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CASE REPORT | ESOPHAGUS

Severe Diffuse Ulcerative Esophagitis Caused by Epstein-Barr Virus/Cytomegalovirus Coinfection in an Immunocompetent Individual

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ABSTRACT

Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) are important causes of viral esophagitis mainly in immunocompromised individuals. Both viruses lead to development of focal ulcerations in the esophagus. While there have been rare case reports of esophagitis in immunocompetent individuals, there has not been a single reported case of coinfection with both CMV and EBV in an immunocompetent individual and presenting with diffuse esophageal ulceration. We report a case of severe diffuse ulcerative esophagitis caused by EBV/CMV coinfection in an immunocompetent individual.

KEYWORDS: Epstein-Barr virus; cytomegalovirus; esophagitis; viral esophagitis; infection

INTRODUCTION

Cytomegalovirus (CMV) is a member of the *Herpesviridae* family and has the largest genome of any herpesvirus.[1] Although immunocompetent individuals can become infected, serious illness is typically seen in immunocompromised patients such as patients with acquired immune deficiency syndrome, organ transplant recipients, and patients on chemotherapy.[1] After colitis, esophagitis is the most common gastrointestinal presentation of CMV infection.[2] It is characterized by odynophagia, dysphagia, and extensive ulceration in the mid-to-distal esophagus, requiring biopsy and pathological examination for diagnosis.[1] Current treatment includes antivirals such as ganciclovir and valganciclovir, with ongoing research into alternative therapies.[3] However, CMV esophageal disease in immunocompromised individuals carries a poor prognosis, significant risk of recurrence, and high 1-year morbidity and mortality rates.[4] Epstein-Barr virus (EBV) infects over 90% of the global population and causes infectious mononucleosis, characterized by fever, lymphadenopathy, pharyngitis, hepatomegaly, and/or splenomegaly.[5] Following primary infection, EBV remains latent in B cells for life, with reactivation occurring uncommonly and usually due to immunological compromise.[5] Primary EBV esophagitis in immunocompetent patients is only sporadically reported.[6] We report a case of severe diffuse ulcerative esophagitis caused by EBV/CMV coinfection in an immunocompetent individual.

CASE REPORT

A 53-year-old woman, with hypertension on medications and recently diagnosed with subclinical thyroiditis, presented with complaints of dysphagia, odynophagia, cough, regurgitation, and vomiting after meals for 2 years. She also reported 8 kg weight loss, decreased appetite, body aches, and weakness. Previous esophagogastroduodenoscopy examinations at other centers showed diffuse esophageal ulceration with nonspecific inflammation on biopsy. She had received proton-pump inhibitors, sucralfate, and iron supplementation without relief. On examination, she appeared pale. There was no history suggestive of diarrhea or colitis. Blood tests indicated iron deficiency anemia (hemoglobin: [7.8 g/dL]; mean corpuscular volume: [59 fL]; mean corpuscular hemoglobin: [28 pg]), hypoalbuminemia (2.8 g/dL), elevated erythrocyte sedimentation rate (36 mm/hr), and occult blood in stool. HIV testing was negative. Esophagogastroduodenoscopy at our center revealed diffuse ulceration throughout the esophagus and pharynx, with marked edematous and erythematous mucosa (Figure 1A). Multiple segmental biopsies were taken. Contrast-enhanced computed

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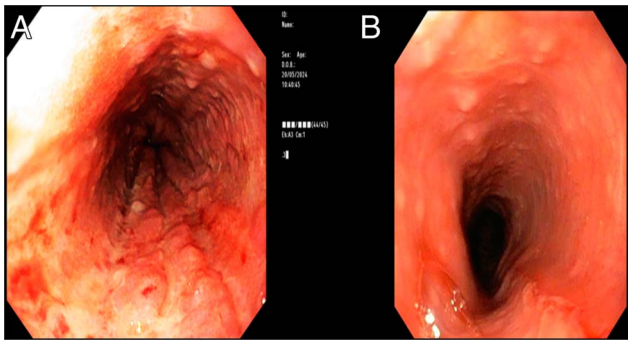

Figure 1. (A) Initial endoscopic examination reveals diffuse ulceration of the esophagus. (B) Endoscopy after 1 month shows near-complete healing of the esophageal ulcerations.

