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CASE REPORT

Cytomegalovirus Colitis in Systemic Lupus Erythematosus: A Case Report

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Abstract

Systemic Lupus erythematosus (SLE), a multisystem autoimmune disease with protean manifestations, is often complicated by infective exacerbations, which may be opportunisticor de novo. Cytomegalovirus (CMV) infection has been linked to retinitis, enterocolitis, myocarditis, pneumonia, and other conditions in SLE patients. We report a case of SLE with CMV colitis, with its sequelae and past tuberculous pericarditis.

Keywords:
CMV colitis, SLE, CMV infection

Introduction

SLE is a heterogeneous autoimmune condition that involves various organ systems. Most of the diagnosed cases of SLE are a combination of immunosuppressive medications along with hydroxychloroquine. Atypical bacterial, viral, fungal, and mycobacterial infections are known to complicate the course of a patient's illness while on immunosuppressive agents. Cytomegaloviral infection is one of them. Numerous manifestations, such as retinitis, enterocolitis, myocarditis, and pneumonia, are reported due to CMV infection in SLE cases. However, the occurrence of CMV in an immunosuppressive naïve patient with SLE is rare; we report one such case of CMV Colitis, which occurred de-novo in a patient with SLE.

Case Report

A 49-year-old female patient with SLE presented with multiple episodes of blood-stained, painless, loose stools for ten days. There was no pain in the abdomen, fever, or vomiting. She had been diagnosed with SLE at the age of 35 years and was on Prednisolone, HCQ, and Azathioprine initially. Nine years ago, she was treated with anti-tubercular therapy and Pericardiocentesis for suspected Tubercular Pericarditis. She was lost for follow-up for five years and has only been taking HCQ since then. On examination, pulse rate was 86/min, blood pressure was 120/80mmHg, and temperature was 98.5 degrees Fahrenheit. There was tenderness in the right iliac fossa, with the remaining systems showing no significant abnormalities.

Complete Hemogram showed Hb of 8.3 gm/dl, lymphopenia (860/µl), and Microcytic hypochromic anaemia. The Direct Coombs test was negative. CRP was 45.42 mg/l (0-5 mg/l). C3 was 96.98mg/dL (Normal 75-135), and C4 was 13.41mg/dL (normal 9 to 36). Serum Immunoglobulin G was 14.54g/L (Normal 7 to 16g/L), Immunoglobulin A was 3.31g/L (Normal 0.7-4g/L), Immunoglobulin M was 1g/L (Normal 0.4-2.3g/L). HIV, HBsAg, and anti-HCV work up were negative.

The ultrasound of the abdomen showed features of Probe tenderness in the right iliac fossa, which was

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suggestiveof acute appendicitis, and she was taken up for laparoscopic appendicectomy.

She continued to have bloody diarrhoea three dayspost-appendicectomy.CECT Abdomen Pelvis revealed diffuse long segment enhancing circumferential wall thickening of the caecum, ascending and transverse colon exhibiting water-halo pattern, with multiple sub-centimetric mesenteric lymph nodes. (*Fig 1 and 2*)

