Multiple drugs

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COVID-19, acute kidney injury and off label use: 2 case reports

This report describes a 59-year-old man and a 37-year-old woman, who developed COVID-19 during immunosuppressive therapy with mizoribine, ciclosporin, prednisone, tacrolimus or mycophenolate mofetil after kidney transplant. Subsequently, both patients developed acute kidney injury during off label treatment with ceftriaxone, moxifloxacin, umifenovir or unspecified cephalosporin for COVID-19 [*routes and time to reactions onset not stated; not all dosages stated*].

Case 1: A 59-year-old man presented with cough and fever for 8 days. He was on various concomitant medications. After kidney transplant, he received long-term maintenance immunosuppression therapy with mizoribine and ciclosporin for 5 years. At presentation, these medications were not continued. His body temperature was 38.2°C, and he had headache, dyspnoea and myodynia, but no chills, fatigue, palpitation, chest pain or night sweats. He also had productive cough and white sputum. He had also been experiencing nausea without abdominal pain, vomiting, diarrhoea, exertional dyspnoea, haemoptysis or chest pain. The 2019-nCov nucleic acid test was positive. He was hospitalised to an outside hospital prior to the admission on 3 February 2020. Total lymphocyte count was 1.28×10^9/L and complete blood cell count was normal. CT scan demonstrated ground-glass opacities in the lower and upper regions of the lung. He was started on off label treatment with umifenovir [arbidol hydrochloride] tablets, unspecified cephalosporin and unspecified antipyretics from 4 February 2020 to 8 February 2020 along with Chinese medicine (shuanghuanglian oral liquid and lianhua qingwen capsules). He also received off label treatment with methylprednisolone for COVID-19. His vital signs were heart rate of 77 bpm, respiratory rate of 24 breaths per minute, BP of 136/76mm Hg, peripheral capillary oxygen saturation of 82% (at 5 L/min oxygen flow) and body temperature of 36.5°C. His renal parameters included serum creatinine of 166 µmol/L, blood urea nitrogen of 9.2 mmol/L and estimated glomerular filtration rate of 38.3 mL/min/1.73m^2. Blood angiotensin converting enzyme (ACE) level was 28 U/L. Laboratory tests also revealed interleukin (IL)-1b of <5.0 pg/mL, IL-6 of 57.47 pg/mL, IL-2 receptor of 659 U/mL, IL-8 of 16.4 pg/mL, IL-10 of 9.6 pg/mL and tumor necrosis factor (TNF-a) of 8.4 pg/mL. He was treated with supplemetal oxygen via nasal catheter (5 L/minute). In the next day of admission, his blood oxygen level could not be maintained. Hence, he was started on non-invasive ventilation (bilevel positive airway pressure). For intravenous nutritional support, he received injection of fat emulsion and glucose. His BP was controlled by urapidil [urapidil hydrochloride], and furosemide was given to control urine volume. Three days after the admission, he developed heartburn, acid reflux, suffocation, chest distress, progressive dyspnoea and progressive deterioration of the renal function. The renal function reassessment revealed serum creatinine concentration of 467 µmol/L, estimated glomerular filtration rate of 11 mmol/L, blood urea nitrogen concentration of 25.8 mmol/L, potassium concentration of 5.41 mmol/L, bicarbonate concentration of 12.7 mmol/L, ALT of 61 IU/L, AST of 87 IU/L, high-sensitivity C-reactive protein concentration of 96.7 mg/L and albumin concentration of 38.4 g/L. He was diagnosed with acute kidney injury, which was thought to be related to COVID-19 along with the antibiotics and antiviral drugs. Five days after the admission, he appeared to be in a state of delirium. Drop in oxygen saturation to 10% was observed, and he died of cardiac arrest without restoration of spontaneous circulation. As his family did not wanted tracheal intubation to cause him pain, invasive rescue was not performed. It was speculated that besides COVID-19, the antiviral and antibiotic led to the acute kidney injury, further leading to the fatal cardiac arrest.

Case 2: A 37-year-old woman presented with cough and fever for 8 days. She was on various concomitant medications. In 2014, she was diagnosed with immune globulin-A nephropathy, for which she underwent haemodialysis in 2015. Subsequently, she underwent kidney transplant. She had been receiving immunosuppressive therapy with prednisone 20mg once a day, tacrolimus 2mg every morning and 1.5mg every night and mycophenolate mofetil. Before hospitalisation, her peak body temperature was 40°C, and her fever was accompanied withdry cough without phlegm, chills, muscle pain, dizziness, chest pain, chest distress, headache and pharyngeal pain. She visited Wuhan union hospital. On the day of presentation, CT scan of the chest showed novel coronavirus infection in the lower region of her left lung, and her 2019-nCov nucleic acid test was positive. She started receiving off label treatment with umifenovir [arbidol hydrochloride] tablets (from 5 February 2020 to 13 February 2020), ceftriaxone (from 5 February 2020 to 12 February 2020), moxifloxacin (from 5 February 2020 to 13 February 2020) and methylprednisolone along with propylene spheres. Thereafter, alleviation of her symptoms were noted, and body temperature remained almost stable for the next 3 days. Chest CT scan, performed on 12 Febraury 2020 showed deterioration. Routine urinalysis revealed 2+ RBCs and 2+protein. Biochemical tests revealed serum creatinine of 167 µmol/L, blood urea nitrogen of 7.7 mmol/L, bicarbonate of 19.5 mmol/L and estimated glomerular filtration rate of 33.4 mL/min/1.73m^2. She was diagnosed with acute kidney injury, which was speculated to be related to COVID-19 along with the antibiotics and antiviral drugs. Mycophenolate mofetil was discontinued after admission and tacrolimus was stopped 10 days later, while moxifloxacin and methylprednisolone (at 40mg once a day) was continued. According to her urine volume, furosemide was administered. A progressive upward trend was observed in serum creatinine. She rested well and received oxygen inhalation, adequate nutrition, gamma globulin infusion and appropriate diuretic treatment. She also avoided nephrotoxic drugs. Her methylprednisolone therapy was changed to oral prednisone 25mg twice a day, which was gradually decreased to 5mg once a day. Eleven days after the admission, tacrolimus was restarted. A satisfactory clinical recovery was noted in body temperature, absorption of the lung lesions and renal function.

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