

## Multiple drugs

S

**Severe acute respiratory syndrome coronavirus 2 infection, renal dysfunction and off label use: case report**

A 66-year-old man developed severe acute respiratory syndrome coronavirus 2 infection during immunosuppressive therapy with mycophenolate and tacrolimus. He also developed renal dysfunction secondary to tacrolimus therapy. Additionally, he received off-label therapy with azithromycin, ceftriaxone and hydroxychloroquine for Covid-19 [dosages not stated; not all routes stated].

The man, who had undergone orthotopic liver transplantation because of end-stage liver disease was admitted to a hospital because of fever and cough during the pandemic of Covid-19, the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Two days prior to this admission, he developed fever, chills, and diffuse myalgias. He also noted a dry cough and nausea and that he had reduced his fluid intake. On the day of admission, he learned that his sister was diagnosed with Covid-19, and he was concerned that his symptoms might also be caused by infection with SARS-CoV-2, prompting him to present to a neighborhood health center. At the health center, he reported mild dyspnoea. His body temperature was 37.8°C, the pulse rate was 125 beats per minute, the blood pressure was 127/78mm Hg, the respiratory rate was 18 breaths per minute, and the oxygen saturation 97% while he was breathing ambient air. He had a history of diabetes, hypertension, hyperlipidemia, obesity, chronic kidney disease, peripheral neuropathy and end-stage liver disease due to alcohol use disorder and hepatitis B virus infection. Twenty-two months prior, renal replacement therapy was initiated for worsening renal function due to the hepatorenal syndrome, and shortly after, he had undergone orthotopic liver transplantation. After the liver transplantation, his renal function improved, and renal replacement therapy was discontinued. On further examination, he had been diagnosed with hepatocellular carcinoma. Current medications included tacrolimus and mycophenolate along with various concomitant medications. He was a ex-tobacco smoker and had stopped drinking alcohol. During periods of heavy drinking, he had used marijuana and cocaine occasionally. On examination, his body temperature was 38.0°C, the pulse rate was 99 beats per minute, the blood pressure was 134/73mm Hg, the respiratory rate was 20 breaths per minute, and the oxygen saturation 94% while he was breathing ambient air. The body mass index was 32.1. Urinalysis revealed a pH of 5.5, a specific gravity of 1.008, 1+ blood, and 1+ protein. Gram's staining of a sputum specimen showed rare polymorphonuclear leukocytes and few mixed gram-positive and gram-negative unspecified organisms. Electrocardiogram revealed sinus tachycardia and nonspecific ST-segment and T-wave abnormalities. The corrected QT interval was 424 msec. Chest X-ray showed low lung volumes with patchy, confluent airspace opacities in the mid-to-lower lungs that were more prominent on the left side than on the right side, with peripheral predominance.

The man received off label-treatment with IV ceftriaxone and oral azithromycin along with sodium chloride [normal saline]. A diagnosis of severe acute respiratory syndrome coronavirus 2 infection was considered. He further received off label therapy with hydroxychloroquine for COVID-19. Additionally, he received atorvastatin, prednisone and the dose of mycophenolate was decreased. During the next 2 days, the body temperature increased to 39.2°C. Chills, myalgias, nausea, and cough continued; dyspnoea increased; and headache, diarrhea, and occasional vomiting developed. Paracetamol [acetaminophen] and ondansetron were administered, and the rate of supplemental oxygen was increased. On the fourth hospital day, the serum level of interleukin-6 was high. On the morning of the fifth hospital day, the oxygen saturation fell below 90% while he was receiving supplemental oxygen. He was unable to speak in full sentences because of dyspnoea, and auscultation of the lungs showed decreased air entry. He was shifted to the ICU. The trachea was intubated, and mechanical ventilation was provided. On admission to the ICU, he was enrolled in a placebo controlled trial (NCT04315298) and received sarilumab. He showed pulmonary infiltrates, an elevated lactate dehydrogenase level, lymphopenia and high levels of inflammatory markers. He had progressive elevations in procalcitonin and ferritin levels and in the erythrocyte sedimentation rate later in his hospitalisation that were concurrent with further development of ventilator-associated pneumonia with *Pseudomonas aeruginosa*. He also had moderate renal dysfunction. The trachea was extubated successfully on hospital day 24. On hospital day 26, he had elevated results of liver-function tests, which aroused concern about allograft rejection. The liver function test abnormalities normalised after the dose of tacrolimus was increased and with the continued administration of prednisone and mycophenolate. His condition gradually improved, and he was discharged to an inpatient rehabilitation facility on hospital day 34.

Fishman JA, et al. Case 29-2020: A 66-Year-Old Man with Fever and Shortness of Breath after Liver Transplantation. New England Journal of Medicine 383: 1168-1180, No. 12, 17 Sep 2020. Available from: URL: <http://doi.org/10.1056/NEJMcpc2004982>

803519437