

Multiple drugs

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Lack of efficacy, off label use and spontaneous iliopsoas haematoma: 2 case reports

In a case series, 2 men were described, among whom a 62-year-old man exhibited lack of efficacy while being treated with off-label dexamethasone, tocilizumab and nafamostat for COVID-19 infection, exhibited lack of efficacy during treatment with favipiravir for COVID-19 infection and developed spontaneous iliopsoas haematoma during treatment with nafamostat, thrombomodulin α and enoxaparin sodium, and a 79-year-old man exhibited lack of efficacy while being treated with off-label dexamethasone, methylprednisolone, nafamostat and tocilizumab for COVID-19 infection, exhibited lack of efficacy during treatment with favipiravir and remdesivir for COVID-19 infection and developed spontaneous iliopsoas haematoma during treatment with nafamostat and heparin [duration of treatments to reactions onsets not stated; not all dosages and routes stated].

Case 1: The 62-year-old man was presented with productive cough, fatigue and cough. The RT-PCR performed on nasal swab turned positive for SARS-CoV-2 infection. Laboratory tests revealed platelet count $178 \times 10^3/\mu\text{L}$, interleukin-6 level 89.1 pg/mL and D-dimer level 0.5 $\mu\text{g}/\text{mL}$. He received favipiravir (loading dose of 1800mg on day 1, followed by maintenance dose of 400mg twice daily for 13 days), off label treatment with IV dexamethasone 6.6 mg/day for 10 days and nafamostat 100 mg/day. Despite initial treatment, he required 10L of oxygen supplementation to maintain oxygen saturation for 3 days following admission. Therefore, he received off-label treatment with IV tocilizumab 8 mg/kg on days 3 and 4. However, his hypoxia continued to worsen. Hence, he was intubated and transferred to the ICU. Then, he received thrombomodulin α [recombinant human soluble thrombomodulin] 12800U twice daily to prevent thrombosis. Five days later, he recovered completely from acute respiratory failure and was extubated. On day 9, he returned to the ward. On the same day, thrombomodulin α was replaced with SC enoxaparin sodium [enoxaparin] 40mg daily. On day 14, he developed severe and sudden pain in his left lower back. His pulse rate was 115 beats/minute and BP was 118/68mm Hg. Laboratory tests showed elevated D-dimer level of 2.6 $\mu\text{g}/\text{mL}$ and decrease in haemoglobin level from 15.7 g/dL to 13.2 g/dL. Contrast-enhanced pelvic and abdominal CT revealed a haematoma in the left iliopsoas muscle spreaded to the retroperitoneal space with extravasation. Subsequently, he underwent urgent transarterial embolisation. Extravasation was seen from the left L3 and L4 lumbar arteries and common iliac arteries. Following the intervention, no active contrast extravasation was noted. He received 6 packed RBCs units with IV fluids due to decrease in haemoglobin level to 7.5 g/dL. On day 33, he was discharged with improvement in haemoglobin level to 12.6 g/dL.

Case 2: The 79-year-old man presented with fatigue and fever and was transferred to the hospital for COVID-19 associated acute respiratory distress syndrome. At another hospital, he received favipiravir, dexamethasone (off-label use), and SC heparin [unfractionated heparin] on the referral day. However, respiratory failure worsened progressively, and he was intubated. Laboratory tests showed platelet count $129 \times 10^3/\mu\text{L}$ and D-dimer level 0.6 $\mu\text{g}/\text{mL}$. Then, he received remdesivir at a loading dose of 200mg on day 1, followed by maintenance dose of 100mg once daily for 10 days, off label treatment with methylprednisolone 1000mg for 3 days followed by dexamethasone 6.6mg for 7 days, nafamostat 100 mg/day and IV tocilizumab 2 consecutive doses of 8 mg/kg. He also received IV heparin [unfractionated heparin] infusion to meet the target-activated partial thromboplastin time. Following extubation, his BP decreased gradually with tachycardia. He also complained of gradual worsening of pain in the right lower back since extubation. Laboratory test showed decreased in haemoglobin level from 12.2 g/dL to 9.7 g/dL, suggestive of haemorrhagic hypovolemic shock. His D-dimer level was 2.2 $\mu\text{g}/\text{mL}$, platelet count $158 \times 10^3/\mu\text{L}$, fibrinogen level 167 mg/dL and activated partial thromboplastin time 42.1 seconds. Contrast-enhanced abdominal CT revealed swelling of the right iliopsoas muscle with retroperitoneal haematoma, small-density area in the left psoas major muscle and extravasation in the right psoas major muscle. Subsequently, heparin was discontinued. He underwent transarterial embolization with rapid volume replacement and packed RBCs transfusion. However, he had cardiac arrest for 4 minutes during preoperative preparations. He responded to resuscitation. He had second episode of cardiac arrest within an hour. His family members did not want further resuscitation attempts. His death was confirmed 18 hours after extubation.