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CASE REPORT | Lower GI Tract

정상 면역 환자에서 구강, 식도, 위 및 대장을 동시에 침범한 거대세포바이러스 감염

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Cytomegalovirus-induced Oral, Esophageal, Gastric and Colonic Ulcers in an Immunocompetent Patient

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Cytomegalovirus (CMV) is a globally prevalent pathogen, with the gastrointestinal (GI) tract being one of the most frequently affected targets. On the other hand, the simultaneous involvement of multiple GI organs in immunocompetent individuals has rarely been reported, and CMV-induced oral ulcers are uncommon. A 70-year-old man presented to the emergency clinic with dyspnea and epigastric discomfort. He had no known conditions that could compromise his immune system and no history of immunosuppressive medication use. A physical examination revealed anemic conjunctiva, and a digital rectal examination revealed melena. GI endoscopy identified ulcers in the oral cavity, esophagus, stomach, and colon, and the histopathological examination confirmed CMV positivity in each ulcer. After a 21-day course of intravenous ganciclovir, follow-up endoscopy revealed healed ulcers. This report shows that CMV can simultaneously affect the oral cavity and multiple GI organs, even in immunocompetent patients. A prompt histopathological evaluation is essential for an accurate diagnosis and timely treatment to prevent further complications. **(Korean J Gastroenterol 2025;85:389-394)**

Key Words: Cytomegalovirus; Ganciclovir; Immunocompetence; Oral ulcer; Peptic ulcer

INTRODUCTION

Cytomegalovirus (CMV) is a globally distributed virus with a high seroprevalence rate of 40–90% in the general population.[1,2] CMV is usually asymptomatic in individuals with intact immune systems. In immunocompromised patients, however, CMV can act as an important opportunistic pathogen, causing severe morbidities such as retinitis, nephritis, pneumonitis, encephalitis, and hepatitis. Recent research has shown that symptomatic CMV infections leading to complications can also occur in non-immunocompromised individuals.[3-6] In particular, the gastrointestinal (GI) system is one of the most commonly affected targets, accounting for 30% of tissue-invasive CMV diseases in immunocompetent patients.[6]

Among the GI organs, the colon is affected most frequently by CMV, followed by the esophagus.[7] A CMV infection can involve any segment of the GI system. Patients may present with GI dysmotility, diarrhea, abdominal pain, or GI bleeding,

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depending on the site of involvement. Although CMV can affect the GI tract in immunocompetent individuals, the simultaneous involvement of multiple GI organs in such patients has rarely been reported.[8] Moreover, a CMV-induced oral ulcer is uncommon and is observed predominantly in immunocompromised patients.[9] This paper presents a case of CMV-induced oral, esophageal, gastric, and colonic ulcers in an immunocompetent patient. This case report was approved as exempt and the waiver of informed consent was obtained from the institutional review board of Ilsan Paik Hospital (exemption number 2025-01-017).

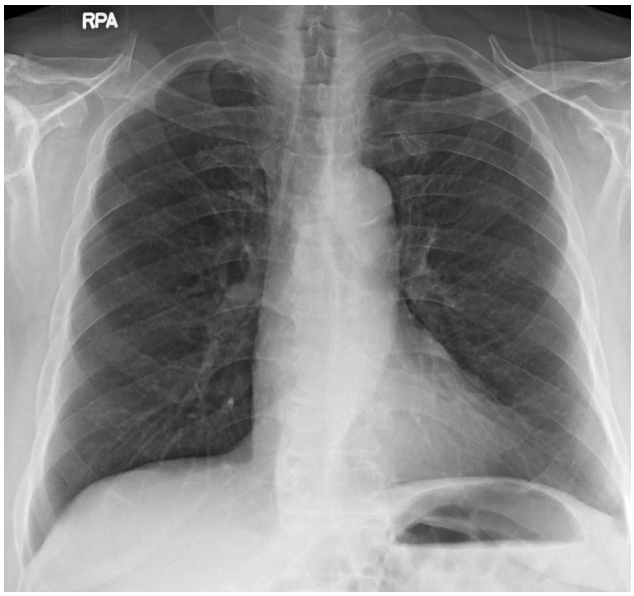

Fig. 1. Initial chest radiograph showing no abnormalities.

