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Case Report

A Rare Case of Cytomegalovirus Colitis with Subsequent Non-tubercular Mycobacteria Immune Reconstitution Inflammatory Syndrome

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Abstract

Cytomegalovirus (CMV) colitis occurs commonly in immunocompromised patients with high mortality. CMV infection has also been reported in immunocompetent individuals and it has a varied clinical presentation. When HIV-infected patients are started on antiretroviral therapy (ART) there is a reconstitution of the immune system which results in the paradoxical worsening of existing conditions or development of new disease conditions known as immune reconstitution inflammatory syndrome (IRIS). In the setting of IRIS one of the most common infections to occur is non-tubercular mycobacteria (NTM). The infection generally develops when the CD4 count is < 50 cells/μL. Here we present a rare case of CMV colitis followed by NTM infection in the setting of IRIS, its management, and treatment outcomes.

Keywords: HIV, IRIS, Cytomegalovirus, Non-tubercular mycobacteria

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Introduction

Cytomegalovirus (CMV) colitis is a well known entity in immunocompromised patients who are either human immunodeficiency virus (HIV) positive, have a history of anti-cancer therapy, inflammatory bowel disease or have undergone a bone marrow transplantation.[1-5] CMV infection has also been reported in immunocompetent individuals and it has a varied clinical presentation. When HIV-infected patients are started on antiretroviral therapy (ART), there is a reconstitution of the immune system, which results in the paradoxical worsening of existing conditions or development of new disease conditions known as immune reconstitution inflammatory syndrome (IRIS). In the setting of IRIS one of the most common infections to occur is non-tubercular mycobacteria (NTM). The infection generally develops when the CD4 count is < 50 cells/μL [6] The diagnosis and clinical management of NTM infections is difficult and it has a very high mortality rate in immunocompromised patients. Here we present a rare case of CMV colitis followed by NTM infection in the setting of IRIS.

Case Report

A 28-year-old woman presented with complaints of multiple eruptions over the face, neck, and chest with recurrent epistaxis, menorrhagia, and gum bleeding. On clinical evaluation, she had pallor with stable vitals and on investigation her hemoglobin level was 9.2 g/L, absolute neutrophil count 1200/uL, platelet count was 50 000/uL, total proteins 6.5 mg/dL and albumin 3.9 mg/dL. Bone marrow aspiration revealed a reactive cellular marrow. She was diagnosed with idiopathic thrombocytopenic purpura (ITP) and treatment was started with positive results. After one year the patient reported back with complaints of watery stools associated with abdominal pain, weight loss of 11 kg in the last 2 months, and inability to open mouth for the last 10 days. Physical examination revealed a weight of just 28 kg, hypotension, cachexia, oral thrush, and mild tenderness in the right iliac fossa without abdominal distension or guarding. Abnormal laboratory findings included hemoglobin of 7.6 g/dL, mean corpuscular volume 77 fL, hematocrit 24%, a CD4 count of 40 cells/μL, HIV viral load of 1.18E06 copies/mL (log6.07), herpes simplex virus IgM/ IgG antibody-non-reactive, cryptococcal antigen negative, sputum for tuberculosis by GeneXpert automated heminested polymerase chain reaction (PCR) negative, with a positive fecal occult blood test (FOBT) and 6-8 pus cells/Hpf in stool microscopic examination. The modified Ziehl-Neelsen stain was positive for cryptosporidium. Hence she was diagnosed with HIV wasting syndrome with cryptosporidiosis and oral candidiasis. She was started on tenofovir 300 mg, lamivudine 300 mg, and dolutegravir 50 mg with nitazoxanide 500 mg twice a day and fluconazole 300 mg daily. However, there was no improvement in diarrhea and the frequency of stools kept on increasing.

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Contrast enhanced computed tomography (CECT) abdomen revealed concentric discontinuous smooth wall thickening (thickness 6.2 mm) involving the entire large bowel suggestive of colitis. A colonoscopy revealed signs of infective colitis (Figure 1). A colonic biopsy was taken which revealed focally ulcerated mucosa with marked edema and architectural distortion. Numerous proliferating capillaries were seen in the lamina propria, which showed endothelial cell enlargement with large oval nuclei containing basophilic intranuclear inclusions surrounding a clear halo (Figure 2). CMV DNA level in plasma by real-time PCR was 97657 copies/ul. The patient was diagnosed with a case of CMV colitis and the treatment was started with valganciclovir 900 mg twice daily for 2 weeks. There was a drastic improvement in the condition of the patient with complete cessation of diarrhea within 7 days of treatment.

