CASE REPORT

EBV colitis with ulcerative colitis: a double whammy

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SUMMARY

We report this case of a 21-year-old immunocompetent man presenting with ulcerative colitis and superimposed Epstein-Barr virus (EBV) colitis. He presented for the first time with symptoms of blood-mixed diarrhoea and raised inflammatory markers. His endoscopic and histological appearances were found to be due to ulcerative colitis for which he was started on standard therapy with intravenous steroids. In spite of this, he continued to be symptomatic and his inflammatory markers continued to rise. A virology screen done showed evidence of previous EBV infection, and in view of poor response to immunosuppression, a superimposed infection was suspected. EBV DNA PCR done on colonic biopsies was found to be positive and the patient was started on intravenous ganciclovir to which he responded well. This case highlights the importance of considering a superimposed infection in patients with poor initial response to steroid therapy in inflammatory bowel disease.

BACKGROUND

Epstein-Barr virus (EBV), a member of herpes virus family, is one of the most common viruses affecting human population worldwide. It is a well-known aetiological agent for infectious mononucleosis, also called glandular fever, which is usually a self-limiting illness. Although EBV had been found in gastrointestinal tissue from patients with inflammatory bowel disease (IBD),^{1 2} EBV infection with gastrointestinal involvement is extremely rare.³ We report the case of a young immunocompetent male patient with first presentation of ulcerative colitis and simultaneous EBV colitis.

CASE PRESENTATION

A 21-year-old immunocompetent Caucasian man presented with 1-week history of being generally unwell with blood-mixed diarrhoea. He was opening his bowels 3–4 times per day passing loose or watery stools with large amount of fresh blood. He also reported having febrile episodes but did not report any abdominal pain, nausea or vomiting. There was no history of recent travel abroad and none of his family members shared his symptoms. He was known to have Asperger's syndrome but other medical history was unremarkable. On clinical examination, he was haemodynamically stable with a normal systemic examination other than some fresh blood noticed on digital rectal examination.

INVESTIGATIONS

Initial blood tests showed raised inflammatory markers with leucocytosis of $14 \times 10^9/L$ (normal up to $11 \times 10^9/L$), C reactive protein (CRP) of 92.5 mg/L (normal <10.0) and erythrocyte sedimentation rate of 30. Renal and liver functions were within normal

limits. Three stool samples for microscopy, culture and clostridium difficile were found to be negative. Plain abdominal radiograph showed no significant abnormality. He underwent a sigmoidoscopy, which showed extensive moderate erythema, mucopurulent exudates and ulceration extending from rectum to proximal sigmoid ([figure 1](#)). The colonic biopsies showed focal active colitis with cryptitis and increased neutrophils in the lamina propria. Given his presentation and endoscopic findings, a diagnosis of ulcerative colitis (UC) was agreed on and he was started on intravenous hydrocortisone 100mg four times a day. After 4 days of therapy, his symptoms improved partially with the bowel frequency going down; however, he kept passing blood in stools and his CRP rose to 108. He also had few spikes of temperature up to 38°C for which a full sepsis screen was done and found to be negative. With the possibility of future treatment with immunomodulators and biologics, full screening workup including viral serology was requested. He was found to be positive for EBV viral capsid antigen (VCA) IgG antibody and nuclear antigen IgG antibody and negative for VCA IgM antibody indicating previous exposure to EBV. He was negative for both cytomegalovirus (CMV) IgG and IgM antibodies on two separate occasions. Other serology results showed previous exposure to varicella-zoster virus but no evidence of HIV, hepatitis B virus or hepatitis C virus. The summary of these results is shown in [table 1](#).

In view of his poor response to intravenous hydrocortisone and spiking temperature, superadded viral infection was suspected. His case was discussed with our consultant virologist who requested further tests on colonic biopsies along with EBV DNA PCR. EBV positive lymphocytes were seen in lamina propria and submucosa on immunohistochemistry and in situ hybridisation ([figure 2](#)). EBV PCR showed 107 320 copies of EBV per millilitre ($\text{Log}=5.03$) with further rise to 169 240 copies/mL ($\text{Log}=5.23$) on repeat test after 5 days. At this point, our patient was still symptomatic with persistently high CRP in spite of being on high-dose steroids for 10 days.

