Toxic Megacolon Associated with Cytomegalovirus Infection in a Patient with Steroid-naïve Ulcerative Colitis

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Abstract

Most cases of cytomegalovirus (CMV) colitis in patients with inflammatory bowel disease (IBD) occur in those treated with immunosuppressants and/or corticosteroids. We herein present the case of a 57-year-old man with toxic megacolon associated with CMV colitis in corticosteroid-naïve ulcerative colitis (UC). To date, there have been only eight previous case reports of CMV colitis in steroid-naïve UC. We discuss the need to consider CMV colitis when making a differential diagnosis of patients with refractory UC who are not receiving corticosteroid treatment.

Key words: toxic megacolon, cytomegalovirus, steroid-naïve, ulcerative colitis


Introduction

Colonic infection with cytomegalovirus (CMV) has been increasingly implicated in inflammatory bowel disease (IBD) (1-3). In an immunocompromised host, a primary CMV infection or the reactivation of a latent CMV infection can cause severe disseminated disease, including colitis (4). Corticosteroids and immunosuppressants are frequently used in the treatment of ulcerative colitis (UC), and their use presents a risk of CMV infection (5).

It has been reported that CMV colitis is rare in patients with IBD who have not been treated with steroids or immunosuppressive agents (6). CMV may be associated with toxic megacolon in some patients with UC (4). We herein report a case of toxic megacolon associated with CMV infection in corticosteroid-naïve UC.

Case Report

A 57-year-old man consulted the outpatient department of our hospital due to being positive for fecal occult blood. He was diagnosed as having the active stage of left-sided-type UC based on typical endoscopic findings and compatible histological findings of chronic inflammation with mild cryptitis and crypt abscesses (Fig. 1). CMV infection was excluded following an immunohistochemical examination for CMV antigens. The patient had been treated with oral 5-aminosalicylic acid (5-ASA) at a dose of 2,400 mg/day for two months. Two months after the completion of the 5-ASA regimen, he presented with a two-week history of watery bowel movements (up to 10 times daily) and associated fa-
tigue, fever and chills. He was admitted for further examination.

On admission, the patient presented with diaphoresis with a temperature of 39.2°C. He had recently experienced 10 episodes of diarrhea. A physical examination revealed discomfort in the abdomen. A chest radiograph and urinalysis were normal. The patient’s white cell count was 10,900/μL with 78.0% neutrophils and 14.9% lymphocytes and his Hb level was 11.4 g/dL. Liver function tests showed that the alanine aminotransferase level was 34 U/L, the alkaline phosphatase level was 463 U/L and the γ-glutamyltransferase level was 127 U/L. Bacterial cultures of the patient’s blood and stool were negative. However, a CMV antigenemia (C7-HRP) analysis showed four positive cells per 72,200 cells (Table 1). On the fourth day after admission, colonoscopy showed moderately inflammatory mucosa (Fig. 2). An immunohistochemical examination of biopsy specimens revealed brown CMV positivity in the mucosa, thus suggesting the presence of a CMV infection superimposed on UC.

On the third day after admission, gancyclovir [9-(1,3-dihydroxy-2-propoxy) methyl]-guanine (DHPG) was administered intravenously at 600 mg/day for 19 days (Fig. 3). Because the patient’s diarrhea and fever did not improve, pulse methylprednisolone therapy was administered for three days starting on the seventh day after admission.

On the twentieth day after admission, although a test for CMV antigenemia (C7-HRP) was negative, toxic megacolon developed, necessitating a subtotal colectomy (Fig. 4). The operative findings showed that the colon was markedly dilated, the transverse colon was dilated to a 10-cm diameter and the intestinal tone had become poor from the sigmoid colon up to the middle of the transverse colon (Fig. 5). The histological findings demonstrated the presence of a bleeding ulcer over the entire colon starting in the ileum with scattered erosions and nuclear inclusion bodies accompanied by a marked cytomegalovirus infection.
Discussion

IBD patients are frequently treated with immunosuppressive agents, including corticosteroids, cyclosporine, azathioprine and methotrexate, either alone or in combination (7, 8). Therefore, severe or refractory IBD patients are thought to be at an increased risk of infection with CMV. In some IBD cases, gastrointestinal CMV infection is resolved without the use of antiviral therapy (9). The incidence of gastrointestinal CMV disease in IBD patients receiving immunosuppressive therapy has been reported to range from 15.8% to 34% (5).

