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Cytomegalovirus hemorrhagic colitis in an immunocompetent patient with COVID-19 infection: A case report

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Abstract

In coronavirus disease-19, we should suspect the opportunistic coinfections even in immunocompetent individuals. In the presence of recurrent gastrointestinal problems, colonoscopy should be done with biopsy and histopathology to diagnose the opportunistic infection, such as cytomegalovirus colitis, in patient with coronavirus disease-19. Here, we report a case of immunocompetent male with coronavirus disease-19 presenting with per rectal bleeding diagnosed as cytomegalovirus colitis.

Keywords

cytomegalovirus, colitis, coronavirus disease-19

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Introduction

Severe acute respiratory syndrome coronavirus disease-19 (SARS-CoV-19) pandemic started from Wuhan on December 2019.[1] The estimated cytomegalovirus (CMV) seroprevalence is 77%–88% in general population.[2] The virus is capable of causing disease during the immunocompromised state.[3] This manifestation is rare in immunocompetent individuals. The CMV and COVID-19 coinfection is a rare association. Here, we present a case of immunocompetent male with COVID-19 presenting with per rectal bleeding diagnosed as CMV colitis.

Case presentation

A 35-year male presented with chief complaints of dry cough, sore throat, low-grade fever, and non-pruritic rashes over extremities for 2 days. He was worked up for SARS-CoV-19 and he was tested positive for COVID-19 by reverse transcriptase–polymerase chain reaction (RT-PCR). After 2 days of admission, he developed pain in peri-umbilical region, had multiple episodes of bloody diarrhea, multiple episodes of non-bilious, non-projectile, and non-blood-stained vomiting. He had no history of diabetes mellitus, hypertension, or tuberculosis. He did not smoke or consumed alcohol occasionally.

On examination, the blood pressure was 120/80 mm of Hg, respiratory rate was 20/min, pulse rate was 73/min, and oxygen saturation was 97% in room air. General physical examination showed multiple, erythematous, non-blanchable macules to plaques along with petechiae and purpura present over bilateral extremities; more over shin, ankles, and dorsum of feet. (Figure 1) There was swelling, tenderness over the joints, and range of motion was painfully restricted. Abdominal examination showed tenderness over epigastrium. Per rectal examination revealed blood staining of fingers. The rest of the examination findings was unremarkable.

The provisional diagnosis of Henoch–Schonlein purpura (HSP) was made initially. The patient was investigated for the markers of vasculitis. The total leukocyte count was elevated; with 85% neutrophils and 8% lymphocytes, platelet

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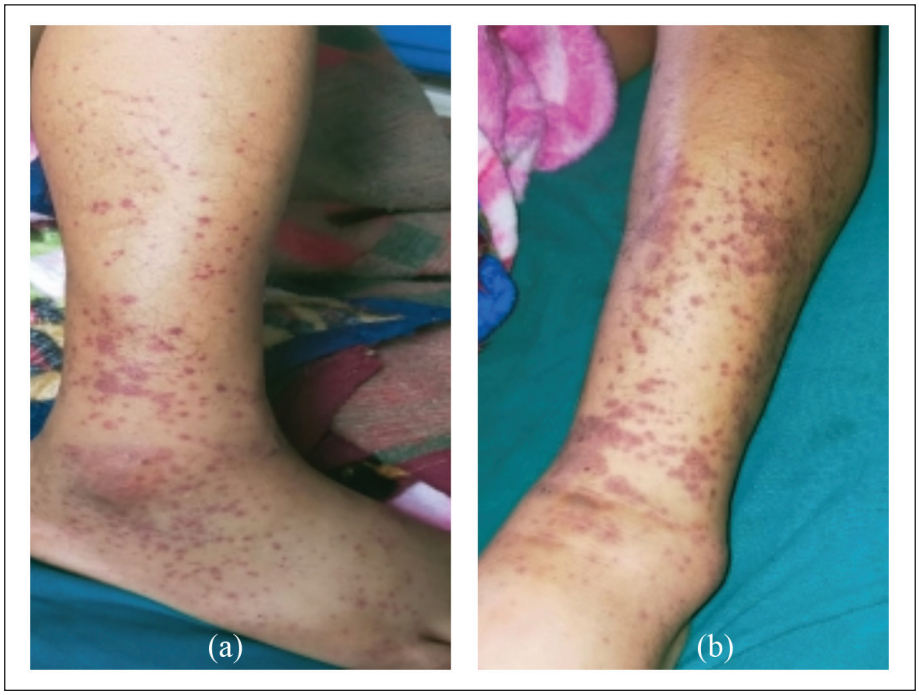

Figure 1. (a, b) Multiple, erythematous, non-blanchable macules to plaques along with petechiae and purpura present over bilateral extremities; more over shin, ankles, and dorsum of feet.

Table 1. Laboratory values.

