EDITORIAL

INTESTINAL RESEARCH

ISSN 1598-9100(Print) • ISSN 2288-1956(Online)
http://dx.doi.org/10.5217/ir.2015.13.1.2
Intest Res 2015;13(1):2-3

A Clinical Significance of Assessing Cytomegalovirus Infection Status in Patients With Ulcerative Colitis

Sooyun Chang, Jae Hee Cheon
Institute of Gastroenterology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea

Article: Usefulness of the Cytomegalovirus Antigenemia Assay in Patients With Ulcerative Colitis **(Intest Res 2015;13:50-59)**

Cytomegalovirus (CMV) is a pathogen implicated in a diverse spectrum of diseases, depending on the immune status of the host. CMV usually leads to asymptomatic infection in immunocompetent individuals, but may cause serious morbidity and mortality in immunocompromised patients.[1,2] CMV is also considered to be the most common viral pathogen involved in IBD. CMV infection is frequently detected using colonic mucosal biopsy in severe cases of UC or CD, but its clinical significance is still controversial. CMV may be the cause of severe colitis flares, or may play the role of an innocent bystander.[3,4]

Recently, noninvasive diagnostic methods such as the serum CMV PCR and CMV antigenemia assay have received a lot of clinical interest owing to the difficulty in diagnosing CMV colitis. In a retrospective study by Kim et al., among 229 moderate-to-severe UC patients, 83 patients (36.2%) had CMV colitis, and the sensitivity and specificity of the CMV antigenemia assay were found to be 47.0% and 81.7%, respectively.[5] Jang et al. also reported similar results in 149 patients with suspected CMV gastrointestinal disease, with the sensitivity and specificity of the CMV antigenemia assay being 54% and 88%, respectively.[6] These results indicate that even though the CMV antigenemia assay could not replace endoscopic biopsy owing to its comparatively low sensitivity, it may still be helpful in diagnosing CMV colitis in some cases because of its high specificity.[5] Although CMV infection has been reported as a risk factor for poor outcomes in two prospective multicenter studies by the IBD Study Group of the Korean Association for the Study for Intestinal Diseases,[7,8] there is little data concerning the relationship between CMV antigenemia assay results and clinical outcomes.

In the present study,[9] the authors retrospectively evaluted the usefulness of the CMV antigenemia assay in predicting clinical prognosis in UC patients in a single academic center. Of 146 patients hospitalized for an exacerbation of moderate-to-severe UC, 43 patients who had undergone the CMV antigenemia assay at the time of admission were included. Twelve of the patients had CMV antigenemia, and 8 (66.7%) were diagnosed with CMV colitis by endoscopic biopsy. Of the 31 patients with negative CMV antigenemia assay results, 4 (12.9%) had CMV colitis. CMV antigenemia was significantly associated with CMV colitis (P=0.001). The sensitivity and specificity of the CMV antigenemia assay for CMV colitis were 66.7% and 87.1%, respectively.

Regarding the clinical course, there was a significant association between CMV antigenemia and refractoriness to corticosteroid therapy (P=0.002). Eleven of 12 (91.7%) patients in the CMV antigenemia-positive group, and 12 of 31 (38.7%) patients in the CMV antigenemia-negative group had refractoriness. In addition, the titer of the antigenemia assay showed a tendency to be higher in patients with steroid-refractory UC than in those with the steroid-responsive UC (P=0.058). Multivariate analysis revealed that steroid refractoriness was significantly increased in CMV antigenemia-positive patients (adjusted OR, 7.73; P=0.030), and in

Received December 2, 2014. **Revised** December 3, 2014.
Accepted December 3, 2014.
Correspondence to Jae Hee Cheon, Department of Internal Medicine, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea. Tel: +82-2-2228-1990, Fax: +82-2-393-6884, E-mail: geniushee@yuhs.ac
Financial support: None. **Conflict of interest:** None.

http://dx.doi.org/10.5217/ir.2015.13.1.2 • Intest Res 2015;13(1):2-3

patients with a shorter duration of UC (adjusted OR, 0.99; *P*=0.025). However, there was no significant difference in the colectomy rate between the positive group (33.3%) and the negative group (22.6%, *P*=0.467). In conclusion, the CMV antigenemia assay showed low sensitivity but high specificity for detecting CMV colitis and predicting steroid-refractory UC.

