Multiple drugs

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COVID-19, off label use and increased serum tacrolimus level following interaction: case report

A 72-year-old man developed COVID–19 during immunosuppressive therapy with tacrolimus and everolimus. Subsequently, he received off-label treatment with hydroxychloroquine, lopinavir/ritonavir, azithromycin and immune globulin for COVID-19. Thereafter, he developed increased tacrolimus level following concomitant administration of tacrolimus and lopinavir/ritonavir [*duration of treatment to reaction onset not stated; not all dosages and routes stated*].

The man, who had a history of dyslipidaemia and hypertension, had undergone a kidney transplantation in 2012. Thereafter, he started receiving immunosuppressive therapy with everolimus and tacrolimus. He presented to the emergency department with general malaise and headache for the previous 3 days. On presentation, he had a normal BP, temperature of 37°C and oxygen saturation of 92% breathing room air. A chest X-ray revealed bilateral pulmonary interstitial infiltrates. Laboratory tests revealed kidney failure and higher levels of tacrolimus compared to his most recent visit. A PCR test of his nasopharyngeal discharge tested positive for COVID-19. Based on these examinations, a diagnosis of COVID-19 secondary to immunosuppressive therapy was made.

Therefore, the man's immunosuppressant therapy was stopped. He was admitted to hospital, and started receiving off-label treatment with oral hydroxychloroquine on day 1 at dose 400mg as loading dose followed by 200mg every 12h for 9 days, oral lopinavir/ritonavir 400mg/100mg every 12h for 1 day on day 2 of admission and oral azithromycin started on day 3 at dose 500mg loading dose followed by 250mg every 24h for 7 days. Additionally, he received supportive treatment with methylprednisolone and antibiotic therapy with ceftizadime. Following five days of admission, he responded favourably. However, an increase in tacrolimus levels was noted, which returned within normal range after 4 days. It was assumed that an interaction between tacrolimus and lopinavir/ritonavir led to an increased serum tacrolimus level. Concomitant kidney failure might have also contributed to increased tacrolimus level. Thereafter, he was discharged from hospital.

Meanwhile, the man was re-started on tacrolimus and everolimus. Seven days later, he returned to the emergency department with fever, gradually increasing dyspnoea and micturition syndrome. At this time, his chest X-ray revealed worsening findings compared to his prior chest x-ray. Laboratory examinations revealed leucocytosis with lymphopenia and elevated acute-phase reactants. Thus, treatment with off-label IV immune globulin 0.4 g/kg every 24h was started. Additionally, he was treated with antibiotic therapy including linezolid and meropenem. Moreover, the immunosuppressive therapy was stopped again. Five days of treatment with immune globulin were completed. He did not present any adverse reactions and did show marked clinical improvement. His dyspnoea disappeared and he showed improvement in chest X-ray findings. On day 6, he was discharged from hospital.

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