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Clinical Features Of Cytomegalovirus Infection In Patients With Hiv Infection

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Abstract

Relevance. According to WHO, mortality from herpes infection is in second place among viral diseases (15.8%) after hepatitis (35.8%) [1]. Cytomegalovirus (CMV) is an important human pathogen that causes a variety of syndromes, from asymptomatic infections to life-threatening lesions.

Objective: to study the role of cytomegalovirus infection as an etiological factor of colitis in HIV-positive patients.

Materials and methods: The study was conducted on the basis of a specialized clinic for infectious diseases of the Republican AIDS Center, 65 patients were examined. By gender, the patients were distributed as follows: 48 men (73.8%) and 17 women (26.1%), 49 (75.3%) patients aged 18 to 35 years, 16 patients aged 36-60 years (24.6%).

Results of the study and their discussion: The study confirms the role of CMV infection in the occurrence of colitis and ongoing diarrhea in HIV-positive patients. After a course of therapy with Ganciclovir, a decrease in disease activity was noted, stool became less frequent, and during colonoscopy: pronounced positive dynamics in the form of partial closure of ulcerative defects and patency of intestinal strictures. Immunohistochemical study of colon biopsies revealed a significant decrease in the expression of cytomegalovirus.

Conclusions: Thus, CMV infection may be a cause of diarrhea in patients with HIV infection. Detection of CMV infection requires consideration of the issue of prescribing antiviral therapy (Ganciclovir) in combination with ART

Keywords: Cytomegalovirus infection, diarrhea, colitis.

Introduction

Combating the spread of HIV infection is a major public health concern due to the global rise in HIV infection, the significant socioeconomic consequences of the epidemic, the lack of reliable specific prevention, and substantial treatment costs. Herpes infection in an individual with a normal immune system is asymptomatic, but in immunosuppressed individuals, it causes severe, often fatal, diseases [1]. According to WHO data, mortality from herpes infection ranks second (15.8%) among viral diseases, after hepatitis (35.8%) [1]. To date, more than 80 members of the Herpesviridae family have been discovered, of which 8 types are pathogenic to humans. All 8 types are DNA-containing viruses with a uniform morphology that cannot be differentiated by electron microscopy [7]. Cytomegalovirus (CMV) is a significant human pathogen that causes a variety of syndromes, ranging from asymptomatic infection to life-threatening lesions. CMV infection of the gastrointestinal tract is a relatively common manifestation in patients receiving immunosuppressive therapy, HIV-infected individuals, and organ and tissue recipients [5]. However, in some cases, immunocompetent individuals can also develop cytomegalovirus disease with intestinal wall involvement. CMV is a DNA-containing virus of the Herpesviridae family. During replication, CMV exerts a cytopathic effect, leading to the formation of giant cells with typical intranuclear and cytoplasmic inclusions [2]. For example, in the UK [3,4] and the USA, 40-60% of adults from middle and high socioeconomic backgrounds are seropositive, compared to 80% in populations with low socioeconomic status. In developing countries, the prevalence of CMV infection is even higher, affecting 80% of children and nearly the entire adult population [8]. Although CMV is a widespread pathogen and most people are infected with it at some point in their lives, the virus is not highly contagious, and its transmission requires close or intimate contact with infected secretions (e.g., blood, urine, saliva, semen, cervical secretions) [8]. It is believed that in almost half (43-53%) of cases, the source of CMV in adults is infected children, who excrete the virus in their urine and saliva for many years [9]. Therefore, the immunocompetence of the patient's body is of great importance in the pathogenesis of CMV. The groups at

highest risk for CMV infection activation include individuals with suppressed immune systems, especially those with HIV, who often develop a disseminated form of the disease that affects nearly all organs and systems [10].

Materials and methods: The study was conducted at the specialized infectious diseases clinic of the Republican AIDS Center. A total of 65 patients hospitalized at the clinic were examined. The presenting complaints upon admission were weakness, lethargy, lack of appetite, and diarrhea lasting more than one month. The gender distribution of patients was as follows: 48 men (73.8%) and 17 women (26.1%). The age distribution was: 49 patients (75.3%) aged 18 to 35, and 16 patients (24.6%) aged 36 to 60. According to the stage of HIV infection, 52 patients (80%) had stage III HIV infection, and 13 patients (20%) had stage IV-A HIV infection.

Results and Discussion: The study revealed that among patients in stages III and IV-A of HIV infection, 38 (58.4%) had a grade 2 intestinal microbial imbalance, and 20 (10.7%) had a grade 3 imbalance. A grade 1 imbalance was less common, observed in 7 patients (4 in stage III and 3 in stage IV-A of HIV infection). Four patients presented with complaints of frequent, loose stools containing mucus, lasting for more than a month and resistant to therapy. These patients underwent a stool culture, which did not reveal any disruption of the intestinal microbial landscape. According to the literature, cytomegalovirus infection of the gastrointestinal tract is a relatively common manifestation in patients receiving immunosuppressive therapy, HIV-infected individuals, or organ and tissue recipients. However, in some cases, immunocompetent individuals may also develop cytomegalovirus disease with intestinal wall involvement. In particular, recent studies have identified a potential link between CMV-induced colitis and various forms of inflammatory bowel disease. In the 4 patients we examined, rectal mucosa biopsy samples were taken during a colonoscopy. The samples were homogenized. Amplification was performed using real-time polymerase chain reaction (PCR). The result was presented as "number of copies per 10^5 tissue cells." A value of over 100 copies per 10^5 tissue cells was considered significant. Three patients were CMV-positive. Taking into account the presence of neutropenia in the blood tests of this patient population, high paraclinical activity, high levels of fecal calprotectin, severe ulcerative intestinal lesions with the development of therapy-refractory disease, and immunohistochemical data, the condition was classified as constantly recurring colitis complicated by cytomegalovirus infection.

