

Methylprednisolone/mycophenolate-mofetil/tacrolimus

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COVID-19 and *Pneumocystis jirovecii* pneumonia: case report

A 55-year-old man developed COVID-19 and *Pneumocystis jirovecii* pneumonia (PJP) during immunosuppressive treatment with methylprednisolone, mycophenolate-mofetil and tacrolimus.

The man, who had a history of chronic kidney disease, underwent kidney transplant in 2013. Then, he started receiving mycophenolate mofetil 0.5g twice daily, tacrolimus 2mg twice daily (concentration was maintained at 4–5 ng/mL) and methylprednisolone 5mg once daily [*routes not stated*]. His medical history was also significant for heart failure, and he had been receiving various concomitant medications. He presented with oliguria for 2 weeks on 31 Jan 2020. A CT scan showed bilateral lung lesions, with a lot of speckle consolidation shadows in both lungs. An oropharyngeal swab was positive for SARS-CoV-2. He was diagnosed with COVID-19. He was isolated in the another hospital for further treatment. On 8 February, he showed a mild cough and developed dyspnoea by 12 February. He was then transferred to the ICU on Feb 13. On admission, A CT scan showed bilateral lung interstitial disease with ground-glass opacities (GGO).

Subsequently, tacrolimus and methylprednisolone were stopped. The man received oxygen delivery via nasal cannula, furosemide and thymalfasin [thymosin-alpha-1] and unspecified immunoglobulin. He responded well to the therapy. Then, he was transferred to a general ward. Due to incomplete improvement in imaging results, high levels of CRP and procalcitonin as well as a positive SARS-CoV-2, he stated receiving an off label treatment with oral lopinavir/ritonavir 1000 mg/day and cefdinir. He also received prophylactic unspecified beta-methylcarbapenem.

During this anti-bacterial and anti-viral therapy period, the man was re-challenged with methylprednisolone 20mg once daily, gradually reduced mycophenolate-mofetil dosage, and an adjusted dosage of tacrolimus, were also re-introduced. Eventually, his condition improved. A chest CT on 24 February (day 11) still showed extensive GGO. His oropharyngeal swab remained positive for SARS-CoV-2. He showed positive serum (1, 3)-beta-D glucan test. A chest CT features long immunosuppressive state. A fungal infection was suspected. He received cotrimoxazole [trimethoprim/sulfamethoxazole] for impaired kidney function. He was treated with off label IV micafungin 50mg gtt once daily for PJP. Additionally, beta-methylcarbapenem was continued empirically. Later, lopinavir/ritonavir was replaced with off label umifenovir 0.2g 3 times daily. After 1 week of micafungin treatment, serum BDG normalised. His clinical symptoms and laboratory findings continued to improve. A chest CT on 1 March 2020 and 8 March 2020 showed gradual absorption of the ground-glass lesions. On 4 March and 7 March, his oropharyngeal swabs showed negative results for SARS-CoV-2. He was discharged on March 11. Then, mycophenolate-mofetil was stopped. The treatment with methylprednisolone 20mg once daily and tacrolimus 1mg twice daily (drug concentration was maintained at 2-3 ng/mL) was continued. He remained well with lower serum creatinine level and improved chest CT images. His retrospectively analysis of sputum collected on 25 February 2020 showed presence of *P. jirovecii*. The levels of *P. jirovecii* in his sputum were almost tenfold higher than those in a PJP positive sputum (collected from a non-COVID-19 patient). He was diagnosed with PJP. Then, he was treated with cotrimoxazole. Eventually, a significant improvement was noted. Further, it was confirmed that, the COVID-19 and *Pneumocystis jirovecii* pneumonia were associated with immunosuppressive therapy of methylprednisolone, mycophenolate-mofetil and tacrolimus.