Investigation	Result	Reference range
Total leukocyte count	26,600/µL	4000–11,000/µL
Neutrophils (%)	85	40–75
Lymphocytes (%)	8	25–45
Platelet count	314,000/µL	150,000–450,000/µL
Hemoglobin level	10.8 gm%	12–16 gm%
Sodium level	138 mEq/L	135–146 mEq/L
Potassium level	2.7 mEq/L	3.5–5.2 mEq/L
Total bilirubin	12 µmol/L	3–21 µmol/L
Direct bilirubin	3 µmol/L	0–5 µmol/L
Aspartate aminotransferase	21 U/L	5–40 U/L
Alanine aminotransferase	18 U/L	5–40 U/L
Urea level	11 mmol/L	1.6–7.0 mmol/L
Creatinine level	104 µmol/L	40–110 µmol/L
Prothrombin time	14 s	10–12 s
International normalized ratio (INR)	1.16	0.8–1.2

count was normal, hemoglobin level was low. The renal function test showed low potassium level and high urea level (Table 1). Serum amylase and lipase were normal. Similarly, the liver function test findings were within normal limits. The serology for Hepatitis-B, C, and human immunodeficiency virus (HIV) was negative. Stool examination showed 10–18 red blood cells (RBCs)/high power field (HPF), and stool occult blood was positive. Serum anti-nuclear antibody (ANA), C-reactive protein (CRP), anti-ds-DNA, C-3, C-4, c-antineutrophil cytoplasmic antibodies (ANCA), p-ANCA, anti-glomerular basement membrane antibody (anti-GBM ab), anti-Sm, anti-RNP, anti-La/anti-SS-B, anti-Ro/anti-SS-A, anti-Scl70, and anti-Jo were negative. Routine and microscopic examination of urine showed traces of albumin and six to eight white blood cells (WBCs)/HPF. The chest X-ray was normal. Ultrasonography (USG) of abdomen and pelvis showed distended stomach along with dilated bowel loops and mild ascites. The contrast-enhanced computed tomography (CECT) of abdomen showed long segment circumferential thickening of small bowel loops with minimal ascites.

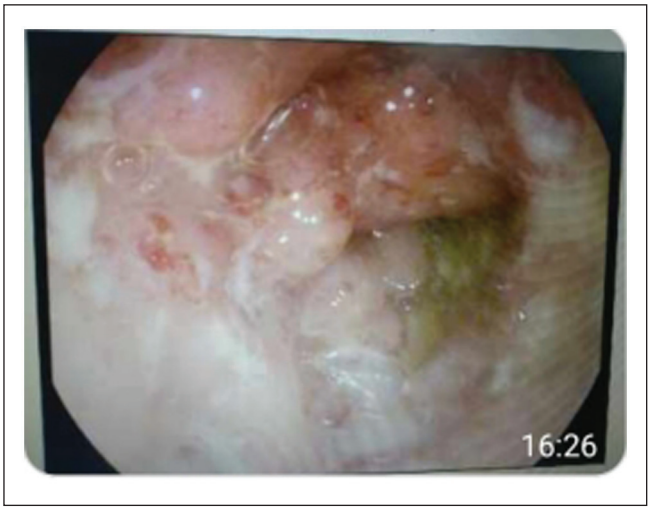

Figure 2. Colonoscopy showed large cecal ulcer, edematous mucosa, and normal ileocecal valve.

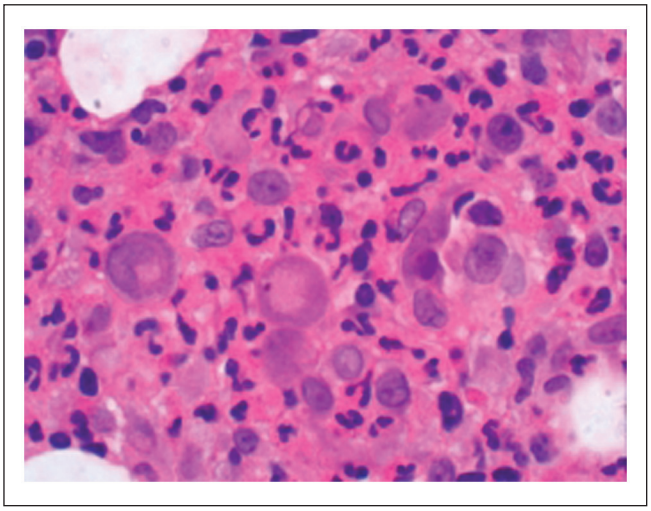

Figure 3. Histopathological examination showed numerous viral cytopathic effects in mesenchymal cells consisting of large cells with nuclear and cytoplasmic inclusion that was consistent with CMV infection.

Upper gastrointestinal (UGI) endoscopy showed normal findings while colonoscopy showed large cecal ulcer, edematous mucosa, and normal ileocecal valve. (Figure 2)

The biopsy was done late due to COVID infection, and the examination of skin biopsy of skin rash was negative for IgM, IgA, IgG, and c1q with minimal c3 dermal staining; thus, suggestive of non-inflammatory pathology. The late biopsy may have yielded negative result. Histopathological examination of colonoscopy-guided biopsied tissue from ulcer bed showed numerous viral cytopathic effects in mesenchymal cells consisting of large cells with nuclear and cytoplasmic inclusion that was consistent with CMV infection. (Figure 3) Until now, we had suspected HSP-related ulcer; but this was a surprise; retrospectively reviewing patient was not immunocompromised as such; but during covid and HSP, he might have got CMV.

