

Multiple drugs

S

Protracted severe COVID-19 pneumonia, hepatotoxicity and lack of efficacy following off label use: case report

A woman in her 70s developed hepatotoxicity during treatment with methotrexate for mixed connective tissue disease. Subsequently, she developed protracted severe COVID-19 pneumonia during treatment with rituximab and exhibited lack of efficacy during off label treatment with immune-globulin and dexamethasone for COVID-19 pneumonia [*not all dosages and routes stated; durations of treatments to reactions onsets not stated*].

The woman was diagnosed with mixed connective tissue disease in early 2018 based on the peripheral arthritis, Raynaud's, oesophageal dysmotility and myositis. She was initially treated with unspecified steroids and methotrexate with partial response. In July 2018, rituximab was added leading to disease remission. Rituximab infusions were repeated every 6 months in addition to methotrexate and methylprednisolone. Thereafter, she developed hepatotoxicity due to methotrexate.

Therefore, the woman's methotrexate therapy was discontinued in late 2019. Afterwards, she remained on rituximab monotherapy plus low dose steroids. On 20 January [*year not stated*], at the age of 76 years, she was seen in the Rheumatology Department and was found asymptomatic, and received rituximab 1g, as scheduled. After few days, her husband developed flu-like symptoms and was tested positive for SARS-CoV-2. On 02 February, she with all her family members living in the same house were screened for SARS-CoV-2 and were all tested positive. Initially, she was asymptomatic but soon developed low-grade fever and fatigue. Gradually, her condition worsened with high-grade fever and cough. On 12 February, she was admitted alongside her husband, who subsequently died due to COVID-19 respiratory failure. On admission, her oxygen saturation was 95% on ambient air. A chest CT revealed ground-glass lesions. She was treated with remdesivir, off label dexamethasone and unspecified low molecular weight heparin according to standard protocol. Gradually, she improved and was discharged to domestic quarantine on 22 February. A few days after her discharge, she started feeling unwell. She reported a low-grade fever. Within the following days, she deteriorated with high-grade fever and dry cough. She was again admitted on 10 March. On admission, she had a positive RT-PCR SARS-CoV-2 test. Her oxygen saturation was 94%, and her blood tests revealed a mild leukopenia, lymphopenia, a two-fold elevation of CRP, a ferritin level of 117 ng/mL whereas antibodies against SARS-CoV-2 were undetectable. Her chest CT showed typical features suggestive of COVID-19 pneumonia. Taking into account that blood cultures and an extensive workout for bacterial, fungal, parasitic and mycobacterial infections was negative, a case of SARS-CoV-2 reactivation was considered. She was treated with broad spectrum antibiotics plus remdesivir and off label dexamethasone. She became afebrile and steadily improved. Following two negative RT-PCR tests for SARS-CoV-2, she was discharged on 22 March. A few days after her discharge, she reported malaise and low-grade fever. She progressively deteriorated with high-grade fever and dyspnoea. On 07 April, she was readmitted. On admission, she again tested positive for SARS-CoV-2 by RT-PCR whereas antibodies were undetectable. She presented with respiratory failure, leukopenia with striking lymphopenia, a five-fold elevation of CRP, a threefold elevation of D-Dimers, a ferritin level of 924 mg/dL whereas immunoglobulin levels were low. A chest CT was significantly worse. She was treated with off label IV immune-globulin [immunoglobulin] 2 mg/kg in total divided into five consecutive days, dexamethasone, broad-spectrum antibiotics and nasal high flow oxygen therapy. Extensive workup for superimposed infections was negative. She gradually got worse and subsequently underwent mechanical ventilation on 29 April. On that day, RT-PCR for SARS-CoV-2 from both nasopharyngeal swabs and bronchial secretions were positive indicating a high viral load. Finally, she died on 06 May due to multi-organ failure.

Daoussis D, et al. Protracted severe COVID-19 pneumonia following rituximab treatment: caution needed. *Rheumatology International* 41: 1839-1843, No. 10, Oct 2021.

Available from: URL: <https://link.springer.de/link/service/journals/00296/index.htm>

803649690