. Immune monitoring data revealed a strong SARS-CoV-2 reactive polyfunctional T-cell response and neutralising capacity of spike protein-specific antibodies. The initial tacrolimus and mycophenolic acid based immunosuppressive therapy was started again on discharge. The patient's SARS-CoV-2 infection and its progression were attributed to the immunosuppressant therapy.

Babel N, et al. Immune monitoring facilitates the clinical decision in multifocal COVID-19 of a pancreas-kidney transplant patient. American Journal of Transplantation 20: 3210-3215, No. 11, Nov 2020. Available from: URL: http://doi.org/10.1111/ajt.16252

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