CASE

A 70-year-old man presented to the emergency clinic complaining of dyspnea and epigastric discomfort that began two weeks prior. The patient had a medical history of diabetes mellitus and hypertension, with no known diseases that could compromise the immune system, such as acquired immune deficiency syndrome or autoimmune disorders. In addition, he denied any use of immunosuppressive medications, including steroids or biologics. For hypertension, he received oral losartan 50 mg once daily. The treatment regimen for managing diabetes mellitus consisted of the oral administration of metformin 500 mg three times daily and glimepiride 3 mg once daily. During the preceding three months, the patient deliberately reduced his food intake for weight reduction and lost approximately 3 kg.

The initial examination revealed a body mass index of 27.3 kg/m^2 (based on a body weight and height of 76 kg and 1.67 m, respectively). His blood pressure, pulse rate, and body temperature were 110/70 mmHg, 90/minute, and 36.2℃, respectively. The physical examination revealed anemic conjunctiva and epigastric tenderness without rebound tenderness. A digital rectal examination revealed melena with no evidence of hemorrhoids. The laboratory findings were as follows: hemoglobin 8.4 g/dL, hematocrit 26.2%, white blood cell count 4,860/mm^3, platelet count 170,000/m^3, creatinine 0.87 mg/dL, fasting glucose 101 mg/dL, HbA1c 6.2%, total protein 5.6 g/dL, albumin 3.1 g/dL, sodium 131 mEq/L, potassium 4.8 mEq/L, and chloride 96 mEq/L. The cardiac markers were within the normal limits. The serological tests for syphilis, hepatitis B and C, and human immunodeficiency virus were

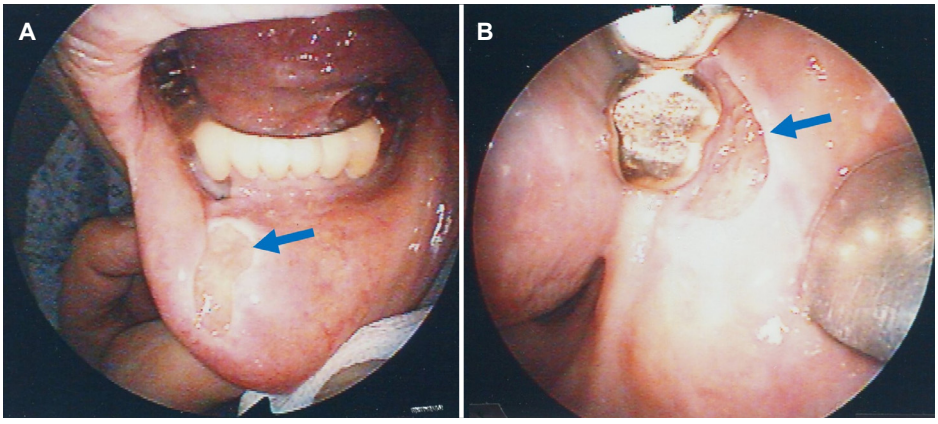

Fig. 2. (A) Oral ulcer on the inner side of the lower lip. (B) Oral ulcer near the molar area.

negative. The chest radiograph showed no abnormalities (Fig. 1).

The patient was admitted for a further evaluation of GI bleeding. Upper GI endoscopy revealed oral ulcers (Fig. 2), esophageal ulcers just above the gastroesophageal junction (Fig. 3A), and gastric ulcers (Fig. 3B). Colonoscopy revealed ascending colonic ulcers (Fig 3C). The biopsies were obtained from each ulcer site. The oral ulcer was biopsied at the Department of Dentistry, and the remaining biopsies were performed during endoscopy. A histopathological examination revealed ulcerative inflammation, with the cells showing enlarged nuclei and intranuclear nucleoli-like inclusions on hematoxylin and eosin staining (Fig. 4A). Immunostaining for CMV was positive (Fig. 4B, 4C).

