

## Multiple drugs

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**Reactivation of Mycobacterium tuberculosis (MTB) and off-label use: case report**

A 44-year-old man developed reactivation of Mycobacterium tuberculosis (MTB) following off-label treatment with dexamethasone, methylprednisolone and tocilizumab for Coronavirus disease-19 (COVID-19) pneumonia. Additionally, he received off-label treatment with azithromycin, ceftriaxone and hydroxychloroquine for COVID-19 pneumonia [not all dosages and routes stated].

The man was admitted for COVID-19-related pneumonia. He started receiving off-label treatment with azithromycin, ceftriaxone, and hydroxychloroquine. However, after 2 days of treatment, he developed worsening hypoxaemia and was intubated. Thus, he was started on empirical antibiotic treatment with cefepime and vancomycin and was shifted to the medical ICU of another hospital. Upon transfer, he had a temperature of 102.8°F, BP of 138/77mm Hg, pulse of 114 beats/min, respirations of 16, and an oxygen saturation of 95% while being mechanically ventilated. He continued on vancomycin and cefepime for 7 days. On day 5, he was started on off-label IV dexamethasone 20 mg/day for 2 days, followed by dexamethasone 10mg daily for 6 days and a single dose of methylprednisolone 40mg. In addition, he was initiated on off-label IV tocilizumab 400mg. Prior to administration of tocilizumab, a QuantiFERON-TB Gold Plus (QFTPlus) test was negative. Within 24 hours of dexamethasone treatment, he became afebrile and dexamethasone was discontinued. After 2 days, his temperature rose to 102°F. Thus, he was initiated on empirical antibiotic therapy with piperacillin/tazobactam and vancomycin for 5 days for possible aspiration pneumonia. On day 16, he was extubated, and was placed on BiPAP (Bilevel Positive Airway Pressure). He was subsequently transitioned to a nasal cannula, and was transferred to general medicine floor. His leukocytosis persisted at 16.7. On day 22, his temperature rose to 101.1°F with a WBC count of 14.7 with a left shift and a newly altered mental status. Thus, he was again treated with piperacillin/tazobactam on the same day for another presumed hospital acquired pneumonia. However, his fever and leukocytosis continued; thus, empirical vancomycin was added on day 24. Subsequently, chest X-ray revealed patchy infiltrates. Additionally, culture showed moderate growth of *Klebsiella pneumoniae*. The isolate was resistant to piperacillin/tazobactam and susceptible to cefepime and carbapenems. Therefore, piperacillin/tazobactam was discontinued and cefepime was started, but his fever and leukocytosis persisted. On day 29, CT scan of the chest and abdomen revealed diffuse opacities, with a 6.6 × 9.4 × 9.5cm consolidation in the right lower lobe with multiple internal air spaces and right hilar lymphadenopathy with calcified subcarinal lymph nodes. Therefore, he started receiving empirical treatment with meropenem, caspofungin, vancomycin, and metronidazole. Caspofungin was discontinued after 2 days and voriconazole was added. He still continued to have leukocytosis with intermittent fever. On day 35, chest CT scan showed an 8cm area of consolidation in the right lower lobe with increased multifocal cavitation. Three sputum smears were tested positive for acid-fast bacilli. A MTB complex was identified by AccuProbe. On further questioning, he reported that he had positive purified protein derivative (PPD) test in the past following travel history to Haiti and had been treated for 3 months in the previous 10 years. Based on all these findings, it was noted that he developed reactivation of MTB secondary to dexamethasone, methylprednisolone and tocilizumab use.

Hence, the man started receiving treatment with isoniazid, rifampicin, ethambutol, and pyrazinamide with pyridoxine. Antibiotics and antifungals were discontinued. Within 5 days, oxygen saturation improved to the high 90s, whereas breathing ambient air and fever and leukocytosis promptly resolved. He was discharged after 3 negative sputum acid-fast smears with appropriate outpatient follow-ups to complete a full course of treatment for MTB.

Sasson A, et al. A Coronavirus Disease 2019 (COVID-19) Mystery: Persistent Fevers and Leukocytosis in a Patient with Severe COVID-19. Open Forum Infectious Diseases 7: 1-5, No. 12, Dec 2020. Available from: URL: <http://doi.org/10.1093/ofid/ofaa558> 803552254

» **Editorial comment:** Details of this case report have previously been published and processed for Adis PV [see Reactions 1828 p161; 803511069]. In this publication, specific corticosteroids were reported as dexamethasone and methylprednisolone.