Mycophenolate-mofetil/prednisone/tacrolimus

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Infections: case report

A 56-year-old man developed methicillin-resistant *Staphylococcus aureus* (MRSA) infection, *Corynebacterium* species infection, vancomycin-resistant *Enterococcus* (VRE) infection, *Klebsiella* pneumonia, *Morganella morganii* infection, *Stenotrophomonas maltophilia* infection, BK polyoma virus DNAaemia, ventilator associated pneumonia and COVID-19 infection following immunosuppressive treatment with prednisone, mycophenolate mofetil and tacrolimus [*routes and durations of treatments to reactions onsets not stated; not all dosages and outcomes stated*].

The man had undergone simultaneous heart-kidney transplant (SHKT) in January 2020 due to chronic renal failure and dilated cardiomyopathy from doxorubicin [adriamycin]. He started receiving immunosuppressive therapy with prednisone 100mg, mycophenolate mofetil 2000mg daily and tacrolimus. The dosage of mycophenolate mofetil was subsequently tapered to 1000 mg daily, and then to 500 mg daily. His immediate postoperative course was complicated by delayed graft function of his kidney. Therefore, he received dialysis on postoperative day (POD) 3 for progressive hyperkalaemia in the setting of oliguria. His sternal and kidney wounds were found to be infected with MRSA and *Corynebacterium* species.

The man was treated with unspecified antibiotics. On POD 22, haemodialysis was stopped with a creatinine of 2.4 mg/dL. In the following week, his ureteral stent was removed in a routine office visit. A couple of days later, he presented with lower abdominal pain, and his creatinine level was found to be elevated from a urinoma. Wound drainage was performed and a percutaneous nephrostomy tube (PNT) was placed. Subsequently, a transplant kidney biopsy revealed acute tubular necrosis without rejection. On POD 36, chest X-ray showed some mild central vascular prominence, a left pleural effusion but no consolidation. On POD 50, he was hospitalised for fever and leucocytosis. A CT scan of the chest, abdomen and pelvis revealed left pleural effusion without any focal consolidation. On POD 57, chest X-ray showed interval progression of interstitial pulmonary oedema with increasing left small pleural effusion. The perinephric collection showed growth of vancomycin-resistant *Enterococcus* (VRE) and blood cultures showed MRSA bacteraemia. Additionally, he developed a low-grade BK polyoma virus DNAaemia. His lymphocyte count was found to be increased than 3 weeks before. He started receiving unspecified antibiotics. The dose of prednisone was reduced to 5mg daily, tacrolimus dose was reduced to trough goal of 5-8 µg/mL and mycophenolate mofetil was discontinued. In view of worsening fluid overload and diuretic resistance, continuous venovenous hemodialysis was initiated. Considering his aspiration event, he required an emergent endotracheal intubation. On POD 60, he was successfully weaned from ventilatory support. Sputum culture showed presence of *Klebsiella* pneumonia, *Morganella morganii*, and *Stenotrophomonas maltophilia*. On POD 77, based on chest X-ray findings, left lower lobe ventilator-associated pneumonia was suspected, and he received unspecified treatment. Subsequently, a low-grade BK polyoma virus DNAaemia worsened. In the setting of weak respiratory drive and failure to thrive from worsening malnutrition, he developed respiratory distress and respiratory failure which required re-intubation in the next week. Thereafter, his initial ventilator settings were weaned down rapidly to minimal support. In view of his persistent cough, weak respiratory drive, recurrent aspirations and malnutrition, an elective tracheostomy was planned to assist with rehabilitation. Prior to surgery, a routine SARS-CoV-2 nucleic acid test (NAT) was found to be positive for COVID-19 infection. He remained to be afebrile on minimal ventilator settings and his chest X-ray findings were improving. Inflammatory markers including ferritin, procalcitonin, LDH and CRP were found to be elevated. He started receiving off-label treatment with hydroxychloroquine 200mg twice daily and azithromycin 250mg daily for 3 days. Two week after the diagnosis, inflammatory markers stabilised. He underwent tracheostomy 18 days after testing positive for COVID-19. On POD-102 chest X-ray revealed pulmonary vascular congestion along with small bilateral pleural effusions and stable bibasilar opacities. On day 26, the virus became undetectable.

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