

Azithromycin/dexamethasone/voriconazole

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Pulmonary aspergillosis following off-label use, and lack of efficacy: case report

A 72-year-old man developed fatal pulmonary aspergillosis during treatment with azithromycin and off-label dexamethasone for COVID-19. Additionally, he exhibited lack of efficacy during treatment with voriconazole for pulmonary aspergillosis [routes not stated].

The man, who had a history of stroke, presented due to staggering gait and exacerbation of dysarthria. After diagnosis of cerebral infarction, he was admitted to another hospital. At admission, he was diagnosed with COVID-19. He had several co-morbidities and was receiving multiple co-medications. An unspecified antiplatelet drug infusion was initiated for cerebral infarction. He also received off-label dexamethasone 6 mg/day for COVID-19. Additionally, he received azithromycin 500 mg/day along with ceftriaxone empirically for a suspected bacterial infection. Due to worsening respiratory condition, he was shifted to another hospital on day 8. A CT scan revealed ground glass shadows throughout both lungs. He was intubated and was kept on an assisted ventilation. Dexamethasone dose was increased to 6.6 mg/day with continued ceftriaxone, and remdesivir was added. He also received heparin [unfractionated heparin] 10 000 U/day for cerebral infarction and as off-label for COVID-19. An improvement in his respiratory condition was noted from day 10. On day 13, a CT scan revealed slightly improved ground glass shadows but a collection of nodular shadows appeared in the right lower lobe. Ceftriaxone and remdesivir were stopped on day 14 and 17, respectively. On day 18, he developed a fever and his laboratory test results deteriorated. A catheter-related blood stream infection was suspected, and he was treated with vancomycin and cefepime. As the shadows on X-ray had worsened, treatment with micafungin was started considering a possibility of fungal infection. A CT scan on day 19 revealed collection of nodular shadows in the right lower lobe and additional nodules appeared in other parts of the right lower lobe. He also developed consolidation in both lower lobes. As his β -D glucan level was high and *Aspergillus fumigatus* was detected in sputum culture, he was diagnosed with COVID-19-associated pulmonary aspergillosis. The pulmonary aspergillosis was attributed to azithromycin and dexamethasone [duration of treatments to reaction onset not stated].

The man's dexamethasone dose was reduced to 3.3 mg/day, and micafungin was switched to voriconazole 500 mg/day. Sputum samples yielded *Aspergillus fumigatus* on days 17 and 20, and *Aspergillus* serum galactomannan test was found positive. He experienced continuous respiratory condition deterioration, and developed frequent episodes of paroxysmal supraventricular tachycardia. Tachycardia was not controlled with medication, and BP dropped. He showed no response to unspecified catecholamine administered on day 23. Despite treatment with voriconazole, his condition progressed. He was shifted on a palliative care, and died on day 26. Autopsy was not performed, but his death was attributed to COVID-19-associated pulmonary aspergillosis.

Imoto W, et al. COVID-19-associated pulmonary aspergillosis in a Japanese man: A case report. *Journal of Infection and Chemotherapy* : Jan 2021. Available from: URL: <http://doi.org/10.1016/j.jiac.2021.02.026>

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