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

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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. 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.

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. 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. 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. 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, there is little data concerning the relationship between CMV antigenemia assay results and clinical outcomes.

In the present study, the authors retrospectively evaluated 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
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 ant-
genemia 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 se-
verity 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 con-
crete conclusion based on these results alone.

However, the present study clearly shows that CMV an-
tigenemia is an independent predictive factor for steroid refractoriness in moderate-to-severe cases of UC. Corticoste-
roid 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, 
CMV testing would be useful to predict the response to ste-
roids 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 ac-
cepted that sigmoidoscopy should be performed to both 
evaluate the disease status itself and determine if CMV infec-
tion 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.

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