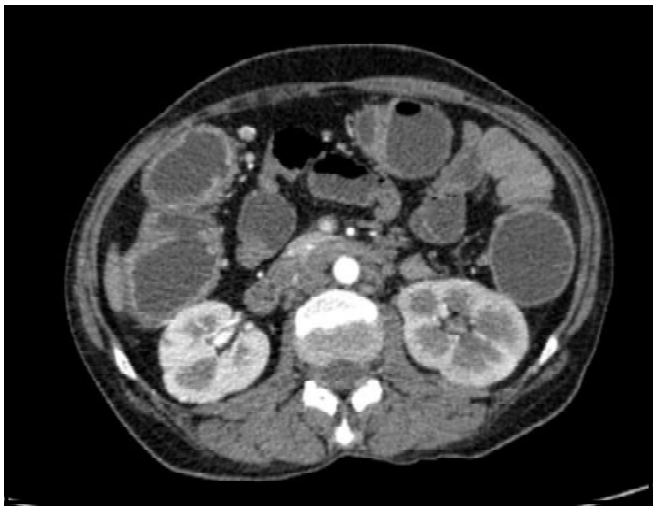

Fig 1– Diffuse long segment bowel wall thickening

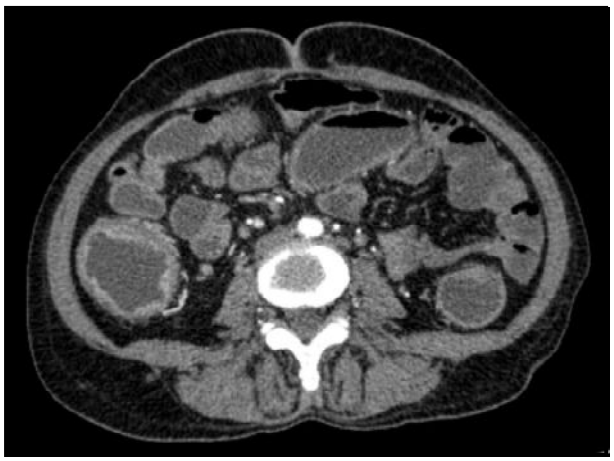

Fig 2 – Water Halo Sign suggestive of submucosal oedema

Colonoscopy showed clean-based ulcers in the terminal ileum and deep guttate ulcers from the caecum to the rectum, with normal intervening mucosa. Biopsy taken from the colonic ulcers showed large areas of ulceration, with exudate and granulation tissue, with occasional cells displaying cytomegaly, with viral inclusions, suggestive of Cytomegalovirus Colitis. (*Fig 3*). CMV Antibody titres were raised, with IgG >180 U/mL (Normal <12) and IgM 38.3 U/mL (Normal <18).

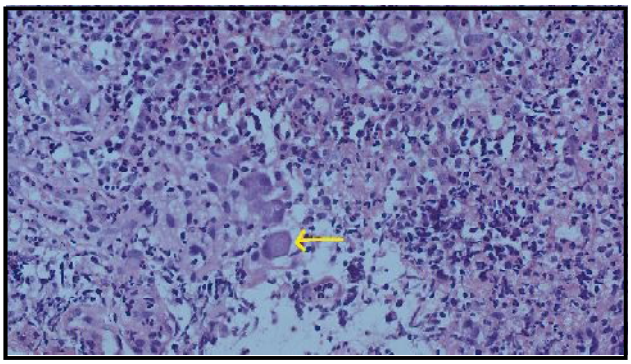

Fig3 – CMV Inclusion Bodies in Colonic Mucosal Biopsy

She was initiated on Inj. Ganciclovir 5mg/kg IV for the first six days, followed by nine days of oral valganciclovir 900mg/day, after which her symptoms resolved, and she is currently under follow-up with no recurrence of bowel symptoms. She had a recurrence of polyarthralgia and low-grade fever with leukopenia, for which she was started on low-dose steroids and hydroxychloroquine.

Discussion

This case highlights the development of opportunistic infections in patients with SLE in the absence of immunosuppressive medications. Usually, such infections are noted in patients on immunosuppressive medications or if Lupus is a consequence of Common Variable Immunodeficiency (CVID). However, CVID was ruled out, with normal immunoglobulin levels. Other differential diagnoses that were considered were lupus enteritis, intestinal tuberculosis, and Inflammatory Bowel Disease. The diagnosis of CMV colitis was established with the demonstration of CMV inclusion bodies.

The background of tubercular pericarditis in the same patient highlights the propensity of SLE cases to develop uncommon, opportunistic infections.

