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Cytomegalovirus Enteritis in a Patient with Rheumatoid Arthritis Receiving Baricitinib

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Address correspondence to Dr. E. Sugawara, 060-0004 N4W7, Chuo-Ku, Sapporo, Japan. Email: e.sugawara@huhp.hokudai.ac.jp. The present study was approved by the Ethics Committee of Tonan Hospital (approval No. 434), and written informed consent was obtained from the patient.

T cells play a central role in immunity against cytomegalovirus (CMV)[1]. Baricitinib, a Janus kinase (JAK) inhibitor, suppresses T cell function by inhibiting JAK-signal transducers and activators of transcription (STAT)[2]. Interferon-γ (IFN-γ) is one of the major T cell cytokines involved in the immunity against CMV[3]. Tacrolimus has a strong inhibitory effect on IFN-γ as well as JAK inhibitors[4].

A 65-year-old male with a 14-year history of rheumatoid arthritis (RA), who was treated with 12 mg/week of methotrexate (MTX) for 14 years, 4 mg of baricitinib, and 2 mg/day of tacrolimus for 6 months, presented abdominal pain and fever. Laboratory tests showed elevated C-reactive protein levels (1.7 mg/dl) and positive CMV antigenemia (102/50,000 cells). Computed tomography scan revealed a thickened distal ileum (Figure 1A). Total colonoscopy showed multiple ulcers in the terminal ileum (Figure 1B). Histopathologic examination

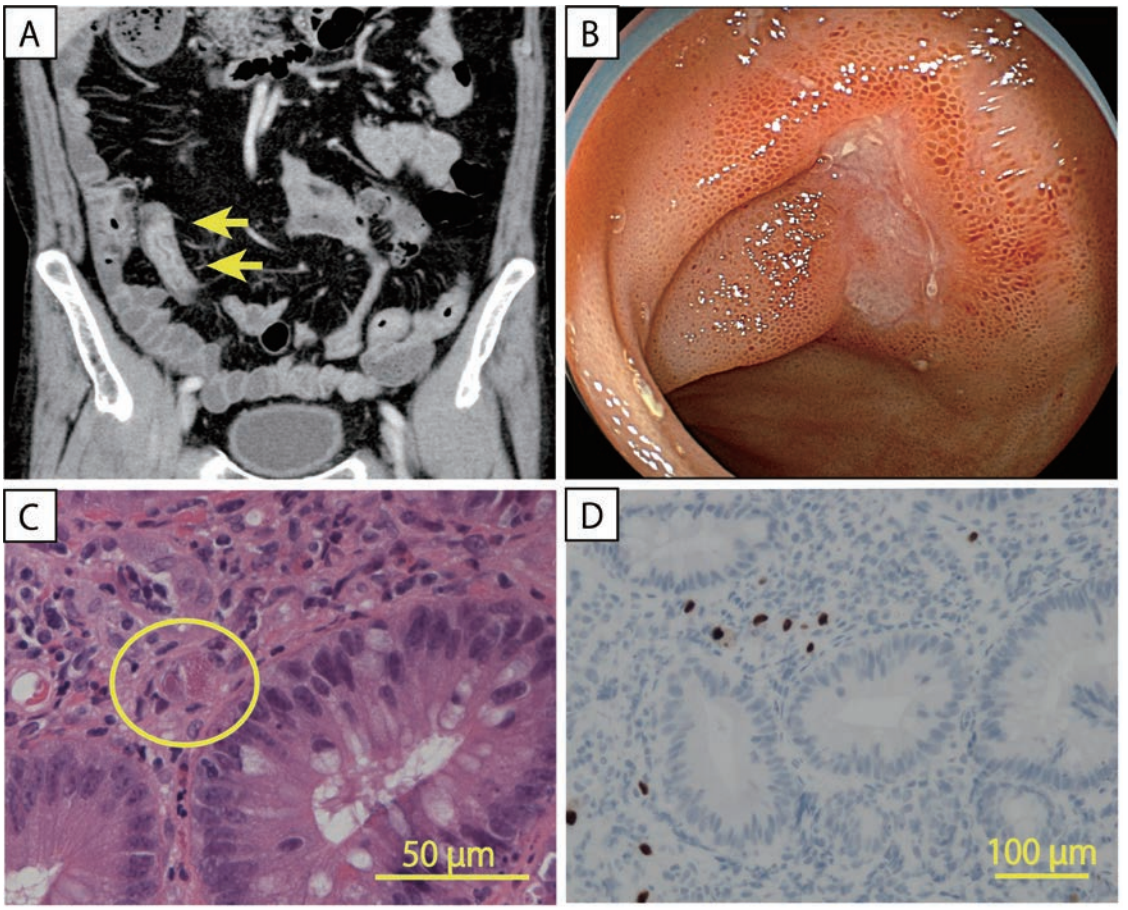

Figure 1. A. Abdominal computed tomography scan showing a thickened distal ileal segment with reactive fluid. B. Endoscopic image of the lower gastrointestinal tract, demonstrating multiple ulcers and erosive changes in the terminal ileum. C. Histologic examinations of the ulcers of the terminal ileum, showing ulcerative changes with inflammatory cell infiltration and cytomegalic changes with intranuclear and intracytoplasmic inclusion bodies in the vascular endothelium by H&E. D. *In situ* hybridization positive for cytomegalovirus.

revealed intranuclear inclusion bodies in the mucosa (Figure 1C), which were positive for CMV (Figure 1D), confirming CMV enteritis. After discontinuation of MTX and baricitinib, he was treated with intravenous ganciclovir for 2 weeks, followed by oral valganciclovir. MTX and baricitinib were readministered after antiviral therapy, while tacrolimus was discontinued. He experienced no flares of RA or CMV enteritis.

Although MTX has been reported to be associated with CMV infection[5], the patient had not experienced CMV infection despite the 14-year history of MTX treatment. Therefore, we hypothesize that CMV infection might have been accelerated mainly by strong T cell dysfunction induced by the combined effects of baricitinib and tacrolimus.

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