Our patient had experienced UC for less than two months before the additional diagnosis of CMV colitis was made, and he had not received concurrent or prior corticosteroid treatment at the time he was diagnosed with CMV infection. Although typical findings of CMV infection were not observed, we detected CMV-positive cells in biopsy specimens obtained from the colonic mucosa, thus indicating an active colonic infection. The positive C7-HRP result also suggested
CMV colitis. Although gancyclovir was administered, the symptoms of colitis did not improve. Therefore, corticosteroid treatment was administered on the seventh day after admission. Toxic megacolon developed, thus necessitating a subtotal colectomy. The histological findings showed a marked cytomegalovirus infection. In the present case, there was no history of corticosteroid use and the mechanism of onset of CMV infection was unknown. The possibility that the corticosteroid treatment administered after admission had led to the development of toxic megacolon could not be ruled out. To our knowledge, only eight case reports have described an association between UC and CMV disease of the colon in patients with no prior use of immunosuppressants (6, 10-15) (Table 2).

Five of these eight cases involved patients who had been diagnosed with UC less than 13 months before the additional diagnosis of CMV colitis was made. Our patient had UC less than two months before the CMV colitis diagnosis was made. Orvar et al. proposed that, in susceptible hosts, viral proteins expressed on the cell surfaces of CMV-infected cells might initiate an immune response that could lead to IBD (12). Corticosteroids and immunosuppressants are frequently used in the treatment of UC, and their use presents well-documented risks of CMV infection (5). CMV may be a potential pathogen, even in non-immunocompromised UC patients.

The presentation of CMV colitis is clinically very similar to and it can sometimes be mistaken for UC flares. Therefore, the diagnosis of concurrent CMV disease in UC patients requires a high degree of certainty. CMV infection can occur regardless of the degree of colonic involvement in UC, i.e., whether the entire colon is involved or only the left side (6, 10-15). The gold standard for confirming CMV disease of the colon includes endoscopic biopsies taken from

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Table 2. Reported Cases of CMV Colitis in Ulcerative Colitis Patients Naïve to Corticosteroids

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Duration of UC</th>
<th>Gancyclovir</th>
<th>Outcome</th>
<th>Extent of colitis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>39</td>
<td>F</td>
<td>1wk</td>
<td>No</td>
<td>Survived</td>
<td>Rectosigmoid</td>
<td>(10)</td>
</tr>
<tr>
<td>27</td>
<td>F</td>
<td>2wk</td>
<td>Yes</td>
<td>Survived</td>
<td>Left-sided</td>
<td>(11)</td>
</tr>
<tr>
<td>33</td>
<td>F</td>
<td>3wk</td>
<td>Yes</td>
<td>Survived</td>
<td>Pancolitis</td>
<td>(12)</td>
</tr>
<tr>
<td>35</td>
<td>M</td>
<td>1mo</td>
<td>Yes</td>
<td>Survived</td>
<td>Left-sided</td>
<td>(12)</td>
</tr>
<tr>
<td>29</td>
<td>F</td>
<td>12yr</td>
<td>Yes</td>
<td>Survived</td>
<td>Pouchitis</td>
<td>(13)</td>
</tr>
<tr>
<td>24</td>
<td>F</td>
<td>13mo</td>
<td>Yes</td>
<td>Survived</td>
<td>Pancolitis</td>
<td>(6)</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>6yr</td>
<td>Yes</td>
<td>Survived</td>
<td>Pancolitis</td>
<td>(14)</td>
</tr>
<tr>
<td>32</td>
<td>M</td>
<td>10yr</td>
<td>Yes</td>
<td>Survived</td>
<td>Pancolitis</td>
<td>(15)</td>
</tr>
<tr>
<td>57</td>
<td>M</td>
<td>2mo</td>
<td>Yes</td>
<td>Survived</td>
<td>Pancolitis</td>
<td>Present case</td>
</tr>
</tbody>
</table>

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the mucosa and ulcer bed. Even in the absence of typical endoscopic findings, we should confirm whether or not a CMV infection may exist by performing endoscopic biopsies.

In conclusion, we herein presented a rare case of CMV colitis superimposed on corticosteroid-naïve UC. Even when IBD patients are not treated with immunosuppressants, clinicians should be aware of the possibility of a CMV infection.

The authors state that they have no Conflict of Interest (COI).

References


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