tomography of the chest and abdomen revealed diffuse esophageal edema with small cervical lymph nodes, fine-needle aspiration of which revealed reactive lymphadenitis. Colonoscopy showed mild nodularity in the terminal ileum with nonspecific inflammation on biopsy. Esophageal biopsy demonstrated dense infiltration of lymphocytes, plasma cells, eosinophils, and granulation tissue, with viral inclusions (Figure 2). Polymerase chain reaction (PCR) assay of esophageal and pharyngeal biopsies detected CMV viral levels of 47,866 copies/mL and EBV viral levels of 9,423 copies/mL. There was no evidence of polyps, colorectal cancer, or lesions suggestive of CMV colitis. The thyroiditis in this patient, although initially thought to be autoimmune, could possibly be due to viral etiology. Autoimmune thyroiditis was not definitively confirmed by anti-thyroid peroxidase antibodies testing, and further investigations such as thyroid ultrasound and thyroid function tests were normal. Endocrinology consultation was sought, and they advised symptomatic management with follow-up thyroid function testing after 3-6 months. A diagnosis of simultaneous CMV and EBV esophagitis was made, and the patient was treated with valganciclovir and acyclovir. A nasogastric tube was placed for enteral feeding. Significant symptomatic improvement, weight gain, and increased hemoglobin and serum albumin levels were observed after 3 weeks. The nasogastric tube was removed, and repeat endoscopy after 1 month showed significant healing of esophageal lesions (Figure 1B). On further 3 months of follow-up, the patient became completely asymptomatic with normal hemogram, albumin levels, and serial thyroid function tests.

DISCUSSION

This case highlights an exceptionally rare presentation of esophagitis due to CMV and EBV coinfection in an immunocompetent individual. The most common cause of esophagitis is gastroesophageal reflux, with other causes including radiation, infections, pill esophagitis, and eosinophilic esophagitis.[7] Among viral causes, CMV, herpes simplex virus (HSV), and rarely EBV are implicated, primarily in immunosuppressed patients. Although CMV and HSV infections are increasingly reported in immunocompetent individuals, there are only

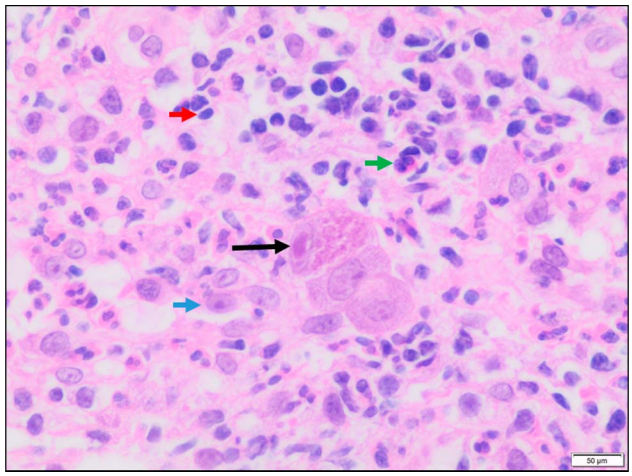

Figure 2. Esophageal biopsy suggestive of dense granulation tissue with neutrophils, eosinophils (green arrow), lymphocytes (red arrow), and histiocytes (blue arrow). Eosinophilic CMV inclusion (black arrow) with surrounding halo is noted in an endothelial cell (hematoxylin and eosin, 400×). Overall findings suggestive of active CMV infection. CMV, Cytomegalovirus.

sporadic cases of EBV-causing esophagitis in this population.[8] Viral esophagitis typically manifests with dysphagia, odynophagia, and diffuse multiple ulcerations, predominantly in the lower esophagus for CMV and HSV, and involvement throughout the esophagus for EBV esophagitis. Diagnosis hinges on histopathological examination demonstrating viral inclusion bodies, with PCR confirming viral presence.[1,5] Coinfection with HSV and CMV esophagitis in an immunocompetent individual has been documented, but coinfection with EBV and CMV presenting as esophagitis has not been previously reported. In our patient, extensive involvement of the pharynx and esophagus with diffuse ulcerations prompted consideration of uncommon etiologies such as viral or eosinophilic esophagitis. Prior negative biopsies for malignancy necessitated segmental biopsies for targeted evaluation, supplemented by saline samples for PCR testing to detect CMV, HSV, and EBV. The thyroiditis in this patient remains of unclear etiology; although subclinical thyroiditis was diagnosed, autoimmune thyroiditis was not definitively the cause as confirmed by negative anti-thyroid peroxidase antibodies testing, and further investigations such as thyroid ultrasound and thyroid function tests were normal, so it was concluded that it could be a part of viral thyroiditis.

In conclusion, this case underscores the importance of considering viral etiologies in patients presenting with diffuse esophagitis, even in immunocompetent individuals. Early diagnosis facilitated prompt initiation of antiviral therapy, resulting in significant clinical improvement and resolution of esophageal symptoms.

DISCLOSURES

Author contributions: Conceptualization, visualization, review, editing: K. Mathur, CL Birda, A. Agarwal. Methodology, writing

draft: all authors. Formal analysis: A. Agarwal. Final approval: All authors. A. Agarwal is the article guarantor.

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