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Single Case

Cytomegalovirus Isolated to a Colon Polyp in a Patient with Ulcerative Colitis on Ozanimod: A Case Report

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Ulcerative colitis · Cytomegalovirus · Colonic polyp · Ozanimod

Abstract
Introduction: Cytomegalovirus (CMV) infection is a notable gastrointestinal infection affecting immunocompromised patients. In the gastrointestinal tract, CMV often presents with patchy or diffuse mucosal involvement and can cause fulminant colitis. However, polypoid CMV lesions are rare. We present a case of a 49-year-old man with ulcerative colitis (UC) in remission on ozanimod who developed CMV isolated to inflammatory colon polyps. ***Case Presentation:*** A 49-year-old patient with UC in clinical remission on ozanimod underwent routine surveillance colonoscopy, which revealed multiple inflamed polyps with white caps. Biopsy results confirmed inflammatory polyps with positive CMV immunostaining, while adjacent tissues and plasma CMV PCR tests were negative. The patient successfully completed a 3-week course of valganciclovir. Follow-up colonoscopy revealed additional inflammatory polyps but no evidence of CMV. He remained in clinical remission and continued ozanimod therapy. ***Conclusion:*** The unusual nature of this presentation suggests a clinically silent CMV re-activation or, alternatively, a primary CMV infection in our patient, with an unclear natural history and optimal management. This report emphasizes the importance of considering CMV in UC patients with unusual endoscopic findings and the need for multidisciplinary collaboration to optimize care.

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Introduction

Cytomegalovirus (CMV) is an opportunistic pathogen that can cause both primary infections and secondary reactivations. After the initial infection, CMV establishes lifelong persistence in various organs and tissues. Reactivations of CMV can lead to severe clinical manifestations in immunosuppressed individuals [1]. The risk of reactivation is particularly high in the intestinal tissues of patients with inflammatory bowel disease (IBD), especially those with ulcerative colitis (UC), often presenting as acute CMV colitis [2]. According to Kwon et al. [2], the likelihood of CMV colitis is 19 times higher in patients with IBD and 31 times higher in those with UC. The prevalence of CMV-associated colitis ranges from 10 to 17% in patients with severe IBD [3].

Grossly and endoscopically, CMV infection in the GI tract can present with a wide variety of appearances, often showing patchy/diffuse mucosal involvement, resembling an IBD flare. However, polypoid CMV lesions in the GI tract are rare. In the following case, we describe a patient with UC in clinical remission on ozanimod, who was found to have CMV isolated to an inflammatory colon polyp.

Case Report

A 49-year-old man with a 2-year history of UC in remission on ozanimod presented to establish care. Mesalamine 1,600 mg daily failed to achieve clinical remission, but he responded well to budesonide. He was then transitioned to ozanimod monotherapy, which he had been on for 10 months. During the visit, he reported having two well-formed bowel movements per week with mild urgency but no rectal bleeding or abdominal pain. His clinical Mayo score was 0. His father had a history of benign colonic polyps, but there was no concerning family history of gastrointestinal malignancies or IBD.

On surveillance colonoscopy, Mayo 1 colitis was found from the rectum to the descending colon with erythema and decreased vascularity. Multiple inflamed polyps (measuring ≤6 mm) with white caps were observed in the sigmoid colon. Two of the largest semi-pedunculated polyps with white caps in the sigmoid colon (13–16 mm, Fig. 1) were resected. Pathology revealed inflammatory polyps with positive CMV immunostaining (Fig. 2). Biopsies of the surrounding tissue and all other colon segments were negative for CMV, with only chronic minimally active colitis in the rectum and sigmoid colon. Plasma CMV PCR assay was negative and there were no signs of systemic infection. The patient was evaluated by an infectious disease specialist and was not found to have extraintestinal CMV. He subsequently completed a 3-week course of valganciclovir.

After completing the course of valganciclovir, a follow-up colonoscopy 6 weeks later revealed similar mucosal findings. Additional polyps in the sigmoid colon with white ulcerations (5–12 mm) were resected. Histopathology of the polyps showed no evidence of CMV or dysplasia, and there was no evidence of CMV in the mucosa surrounding the polyps (Fig. 3).