There are some limitations to the present study. Selection bias may have been introduced when performing the CMV antigenemia assay, which could have influenced the results by leading to higher chances of testing CMV antigenemia in severe patients. Whether and when to examine for CMV colitis is generally decided by the attending physician, the severity of the disease, and/or steroid refractoriness. In future studies, it would be beneficial to establish certain objective criteria for the CMV antigenemia assay, and to determine the optimal timing for blood sampling. Furthermore, the sample size was small, and the analysis was retrospective and based on medical charts, which makes it difficult to draw a concrete conclusion based on these results alone.

However, the present study clearly shows that CMV antigenemia is an independent predictive factor for steroid refractoriness in moderate-to-severe cases of UC. Corticosteroid therapy is currently a significant tool in the management of acute exacerbation of UC. Moreover, a history of CMV has been shown to be predictive of nonresponse to infliximab.[10] CMV testing would be useful to predict the response to steroids earlier in the treatment course. Therefore, testing for CMV should be routinely performed before corticosteroid or infliximab therapies in acute, severe cases of UC. However, a positive antigenemia test result is not sufficient to confirm a diagnosis of CMV colitis in cases of UC. It is generally accepted that sigmoidoscopy should be performed to both evaluate the disease status itself and determine if CMV infection is involved. Given that CMV antigenemia testing has a relatively high specificity as revealed by several studies, and that immunohistochemical staining of CMV takes 3–5 days before providing final results, the CMV antigenemia assay should be considered as a preliminary test in acute, severe cases of UC.

REFERENCES

1. Cohen JI, Corey GR. Cytomegalovirus infection in the normal host. Medicine (Baltimore) 1985;64:100-114.
2. Montejo M. Key definitions and concepts in cytomegalovirus: infection versus disease. Replication, viral load, universal prophylaxis. Preemptive therapy. Enferm Infecc Microbiol Clin 2011;29(Suppl 6):4-5.
3. Kommareddy S, Chun CL, Rogers W, Triadafilopoulos G. Always a suspect: CMV in ulcerative colitis. Dig Dis Sci 2013;58:1838-1840.
4. Kim JJ, Simpson N, Klipfel N, Debose R, Barr N, Laine L. Cytomegalovirus infection in patients with active inflammatory bowel disease. Dig Dis Sci 2010;55:1059-1065.
5. Kim JW, Boo SJ, Ye BD, et al. Clinical utility of cytomegalovirus antigenemia assay and blood cytomegalovirus DNA PCR for cytomegaloviral colitis patients with moderate to severe ulcerative colitis. J Crohns Colitis 2014;8:693-701.
6. Jang EY, Park SY, Lee EJ, et al. Diagnostic performance of the cytomegalovirus (CMV) antigenemia assay in patients with CMV gastrointestinal disease. Clin Infect Dis 2009;48:e121-e124.
7. Kim YS, Kim YH, Kim JS, et al. Long-term outcomes of cytomegalovirus reactivation in patients with moderate to severe ulcerative colitis: a multicenter study. Gut Liver 2014;8:643-647.
8. Kim YS, Kim YH, Kim JS, et al. The prevalence and efficacy of ganciclovir on steroid-refractory ulcerative colitis with cytomegalovirus infection: a prospective multicenter study. J Clin Gastroenterol 2012;46:51-56.
9. Chun JY, Lee CH, Kwon JE, et al. Usefulness of the cytomegalovirus antigenemia assay in patients with ulcerative colitis. Intest Res 2015;13:50-59.
10. Park SH, Yang SK, Hong SM, et al. Severe disease activity and cytomegalovirus colitis are predictive of a nonresponse to infliximab in patients with ulcerative colitis. Dig Dis Sci 2013;58:3592-3599.