STUDENTS' CORNER
CASE REPORT

Asymptomatic cytomegalovirus gastritis in an immunocompetent COVID-19 patient: A case report

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Abstract

A number of complications are associated with COVID-19 due to reduced immunity. Of these, opportunistic infections are of great significance because of their atypical presentation and low detection rates. Co-infection of various parts of the gastrointestinal system with cytomegalovirus (CMV) is a common occurrence in COVID-19 patients. Dysphagia and odynophagia are the main complaints of oesophagitis caused by CMV. Colitis due to CMV presents with melena, diarrhoea, or constipation. However, gastritis due to the same agent can be asymptomatic or associated with atypical symptoms like fever and epigastric pain. Cytomegalovirus gastritis can be fatal if not detected early. Hence, continued monitoring of routine baseline investigations is imperative until the complete resolution of COVID-19, as prompt diagnosis improves the outcomes.

Keywords: Cytomegalovirus, Cytomegalovirus Infections, case report, COVID-19.

Introduction

The COVID-19 pandemic is one of the most highly virulent infections as, globally, over 759 million confirmed cases and over 6.8 million deaths were reported till March 5, 2023, according to WHO.[1] Due to the development of effective vaccines and widespread efforts to raise awareness regarding its prevention, the number of new cases of COVID-19 infection and its associated deaths has reduced significantly. However, the number of cases with complications due to COVID-19 is increasing. Post-COVID sequels like opportunistic infections with life-threatening organisms such as tuberculosis, fungal infection, and other viruses, such as Ebstein–Barr Virus (EBV) and cytomegalovirus (CMV), are common due to the disrupted immune system.[2] These are fatal if not detected early and managed accordingly.[2]

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CMV is a double-stranded deoxyribonucleic acid virus from the Herpesviridae family. Most infections associated with CMV are either asymptomatic or present with mild symptoms like fever and malaise.[3,4] However, CMV infection can be severe due to any condition that weakens the immune system, like acquired immunodeficiency syndrome (AIDS) and patients on immunosuppressive therapy.[4] Similarly, in severe COVID-19 infection, the number of circulating T-lymphocytes, specifically CD4+ and CD8+ T cells, is reduced, rendering the host prone to CMV gastritis.[3]

CMV gastritis can present with fever and non-specific symptoms in its uncomplicated form. However, when the infection invades the mucosa of the gastrointestinal tract, the normal absorptive function, particularly of the large intestine, is disrupted, resulting in watery diarrhoea, which can further develop into bloody diarrhoea which is indicative of CMV colitis.[4] Moreover, the ongoing inflammation can also cause colonic obstruction due to the formation of inflammatory polyps, in which case the presenting complaint will be constipation and bloating.[4] CMV colitis should be suspected in patients with severe COVID-19 infection if they develop gastrointestinal symptoms like melena and diarrhoea.[5,6] However, a sudden and asymptomatic drop in haemoglobin is highly suggestive of CMV gastritis.[7] The diagnosis can be confirmed by CMV serological tests (CMV DNA PCR, CMV antigen assay, CMV IgG, and IgM) followed by endoscopy and histopathological examination of the sample acquired.[8,9] The management should include normalising the haemoglobin levels with blood transfusions, if indicated, and initiating appropriate anti-viral therapy to combat the CMV infection.[10] Follow-up with serial monitoring of CMV levels is imperative.[10]

Case Report

A 72-year-old male presented to the emergency room of Shifa International Hospital, Islamabad on November 25, 2020, complaining of worsening shortness of breath for seven days. He was a diagnosed case of type 2 diabetes mellitus, hypertension, benign prostatic hyperplasia, coronary artery disease, and chronic obstructive pulmonary disease with history of pulmonary tuberculosis.

Table: Laboratory Investigations After Admission.

Investigations	Patient value	Normal value
Haemoglobin (g/dL)	12.6	M (13-18), F (11.6-16.5)
WBC (/UL)	20,730	4,000-11,000
Platelets (/UL)	259,000	150,000-400,000
RBG (mg/dL)	249	200
Sodium (mEq/L)	131	136-145
Chloride (mEq/L)	97	98-107
BUN (mg/dL)	22	8-23
Potassium (mEq/L)	4	3.5-5.1
Bicarbonate (mEq/L)	26	22-29
Creatinine (mg/dL)	0.7	M (0.7-1.25), F (0.571.11)

WBC= White Blood Cell, RBG= Random Blood Glucose, BUN= Blood Urea Nitrogen.