At 1-month follow-up, the patient remained in clinical remission. He chose to continue ozanimod due to its effectiveness in maintaining clinical remission of his UC. A multidisciplinary team, including his infectious disease specialist, advised that switching to another treatment offered no assurance against opportunistic infections or improved control of his UC. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000545642).

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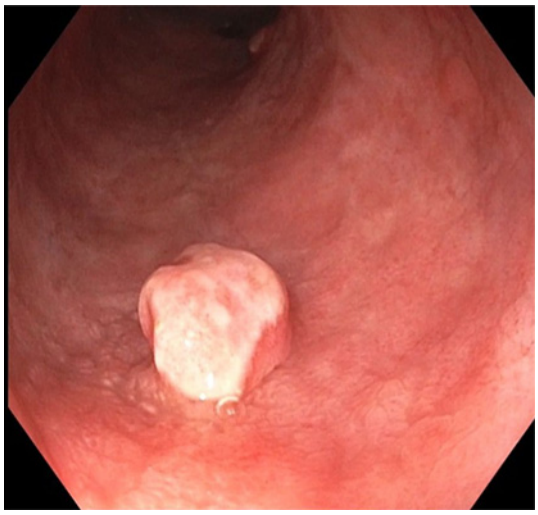

Fig. 1. Sigmoid colon inflammatory polyp.

Discussion

This is the first reported case of CMV isolated to a colon polyp in a patient with UC taking ozanimod. The risk of serious infections, including CMV colitis, is known to be elevated in IBD patients receiving JAK inhibitors, particularly when used in combination with corticosteroids [4, 5]. However, to date, there are no reported cases of CMV infection in IBD patients treated with S1P modulators such as ozanimod.

In patients with UC, CMV may either cause a primary infection or reactivate as seropositive individuals carry latent CMV in the digestive tract [6]. Primary infection/reactivation of latent virus in UC occurs due to various factors, including the disease itself, immunosuppressive treatments, malnutrition, and impaired host defense mechanisms [2, 3, 7]. The inflammation and mucosal damage in the bowel lead to the release of proinflammatory cytokines, which attract CMV-infected macrophages. This progressive inflammation and vasculitis result in severe ischemia and transmural necrosis. Consequently, CMV is typically found in the ulcer beds and granulation tissue. The white caps on the inflammatory polyps represented granulation tissue in our patient and was the likely site where the CMV was found.

It is unclear whether CMV reactivation exacerbates underlying IBD, or if inflammation from IBD triggers CMV reactivation, with CMV merely serving as an innocent bystander. CMV is frequently detected in actively inflamed tissue, appearing in 4.5% of newly diagnosed, treatment-naïve UC cases and 13.8–40% of steroid-refractory cases, often mimicking an IBD flare [8]. However, in these severe UC cases, CMV presence seems transient, often resolving alongside clinical improvement of IBD without antiviral therapy [9]. Furthermore, while up to one-third of steroid-refractory UC patients may have detectable CMV antigens in the colon, their presence does not appear to worsen disease outcome [9]. These findings suggest that CMV reactivation in most moderate to severe UC cases is a secondary phenomenon that does not affect prognosis. On the other hand, the absence of antiviral treatment in CMV-positive patients has been associated with a higher risk of colitis relapses, hinting at a potential role for CMV in aggravating IBD [10]. The interpretation of these findings, however, is limited by inconsistencies in study quality and variations in reporting standards across the available literature.

Symptoms can vary from abdominal discomfort, diarrhea, and rectal bleeding to severe complications like fulminant colitis, toxic megacolon, or even bowel perforation [2].

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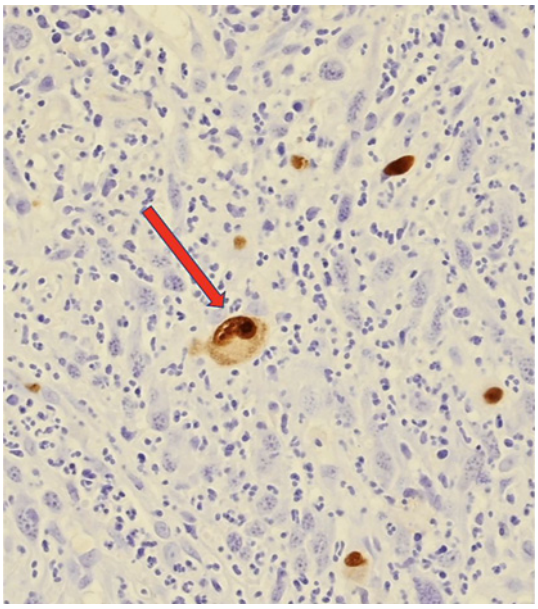

Fig. 2. Sigmoid colon polyp pathology revealing CMV inclusion bodies (red arrow) using immunohistochemical staining (original magnification, ×400).

