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CMV Colitis in a Systemic Lupus Disease Patient: Case Report and Review

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Abstract | **Case Report**

Introduction: Cytomegalovirus (CMV) infections are common, particularly among immunocompromised patients. They are usually asymptomatic, but can be responsible for severe symptoms and complications especially in immunocompromised individuals including those with human immunodeficiency virus infection or receiving long-term treatments with corticosteroids or immunosuppressive therapy. CMV colitis is the second most common presentation of end-organ disease. ***Case presentation:*** We report the case of a 27-year-old female patient, followed since the age of 15 for systemic lupus with cutaneous, articular, hematological and grade 4 renal impairment, on long-term corticosteroid therapy, mycophenolate mofetil (MMF) and hydroxychloroquine, admitted to hospital for altered general condition, generalized muscle weakness, and hematochezia. Clinical examination on admission revealed generalized mucocutaneous pallor, right hemiparesis, and normal proctological examination. She was referred to our digestive endoscopy unit for colonoscopy. Endoscopic examination revealed the presence of 3 large ulcers in the sigmoid colon, and a subcentimetric ulcer in the right colo, with normal intercalary mucosa. Biopsies taken from the ulcer margins showed positive CMV PCR. The diagnosis of CMV colitis was thus made and the patient was put on IV Ganciglovir. ***Conclusion:*** CMV colitis could occur in lupus patient under corticosteroids or immunosuppressive therapy. It should be included in the differential diagnosis in these patients who present to emergency department with bloody stools, acute abdominal pain or diarrhea.

Keywords: CMV, Colitis, Lupus, MMF, Case Report.

INTRODUCTION

CMV is an ubiquitous Herpes virus, known as human herpesvirus 5 and belongs to the *Betaherpesvirinae* subfamily of *Herpesviridae*. It is responsible for infection in about 40 to 100 per cent of adults worldwide [1]. The infection is generally asymptomatic, with the virus remaining latent in white blood cells for the life of the host [2]. Clinically significant disease is most likely to occur in individuals with impaired cell-mediated immunity, particularly among transplant patients, AIDS patients, those undergoing chemotherapy, immunosuppressive therapy, or corticosteroids. It can affect multiple organs, with colitis being the second most common manifestation of end-organ disease [3]. Systemic lupus erythematosus (SLE) patients are generally at high risk of CMV infection. Digestif symptoms linked to CMV infection, such as abdominal pain, diarrhea, melena, and perforation, can closely resemble those of lupus enterocolitis, leading to potential confusion in diagnosis [4]. Therefore, it is essential to differentiate whether these symptoms are due to an exacerbation of SLE or a CMV infection.

Herein, we describe the case of a SLE patient who developed CMV colitis following immunosuppressive therapy, leading to colonic ulcers with bloody stool.

CASE PRESENTATION

We report the case of a 27-year-old female patient, followed since the age of 15 for SLE, diagnosed on the basis of skin involvement with malar erythema and photosensitivity, joint involvement with inflammatory polyarthralgia of the large and small joints, hematological involvement with bicytopenia (anemia and thrombocytopenia), and renal involvement confirmed by renal biopsy that revealed type IV lupus

glomerulonephritis, initially treated with bolus methyprednisolone (3 courses) and cyclophosphamide, then switched to mycophenolate mofetil (MMF), hydroxychloroquine and long-term corticosteroid therapy. The patient was admitted to hospital with an altered general condition, generalized muscle weakness and hematochezia. Clinical examination on admission revealed a hemodynamically stable patient with generalized mucocutaneous pallor, right hemiparesis and a normal proctological examination.

Biological findings included normocytic normochromic anemia with hemoglobin at 8g/dl, lymphopenia at 800/mm3 and creatinine at 26mg/l. A cerebral CT scan was performed to investigate the motor deficit, which revealed multiple foci of chronic ischemic stroke in different territories, probably related to lupus vasculitis. The patient was referred to our digestive endoscopy unit for colonoscopy to explore the hematochezia. Endoscopic examination revealed 3 large ulcers in the sigmoid colon and a subcentimetric ulcer in the right colon, with normal intercallary mucosa. Multiple biopsies were taken from the edges of the various ulcers, and sent for anatomopathological and virological studies. Anatomopathological study revealed severe colitis, with no indentification of CMV inclusions or other pathogens. CMV PCR was positive on all biopsies. The diagnosis of CMV colitis was thus confirmed, and the patient was put on intravenous (IV) Ganciclovir 5mg/Kg/12h.

The evolution was marked by the onset of consciousness disorders with a glascow score of 8/15 and the occurrence of 2 partial convulsive seizures, prompting her admission to intensive care unit (ICU). A CT scan revealed an ischemic stroke in the superficial territory of the middle cerebral artery and the anterior cerebral artery. The patient died few days later in the ICU due to stroke complications.

