LETTERS TO THE EDITOR

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Author's Reply

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We thank Dr. Kim for her thoughtful comments[1] regarding our article entitled "Usefulness of the cytomegalovirus antigenemia assay in patients with ulcerative colitis".[2] We agree with Dr. Kim that the cytomegalovirus (CMV) antigenemia assay is not sufficient to confirm a diagnosis of CMV colitis in patients with ulcerative colitis (UC). In this study,[2] CMV colitis (defined as the presence of inclusion bodies in H&E-stained sections and/or positive immunohistochemical staining for CMV in the colonic mucosa) was diagnosed in eight (66.7%) of 12 patients positive for CMV antigenemia. In contrast, four (12.9%) of 31 patients negative for CMV antigenemia had CMV colitis. Although positive CMV antigenemia was strongly associated with CMV colitis (P=0.001), the CMV antigenemia assay has high specificity (87.1%) but low sensitivity (66.7%) for detecting CMV colitis in patients with active UC. Therefore, the CMV antigenemia assay may not be useful for the detection of CMV colitis in patients with UC due to its high false-negative rate.

As pointed out by Dr. Kim,[1] histologic evaluation including H&E staining for the presence of cytomegalic cells and immunohistochemical staining for CMV in colonic tissues is the gold standard for diagnosing CMV colitis.[3,4] In addition, colonic tissue PCR for CMV DNA is useful for detecting CMV infection,[5] and recommended for evaluating CMV colitis in patients refractory to immunosuppressive therapies.[6] All of these methods require colonoscopy or sigmoidoscopy in patients at high risk of developing procedure-related complications. However, it is generally accepted that sigmoidoscopy should be considered to assess the severity and extent of colonic inflammation as well as to define the presence of concomitant CMV infection in all patients with active UC, except those at high risk for perforation, such as patients with toxic megacolon.[7,8]

The CMV antigenemia assay detects the CMV pp65 antigen in the leukocytes of circulating blood using fluorescent antibodies specific for pp65.[3] Thus, the CMV antigenemia assay reflects systemic CMV reactivation rather than CMV gastrointestinal disease.[4] The low sensitivity of the CMV antigenemia assay for diagnosing CMV colitis may result from the possibility of localized CMV colonic infection without systemic CMV viremia. The strength of the CMV antigenemia assay should be focused on systemic CMV reactivation parameters rather than the diagnosis of CMV colitis.

Active UC patients with aggravated symptoms despite appropriate oral medication should be hospitalized for intravenous steroid therapy.[9] However, approximately 27% of the patients require early colectomy after corticosteroid therapy.[10] Thus, it is critical to identify early predictors for steroids-refractory UC in order to facilitate the initiation of rescue therapy and avoid colectomy. In this study, we determined that positive CMV antigenemia was an independent predictor for steroid refractoriness in patients with moderate-to-severe UC who required intravenous steroids. In a multicenter cohort study, UC patients who experienced CMV reactivation showed poor clinical outcomes in terms of colectomy and disease flare-ups.[11] Therefore, patients positive for CMV antigenemia might be at high risk for steroid refractoriness and need early ganciclovir therapy because of systemic CMV reactivation, although whether CMV is the cause of colitis exacerbation or plays the role of an innocent bystander in the exacerbation of UC remains controversial.[3]

Considering the short processing time and high specificity for CMV colitis, the CMV antigenemia assay is clinically use-

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ful for the early detection of CMV reactivation in active UC patients. Therefore, we suggest that the CMV antigenemia assay might be considered as a preliminary test for CMV reactivation and a predictor of steroid refractoriness in all patients with moderate-to-severe UC who require systemic steroids.

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