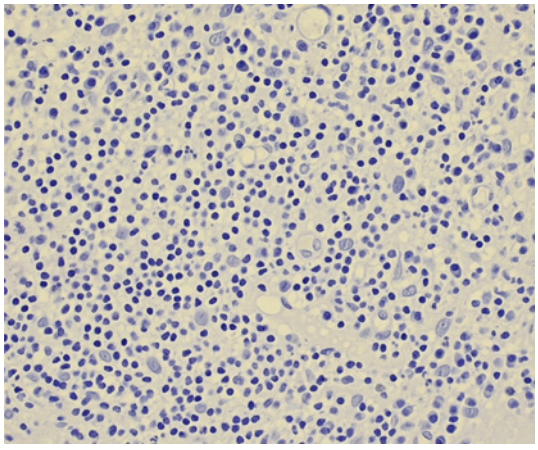

Fig. 3. Sigmoid colon polyp with no evidence of CMV after valganciclovir treatment (original magnification, ×400).

Colonoscopy examination may reveal punched-out ulcers, diffuse mucosal defects, exudates, and pseudo polyps, with no definitive endoscopic findings to differentiate UC exacerbation from CMV colitis [11]. However, CMV colitis in minimally active or mild UC is rare, and CMV isolated to a colon polyp in the presence or absence of UC is unusual [12]. This may represent clinically silent CMV reactivation or a primary CMV infection with the potential to cause long-term consequences. It has been previously described once in an elderly UC patient in clinical remission on methotrexate and sulfasalazine, who did not undergo antiviral treatment [13]. In our case, the endoscopic findings were identical following valganciclovir therapy. This suggests that, while valganciclovir is effective in eradicating CMV, the observed mucosal changes were unlikely attributable to CMV infection and were instead thought to reflect chronic UC. Therefore, this was considered an incidental finding that proved to be benign.

CMV can be diagnosed through highly specific histological examination, immunohistochemistry, or gold standard-quantitative real-time PCR [7]. Interpreting these test results is challenging as it remains unclear whether CMV DNA detection reflects incidental reactivation

from immunosuppression or a primary trigger [14]. When CMV is detected in intestinal tissue, there is a common tendency (82%) among gastroenterologists to initiate antiviral therapy [15], especially in cases of severe colitis, large/multiple colonic ulcers, or steroid resistance [16]. However, as no prior data or guidelines exist on the natural history and optimal management of isolated CMV polyps, the decision to undergo antiviral treatment for our patient was clinician based. Extrapolating from the 90.5% clinical and laboratory remission rates with antivirals among patients with severe CMV colitis and UC flares with high CMV viral load, ganciclovir or valganciclovir can be promising treatments for CMV localized to polyps [17]. However, in CMV tissue-positive patients without colonic ulcers and low viral loads, indicating latent CMV, watchful follow-up with UC medications is viable due to the absence of progression, reactivation, or complications [17]. Thus, while antiviral treatment may not be warranted for patients with low viral DNA levels, the management of those with CMV isolated to colonic polyps remains uncertain.

In summary, we report an unusual case of gastrointestinal CMV presenting as isolated inflammatory polyps in an asymptomatic patient with UC in clinical remission on ozanimod. This case emphasizes the need to consider CMV in UC patients receiving immunosuppressive therapy, especially when granulation tissue, such as inflammatory polyps, is observed. Close communication with pathologists is necessary to ensure biopsy samples are assessed for CMV in cases where it is a clinical concern.

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Manuscript writing: Zehra Naseem, Ahmed Nadeem, Aidan J. David, Aun Muhammad, and Fatima Zehra Shah. Conception, critical review, and final approval of the manuscript: Brian M. Fung, Stephen B. Hanauer, and Joseph David.

Data Availability Statement

The data that support the findings of this study are not publicly available as their containing information can compromise the privacy of the patient of this care report but are available from the corresponding author (Z.N.) upon reasonable request.

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