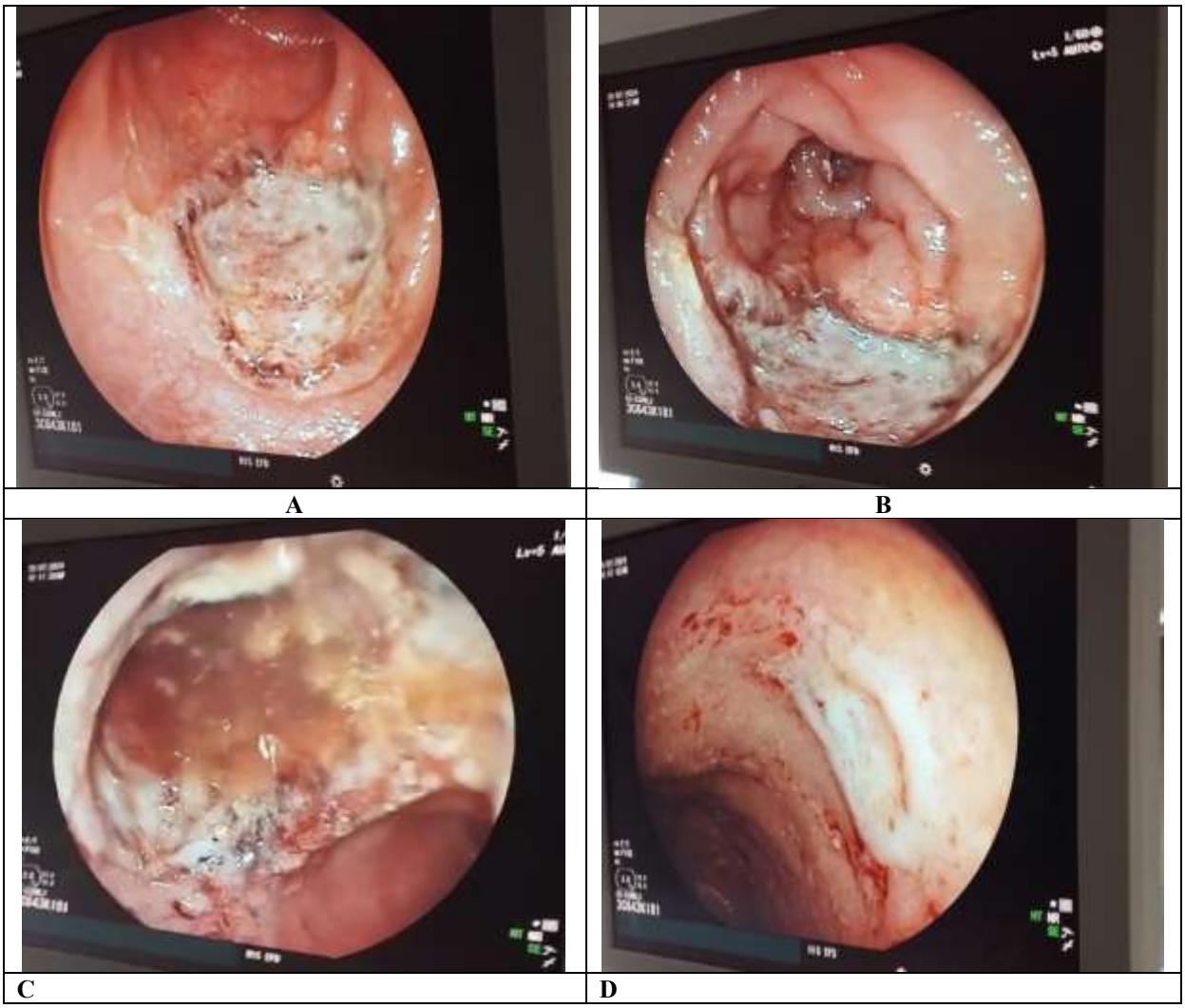

Figure A, B and C: 3 large and deep ulcers in the sigmoid colon
Figure D: subcentimetric ulcer in the right colon

DISCUSSION

CMV, a double-stranded DNA virus and part of the herpesvirus family, is a widespread viral infection affecting many people in the general population. The seroprevalence of CMV ranges from 40% to 100% and is influenced by factors such as age and geographic location [5]. T-cells play a crucial role in controlling viral replication during primary CMV infection but are unable to completely eradicate the virus [6, 7]. This indicates that anyone could be at risk for CMV-related complications if the virus reactivates when they become immunocompromised.

In healthy individuals, CMV typically causes a mild, self-limiting illness, but in immunocompromised patients, reactivation or reinfection can cause severe diseases such as pneumonitis, hepatitis, pancreatitis, colitis, encephalitis, retinitis, or pericarditis, leading to significant morbidity and mortality [8]. CMV colitis is the second most common manifestation of end-organ disease [3], and is believed to negatively affect the clinical outcome of those patients [9].