The serological tests revealed negative CMV-specific IgM and positive CMV-specific IgG, but a blood polymerase chain reaction (PCR) for CMV DNA was not performed. The patient was diagnosed with a CMV GI infection involving multiple sites, including the oral cavity, esophagus, stomach, and colon.

Oral rabeprazole 20 mg once daily was initiated according to the diagnosis of esophageal and gastric ulcers. After CMV detection, he was administered intravenous ganciclovir (5 mg/kg) twice daily for 21 days. During administration, the patient experienced no adverse reactions such as hematological toxicity, nephrotoxicity, or hepatotoxicity.

Follow-up upper GI endoscopy and colonoscopy were recommended after a three-week course of ganciclovir, but the patient declined, and he was discharged with improved dyspnea and epigastric discomfort. Oral rabeprazole was continued for three months. Outpatient follow-up endoscopies performed two months after discharge revealed healed ulcers (Fig. 5).

DISCUSSION

CMV is a double-stranded DNA virus that belongs to the Herpesviridae family. CMV disease is rare in non-immunocompromised individuals because cell-mediated host immunity typically prevents the development of an overt CMV infection.[10,11] In recent years, however, CMV disease among immunocompetent patients has increased, particularly in the GI tract.[10,12] CMV can affect any part of the GI system, from the oral cavity to the rectum.[8] Oral CMV ulcers could occur at various intraoral sites, most commonly involving the hard and soft palates.[9,13]

Diagnosing a CMV infection of the oral cavity and GI tract can be challenging because there are no pathognomonic findings, and mucosal ulceration is the most common presentation. CMV ulcers are typically characterized by deep ulcers with clear margins.[3,9] A histopathological examination is the gold standard for diagnosis. Therefore, it is important to suspect CMV disease and obtain biopsies from ulcers. The histopathological findings included enlarged nuclei with intranuclear, nucleoli-like inclusions (Owl's eye sign) or positive immunohistochemical staining for CMV.[14,15] In the present case, both histopathological features were observed in the biopsies obtained from the oral, esophageal, gastric, and colonic ulcers, confirming the diagnosis of a CMV infection.

Although CMV blood tests such as serum antibodies, antigenemia, and PCR for CMV DNA can provide useful information, they are not definitive diagnostic tools for CMV GI infection. Even in patients with active CMV GI disease, more

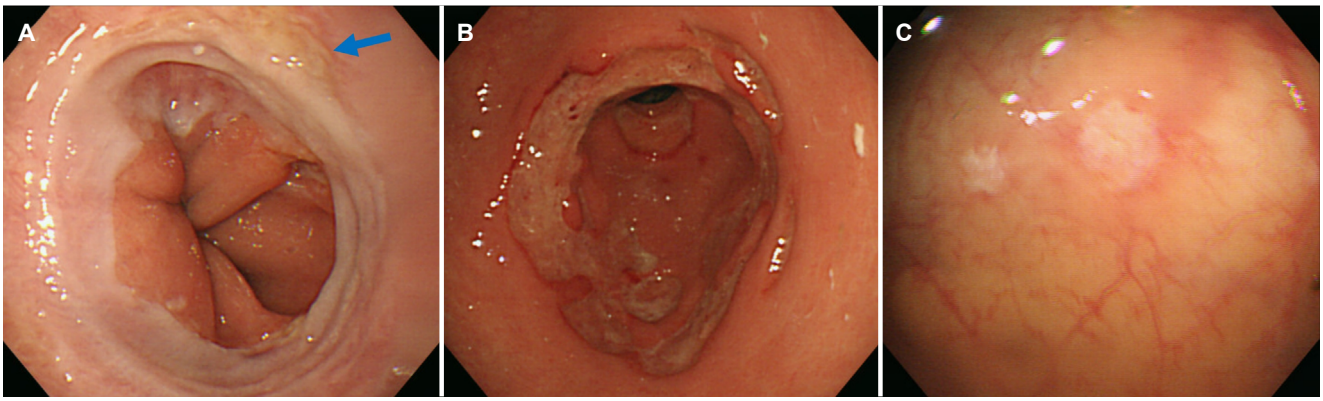

Fig. 3. (A) Esophageal ulcer just above the gastroesophageal junction. (B) Gastric ulcers in the gastric antrum. (C) Colonic ulcers in the ascending colon.

than 40% had negative CMV-specific serum IgM,[15] and only 60% showed a viral load in blood CMV PCR.[12] Nevertheless, when blood CMV PCR is positive, serial measurements can help guide the duration of antiviral therapy; a decrease in or loss of viremia indicates a favorable treatment response. In the present patient, the serum IgM was negative, and CMV PCR testing was not performed.

