Letter

Cytomegalovirus Enteritis Induced by Baricitinib and Tacrolimus: Association or Coincidence?

To the Editor:

We read the recent article by Sugawara et al with great interest.¹ The authors described a 65-year-old patient with rheumatoid arthritis who had been treated with methotrexate for 14 years without any adverse effects, yet within the last 6 months had developed fever and abdominal pain when treated with 2 mg/day of tacrolimus and 4 mg of baricitinib. He was definitively diagnosed with cytomegalovirus (CMV) enteritis by computed tomography scan, total colonoscopy, histopathologic examination, and CMV testing. However, there are certain details that require further clarification.

First, gastrointestinal (GI) viral infections are well recognized as a complication of immunosuppression. CMV enteritis is a rare but fatal disease that has been underdiagnosed and is an opportunistic infection not only in immunocompromised patients but also in immunocompetent individuals.² The diagnosis of CMV enteritis remains difficult due to the various clinical presentations, the generally critical condition, and the frequent need for repeated biopsies. It is essential for clinicians to have a low threshold for suspecting a viral etiology of mucosal ulceration and inflammation, and to prioritize empirical antiviral therapy in immunosuppressed patients. Second, a study by Yeh et al found that a history of radiotherapy and higher C-reactive protein (CRP) levels were poor prognostic factors for increased in-hospital mortality in CMV enteritis.³ Higher CRP levels represent severe infection and inflammation.⁴ The patient in this article did not have high CRP levels, indicating that the mucosal damage and inflammation were not severe, which implies a good prognosis.¹ Finally, radiation therapy, immunodeficiency, and CMV colitis have been shown to be risk factors for CMV enteritis.⁴ It is unclear whether factors predisposing to mucosal injury, such as a history of radiation examinations including the lower spine and pelvis, were present during the disease in this patient. Radiation therapy can lead to chronic and acute intestinal mucosal injury, which in turn leads to inflammation, swelling of the endothelial lining of arterioles, ischemia, mucosal cell loss, and neovascularization. All these contribute to mucosal fibrosis and friability, and ultimately increase the risk of vulnerability and superimposed infection.⁵ CMV colitis is a risk factor for CMV enteritis because they share similar risk factors. In addition to the patient's own immunocompromised status, corticosteroid exposure, chronic renal disease, and crit-

ical illness (eg, concurrent pneumonia, shock, sepsis) can also contribute to immunodeficiency,⁶ so the authors should describe in detail whether there were other conditions that contribute to the immunocompromised status in this article.¹ The hypothesis that CMV infection might be accelerated mainly by strong T cell dysfunction induced by the combined effects of tacrolimus and baricitinib merits consideration.

In summary, although some of the details in this article need to be further elucidated, this study reveals a case of immunosuppression leading to the risk of serious infectious GI complications, and supports the growing concern regarding immunosuppression-induced adverse drug reactions.

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The authors declare no conflicts of interest relevant to this article.

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