Meropenem/piperacillin/tazobactam

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Drug resistance: case report

An adult man [aged between 45–55 years; *exact age not stated*] developed drug-resistance during treatment with meropenem and piperacillin/tazobactam for ventilator-associated pneumonia [*routes not stated*].

The man was diagnosed with COVID-19 in 2020 and initially asymptomatic. Twenty days following the initial SARS-CoV-2 positive test, he was hospitalised due to Type-1 respiratory failure (hypoxaemia) and required mechanical ventilation. Thereafter, his endotracheal sample did not detect SARS-CoV-2, that indicated cleared viral infection. However, after one week of ICU admission, he developed ventilator-associated pneumonia. His culture test showed susceptible *Pseudomonas aeruginosa* with a minimum inhibitory concentration (MIC) of 0.5 mg/L (meropenem) and 8 mg/L (piperacillin/tazobactam). Hence, he received piperacillin/tazobactam 4.5g every 6 hours for seven days and was clinically recovered. However, eight days following treatment with piperacillin/tazobactam, his culture test confirmed recurrence of ventilator-associated pneumonia (*P. aeruginosa*). At this time, the MIC of piperacillin/tazobactam was >16 mg/L.

Therefore, he received meropenem 1g every 8 hours for seven days and showed clinical improvement. However, two days after completion of meropenem therapy, his culture test showed recurrence of ventilator-associated pneumonia (*P. aeruginosa*), which was resistant to both piperacillin/tazobactam and meropenem. The MIC of piperacillin/tazobactam was >16 mg/L and meropenem was >8 mg/L. A week later, he was discharged to the respiratory ward following improvement. At a 3-week follow-up, he reported symptoms of breathlessness and myalgia and a decrease in oxygen saturation following mild exertion. Eight months after his initial positive test, he still reported fatigue and breathlessness, which were considered as common symptoms of the newly defined long COVID condition. Hence, to understand the cellular and molecular dynamics of post-acute COVID-19, he was enrolled in the DISCOVER study (Diagnostic and Severity markers of COVID-19 to Enable Rapid triage study) that collected and analysed longitudinal samples from 30 March 2020 till the time of report of COVID-19 patients. The metagenomic analysis showed antimicrobial resistance genotype and immunological analysis showed massive and escalating levels of T-cell activation. Hence, it was speculated that because of COVID-19 infection, he displayed a heightened immune system that further stimulated by the recurrent *Pseudomonas aeruginosa* infection leading to bystander activation of T cells specific for antigens unrelated to either COVID-19 or *P. aeruginosa*.

Gregorova M, et al. Post-acute COVID-19 associated with evidence of bystander T-cell activation and a recurring antibiotic-resistant bacterial pneumonia. eLife 9: 17 Dec 2020. Available from: URL: http://doi.org/10.7554/eLife.63430