A 58-year-old male received a diagnosis of rheumatoid arthritis (RA) in September 2011, involving shoulders, elbows, hands, knees, ankles, and feet with bony erosions. He had a pulmonary tuberculosis history (Figure 1a) complicated by restrictive pericarditis, successfully managed by antibiotics and pericardiectomy in 1995. Biweekly injection of 40 mg adalimumab, a tumor necrosis factor monoclonal antibody (mAb), was initiated in May 2014 due to refractory responses to prednisolone 10 mg/day and disease-modifying antirheumatic drugs (hydroxychloroquine, leflunomide, methotrexate, and sulfasalazine). After adalimumab therapy, there was a low disease activity (DAS28 < 3.2) with reduced medication regimen to prednisolone 5 mg/day and methotrexate 15 mg/week.1 Negative results of QuantiFERON test, a whole-blood interferon-γ release assay helpful for tuberculosis diagnosis,2 were obtained before and after adalimumab therapy. In September 2017, he was admitted with dyspnea and cough for 1 week. Diffuse pulmonary ground-glass infiltrations were found (Figure 1b) with negative microbiological survey. Under the suspicion of drug-induced lung injury (DILI), methotrexate use was terminated with the prescription of high-dose glucocorticoids, leading to resolved pulmonary infiltrations 1 month later (Figure 1c). There was a switch of biologics use due to a worsening activity without methotrexate therapy. Infusion of rituximab, a B-cell depleting mAb, was initiated in July 2018, 1 g every 2 weeks for two doses repeated every 6 months, together with prednisolone 10 mg/day and hydroxychloroquine 400 mg/day. There was a disease remission (DAS28 < 2.6) after rituximab therapy.

The patient received rituximab infusions on June 14 and 30, 2022. Owing to the admission for percutaneous intervention of occluded coronary arteries, nasopharyngeal SARS-CoV-2 polymerase chain reaction test was done with negative results on June 17, 2022. There was no known COVID-19 vaccination history. He visited the Emergency Department with acute onset of dyspnea and cough on July 4, 2022. There were diffuse pulmonary ground-glass infiltrations (Figure 1d) and positive results of SARS-CoV-2 test (cycle threshold 18.8), establishing a diagnosis of COVID-19 pneumonia. Despite the use of mechanical ventilation and antiviral (molnupiravir and remdesivir) and immunomodulating (dexamethasone and tocilizumab) therapy,3 he succumbed to acute respiratory distress syndrome and multiorgan failure 15 days later.

During the COVID-19 pandemic, owing to associated comorbidities and activity/medication-related immunosuppression, inflammatory rheumatic diseases might form a vulnerable group at increased risk of severe SARS-CoV-2 infection.4,5 Higher prescribed glucocorticoids dosages (more than 10 mg/day prednisolone-equivalent dose) in such patients have greater odds of COVID-19-related death.5 Furthermore, B-cell depletion therapy can compromise humoral immune responses with difficulties in the clearance of SARS-CoV-2.4-6 Notably, rituximab use in systemic lupus erythematosus is associated with increased hospitalization and death outcome as well as poor vaccination efficacy with lower seroconversion rates and antibody levels.6 Despite the remarkable efficacy, rituximab therapy in our patient might be a COVID-19-associated death risk other than male sex, cardiovascular comorbidity, and glucocorticoids use.

Besides disease activity with lung involvement, acute diffuse pulmonary complications in RA are due to treatment-related adverse drug reaction (ADR) and infection.7,8 DILI can occur during methotrexate therapy in RA, a reversible condition if under earlier management such as the pneumonitis episode in this case.8 Indeed, COVID-19 pneumonia should be a differential diagnosis of acute diffuse pulmonary complications in RA patients receiving rituximab therapy.

**Note of Authors**

Increasing evidences support the association of severe SARS-CoV-2 infection in RA patients receiving rituximab therapy regardless of their vaccination status.5,9 We reported a possible ADR of rituximab in this patient to the Food and Drug Administration through the National Adverse Drug Reaction Reporting System on August 24, 2022.10
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