Multiple drugs

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Various toxicities, lack of efficacy following off label use and vaccine failure: case report

A patient in their 60s [*exact age not stated; sex not stated*] developed COVID-19 infection, *Clostridium innocuum* infection, *Pseudomonas aeruginosa* infection, *Candida albicans* infection, humoral immune defect and cytomegalovirus (CMV) infection during immunosuppressive treatment with prednisone, tacrolimus and mycophenolate. Subsequently, the patient exhibited lack of efficacy during treatment with remdesivir, off label dexamethasone and off label tocilizumab for COVID-19 infection, and developed thickening of the sigmoid colon during off label treatment with tocilizumab for COVID-19 infection. Additionally, the patient exhibited vaccine failure due to humoral immune defect following vaccination with Ad26.COV2-S for immunisation against COVID-19 [*routes and dosages not stated; not all durations of treatments to reactions onsets stated*].

The patient, who had undergone lung transplantation >5 years previously, received Ad26.COV2.S vaccine in March 2021. The patient had excellent allograft function and there was no history of recent rejection. At the time of vaccination, the patient was receiving immunosuppressive therapy with stable doses of prednisone, tacrolimus and delayed-release mycophenolate. After 62 days from the vaccination, the patient developed cough, fever and dyspnoea. The patient had a remarkable history of work at a correctional facility associated with >250 cases of COVID-19. Therefore, on day 5 of illness, the patient was admitted. The patient tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on polymerase chain reaction (PCR) test. Hence, a diagnosis of COVID-19 infection was confirmed. Sequencing demonstrated a B.1.1.7 (Alpha) variant. Chest radiograph showed diffuse pulmonary infiltrates. The immunosuppressive therapy was considered as risk factor for COVID-19 infection.

Therefore, on admission, the patient's treatment with mycophenolate and prednisone was discontinued. Thereafter, the patient received remdesivir and off label treatment with dexamethasone. Despite prompt treatment with dexamethasone and remdesivir, 3 days after admission, the patient required intubation (lack of efficacy). At that time, the patient received off label tocilizumab. However, the patient further experienced a series of complications including renal dysfunction requiring dialysis and severe hypoxaemia. Therefore, lack of efficacy was considered for remdesivir, off label dexamethasone and off label tocilizumab. On day 16 of illness, the patient developed progressively worsening shock. In the setting of listed penicillin allergy, empiric treatment was started with vancomycin and aztreonam. Subsequently, the patient's condition progressed, and the patient received nearly maximal unspecified vasopressor support and supplemental oxygen delivery. Anamnesis revealed prior carbapenem tolerance. Therefore, the patient's treatment was changed to vancomycin, micafungin, meropenem, and voriconazole. Over the course of several hours, the patient's vasopressor requirement improved dramatically. On day 17 of illness, computed tomography (CT) of the chest revealed diffuse pulmonary infiltrates with a ground-glass predominance and coalescent consolidations, suggesting pneumonia. Simultaneous CT of the abdomen demonstrated significant thickening of the sigmoid colon. Tocilizumab therapy was considered as additional risk factor along with shock for thickening of the sigmoid colon. Despite initial clinical improvement with empiric antimicrobials, on day 17 of illness, the patient sustained a fatal cardiac arrest. Tracheal aspirate yielded purulent secretions, which subsequently grew mucoid *Pseudomonas aeruginosa* and *Candida albicans*. The patient's pneumonia was considered secondary to *Pseudomonas aeruginosa* infection. Blood cultures grew *Clostridium innocuum* and *Candida albicans*. PCR results for serum CMV were 267 IU/mL. Stool PCR for *Clostridioides difficile* revealed a negative result. Immunosuppressive therapy was considered as risk factor for *Clostridium innocuum* infection, *Pseudomonas aeruginosa* infection, *Candida albicans* infection and CMV infection. On day 16 of illness, qualitative SARS-CoV-2 anti-spike immunoglobulin G (IgG) obtained was positive. Subsequently, on day 17 of illness, semi-quantitative SARS-CoV-2 anti-spike IgG obtained was positive, which was detected at a concentration of 70.4U/mL. Despite vaccination with Ad26.COV2-S, the patient developed COVID-19. Therefore, vaccine failure was considered for Ad26.COV2-S. The humoral immune defect due to immunosuppressive therapy was considered as contributory factor to vaccine failure.

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