COVID-19 Recovery Without B Cells or Antibodies in Patients Receiving Rituximab for Autoimmune Disease

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To the Editor;

There is a critical need to better understand the outcomes of patients with autoimmune disease treated with rituximab who contract severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Neutralizing antibodies to SARS-CoV-2 are purported to be a significant driver of immunity. Indeed, nearly all patients surviving infection with SARS-CoV-2 develop antibodies by three weeks.[1] Moreover, vaccines involve the generation of neutralizing antibodies. However, there is growing concern over the protective role and durability of the antibody response to SARS-CoV-2.[2,3] On the other hand, there is growing recognition of T cells in the adaptive response to SARS-CoV-2. Recent reports have found circulating virus-specific $CD4^+$ and $CD8^+$ T cells in most convalescent patients who had coronavirus disease 2019 (COVID-19).[4] Herein, we describe our observations of patients receiving rituximab for autoimmune disease who recover from COVID-19 without B cells and without detectable anti-SARS-CoV-2 antibodies.

We retrospectively analyzed 516 adult patients with autoimmune disease treated with rituximab-induced B cell depletion at our center during the COVID-19 era. We identified six patients with COVID-19. Four patients had antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), and 2 patients had idiopathic focal segmental glomerulosclerosis. All six patients fully recovered from COVID-19. The median (range) time from symptom onset to last fever was 17.5 days (0 – 44). Two patients were admitted to the ICU and received remdesivir. One also received convalescent serum. One patient was admitted to the hospital floor and monitored without specific treatment. The remaining three patients improved without intervention while self-quarantining at home.

Patient one, who was previously admitted to the ICU and treated with remdesivir, tested positive by PCR at one of 2 sites on the nucleoprotein gene on day 120. She had on-going symptoms of cough,

Patients with Undetectable Circulating B Cells During Their Infection

Patient	Day of Last Fever Since First Symptom	Day of 1st of 2nd Consecutive Negative RNA Tests	Day of Antibody Test	Antibody Test Result
1	44	85	28 RBD	Negative
			31 Roche	Negative
			34 RBD	Negative
			74 Roche	Negative
			74 RBD	Negative
2	20	56	73 Roche	Negative
			73 RBD	Negative
3	41	32	34 Roche	Negative
4	15	36	14 RBD	Negative
			64 Roche	Negative
			64 RBD	Negative
5	0	27	48 Roche	Negative
			48 RBD	Negative
			70 Roche	Negative
			70 RBD	Negative
6	15	52	48 Quest	Positive
			67 Roche	Negative
			67 RBD	Positive

Abbreviations: Roche, roche elecsys anti-SARS-CoV-2 total antibodies test; RBD, receptor-binding domain IgG, IgA, IgM ELISA (medrxiv.org/content/10.1101/2020.07.18.20155374v1); Quest, Quest-SARS-CoV-2 Ab IgG.

shortness of breath and nausea. In addition to rituximab, she was on azathioprine and prednisone 10 mg daily for the duration of her infection. On day 120, she was started on prednisone 40 mg daily for 10 days and her symptoms abated.

Five of the six patients had documented undetectable circulating B cells during their infection. All five patients had undetectable anti-SARS-CoV-2 antibodies (Table). The sixth patient had partial B cell recovery (30 cells/µL; reference range: 90 to 660 cells/µL) when measured three weeks after clearing viral RNA. She had detectable SARS-CoV-2 antibodies on two of three assays.

Our series highlights 6 patients with autoimmune disease receiving B cell depletion therapy with rituximab who contracted COVID-19 and fully recovered. Even though rituximab prevented antibody development to SARS-CoV-2 through its B cell depleting effect, the patients in our series demonstrated an ability to clear the virus. We speculate this is due to the T cell response. These observations offer insight into the adaptive immune response to SARS-CoV-2 and potentially suggest that the T cell response may be as or more important than the B cell response.

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