TREATMENT

A decision was made to start him on intravenous ganciclovir at a dose of 5 mg/kg/day and to continue with high-dose steroids.

OUTCOME AND FOLLOW-UP

After 7 days on this combination, the patient improved clinically and his CRP dropped down to 30. His repeat EBV DNA PCR also dropped to 5855 copies/mL ($\text{Log}=3.77$). He was discharged on mesalazine and reducing dose of prednisolone with outpatient clinic follow-up.

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Figure 1 Sigmoidoscopy picture showing extensive moderate erythema, mucopurulent exudates and ulceration extending from the rectum to the proximal sigmoid.

DISCUSSION

IBD is a chronic relapsing and remitting illness of unknown aetiology. Among different hypothesis regarding the cause of IBD, infections with various pathogens including viruses have been documented. EBV is one of these pathogens which may have a role in the pathogenesis of IBD.¹ EBV has been found in colonic biopsies from patients with IBD but its relation to IBD pathogenesis is not clear. Most of the IBD cases where EBV was documented on colonic biopsies were immunocompromised due to treatment with immunosuppressants like azathioprine.⁴ In contrast to such cases, it is extremely rare to have colonic infection by EBV in an immunocompetent patient.^{3,5} Clayton *et al* reported one such case where a 24-year-old man with no known medical illness presented with fever, malaise and rectal bleeding and was required to have right hemicolectomy due to uncontrolled bleeding from caecal ulceration secondary to EBV infection.⁵

Our patient neither had a history of immunosuppressants nor was he known to have IBD. He presented with clinical and endoscopic features of ulcerative colitis but failed to respond to standard therapy for this. His colonic biopsies supported the diagnosis of ulcerative colitis but also documented EBV-positive lymphocytes on immunohistochemistry and in situ hybridisation. As presence of EBV on colonic biopsies is not always pathological, we were unsure if this needed to be treated as EBV colitis. However, rising titres of EBV on PCR was highly suggestive of a pathological role for EBV in his colonic disease. Our virologist therefore recommended antiviral therapy along with high-dose steroids. This produced both a clinical and virological response along with a decrease in inflammatory markers. One of the two possibilities here was that his first presentation with ulcerative colitis (UC) was complicated by reactivation of his latent EBV infection when he was treated with high-dose steroids. The other possibility was that he had a preclinical UC, which became symptomatic with superadded EBV infection that led to his presentation, that is, a synchronous UC and EBV colitis similar to what has been reported previously in a case of CMV colitis.^{6,7}

Table 1 Summary of viral serology

Viral Serology	Result
EBV IgG	Positive
EBV IgM	Negative
CMV IgG	Negative
CMV IgM	Negative
VZV IgG	Positive
VZV IgM	Negative
HIV	Negative
HBV	Negative
HCV	Negative

CMV, cytomegalo virus; EBV, Epstein-Barr virus; HBV, hepatitis B virus; HCV, hepatitis C virus; VZV, varicella-zoster virus.

Figure 2 Epstein-Barr virus positive lymphocytes seen in lamina propria and submucosa on immunohistochemistry and in situ hybridisation.

Learning points

- This case highlights the importance of considering superimposed or simultaneous infections in cases of ulcerative colitis, which fail to respond to standard therapy. Gastroenterologists are generally well aware of superadded CMV infection in ulcerative colitis patients but Epstein-Barr virus (EBV) is less thought of. It is imperative to perform full screening workup including not only CMV and clostridium difficile but also EBV serology in such cases. It also applies to screening workup before starting immunomodulators in these patients.
- Further inputs are needed to explore the role of EBV in the disease presentation of inflammatory bowel disease.
- By sharing this case, we hope to improve clinicians' awareness of such cases, which will lead to better care and outcomes for the patients.

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