

## Tacrolimus

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**COVID-19 infection: case report**

A 37-year-old man developed COVID-19 infection during immunosuppressant treatment with tacrolimus.

The man was diagnosed with liver cancer and admitted to hospital for a liver transplant on 14 January 2020. Three months prior to admission, he experienced ongoing episodes of sharp pain in his right abdomen. He had multiple hepatic masses. He reported 19 years of hepatitis B virus (HBV) infection. He underwent a hepatic arterial chemoembolization on day 4. On the next day, he had fever and his neutrophil counts increased to  $7.51 \times 10^9/L$ , and his lymphocyte counts dropped to  $0.64 \times 10^9/L$ . Chemoembolisation-associated sterile inflammation was suspected, and he was prescribed cefdinir. After a routine evaluation to determine eligibility for transplantation, an orthotopic liver transplantation was scheduled on day 7. The pathological diagnosis on explant revealed hepatocellular carcinoma (HCC). He started receiving an immunosuppressive drug tacrolimus [*route and dosage not stated*] and concomitant unspecified systemic glucocorticoids. Also, escalation and combination of antimicrobial agents including imipenem/cilastatin and linezolid were started immediately following transplantation. Also, caspofungin was added as a prophylactic treatment for fungal infection. On day 9, due to persistent fever, a CT thorax was performed, which revealed bilateral hypostatic change and minor pleural effusion in the right thoracic cavity. Microbiologic cultures yielded gram-positive cocci and gram-negative bacilli in his sputum. His repeat thorax CT revealed multicentric subpleural ground glass opacification in the left lobes on day 18. Due to the COVID-19 outbreak in Wuhan area, a COVID-19-specific real-time PCT (RT-PCR) was performed on nasopharyngeal aspirate and was confirmed positive on day 19. His nasopharyngeal aspirate was negative for other respiratory viruses. Thus, a diagnosis of COVID-19 infection secondary to tacrolimus was made [*time to reaction onset not stated*].

The man received off-label treatment with moxifloxacin, oseltamivir, IV immune globulin [immunoglobulin], cefoperazone/sulbactam and unspecified recombinant human granulocyte colony-stimulating factor for COVID-19 infection. Due to an acute phase after transplantation, tacrolimus and glucocorticoids were maintained and gradually titrated to lower doses. His oxygen saturation was maintained between 95% and 99% with high-flow nasal cannula oxygen therapy. His fever subsided on day 33, and a repeat chest CT scan revealed resolution of the infiltrate in the left lobe, and on day 36, progression of pleural effusion in the right lung. A blood test indicated persistent lymphopenia. Acute cellular rejection [*aetiology unknown*] was suspected, and the dose of tacrolimus was increased starting on day 40. Repeat COVID-19 RT-PCR test was negative from day 34 to day 52. However, RT-PCR showed COVID-19-positive again on day 53 and returned to negative 3 days later without any additional treatment. He was discharged on 12 March 2020. He had no signs of multisystem organ failure during hospitalisation.