

## Case Report

# Acute Fulminant-Onset Synchronized CMV-Ulcerative Colitis

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Cytomegalovirus (CMV) is an agent which exists asymptotically in most individuals and may cause latent life-time infection following contamination. Symptomatic CMV infection develops most commonly in organ transplant recipients and in individuals who receive immunosuppressive drugs, undergo haemodialysis or have acquired immunodeficiency syndrome. The link between ulcerative colitis and CMV infection and the efficacy of antiviral therapy in these individuals have been demonstrated. Due to the fact that synchronous onset of CMV and ulcerative colitis is a very rare clinical condition, we present here a synchronous-onset fulminant CMV and ulcerative colitis in a 58-year-old man without any other co-morbidities.

**Keywords:** Cytomegalovirus, Fulminant colitis, Ulcerative colitis

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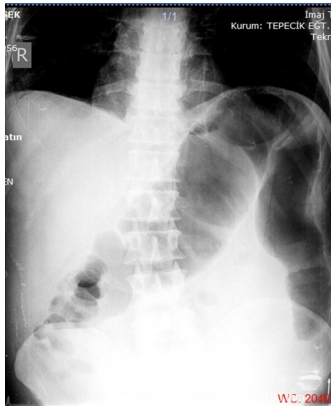
**Introduction**

Cytomegalovirus (CMV) is an agent which exists asymptotically in most individuals and may cause latent life-time infection following contamination.<sup>1</sup> CMV-associated symptomatic infection occurs following reactivation of the virus. Symptomatic CMV infection develops most commonly in organ transplant recipients and in individuals who receive immunosuppressive drugs, undergo haemodialysis or have acquired immunodeficiency syndrome.<sup>2,3</sup> The link between ulcerative colitis and CMV infection and the efficacy of antiviral therapy in these individuals have been demonstrated.<sup>4</sup> In a study performed with murine species in 2009, CMV and norovirus alone were shown to play a triggering role for ulcerative colitis and Crohn's disease.<sup>5-7</sup> There are 16 cases in the literature that describe an onset with CMV colitis. These cases do not include a case with a fulminant-onset, as in our case. We deemed presenting this case would be appropriate since it involves a fulminant synchronized CMV-ulcerative colitis with an acute onset and showed dramatic response to antiviral therapy with steroid treatment.

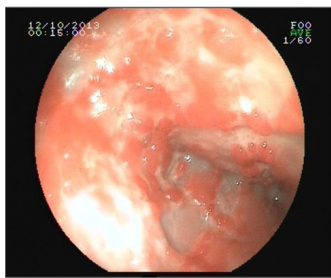
**Case Report**

Written informed consent was obtained from the patient. A 58-years-old male with no history of travel, drug use and known co-morbidities was admitted to the hospital with abdominal pain and bloody diarrhea 8–10 times a day for three weeks. He has also had no family history for bowel disease. Deleted vascular structures and granular mucosa structures that affected the whole colon were observed on the colonoscopy. The patient was diagnosed with ulcerative colitis due to mild pancolitis. Treatment with 4800 mg/d

mesalazine per-oral was started. The patient presented to the emergency department of our hospital on day 10 of treatment due to worsening of abdominal pain and bloody diarrhea. At presentation, daily defecation count was more than 15 times. His blood pressure was 80/50 mm Hg, heart rate was 110/min and body temperature was 37.8°C. He had tenderness generalized to the whole abdomen. His hemoglobin count was 9.04 gr/dl, sedimentation was 86 mm/h, CRP: 6.61 mg/dL (n:0–0.8), total protein was 4,6 g/dL, albumin was 2.4 g/dL, while other biochemical and hematologic measurements were normal. Pronounced dilatation (up to 8 cm) of the left colon and transverse colon distal colonic folds was observed with abdominal X-ray (Figure 1). Patient's colonoscopy was consistent with severe pancolitis (widespread erythema, edema, granularity, spontaneous bleeding, dense mucopurulent material and diffuse deep and superficial ulcers) (Figure 2). The patient was admitted for inpatient care for toxic megacolon secondary to ulcerative colitis. Patient's stool examination was negative for the *Clostridium difficile* toxin with no bacterial agents. Metronidazole (1500 mg/d) + ceftriaxone (2 g/d) + methylprednisolone (60 mg/d) parenteral treatments were started. The biopsy of colonoscopy was consistent with acute ulcerative colitis (diffuse mononuclear inflammatory infiltrate in lamina propria, crypt abscesses (neutrophils in glandular lumen) and cryptitis) and CMV inclusion was not detected. CMV DNA (with real-time PCR) was investigated due to absence of clinical, radiological or endoscopic response despite 1-week treatment and was  $5.01 \times 10^3$  copies/mL and CMV immunoglobulin M was positive. Ganciclovir 1000 mg/d parenteral treatment was initiated. Clinical, radiological



**Figure 1.** Abdominal X-ray of Patient at Emergency Room. Pronounced (up to 8 cm) dilatation at the left colon and transverse colon.



**Figure 2.** Colonoscopy Image of the Patient Admitted to the Hospital; severe pancolitis (widespread erythema, edema, granularity, spontaneous bleeding, dense mucopurulent material and diffuse deep and superficial ulcers).