Following this, the patient was managed with intravenous antibiotics, fluids, and potassium chloride. Hydrocortisone and oral mesalazine were started in view of HSP and vasculitis-related colonic ulcer while awaiting the biopsy reports, and the arthritis was resolved. Later biopsy showed CMV and valganciclovir was given for 4 weeks; rashes, joint pain, and bleeding were resolved; colonoscopy was done again after 4 weeks, ulcer was resolved almost completely. After 6 days of hospital admission, patient's RT-PCR for COVID-19 was negative. Patient was started on oral valganciclovir.

Discussion

COVID-19 pandemic has affected millions of people over the world and presented with wide varieties of symptoms. Although respiratory symptoms are the most common manifestations of COVID-19 disease, gastrointestinal symptoms are increasingly noted and gaining significance. The common gastrointestinal symptoms noted in COVID are anorexia, nausea, vomiting, diarrhea, and abdominal pain.[4]

CMV, a double-stranded DNA virus, is the member of Herpes viridae family. It is frequently seen in the immunocompromised conditions, such as HIV infection, diabetes mellitus, solid organ transplant recipients, ulcerative colitis, and malignancy.[5] The transmission of virus usually occurs via exposure to body fluids, such as saliva, blood, tears, semen, and tissue.[6] The virus usually enters the latent phase and persists lifelong in the host cell.[7] The virus usually reactivates during the conditions of immunosuppression, whereas the host immunity checks the replication and dissemination of the virus in immunocompetent hosts.[6] The role of CMV reactivation in SARS-CoV-19 is unclear. The multifactorial role of age, comorbidities, various immunosuppressive treatments, and presence of critical illness is implicated, but neither of them was present in the case of our patient. The petechiae and purpura in our case could be because of COVID-19 or CMV. There have been reported cases of petechiae on COVID-19 though less common.[8,9] There are multiple suggested causes for skin rashes in individuals with COVID-19. One possible explanation is the occurrence of widespread inflammation in the small blood vessels, known as diffuse microvascular vasculitis, which is triggered by the activation of the complement system. A study revealed substantial accumulation of complement proteins in the capillaries of the skin, along with the presence of neutrophils in the surrounding tissue and evidence of leukocytoclasia, indicating the involvement of vasculitis.[10] There are reported cases of purpura secondary to CMV infection; however, they are associated more with thrombocytopenia.[11]

The CMV colitis usually presents with hematochezia, abdominal pain, diarrhea, nausea, vomiting, melena, and fever.[5] Hematochezia is seen more in immunocompetent

hosts, while pain abdomen and diarrhea are more common in immunocompromised hosts.[12] Severe vasculitis and inflammation may predispose to bowel ischemia and perforation causing peritonitis.[13] The endoscopic findings range from minor mucosal inflammation, erythema, diffuse edema to pseudotumor, and deep ulcers.[14] The diagnosis of tissue-invasive gastrointestinal (TI-GI disease) CMV is confirmed by the histopathological demonstration of CMV in infected tissue, and sensitivity is 82.6% on hematoxylin and eosin staining, and 95.7% with immunohistochemical (IHC) staining.[15] Cytopathic effects, such as inclusion bodies, are seen in 65% of the virus-infected cells. The infected cells are enlarged and nuclei exhibit owl's eye appearance due to eosinophilic inclusions surrounded by halo of empty space.[16] IHC staining and mucosal PCR techniques appear as complementary methods. The sensitivity of quantitative PCR (>250 copies/mg) for the detection of CMV colitis in inflammatory bowel disease (IBD) patients was 79%.[17] The treatment guideline consists of intravenous ganciclovir followed by oral valganciclovir. A metanalysis on the outcome of CMV infection in immunocompetent hosts showed spontaneous remission in 31.8% and 50% in patients aged more and less than 55 years of age, respectively.[18]

TI-GI disease is also found in significant portion of patients with IBD mainly. Steroid-resistant ulcerative colitis signifies worse prognosis.[19] As CMV colitis presenting as isolated colitis is rare and it may mimic with IBD due to common clinical features, endoscopic, and histology; misdiagnosis and treatment with immunosuppressants can lead to worsening of symptoms.[15] Some studies suggest the destruction of adaptive immune cells and upregulation of T cells killing and dysregulation of immune system in COVID-19 patients which may be the potential cause for the reactivation of CMV.[20]

Conclusion

CMV colitis should be considered differential diagnosis of gastrointestinal symptoms and vascular gastrointestinal pathology in COVID-19 patient for early diagnosis and management, and improving the prognosis.

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Author contributions

N.M. and S.S. wrote the original article, reviewed, and edited the original article. N.M., S.S., M.B., R.C., A.J., A.M., and D.K. revised and edited the original article, and were in charge of the case.

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Ethical approval

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Informed consent

Written informed consent was obtained from the patient for the anonymized information to be published in this article.

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