Multiple drugs

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Various toxicities: case report

A 70-year-old woman exhibited lack off efficacy during treatment with remdesivir and off label methylprednisolone for COVID-19 pneumonia. Subsequently, she developed mucormycosis along with methicillin resistant Staphylococcus aureus during treatment with methotrexate and methylprednisolone. Additionally, she developed pancytopaenia during treatment with amphotericin-B and methotrexate [*not all routes and dosage stated*].

The woman presented with a history of breathing discomfort, fever and cough from previous 3 days. Her medical history included diabetes for which she was receiving oral hypoglycemic agents (OHA); interstitial lung disease (ILD) for which she was receiving methotrexate 15mg/week and low dose unspecified steroids; old left sided hemiparesis for which she was receiving aspirin [Ecosprin]. On the current presentation, she was found positive for COVID-19 and was diagnosed with COVID-19 pneumonia. Thereafter, she started receiving remdesivir injection for 5 days, off label IV methylprednisolone 40mg three times a day and enoxaparin-sodium [Clexane]. However, her dyspnoea remained persistent. Hence, a lack of efficacy was reported for remdesivir and methylprednisolone. In view of persistent dyspnea, she was shifted to the medical ICU. Subsequently, she received bilevel positive airway pressure (BiPAP) support and off label convalescent-anti-SARS-CoV-2-plasma two units. She continued receiving same line of management and gradually her was BiPAP support was weaned. Thereafter, she was discharged with unspecified steroids, unspecified OHA and other medications in a stable condition. After 2 months, she presented again with the history of eye pain, right sided headache and vomiting. Examination revealed that, she had tachycardia and SpO2 of 88% on rheumatoid arthritis (RA) with facial edema and redness over right eye. Therefore, she was admitted. Subsequent, blood investigations through haemogram revealed revealed haemoglobin (Hb) level of 11g%, total leukocyte count (TLC) of 24000, platelet count of 232 lakhs and creatinine level of 2.92. Thereafter, magnetic resonance imaging (MRI) of brain showed microvascular changes. Since, there was a possibility of fungal sinusitis, High resolution CT paranasal sinuses (PNS) was performed, which revealed sinonasal inflammatory process. Subsequently, urgent MRI paranasal sinus and orbit raised a suspicion of invasive fungorhinosinusitis, optic neuritis and orbital cellulitis. Thereafter, the presence of orbital cellulitis with impending optic neuritis was confirmed. Nasal swab revealed a result negative for fungus. Thereafter, she received a functional endoscopic sinus surgery (FESS); Pus obtained was sent for culture, which revealed positive results for mucor with *Staphylococcus aureus*. Hence, she was considered to have mucormycosis. It was reported that, during FESS, she was intubated.

Subsequently the woman's treatment was started with amphotericin-B (lipid formulation) 250 mg/daily and unspecified sensitive IV antibiotics for methicillin resistant *Staphylococcus aureus*. After 5 days from the therapy, her blood investigations showed a platelet count of 115 lakhs, a Hb of 9.7g% and TLC 2.91 along with normalisation of kidney function tests. On the day 10th of hospitalisation, her TLC was 1.24, platelet was 53000 and Hb was 8.7g%. Thereafter, the peripheral smear revealed pancytopenia with lymphocytosis. Iron profile showed a low iron and a low total iron binding capacity. Additionally, her folate and vitamin B12 were normal. Thereafter, direct coombs test and indirect coombs test revealed a negative result hence, the possibility of haemolysis was ruled out. Thereafter, she started experiencing nasal bleed [aetiology unknown]. Subsequent investigations revealed D-dimer level of 927, a normal International normalized ratio and normal fibrin degradation products. Hence, the possibility of disseminated intravascular coagulation (DIC) was ruled out. Thereafter, in the view of ongoing epistaxis, she received platelets and fresh frozen plasma. The development of pancytopenia was initially attributed to the methotrexate. Subsequently, her treatment with methotrexate was discontinued. Thereafter, she started receiving folinic acid. However despite stopping methotrexate, she continued experiencing pancytopenia. Hence, finally, the development of pancytopaenia was attributed to both methotrexate and amphotericin-B. Hence, she started receiving G-CSF injections with erythropoietin. Subsequently, she was switched on to amphotericin-B-liposomal [liposomal ampho-B]. On day 15, her repeat haemogram showed a platelet level of 112000, Hb level of 12.1 g% and a TLC level of 5.41. After receiving 5 days of ventilatory support and 14 days of amphotericin B in hospital, she was discharged with OHA, amphotericin-B-liposomal [Ambisome] and posaconazole. From that time she was asymptomatic and currently, at the time of this manuscript writing she was doing well. Ultimately, the development of mucormycosis with methicillin resistant Staphylococcus aureus was attributed to methylprednisolone and methotrexate [*durations of treatments to reactions onset not stated*].

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