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Letter to the Editor

A Case of Ulcerative Colitis Relapse Characterized by Systemic Type I Interferon Responses after COVID-19 Vaccination

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To the Editors:

The newly developed messenger RNA (mRNA)–based vaccines against severe acute respiratory syndrome coronavirus 2 are effective for the prevention of coronavirus disease 2019 (COVID-19). However, the induction of efficient immune responses by COVID-19 vaccination is concomitant with a wide variety of side effects.[1] Although a significant population of patients with ulcerative colitis (UC) experience disease flares after COVID-19 vaccination,[2,3] the immune responses accounting for UC flares following COVID-19 vaccination are poorly understood.

A 22-year-old woman developed watery diarrhea, bloody stool, and abdominal pain 4 days after the first dose of BNT162b2 vaccination (BioNTech-Pfizer). She was diagnosed with UC at 12 years of age and had maintained complete remission without medication since then. No major abnormalities were seen in blood tests except elevation of C-reactive protein levels (1.71 mg/dL, normal range <0.14 mg/dL). Colonoscopy showed edema, redness, small erosions, and disappearance of vascular networks in the rectum, transverse colon, and cecum. Massive infiltration of immune cells, destruction of crypt architecture, and crypt abscesses were observed in the colonic biopsy samples (Figure 1A). These results were consistent with UC relapse after COVID-19 vaccination, and she was treated with 5-aminosalicylic acid (5-ASA) (4800 mg/d). Three weeks after the initiation of 5-ASA treatment, symptom relief was achieved. The patient received a second dose of COVID-19 vaccination without exacerbation of UC.

mRNA induces strong type I interferon (IFN) responses upon sensing by pattern recognition receptors.[1] Thus, it is possible that enhanced type I IFN responses following immunization with the mRNA-based COVID-19 vaccine underlie the immunopathogenesis of relapse in this case. To examine this possibility, serum concentrations of IFN-α, IFN-β, tumor necrosis factor α, and interleukin-6 were measured as previously described.[4] Serum concentrations of IFN-α, IFN-β, and interleukin-6 decreased after induction of remission by 5-ASA (Figure 1B). Thus, UC relapse was associated with type I IFN responses caused by COVID-19 vaccination in this case. This idea is supported by the recent finding that type I IFN responses are enhanced in the colonic mucosa of patients with UC.[5]

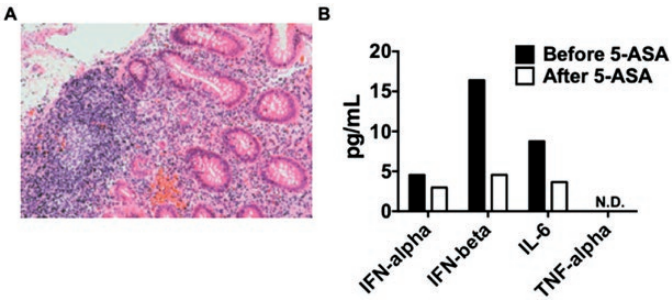

Figure 1. Relapse of ulcerative colitis after coronavirus disease 2019 vaccination. A, Hematoxylin and eosin staining of colonic biopsy samples; massive infiltration of immune cells, destruction of the crypt architecture, and crypt abscess were seen in the biopsy samples obtained from the cecum. Magnification ×400. B, Serum concentrations of interferon (IFN)-α, IFN-β, interleukin (IL)-6, and tumor necrosis factor(TNF)-α before and after the treatment with 5-aminosalicylic acid (5-ASA). N.D., not detected.

Although COVID-19 vaccination has been identified as a risk factor for UC flares, the immunopathogenesis of these flares remains poorly defined. In this case of UC relapse following COVID-19 vaccination, type I IFN responses were parallel to disease progression. Thus, type I IFN responses due to mRNA sensing by PRRs may result in the exacerbation of UC. However, it should be noted that confirmation of this idea requires large-scale cytokine analyses in UC patients exhibiting flares after COVID-19 vaccination.

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Author Contributions

Y.M. and T.W. drafted the manuscript and measured the serum concentrations of the cytokines. K.M. and M.K. revised the manuscript.

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Conflict of Interest

No conflicts of interest are declared.

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