Infections are a critical problem in the management of SLE, especially when a patient presents with pyrexia of unknown origin, which often mimics a flare of SLE. It is well known that infections are the second leading cause of death in SLE patients (25%), ranking just after complications related to disease activity (26%). [1] Factors increasing the propensity of infections in SLE patients are background use of immunosuppressive therapy (Steroids, Cyclophosphamide, Mycophenolate and Azathioprine), increasing disease activity and prolonged hospitalization. [2]

There are numerous mechanisms proposed to reason out of infections in SLE, namely,

- Reduced $CD4^+$ T cells (due to disease and/or corticosteroids)
- Reduced $CD25^+$ T-Reg cells
- Abnormal T-cell mediated cytotoxicity.
- Impaired chemotaxis and phagocytosis of macrophages and polymorphonucleate
- Complement deficiency.
- Decreased expression of cellular complement receptors (CR1, CR2, CR3)
- Mannose-binding lectin deficiency
- Low levels of soluble Fc gamma receptor III
- Chronic inflammation and tissue damage.[3]

Among opportunistic infections, cytomegalovirus (CMV) is particularly dangerous in SLE, being a problem for the differential diagnosis of SLE flare and for treating SLE flare with immunosuppressives. Cytomegalovirus is a double-stranded DNA virus belonging to the family of Herpesviridae. It remains dormant in the host after an acute infection, like other viruses of this family. Among all herpes viruses, CMV carries the maximum number of genes that are coded to evade innate and adaptive immunity in the host. CMV bears a lifelong burden of antigenic T-cell surveillance and immune dysfunction. It is known to cause a wide range of infections like CMV Encephalitis, Pneumonitis, Myocarditis, Hepatitis, Colitis,and Retinitis.[4]

Cytomegalovirus Colitis is usually diagnosed by a high index of suspicion with the help of Serum CMV IgM Titres, CMV PCR, or the gold standard test, "CMV Inclusion Bodies" on histopathology.Once diagnosed, highly selective treatment options like Ganciclovir, Valganciclovir, Foscarnet, and Cidofovir are available.

There are very few reported cases of SLE complicated by CMV Colitis. Ikeda *et al*. in 2017 [5] describe a 31-year-old female with lupus nephritis who developed CMV Colitis and was operated on.Berman et al. in 2016 [6] reported a case of CMV Colitis in SLE in a patient who was on Belimumab. Tachikawa *et al*. in 2016 [7] describe the case of an elderly female patient with multiple bleeding colonic ulcers, which was resected; however, the patient did not survive beyond ten days. Takei *et al.* in 2005[8] describe a 30-year-old female patient who developed CMV Colitis along with Pneumocystis carinii pneumonia in the setting of SLE with high disease activity. Sakamoto *et al.* in 2001[9] describe a 44-year-old female case of SLE who developed CMV Colitis and HLH and eventually succumbed to the illness.However, in the above cases, patients were on active immunosuppressive medications prior to admission, which made them much more susceptible to developing CMV infections, unlike our case, which was off immunosuppressants.

There are few other cases reported where CMV retinitis has occurred in cases of SLE, described by Haze et al. in 2017[10], who had rhegmatogenous retinal detachment and underwent vitrectomy, Berman *et al*. in 2016[6] describe cases of CMV Pneumonitis in SLE and CMV Encephalitis in SLE.

According to the European League Against Rheumatism (EULAR), every case of Lupus should be screened for HIV, HCV, HBV, and CMV infection before beginning immunosuppressive therapy, including steroids[11]. However, clear guidelines in the management of CMV infections in patients with autoimmune diseases are lacking.

In addition, the potential role of IVIG should be considered for the management of SLE patients with disease flare and concomitant CMV infection; however, the scientific evidence for the efficacy of IVIG as a therapy for SLE manifestations is poor [12,13]

Conclusion

Cytomegalovirus infection, especially colitis, is rare in patients with SLE who are not on immunosuppressive drugs, and numerous molecular and genetic mechanisms can explain the occurrence of such catastrophic atypical infections. Prompt diagnosis is critical to providing the proper treatment, failing which, the complications can prove deadly to the patient. Management of active infection in an immunological condition requiring immunosuppression is quite a challenge, and if done right, it can significantly reduce morbidity and mortality in these patients.

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Conflicts of Interest: None

Consent: Has been obtained from the patient and her daughter prior to preparing the case report.

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