Mild COVID-19 in ANCA-associated vasculitis treated with rituximab

Treatment for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis usually raises questions about the risk of infections. Particular attention has been given to the impact of drugs such as cyclophosphamide and B-cell deleterious therapies on the severity of COVID-19. Monti et al. suggest that receiving biological disease-modifying antirheumatic drugs may not increase risk of COVID-19. Furthermore, Guilpain et al. reported a woman treated with rituximab and low-dose prednisone due to granulomatosis with polyangiitis proteinase 3-antineutrophil cytoplasmic antibody (PR3-ANCA) vasculitis, who developed pneumonia associated with COVID-19 with a milder evolution than expected in other series.

Here, we present a 64-year-old woman diagnosed of myeloperoxidase-ANCA microscopic polyangiitis in 2014, with secondary hypertrophic pachymeningitis, sinusitis and constitutional syndrome. Her main comorbidities were hypercholesterolaemia and areata alopecia. On 25 November 2019, vasculitis relapsed and was treated with two infusions of 1000 mg rituximab given 2 weeks apart, in addition to three bolus of 125 mg methylprednisolone. The patient improved and received maintenance treatment with 7.5 mg/day prednisone and a double-strength tablet of trimethoprim-sulfamethoxazole 3 days a week.

While on holidays at her daughter’s house in The Netherlands, on 7 March 2020 her husband developed fever >38°C, odynophagia, discomort and dyspnoea. He was finally admitted to a hospital and diagnosed with COVID-19 infection by reverse transcription PCR (RT-PCR) on a nasopharyngeal swab. At the same time, she presented feverish, asthenia, myalgia, lack of appetite, headache, anosmia and dysgeusia, and was treated with paracetamol at home, improving after 2 weeks. One month later, after returning home in Spain, she came to our clinic for evaluation due to her exposure to COVID-19.

Blood test results showed positive immunochromatographic-specific IgG antibodies assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). IgM antibodies and nasopharyngeal swab (RT-PCR) were both negative. Cytometric studies revealed 10 B lineage cells. Serum immunoglobulin showed moderately decreased IgM (0.23 g/L), and normal IgG and IgA concentrations. A test for ANCA was positive, with a perinuclear staining pattern, and an ELISA confirmed the presence of myeloperoxidase ANCA at a titre of 5.3 U/mL (reference range <1).

Patients with compromised immune systems represent a susceptible population in which infections may have devastating consequences. The impact of rituximab treatment on SARS-CoV-2 infection remains to be clarified. As hyperinflammation underlies the mechanism of severe COVID-19, the immunocompromised situation may prevent them from virus-induced cytokine storm syndrome. Transcriptome data including RNA-seq and GeneChip human genome arrays show that glucocorticoids and some disease modifying anti-rheumatic drugs (DMARDs) (foliculizumab, methotrexate, hydroxychloroquine, tocitabimib, azathio-prine and so on) could suppress the cytokine profile represented in severe COVID-19, but there are scarce data about rituximab. Rituximab largely depletes peripheral B cells, including memory B cells, from blood. It also modulates the immune system through different mechanisms including antibody-dependent cellular cytotoxicity, complement-dependent cytotoxicity and apoptosis induction. In addition, early stem cells and B-precursors do not express CD20 on their surface, which gives them resistance to the effect of rituximab. However, studies have shown that patients treated with anti-CD20 agents had a severely impaired immunogenicity to vaccines and therefore, against emerging infections such as COVID-19.

Our patient’s presentation of COVID-19 with mild symptoms did not fit the expected clinical course in an immunosuppressed patient. This suggests that B-cell depletion therapy may not be a risk factor for severe forms of COVID-19 but favour a milder course of the disease and the generation of specific antibodies, whose future protective role remains unclear.

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