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Investigation of Ulcerative Colitis for Herpes Simplex Virus and Cytomegalovirus Genomic Sequences by the Polymerase Chain Reaction

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Dear Editor,

Given the importance of inflammatory bowel disease (IBD) as the unknown etiology and that detection of an infectious agent in patients with ulcerative colitis (UC) might have important implications in treatment and prevention, the authors investigated the prevalence of herpes simplex virus (HSV) and cytomegalovirus (CMV) in patients with UC in comparison with healthy subjects using the polymerase chain reaction (PCR) technique.

Inflammatory Bowel Disease represents a group of idiopathic chronic inflammatory intestinal conditions. Patients with IBD are occasionally hospitalized due to fever, abdominal pain, and diarrhea, which are commonly attributed to an exacerbation of their underlying disease. Ulcerative Colitis is one of the two major types of IBD, along with Crohn's disease (CD). It is a form of IBD that causes inflammation and ulcers in the colon. Unlike CD, which can affect any part of the gastrointestinal tract, UC characteristically involves the large bowel (1-3). Ulcerative Colitis is three times more common than CD. It is slightly more common in females than in males. Furthermore, UC has an incidence of 1 to 20 cases per 100000 individuals per year, and a prevalence of 8 to 246 per 100000 individuals (4). In the United States about one million people are affected by UC (5). It is more common in the Western and Northern hemispheres; the incidence is low in Asia and the Far East. The exact etiology of UC is unknown, but the disease appears to be multifactorial and polygenic; the proposed causes include environmental factors, immune dysfunction and a likely genetic predisposition. In the recent years, cases of IBD associated with herpes virus infections have occasionally been reported (6-9).

Herpes Simplex Virus and CMV are ubiquitous herpes viruses and establish persistent infections in the host. Furthermore, HSV and CMV are transmitted through close personal contact with body fluids, including blood, urine and saliva, while HSV and CMV infections can also occur in immunocompromised patients such as recipients of organ transplants, patients undergoing hemodialysis, patients receiving immunosuppressive drugs, and patients with acquired immunodeficiency syndrome. In IBD patients, herpes viruses have been recognized in colonoscopic biopsy specimens obtained during evaluation and management of IBD or diagnosed after pathologic examination of the colon. However, prospective studies examining prevalence of HSV and CMV genome in patients with IBD in comparison with a control population are limited. Patients with UC are treated with corticosteroids, anti-inflammatory agents, anti-diarrheal agents and rehydration. de Saussure et al. (10) treated three CMV-positive IBD cases with antiviral therapy, and only one patient had remission. Kandiel et al. (11) used antiviral drugs for the treatment of CMV positive colitis, and achieved a remission rate of 67-100%.

During the recent years, a clear association between complicated courses of UC and the presence of herpes viruses has been established. The exact pathogenic role of herpes viruses in these patients remains unclear despite a great number of published reports. Powell et al. (12) first reported the association of CMV with UC in 1961. However, the role of HSV and CMV in UC patients has not been reported in Iran until now, as indicated by the literature search. This is the first study to investigate the prevalence of HSV and CMV in UC patients in Iran. In UC patients we detected HSV DNA in 80% and CMV DNA in 80% of samples. In the healthy control group 10% had HSV DNA and 30% had CMV DNA. There was an association between HSV and CMV DNA presence and occurrence of UC as compared with the control group tissue samples.

Herpes viruses infection in UC patients, especially in those who are immune-compromised by steroid therapy, can produce severe systemic disease and often leads to colectomy, yet coincidental diagnosis of UC and herpes virus colitis has also been reported (13-15). However, the importance of herpes virus, as an exacerbating factor of UC, has been neglected by many clinicians. Polymerase Chain Reaction has emerged as the most sensitive laboratorial method, and immunohistochemistry or in situ hybridization has been reported for diagnosis of viral infection including that with herpes viruses (6, 16-20). The current study suggests that the presence of HSV and CMV in UC tissues and non-malignancy by the PCR method reflect the ability of the virus to infect different colon cells. In the study of Dimitroulia et al. (15) on intestinal tissue, CMV genome was detected in 32.9% of patients with IBD and only in 2.4% of the controls; also a significant association was detected between CMV intestinal infection and either UC or CD, although the association was even stronger for patients with UC. Hommes et al. (21) evaluated the pathogenicity of CMV in patients with IBD; their results showed that CMV causes significant clinical morbidity in patients with IBD. Kishore et al. (16) investigated infection with CMV in patients with IBD; sixty-three patients with IBD (both UC and CD) were selected, and the results showed CMV infection in patients with IBD might be common. These findings have definite clinical significance and therefore should not be ignored. Although our results confirmed the results of Dimitroulia et al. (15), Hommes et al. (21) and Kishore et al. (16) indicating that there is an association between CMV infection and progression of IBD, yet, in other studies, no evidence of a direct association between IBD and CMV infection was found (14, 22) In the study by Yi et al. (14) on the prevalence and risk factors of CMV infection in IBD in Wuhan, central China, 226 patients with IBD (189 UC and 37 patients with CD) were selected; CMV DNA was detected by nested PCR, and no risk factor was found to be significantly correlated with CMV infection in risk factor analysis. Also, Leveque et al. (22) found no relationship between CMV viral load and disease severity in patients with active IBD.

In summary, UC patients have a predisposition to HSV and CMV infections as compared to healthy individuals. Although the results demonstrate a direct molecular evidence to support the association of HSV and CMV with UC, yet the etiological link between UC, HSV and CMV infections needs to be studied.

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