

## CLINICAL VIGNETTE

# CMV and *C. difficile* Co-Infection in Patient on Immunotherapy

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### Case

A 75-year-old-female with a recurrent *C. difficile* colitis and breast cancer was brought in by emergency services following a syncopal episode. Two weeks prior, the patient developed right upper quadrant and epigastric abdominal pain. She also reported worsened nausea and diarrhea with urgency and rectal bleeding. Her inflammatory breast cancer was s/p right radical mastectomy and currently treated with trastuzumab and pertuzumab.

On admission, the patient was tachycardic and hypotensive. Labs were notable for WBC 3.4, Hb 8.6, AST 53, ALP 128, CRP 44.3, Albumin 1.6. An abdominal ultrasound demonstrated acute cholecystitis. CT abdomen and pelvis demonstrated marked wall thickening and mucosal hyper-enhancement of the descending colon, sigmoid colon, and rectum. *C. diff* PCR and toxin were positive. The patient underwent laparoscopic cholecystectomy and was treated with fidoxamicin and metronidazole for her *C. diff* colitis. This was the patient's third episode of *C. diff* colitis.

Given concern for possible concomitant immunotherapy associated colitis, a flexible sigmoidoscopy was performed which demonstrated moderately congested mucosa with areas of mild superficial ulceration in the rectum, rectosigmoid colon, and sigmoid colon. Pathology demonstrated CMV colitis. The patient continued treatment with fidoxamicin and metronidazole for *C. difficile* colitis and started gancyclovir for CMV colitis. Her symptoms improved over the following days and she was discharged home within the week.

### Discussion

Both *C. difficile* and CMV are common colonizers in patients. Active infections usually occur in the setting of antibiotics (in the case of *C. difficile*) or immunosuppression.<sup>1-3</sup> Co-infection with *C. difficile* and CMV is rare, but has been previously reported. Patients with *C. difficile* and CMV co-infection have poorer outcomes with high mortality rates.<sup>4</sup>

*C. difficile* colitis is characterized by fevers, abdominal cramping, and watery diarrhea. CMV colitis presents similarly to *C. difficile*; however, is more often associated with rectal bleeding. Endoscopically, *C. difficile* colitis is commonly characterized by pseudomembranes whereas CMV colitis is characterized by punched out ulcerations with or without exudates.<sup>5,6</sup>

Immunohistochemistry demonstrating intranuclear inclusion bodies is required to make the diagnosis of CMV colitis.

Co-infections are more likely to occur in the setting of immunosuppression, such as cancer immunotherapy. Our patient developed active co-infection with *C. difficile* and CMV in the setting of immunotherapy with trastuzumab and pertuzumab. Trastuzumab is a monoclonal antibody against the human epidermal growth factor receptor 2 (HER2) receptor. Pertuzumab is a monoclonal antibody that inhibits HER2 dimerization, preventing its activation. Both drugs result in cessation of HER2 signaling, resulting in cellular death. Both agents increase the risk of infection, including gastrointestinal infections, given their immunosuppressive properties.<sup>7</sup>

This case highlights the importance of thorough evaluation for causes of gastrointestinal infection including stool studies and endoscopy, to avoid missing concomitant infections.

### REFERENCES

1. **Anastasopoulou A, Samarkos M, Diamantopoulos P, Vourlakou C, Ziogas DC, Avramopoulos P, Kouzis P, Haanen J, Gogas H.** Cytomegalovirus Infections in Patients Treated With Immune Checkpoint Inhibitors for Solid Malignancies. *Open Forum Infect Dis.* 2023 Mar 28;10(4):ofad164. doi: 10.1093/ofid/ofad164. PMID: 37065986; PMCID: PMC10099470.
2. **Ruiz-Camps I, Aguilar-Company J.** Risk of infection associated with targeted therapies for solid organ and hematological malignancies. *Ther Adv Infect Dis.* 2021 Feb 19;8:2049936121989548. doi: 10.1177/2049936121989548. PMID: 33680453; PMCID: PMC7897815.
3. **Vasavada S, Panneerselvam K, Amin R, Varatharajulu K, Okhuysen PC, Oliva ICG, Wang J, Grivas P, Thomas AS, Wang Y.** *Clostridioides difficile* infection in cancer patients receiving immune checkpoint inhibitors. *Ann Gastroenterol.* 2022 Jul-Aug;35(4):393-399. doi: 10.20524/aog.2022.0722. Epub 2022 Jun 2. PMID: 35784625; PMCID: PMC9210781.
4. **Chung R.** Co-Colitis: A Rare Case of *C. difficile* and CMV Coinfection in an IBD Patient. *Am J Gastroenterol.* 2015 Oct;110():p S310.
5. **Neumann H, Pohl J.** Endoscopic imaging of *Clostridium difficile* colitis. Available at: [https://www.videogie.org/article/S2212-0971\(13\)70147-X/fulltext](https://www.videogie.org/article/S2212-0971(13)70147-X/fulltext).

6. **Yoon J, Lee J, Kim DS, Lee JW, Hong SW, Hwang HW, Hwang SW, Park SH, Yang DH, Ye BD, Myung SJ, Jung HY, Yang SK, Byeon JS.** Endoscopic features and clinical outcomes of cytomegalovirus gastroenterocolitis in immunocompetent patients. *Sci Rep.* 2021 Mar 18;11(1):6284. doi: 10.1038/s41598-021-85845-8. PMID: 33737711; PMCID: PMC7973552.
7. **Nami B, Maadi H, Wang Z.** Mechanisms Underlying the Action and Synergism of Trastuzumab and Pertuzumab in Targeting HER2-Positive Breast Cancer. *Cancers (Basel).* 2018 Sep 20;10(10):342. doi: 10.3390/cancers10100342. PMID: 30241301; PMCID: PMC6210751.