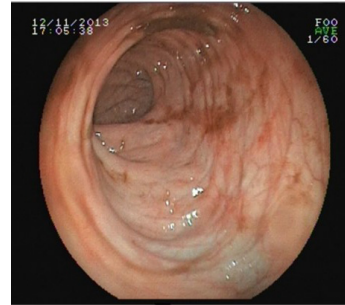
and endoscopic response began to be achieved at week 1 of follow-up, and the steroid treatment was tapered gradually and was maintained with mesalazine treatment (Figure 3). Achieving almost complete improvement clinically, radiologically and endoscopically following 21 days of treatment, ganciclovir treatment was discontinued. The patient was discharged by adding azathioprine 50 mg/d to the mesalazine treatment. At the third month control, the patient had a near-total remission on colonoscopy with mesalazine and azathioprine treatment (Figure 4). The patient was followed to remission with mesalazine and azathioprine treatments for one year. At the end of one year, the patient was referred to our clinic with findings of ulcerative colitis activation after he cut off his treatment with his own request. We started mesalazine 4800 mg/d per-oral again and achieved remission in 3 weeks.

### Discussion

CMV is an infectious agent from the beta herpesvirus family with dual DNA chains which can frequently be demonstrated in colonic biopsies in patients with ulcerative colitis and is present in about 20–40% of steroid-refractory patients.<sup>8</sup> A recent Korean study determined CMV virus in 43–67% of steroid-refractory ulcerative colitis patients with moderate and severe disease through investigations in the tissue using both serological (immunoglobulin M



**Figure 3.** Colonoscopy Image after the 1 Week Treatment with Ganciclovir. Pseudopolyps were seen when the clinical progress of patient getting better.



**Figure 4.** colonoscopy image in the third month of treatment which a near-total remission was obtained.

antibody levels) and immunohistochemical staining and polymerase chain reaction.<sup>9</sup> Whether demonstrating the virus in the tissue of ulcerative colitis patients indicates a pathogen that leads to exacerbation or an innocent host is still a matter of debate.<sup>6</sup> While some studies indicate that presence of CMV in the tissue increases disease severity and leads to steroid non-responsiveness and poor prognosis, others demonstrated that presence of CMV did not lead to a significant difference.<sup>10</sup> Diagnosing CMV colitis is difficult since its onset resembles an ulcerative colitis exacerbation. It can be established by presence of histopathologic effects induced by the viral antigen on the colonic tissue immunohistochemically or by hematoxylin & eosin (H&E) staining or via identifying viral DNA with PCR.

The most common endoscopic evidence observed in CMV colitis is the presence of multiple ulcers. In cases such as ours where the whole colon is involved, the lesions appear to have a skipping pattern. Synchronized onset of CMV colitis with ulcerative colitis was first described in 1990.<sup>11</sup> Sixteen cases were reported since then. It is quite difficult to demonstrate inclusion bodies specific to CMV with H&E in pathology samples. In a study by Kim et al evaluating historical pathology samples taken at time of initial diagnosis immunohistochemically, CMV colitis was demonstrated in 5 out of 61 cases (8.2%).<sup>12</sup> It was seen that none of these patients were taking CMV colitis treatment. This suggests that patients with CMV colitis may be missed in daily practice.

Clinical diagnosis of CMV colitis is difficult because the clinical presentation and colonoscopic appearance could be similar to an exacerbation of ulcerative colitis. CMV can be detected in colonic tissue by immunohistochemistry (IHC) of viral antigens, recognition of viral histopathological effects in H&E stained tissue, or PCR detection of viral DNA. These methods are the best ways to detect CMV colitis, but it should not be forgotten that sometimes negative results may be obtain. Diagnostic blood tests for CMV include serum antibody measurements, the CMV antigenemia assay, and polymerase chain reaction (PCR) of CMV DNA are non-invasive diagnostic methods where CMV cannot be demonstrated in colonic tissue samples like our case.<sup>1,5-12</sup> There was no response to initial therapies such as mesalazine and steroid in our patient and we added ganciclovir after we detected CMV DNA and CMV IgM was positive. Clinical response was achieved after ganciclovir therapy and pseudopolyps occurred. We achieved remission again after we restarted mesalazine therapy one year later when the patient stopped his treatment. Hence, the patient has been in remission after mesalazine therapy was started again so we thought that the patient had synchronous onset of CMV colitis and ulcerative colitis at first.

In conclusion, CMV reactivation obviously leads to clinical worsening in ulcerative colitis patients.<sup>6,13-15</sup> Presence of a possible synchronized disease should also be kept in mind. While it is the standard approach to demonstrate presence of infection in the tissue histologically, false negative results may occur due to some reasons such as the choice of biopsy site and availability of an experienced pathologist. Thus, in patients with no clinical response or in cases where we still have doubts over the course of fulminant disease based on colonoscopic findings, it should be remembered that histological DNA level determination with immunoglobulin M and PCR might save the patient from total colectomy or even from death.

#### Authors' Contribution

Concept: OBB. Design: OBB. Supervision: SOS. Materials: OBB, SOS. Data collection and/or processing: OBB. Analysis and/or interpretation: SOS, OBB. Literature search: OBB. Writing: OBB. Critical reviews: OBB, SOS.

#### Conflict of Interest Disclosures

The authors have no conflicts of interest.

#### Informed Consent

Informed consent was obtained from the patient who participated in this study.

#### Financial Disclosure

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