The patient had a history of recent COVID-19 infection. A CT pulmonary angiogram revealed a lower lobe air embolism. Examination revealed normal temperature, blood pressure of 150/70 mmHg, a pulse of 90/min, and respiratory rate of 27/min with a SpO_2 of 89%. Chest auscultation revealed bilateral crepitations which were more pronounced on the left side. The baseline investigations are shown in Table. Chest X-ray showed infiltrates on the left side and haze on the right side. Initially, the patient was admitted to the intensive care unit (ICU) for the management of pulmonary embolism. After three days, the patient's condition improved and he was shifted to the floor for further monitoring. On day 13, an asymptomatic drop in the patient's haemoglobin was observed from 12.6 g/dL to 7.6 g/dL. The patient did not report any hematemesis, bleeding per rectum, or melena. Relevant investigations including folic acid, vitamin B12, and serum iron were negative but stool occult blood was positive. The patient was transfused one unit of packed red blood cells which improved the haemoglobin to 8.7 g/dL. On day 15, the patient underwent an oesophagogastroduodenoscopy which revealed erosive oesophagitis, erosive gastritis, and mild duodenitis. A small biopsy tissue report revealed moderate chronic severe active CMV gastritis as shown in Figure. The patient was started on IV Ganciclovir (5mg/kg) and then switched to tablet Ganciclovir (5mg/kg). A CMV DNA by PCR Quantitative test was carried out on day 21, in which CMV DNA was detected at a quantity of 4190. Daily CBC tests monitored the patient's haemoglobin, which improved to 9.9 g/dL. The patient was discharged on December 18, 2020, with 92% oxygen saturation and was counselled about compliance with home medicines, diet, and home care. The patient was also advised to take Valganciclovir tablet 450mg with a regimen of 900mg orally once a day for eleven days. The patient returned for a follow-up after five days on December 23, 2020, with the report of CMV DNA PCR in which CMV DNA was detected again but was reduced to 1409.

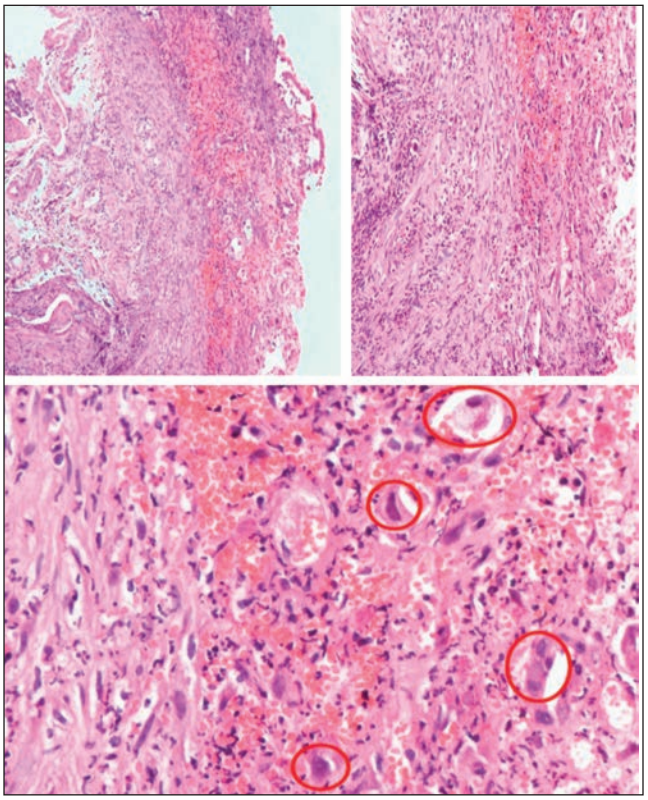

Figure: Histological examination images of the gastric biopsy indicating CMV inclusion bodies (highlighted as red circles).

Discussion

Despite COVID-19 causing several complications, the number of cases of CMV-associated gastrointestinal infection is significantly low. Most of the reported cases, including the one presented above, occur in old-age patients.[3-6,8,10] However, two cases of CMV-associated gastrointestinal infection have been reported in middle-aged individuals.[7,9] Only three reported cases had no known co-morbidity, which differs from this case as multiple co-morbid conditions were present. In all the reported cases, the COVID-19 infection presented with severe intensity, as indicated by ICU admissions and decreased SpO_2, which was also observed in this case.[3,10] In this case, the treatment for COVID-19 involved the administration of Remdesivir and steroids. In four reported cases, Tocilizumab was also used.[4,7,9,10] Of these, only one case reported CMV-associated GI infection due to immunosuppression from administering relatively higher doses of Tocilizumab.[4] Another unique aspect of this case is the involvement of the stomach by CMV, as only two such cases have been reported.[9,10] CMV infection of the gastrointestinal tract occurred in the post-COVID duration in only one of the reported cases, which is different from this case as the CMV co-infection occurred while the patient was positive for COVID-19 and was suffering from another non-infectious complication of COVID-19.[9] In all

the reported cases, the diagnosis of CMV was made not only based on endoscopic procedures followed by histopathological examination of the biopsy sample but also involved CMV serological tests, which are also similar to this case.[3-10] Ganciclovir was used as the primary anti-viral drug against CMV in all the reported cases including this one.[3-10] However, one unique aspect regarding this case is that a lower dose oral regimen of Ganciclovir was used during the post-discharge period.

