Anakinra/hydroxychloroquine

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Long-QT-syndrome, *Klebsiella pneumoniae* and *Proteus mirabilis* infection: case report

A 53-year-old woman developed long-QT-syndrome during off-label treatment with hydroxychloroquine for COVID-19. She also developed *Klebsiella pneumoniae* and *Proteus mirabilis* infection following treatment with anakinra for cytokine storm syndrome [*not all dosages and routes stated; time to reaction onsets not clearly stated*].

The woman was admitted on 20 March 2020 in a hospital in Germany with cough, persistent fever and progressing dyspnoea for 4 days. Due to suspected COVID-19, quarantine measures and oxygen therapy by face mask was initiated with transfer to the ICU. Her medical history was significant for noninsulin-dependent diabetes mellitus type 2, asymptomatic, non-progressing meningeal tumour, arterial hypertension, hepatic steatosis, psychiatric borderline syndrome and alcohol abuse disorder; however, she had stopped drinking 6 months previously. She was receiving metformin and unspecified antihypertensive therapy. Following further investigations, SARS-CoV-2 RNA was detected, confirming COVID-19. She started receiving off-label treatment with hydroxychloroquine on day 1. Subsequently, she developed long-QT-syndrome secondary to hydroxychloroquine.

The woman's treatment with hydroxychloroquine was discontinued on day 5. Within 12h of admission, worsened hypoxia was observed, and a diagnosis of acute respiratory distress syndrome secondary to COVID-19 was considered. She required mechanical ventilation. Prone positioning was also started. On day 7 after admission, she developed high fever and high CRP without elevated procalcitonin level. Based on these findings, a reactive haemophagocytic lymphohistiocytosis and cytokine storm syndrome was suspected. She was initiated on SC anakinra 100mg from day 7 to day 11, along with unspecified antibiotic prophylaxis. The following day, fever and inflammatory markers decreased, while improved respiratory situation was noted. On admission day 12, anakinra therapy was stopped for 48h, which resulted in relapsed inflammatory markers and fever on day 14. The anakinra therapy was re-started and administered until day 18 with clinical improvement. She received total 9 doses of anakinra over 12 days. On admission day 19, she underwent bronchoscopy and chest CT, which showed persistent bilateral pulmonary infiltrates with primary affection of the dorsal segments. The same day, her clinical condition again worsened with sepsis and impaired oxygenation. She was started on empirical treatment with meropenem and ciprofloxacin. Microbiologic cultures revealed positive findings for *Klebsiella pneumoniae* in peripheral blood and in bronchoalveolar lavage. Also, *Proteus mirabilis* was noted in bronchoalveolar lavage. On day 22, her CRP and procalcitonin level was noted to be massively increased. She was initiated on continuous haemodiafiltration for acute renal failure secondary to COVID-19. Her inflammatory markers normalised with improvement of respiratory and circulatory parameters. Her renal replacement therapy was subsided to intermittent haemodialysis, and was later discontinued due to improvement in renal function. SARS-CoV-2 RNA was not found in bronchoalveolar lavage and nasopharyngeal swab. On admission day 27, she underwent tracheotomy. Her condition improved. She was discharged for postacute care at a rehabilitation centre, and she was able to breath spontaneously without mechanical support. The *Klebsiella pneumoniae* and *Proteus mirabilis* infection was considered to have developed secondary to anakinra.

Kaps L, et al. Treatment of cytokine storm syndrome with IL-1 receptor antagonist anakinra in a patient with ARDS caused by COVID-19 infection: A case report. Clinical Case Reports 8: 2989-2993, No. 12, 2020. Available from: URL: http://doi.org/10.1002/ccr3.3307

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