Lupus disease itself and the use of immunosuppressive therapies increase the risk of opportunistic infections. The acute onset of CMV infection has been described in up to 46% of patients with connective tissue disorders undergoing immunosuppressive therapy (10). It has also been noted that these patients are at high risk for reactivation of latent CMV disease [11]. MMF is a key immunosuppressant commonly used to treat autoimmune diseases, and it is recommended as a first-line therapy for both the induction and maintenance of remission in patients with SLE and lupus nephritis (LN) [12]. However, the side effect profile of MMF has not been thoroughly assessed, particularly concerning infections. A recent study in Japan followed 452 adult patients with LN taking MMF for 6 months showed that the most common adverse effects of MMF were herpes zoster, diarrhea, and CMV infection [13].

CMV can impact any part of the gastrointestinal tract, with colitis being the most prevalent manifestation. This condition can occur independently or alongside other systemic involvements. CMV colitis typically presents with symptoms such as fever, abdominal pain, diarrhea, or bleeding. Hematochezia was the main symptom in our case. The virus directly infects the bowel, leading to mucosal erosions or ulcerations. In more severe cases, it can result in tissue necrosis and perforation of the bowel wall [14].

Endoscopic findings are generally nonspecific. The most notable independent finding is the presence of ulcerations that have a well-defined, punched-out appearance [15, 16], just like in our case. The prevalence of mucosal ulcerations in CMV colitis is quite high, ranging from 70% to over 80% [17, 18]. Additionally, irregular ulcerations and a cobblestone-like appearance are also associated with this condition [19]. Histological studies have shown that the number of CMV inclusion bodies is significantly greater in patients with punched-out lesions [19]. Occasionally, CMV colitis may present as toxic megacolon with pseudomembrane formation or as ischemic colitis [20, 21]. Two recent case reports indicated that CMV colitis was misdiagnosed as a rectal malignancy, presenting as an inflammatory tumor-like mass in an immunocompetent patient [21, 22]. Consequently, diagnosing CMV colitis necessitates a histological evaluation of biopsy tissue, ideally obtained from both the base and edge of the ulcers [23].

Blood serology has no diagnostic value for CMV colitis since the seroprevalence of CMV within the adult population is high [24].

Hematoxylin and eosin (H&E) staining can reveal the characteristic viral inclusions associated with CMV colitis, known as “owl eye” inclusions. When present, this histological feature is highly specific for CMV. However, this method has demonstrated lower sensitivity compared to immunohistochemistry (IHC) and tissue polymerase chain reaction (PCR) [25, 26].

The gold standard for detecting CMV in gastrointestinal mucosal biopsies is CMV-specific immunohistochemistry (IHC), which labels the CMV antigen in infected cells [27]. Zidar *et al*., [23] demonstrated that no positive cells were detected by IHC in tissues that were not infected with CMV.

While quantitative plasma PCR is used to diagnose systemic infection, PCR in colonic tissue has proven to be more sensitive than IHC. The European Crohn’s and Colitis Organization (ECCO) guidelines recommend using PCR on gastrointestinal biopsy tissue to diagnose CMV colitis in patients with inflammatory bowel disease (IBD) [28]. This method is objective, fast, and highly standardized [29]. McCoy *et al*., [24], showed that PCR increased sensitivity to detect CMV in histologically negative biopsies from patients with subsequent positive CMV colitis, just like our case. Thus, the use of PCR has been suggested when there is a strong clinical suspicion of CMV infection and IHC is negative [16].

Concerning treatment, the drug of choice for CMV colitis in adults is ganciclovir, administered either orally or intravenously at a dose of 5 mg/kg/12h [30, 31]. According to ECCO guidelines, after 3–5 days of intravenous ganciclovir, patients can switch to oral valganciclovir at a dose of 900 mg twice daily to complete the remaining 2–3 weeks of therapy. Foscarnet can be used as an alternative treatment for patients who have developed resistance to or cannot tolerate ganciclovir [31].

The necessity of medical treatment for immunocompetent patients with CMV disease remains a subject of debate. Antiviral medications carry significant side effects, including myelosuppression, central nervous system disorders, hepatotoxicity, and nephrotoxicity [20]. However, untreated CMV disease is linked to increased morbidity and mortality. Current recommendations suggest that antiviral treatment should be considered for immunocompetent patients only if they are males over 55 years of age or have comorbidities that compromise the immune system, such as diabetes or chronic renal insufficiency [30].

CONCLUSION

In summary, we report the case of CMV colitis in a systemic lupus patient under corticosteroids and MMF, who presented with hematochezia and deep large colonic ulcers in endoscopy. This case underscores the importance of exploring the possibility of CMV colitis as a differential diagnosis in SLE patients presenting with gastrointestinal symptoms especially those under immuno-suppressive drugs.

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