Furthermore, in one of the reported cases, due to delayed response to Ganciclovir, Foscarnet and Ustekinumab were also used for CMV infection.[7] Only a single case has been reported in which treatment of CMV infection required an emergency laparotomy due to fatal loss of blood.[4] The reported cases presented with gastrointestinal symptoms like melena, diarrhoea, rectal bleeding, and dysphagia which is different from this case as the presentation of CMV infection was asymptomatic, detected only by a sudden drop in haemoglobin.[3-10]

Conclusion

COVID-19 infection is one of the most deadly diseases because of its acute presentation, fatality, and varied complications. Of these, CMV-associated infection of the gastrointestinal tract is a rare but self-limiting problem in immunocompetent individuals. The presentation of these opportunistic infections can be asymptomatic, and routine baseline investigations should be carried out for early detection. If suspected, the diagnosis should be confirmed through invasive and non-invasive specific tests for CMV. Ganciclovir has proven to be an effective agent against opportunistic CMV infection in COVID-19 patients. However, the side effects of this drug should be considered before starting therapy, and adequate monitoring should be carried out during its administration.

Consent: The patient provided written consent for publishing his case for the promotion of science.

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References

1. World Health Organisation Coronavirus disease (COVID-19) Weekly epidemiological update on COVID-19. [Online] [Cited 2023 March 08]. Available from: URL: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---8-march-2023
2. Abdoli A, Falahi S, Kenarkoohi A. COVID-19-associated opportunistic infections: a snapshot on the current reports. Clin Exp Med. 2022; 22:327-46. doi: 10.1007/s10238-021-00751-7.
3. Bakir M, Rebh F, Mahdi E, AlFiaar A, Mansoor GS. A Case of Cytomegalovirus Colitis in an Immunocompetent COVID-19 Patient. Cureus. 2022; 14:e23203. doi: 10.7759/cureus.23203.
4. Khatib MY, Shaik KS, Ahmed AA, Alwraidat MA, Mohamed AS, Abou Kamar MR et al. Tocilizumab-induced cytomegalovirus colitis in a patient with COVID-19. Clin Case Rep. 2020; 9:148-52. doi: 10.1002/ccr3.3487.
5. Marchi G, Vianello A, Crisafulli E, Maroccia A, Crinò SF, Pecori S, et al. Cytomegalovirus-Induced Gastrointestinal Bleeding and Pancreatitis Complicating Severe Covid-19 Pneumonia: A Paradigmatic Case. Mediterr J Hematol Infect Dis. 2020; 12:e2020060. doi: 10.4084/MJHID.2020.060.
6. Leemans S, Maillart E, Van Noten H, Oliveira Dos Santos L, Leahu LM, Kamgang P, et al. Cytomegalovirus haemorrhagic colitis complicating COVID-19 in an immunocompetent critically ill patient: A case report. Clin Case Rep. 2020; 9:e03600. doi: 10.1002/ccr3.3600.
7. Carll WC, Rady MY, Salomao MA, Patel B, Singh VP, Sen A. Cytomegalovirus haemorrhagic enterocolitis associated with severe infection with COVID-19. BMJ Open Gastroenterol. 2021; 8:e000556. doi: 10.1136/bmjgast-2020-000556.
8. Shah M, Kakar A, Gogia A, Langer S. Convalescent plasma, cytomegalovirus infection, and persistent leukopenia in COVID-19 recovery phase: What is the link? J Postgrad Med. 2021; 67:100-2. doi: 10.4103/jpgm.JPGM_1168_20.
9. Taherifard E, Mortazavi R, Mokhtari M, Taherifard A, Kiani Salmi S, Taherifard E. Cytomegalovirus gastritis in a patient with severe acute respiratory syndrome coronavirus 2 infection: A case report and literature review. Respir Med Case Rep. 2022; 37:101644. doi: 10.1016/j.rmcr.2022.101644.
10. Robertson, Wesley A, Narang, Natasha, NovoaTakara, Louis, et al. CMV-Induced Small Bowel Bleeding Complicating Severe COVID-19 Respiratory Failure. ACG Case Rep J. 2022; 117:e1700-1. doi: 10.14309/01.ajg.0000866876.15285.

Author Contribution:

FN: Concept, design, collection and assembly of data and drafting.
MI: Critical revisions.
SMMA: Literature review and comparison of other reported cases with the presented case.
TI: Concept and provision of the diagnostic and treatment details.