Multiple drugs

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Lack of efficacy and off label use: 2 case reports

In a case series, a 31-year-old woman (case 1) and a 40-year-old woman (Case 2) exhibited lack of efficacy while receiving norepinephrine. Additionally, both the women received off label treatment with lopinavir/ritonavir, tocilizumab, chloroquine, azithromycin, ceftriaxone, meropenem, linezolid, rifaximin or fluconazole for COVID-19 pneumonia [*not all dosages and routes stated*].

Case 1: The woman, who had alcoholic liver disease (ALD), was admitted to hospital because of dyspnoea, cough and fever. Following invetigation, she was diagnosed COVID-19 pneumonia. She also developed symptoms of liver decompensation. Subsequently, she was started on off label treatment with oral chloroquine 500mg twice daily, oral azithromycin 500mg once daily, IV ceftriaxone 2g once daily. Additionally, she received IV albumin infusions 20g twice daily. She received diuretics including spironolactone, furosemide, ornithine aspartate [L-aspartate-L-ornithine] infusions and hepatoprotective drugs silibinin and ornithine aspartate. The next day, oral lopinavir/ritonavir (400mg/100mg) twice daily was added. On day 3 of admission, there was rapid deterioration. Pulse oximetry decreased, abdominal swelling worsened and rhonchi and crackles appeared during the lung auscultation. Due to respiratory failure, she was intubated, received invasive mechanical ventilation and deep sedation. Arterial blood gas analysis was consistent with moderate acute respiratory distress syndrome (ARDS). She received norepinephrine due to haemodynamic instability. Diuretics were administered in the continuous IV injection. Enteral nutrition was administered. However, on day 4 of the ICU stay, total parenteral nutrition was initiated due to active gastrointestinal bleeding. Despite intensive treatment, further increases of the inflammatory parameters was observed and her body temperature increased. She received tocilizumab 600mg infusion, which was repeated on two consecutive days. On day 5, ceftriaxone was replaced by IV meropenem 1g 3 times daily, IV linezolid 600mg twice daily, oral rifaximin 400mg 3 times daily and IV fluconazole 200 mg/day. Afterwards, an antiarrhythmic treatment with amiodarone was initiated. On day 7, gastrointestinal haemorrhage was noted and she required a transfusion of blood products and fresh-frozen plasma. Continuous IV injection of a proton pump inhibitor, tranexamic acid, and etamsylate [cyclonamine] was administered to stop the active gastrointestinal bleeding. Albumin infusion were continued. In the subsequent days, she required another transfusion of RBC. She became hyperpyretic without response to the antipyretic drugs and physical cooling. Her serum level of interleukin-6 (IL-6) increased. Severe impairment was noted in the coagulation parameters such as activated partial thromboplastin time (APTT) and international normalized ratio (INR). The ammonia levels were also increased. Eventually, she developed intractable hepatorenal syndrome, and her haemodynamic instability worsened. On day 9 of admission, she died of multi-organ failure.

Case 2: The woman was admitted to the hospital because of jaundice, ascites, and fever. She was diagnosed with COVID-19 infection and laboratory tests were suggestive of ALD. Subsequently, she was started on off label treatment with lopinavir/ritonavir and tocilizumab. Additionally, she received oral chloroquine 500mg twice daily, oral azithromycin 500 mg/day, IV ceftriaxone 2 g/day and IV albumin infusions 20 g/day. She received diuretics including spironolactone, furosemide and vitamin K supplementation. Other hepatoprotective drugs included silibinin, ornithine aspartate and subsequently oral lopinavir/ritonavir (400mg/100mg) twice daily and steroids. On day 4 of admission, a rapid deterioration was observed. Her pulse oximetry decreased, ascites increased and rhonchi and crackles appeared during lung auscultation. Due to respiratory failure, she was intubated and received invasive mechanical ventilation and deep sedation. Arterial blood gas analysis was consistent with moderate acute respiratory distress syndrome (ARDS). She was mechanically ventilated. Neuromuscular blockade was used due to severe hypoxaemia. She received norepinephrine due to haemodynamic instability. Afterwards, diuretics were given in fractional doses and then in the continuous IV injection. Blood and endotracheal aspirate cultures were negative. Enteral nutrition was administered in the ICU. However, partial parenteral nutrition had to be added as she was unable to achieve adequate nutrition. She developed ascitic hydrothorax of the right pleura and a pleural cavity drainage was performed. There was a temporary improvement of gas exchange and further increases in the inflammatory parameters were noted. CRP showed a downward trend and the procalcitonin level was normal. The antibiotic regime was switched from ceftriaxone to IV meropenem 1g 3 times daily and IV linezolid 600mg twice a day. The dosage of vasopressors was increased. Severe anaemia was noted, and she required a transfusion of blood products. The patient became hyperpyretic and tachyarrhythmia appeared. A massive ascites was developed requiring paracentesis. Blood appeared in the nasogastric tube, indicating gastrointestinal haemorrhage. Due to the impaired gas exchange, a percutaneous tracheostomy was performed on day 12. However, there was no improvement. Despite intensive therapy, she developed uncontrollable haemodynamic instability as well as profound hypoxia. On the same day, she died of cardiopulmonary insufficiency.

Wisniewska H, et al. Nosocomial COVID-19 infection and severe covid-19 pneumonia in patients hospitalized for alcoholic liver disease: A case report. American Journal of Case Reports 21: 1-8, Jan 2020. Available from: URL: http://doi.org/10.12659/AJCR.927452