Immunosuppressants

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COVID-19 pneumonia: 6 case reports

In a case series, six kidney transplant recipients (all male patients) aged 41–65 years were described who were admitted to a hospital in Italy due to the development of COVID-19 pneumonia secondary to ongoing transplant related immunosuppressive therapies that included antithymocyte-globulin, tacrolimus, mycophenolate-mofetil, prednisone, methylprednisolone, unspecified steroids and unspecified glucocorticoids [*not all routes, dosages and duration of treatments to reaction onsets stated*].

Case 1: A 41-year-old man, who had a history of hypertension and had undergone kidney transplant from a deceased donor 15 years prior, presented with few days of fever and cough. His ongoing immunosuppressive therapy included tacrolimus and prednisone. A diagnosis of COVID-19 pneumonia was confirmed on 25 March 2020. Hence, his tacrolimus therapy was stopped. His treatment was started with off label methylprednisolone 20mg daily, darunavir/ritonavir 800/100mg, hydroxychloroquine and cefepime. Due to rapid worsening of his respiratory status, he also received off label tocilizumab 8 mg/kg on day 7 and on day 8. A significant deterioration was noted in his kidney function and he developed fluid overload, which was difficult to manage. Therefore, continuous renal-replacement therapy was started. Off label antibacterial therapy was also started with azithromycin; however, he developed respiratory failure and required mechanical ventilation from day 15. Two days later, he died due to sepsis.

Case 2: A 65-year-old man, who had a history of hypertension, diabetes mellitus and cardiovascular disease, and had undergone kidney transplantation from a deceased donor in March 2020, developed fever and cough eight days after the transplant procedure. Positive contact with COVID-19 positive patients was not reported in the days before the transplant procedure. His induction immunosuppressive therapy included antithymocyte globulin [thymoglobulin] for three days and methylprednisolone. Maintenance immunosuppressive therapy included tacrolimus (levels 10–12 ng/mL), mycophenolate-mofetil and prednisone. He also received ganciclovir for CMV prophylaxis as the donor was CMV IgG+. Subsequent swab test confirmed COVID-19 pneumonia. Therefore, his tacrolimus and mycophenolate-mofetil therapies were stopped. Off label treatment was started with methylprednisolone 20mg daily, hydroxychloroquine 200mg daily and darunavir/ritonavir 800/100mg daily. He remained haemodynamically stable with low oxygen saturation of 94–95% with low-flow oxygen through nasal cannula. He received off label tocilizumab 8 mg/kg on day 4 and day 5. On day 6, the arterial partial pressure of oxygen decreased, and he required non-invasive ventilation. Mechanical ventilation was initiated on day 7 after a further deterioration was noted in his pulmonary status. On Day 8, culture tests of both urine and blood showed positive result for multi-sensitive *Klebsiella pneumoniae*. His urine culture was also positive for *Enterococcus faecalis*. Therefore, his antibacterial treatment was changed from amoxicillin/clavulanic-acid to cefepime. Later, he also received antibacterial treatment with gentamicin, piperacillin/tazobactam and daptomycin. Later, he developed oliguria, and continuous renal-replacement therapy was started on day 12. On day 17, he died.

Case 3: A 54-year-old man, who had a history of cardiovascular disease (on unspecified oral anticoagulant therapy), and had undergone his third kidney transplantation in 2014, reported experiencing fever, emesis and diarrhoea. His ongoing immunosuppressive therapy consisted of unspecified glucocorticoids and tacrolimus. COVID-19 pneumonia was confirmed on 03 April 2020. Hence, the tacrolimus therapy was stopped. His treatment was started with off label methylprednisolone 20mg daily and hydroxychloroquine 200mg daily. On day 2, he developed haemoptysis and his respiratory status worsened. His unspecified anticoagulant therapy was stopped, and unspecified low molecular weight heparin was started. Also, he was placed on non-invasive ventilation. He received off label tocilizumab 8 mg/kg on day 2 and day 3. On day 12, improvement was noted and non-invasive ventilation was suspended. On day 20, he was discharged from the hospital on prednisone as immunosuppressive therapy. During follow-up examination (26 days after discharge), his pulmonary function was noted as normal.

Case 4: A 62-year-old man, who had a history of hypertension, cardiovascular disease, resolved HCV infection, and had undergone his second kidney transplantation in 2007, reported experiencing fever, dyspnoea and diarrhoea. His ongoing immunosuppressive therapy consisted of tacrolimus, mycophenolate mofetil and unspecified steroids. COVID-19 pneumonia was confirmed on 22 March 2020. Hence, the tacrolimus and mycophenolate mofetil therapies were stopped. His treatment was started with off label methylprednisolone 20mg daily, hydroxychloroquine 200mg daily, piperacillin/tazobactam and fluconazole. On day 1 after diagnosis, a rapid worsening of respiratory status was noted that required mechanical ventilation. He received off label tocilizumab 8 mg/kg on day 16; however, no improvement was noted in his respiratory status and he died on day 26 due to sepsis.

Case 5: A 49-year-old man had a history of cardiovascular disease, resolved HCV infection, and had undergone kidney transplantation 18 years prior. On 24 March 2020, he was admitted to the emergency department due to two days of fever and cough. Swab tests confirmed COVID-19 pneumonia. His ongoing immunosuppressive therapy consisted of tacrolimus, mycophenolate mofetil and unspecified glucocorticoids. Subsequently, his mycophenolate-mofetil therapy was stopped and the dose of tacrolimus was reduced. His treatment was started with off label methylprednisolone 20mg daily, hydroxychloroquine 200mg daily and ceftaroline-fosamil [ceftaroline]. On day 4, progressive worsening of his respiratory status was noted. Hence, tacrolimus was stopped, and off label tocilizumab 8 mg/kg and non-invasive ventilation were started. On day 11, he started receiving off label immune-globulin [IVIg] 0.2 g/kg/day for four days. On day 16, the dose of methylprednisolone was increased to 40mg daily*. Non-invasive ventilation was suspended on day 17, and he was discharged from the hospital on day 21. During follow-up examination (12 days after discharge), complete recovery of pulmonary function was noted. Tacrolimus was gradually increased to target trough level of 4–5 ng/mL and the dose of methylprednisolone was maintained.

Case 6: A 62-year-old man had a history of hypertension, cardiovascular disease, and had undergone kidney transplantation in 2011. His ongoing immunosuppressive therapy included tacrolimus and unspecified glucocorticoids. On 03 April 2020, he was admitted to the emergency department for fever and dyspnoea, and a diagnosis of COVID-19 pneumonia was confirmed. Hence, tacrolimus was stopped. His treatment was started with off label methylprednisolone 20 mg/day, hydroxychloroquine 200mg daily and amoxicillin/clavulanic-acid 1g twice a day. On the same day (i.e. day 1), he was placed on mechanical ventilation. He received off label tocilizumab 8 mg/kg on day 2 and day 3. Despite the treatments, his pulmonary function progressively deteriorated and he died on day 8 due to sepsis.

* Discrepancy was noted in the dose of methylprednisolone, which was mentioned as 40mg twice daily in the text, but was mentioned as 40mg daily in figure 1. The dose in the figure was considered.

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