Antiviral agents such as ganciclovir or valganciclovir are recommended as first-line therapy for treating CMV disease.[10,15] Intravenous ganciclovir (5 mg/kg twice daily) or oral valganciclovir (900 mg twice daily) for two to three weeks is generally used in patients with a normal kidney function.[10] Both can induce hematological toxicity (including neutropenia, anemia, and thrombocytopenia), as well as hepatotoxicity, nephrotoxicity, and potential effects on fertility. Foscarnet and cidofovir serve as alternative options in cases of ganciclovir-resistant CMV, but they also pose risks of hematological toxicity, nephrotoxicity, and electrolyte imbalance. Although the treatment strategies for CMV infections are well established in immunocompromised individuals, no definite guidelines exist for immunocompetent patients. Whether immunocompetent patients with CMV infection require antiviral therapy or can be managed conservatively remains controversial, and the optimal duration of antiviral treatment in such populations remains unclear. Moreover, no consensus exists on the maintenance therapy for CMV infection in immunocompetent patients. Therefore, antiviral treatment should be determined for each specific clinical situation. In the present case, antiviral treatment was initiated based on the patient's advanced age (70 years) and extensive distribution of CMV ulcers from the oral cavity to the colon. Intravenous ganciclovir was administered for 21 days, and the patient experienced no adverse reactions. Follow-up endoscopy revealed healed ulcers, and maintenance therapy was not administered.

Numerous cases of CMV GI infection and multiple studies on CMV GI involvement in immunocompromised and immunocompetent patients have been reported.[3,5,12,16] Nevertheless, CMV oral ulcers are relatively rare, and most case reports of CMV oral ulcers involve immunocompromised hosts.[9]

A literature review searched all relevant studies in two electronic databases (PubMed and the Cochrane Library) in consultation with an expert research librarian. In addition, at-

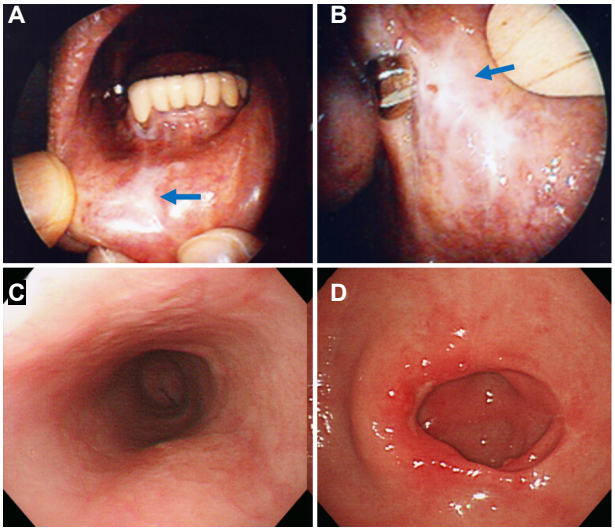

Fig. 5. (A, B) Healed oral ulcers. (C) Healed esophageal ulcers. (D) Healed gastric ulcers.

