

Multiple drugs

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Various toxicities and off label use: 5 case reports

In a prospective study involving 22 patients admitted to a hospital in Germany with the diagnosis of COVID-19 infection between March 2020 and April 2020, 5 patients in their 50s–60s including two patients aged 58 years and 66 years [4 men and 1 woman; *not all exact ages not stated*] were described, who developed acute kidney injury, exanthema, ventilator associated pneumonia, septic shock or pneumothorax during treatment with lopinavir/ritonavir, hydroxychloroquine, spiramycin, azithromycin, meropenem, piperacillin/tazobactam or vancomycin. Of the treatments, lopinavir/ritonavir, hydroxychloroquine, spiramycin and azithromycin were off label therapies for the COVID-19 infection [*time to reactions onsets, routes, dosages and outcome not stated*].

Patient 3: The man in his 50s was admitted to a hospital in Germany with the diagnosis of COVID-19 infection. Subsequently, he started receiving treatment with off label lopinavir/ritonavir [Kaletra]. He also received off-label hydroxychloroquine with azithromycin for two days. Additionally, he received antibacterial therapy with meropenem for suspected superinfection (respiratory tract infection). During the treatment, he developed treatment related acute kidney injury (related to lopinavir/ritonavir) and exanthema (related to hydroxychloroquine and azithromycin). On hospitalisation day 26, he was discharged from the hospital.

Patient 5: The man in his 50s was admitted to a hospital in Germany with the diagnosis of COVID-19 infection. Due to suspected superinfection (respiratory tract infection), he was started on piperacillin/tazobactam. However, during the treatment, he developed treatment related ventilator-associated pneumonia and septic shock. On hospitalisation day 29, he was discharged from the hospital.

Patient 6: The man in his 60s was admitted to a hospital in Germany with the diagnosis of COVID-19 infection. Subsequently, he started receiving treatment with off label hydroxychloroquine with spiramycin for four days. Additionally, he received antibacterial therapy with meropenem for suspected superinfection (respiratory tract infection). During the treatment, he developed acute kidney injury, which was considered as related to the hydroxychloroquine and spiramycin therapy. On hospitalisation day 76, he was discharged from the hospital.

Patient 13: The man aged 58 years was admitted to a hospital in Germany with the diagnosis of COVID-19 infection. Due to suspected superinfection (sepsis, respiratory tract infection and urogenital tract infection), he was started on piperacillin/tazobactam, vancomycin and meropenem. Later, pathological examinations confirmed *Staphylococcus aureus* and *Klebsiella pneumoniae*. However, during the treatment, he developed treatment related ventilator-associated pneumonia and septic shock. On hospitalisation day 42, he was died due to the COVID-19 infection. Autopsy showed reactive pneumocyte changes ("Napoleon hat sign") consistent with viral infection. Tissue samples showed areas of beginning, patchy fibrosis with a foreshadowing of honeycombing.

Patient 16: The woman aged 66 years, who had a history of rheumatic disease, was admitted to a hospital in Germany with the diagnosis of COVID-19 infection. Due to suspected superinfection (respiratory tract infection), she was started on meropenem. However, during the treatment, she developed treatment related Pneumothorax. On hospitalisation day 26, she was discharged from the hospital.