However, the patient reported to HIV centre again after four weeks of cessation of diarrhea with increased weakness and weight loss of more than 2 kg. CECT of the chest was done and a necrotic mediastinal lymph node was identified. An endobronchial ultrasonography-guided lymph node aspirate was found to have acid fast bacilli in Ziehl-Neelsen stain, however liquid tubercular culture by Mycobacterial Growth Indicator Tube (MGIT) was negative, thus suggesting infection by NTM. Hence she was diagnosed as a case of NTM with IRIS. The patient was initially started on anti-tubercular therapy (ATT) empirically on suspicion of tubercular infection. However, she developed ATT-induced hepatitis and subsequent hepatic failure resulting in the death of the individual.

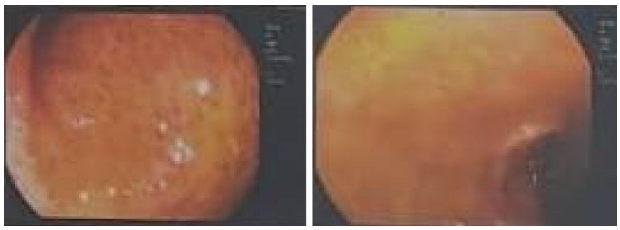

Figure 1. Patchy erythema involving the entire mucosa of the colon

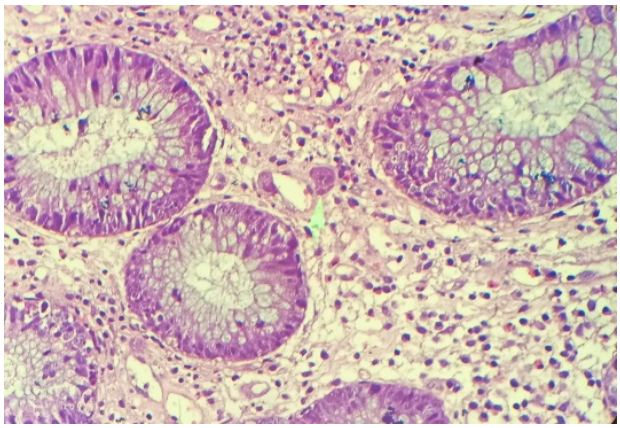

Figure 2. Enlarged endothelial cell with a large nucleus containing basophilic inclusion

Discussion

CMV colitis is one of the commonest infections occurring in immunocompromised presenting with diarrhea, bloody stool, nausea, fever, and abdominal pain.[7] Involvement of the colon and rectum is the most common cause of symptoms in CMV infection.[8] Our case presented with a very low CD 4 count with oral candidiasis and cryptosporidium in stool, which were treated without any relief to the patient causing a delay in the diagnosis of CMV colitis that was confirmed on histopathology with characteristic nuclear and cytoplasmic inclusion giving Owl eye appearance and PCR. Immune reconstitution occurs in cases of HIV who have a very low CD4 count and are started on ART. It is a strong virological and immunological response to ART.[9] IRIS may also be caused by other conditions like malignancies, autoimmune disorders, and infections. It causes paradoxical worsening of symptoms or unmasking of previously untreated or subclinical infection.[10] NTM infection is common in the setting of IRIS. It most commonly presents as necrotic lymph nodes, pulmonary infiltrates, and weight loss. The route of infection is generally oral.[9,11] This may be confused with mycobacterial tubercular infection because of similar clinical and radiological findings. The institution of ATT in these patients has a high incidence of liver failure.[12] IRIS has high mortality of approximately 21% with 3% mortality in tuberculosis-related cases.[6,13] Our case was also started empirically on ATT resulting in features of liver cell failure and death.

Authors' Contribution

All authors have contributed equally to patient management, follow-up, manuscript preparation, and review of the literature. RP is the corresponding, and guarantor for the manuscript.

Competing Interests

The authors declare no conflict of interest related to this work.

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