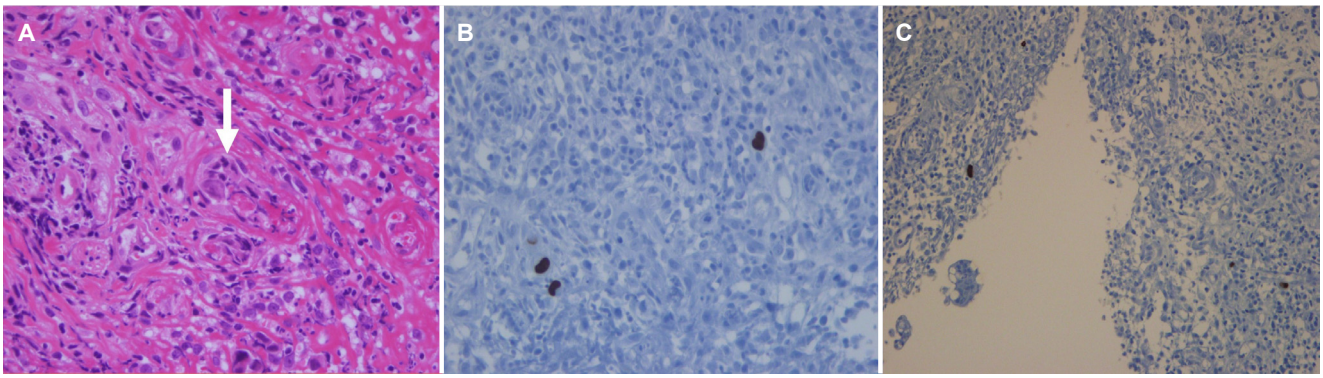

Fig. 4. Histopathological examination. (A) Ulcerative inflammation with some cells (arrow) exhibiting enlarged nuclei with intranuclear nucleoli-like inclusions (oral cavity, hematoxylin and eosin stain ×400). (B) Immunohistochemical stain for cytomegalovirus showing positive cells (stomach, immunohistochemical stain ×400). (C) Immunohistochemical stain for cytomegalovirus showing positive cells (colon, immunohistochemical stain ×200).

Table 1. Simultaneous Cytomegalovirus-induced Oral and Gastrointestinal Tract Ulcers: A Review of Literature

Authors	No of case	Sex	Age	Involved organs	Underlying disease	Limitation
Oliveira et al.[17] (2017)	1	F	67	Tongue, esophagus, stomach, colon	Pemphigus vulgaris	- CMV infection was confirmed by autopsy.
Lu et al.[18] (2001)	1	M	50	Oral cavity, colon	Pellagra	- Oral ulcers were not biopsied and may have represented pellagra - The authors considered that CMV colitis caused pellagra.
Our case	1	M	70	Oral cavity, esophagus, stomach, colon	No immuno-suppressive disease	

tempts were made to search the grey literature using Google Scholar. The search terms were ['cytomegalovirus' AND 'oral ulcer' AND ('stomach ulcer' OR 'colitis, ulcerative' OR 'esophagitis, peptic' OR 'duodenal ulcer' OR 'digestive system')]. Five articles were retrieved from the two databases (four from PubMed and one from the Cochrane Library), none reporting simultaneous oral and GI-tract ulcers. Two additional articles were identified through grey literature searches. Table 1 lists all cases. Oliveira et al.[17] reported a case of simultaneous CMV oral and GI ulcers in a patient with pemphigus vulgaris treated with immunosuppressive agents, including corticosteroid and mycophenolate mofetil. The patient presented with extensive pemphigus vulgaris facial lesions, oral and extensive GI mucosal ulcers, and pneumonia and ultimately died of a massive pulmonary embolism. The autopsy confirmed a CMV infection involving the tongue and GI tract (esophagus, stomach, and colon). Lu et al.[18] described a case of CMV colitis with oral ulcers in a patient with pellagra, but the oral ulcers were not biopsied and may have represented pellagra rather than a CMV infection. To the best of the authors' knowledge, the present report is the first to describe a CMV infection affecting multiple GI organs, including the esophagus, stomach, colon, and the oral cavity, in an immunocompetent patient.

In summary, the present case showed that a CMV infection can simultaneously affect the oral cavity and multiple GI organs, including the esophagus, stomach, and colon, even in immunocompetent patients. A histopathological evaluation is essential for an accurate diagnosis and prompt treatment to prevent further complications.

AUTHOR CONTRIBUTIONS

Conceptualization: SK, NHK. Data curation: SK, NHK. Validation: SK, NHK. Writing – original draft: SK. Writing – review & editing: NHK.

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