Patients undergoing antiretroviral therapy were prescribed antiviral therapy for the Herpes infection—Ganciclovir at a dose of 10 mg/kg/day intravenously for 10 days. Following the course of therapy, a decrease in disease activity was noted: bowel movements became less frequent, and colonoscopy revealed pronounced positive dynamics, including partial healing of ulcerative defects and the resolution of intestinal strictures. An immunohistochemical examination of colon biopsies after the course of antiviral therapy revealed a significant decrease in cytomegalovirus expression. The CMV antigen, appearing as pale brown granules, was detected in the cytoplasm of isolated stromal cells. Notably, the CMV antigen was absent in glandular cells and the microvascular endothelium.

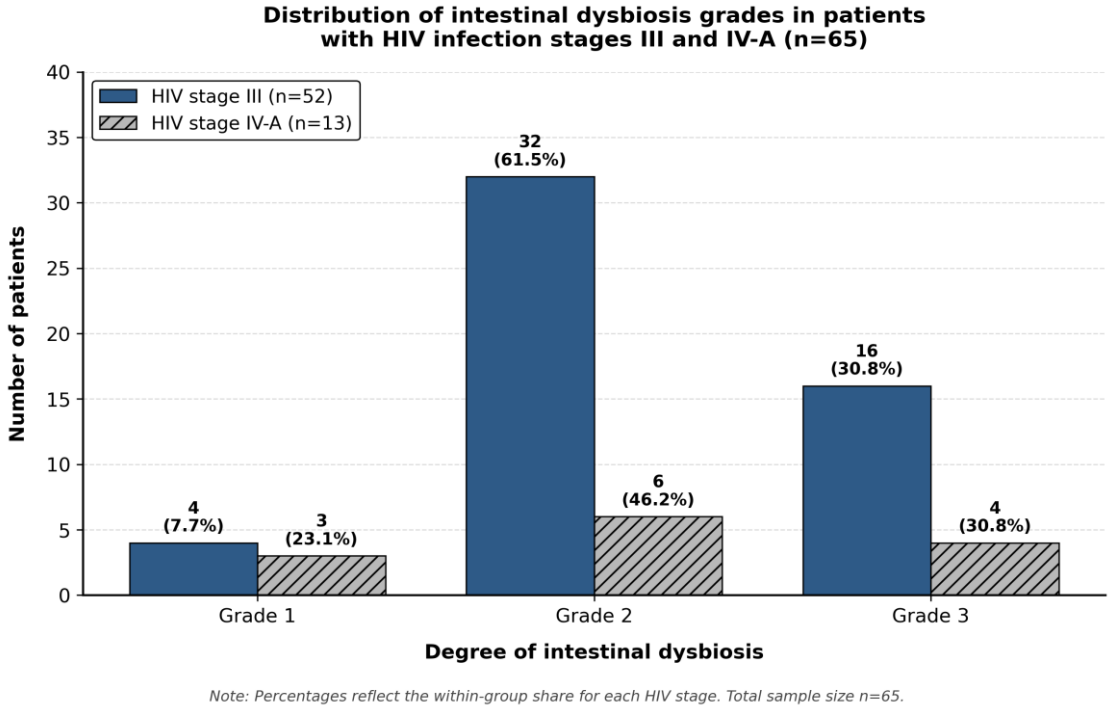

Figure 1. Distribution of intestinal dysbiosis grades in patients with HIV infection stages III and IV-A (n=65).

Note. Percentages reflect the within-group share for each HIV stage. Grade 2 dysbiosis predominates in stage III patients (61.5%), whereas patients with stage IV-A demonstrate a higher combined share of more severe forms (grades 2 and 3 together account for 76.9%).

Table 1. Clinical and laboratory parameters in CMV-positive patients before and after ganciclovir therapy (n=3).

Parameter	Before treatment	After treatment	Dynamics
Stool frequency (per day)	6–8 episodes, loose, with mucus	2–3 episodes, formed	**Marked decrease ↓**
Mucus in stool	Persistent (++/+++)	Sporadic / trace (±)	**Near-complete resolution ↓**
Ulcerative defects on colonoscopy	Multiple, deep ulcerative lesions, therapy-refractory	Partial healing, superficial defects	**Positive dynamics ↓**
Intestinal strictures	Present (refractory)	Resolved / regressed	**Complete regression ↓↓**
CMV antigen expression (IHC)	>100 copies per 10^5 tissue cells; numerous intranuclear and cytoplasmic inclusions	Faint pale-brown granules in isolated stromal cells; absent in glandular cells and microvascular endothelium	**Marked reduction ↓↓**
Faecal calprotectin	Elevated (marker of high paraclinical activity)	Substantially decreased	**Reduced inflammation ↓**
Neutropenia (CBC)	Present	Approaching normal range	**Improvement ↑**
Overall clinical status	Weakness, lethargy, anorexia, diarrhoea lasting >1 month	Appetite restored, condition stabilized	**Clinical remission ↑↑**

Note. Treatment regimen — ganciclovir 10 mg/kg/day intravenously for 10 days, administered against the background of antiretroviral therapy. CMV diagnosis was established in rectal mucosa biopsy specimens by real-time PCR (expressed as copies per 10^5 tissue cells; a value of >100 copies was regarded as significant) and by immunohistochemical (IHC) analysis. After completion of the antiviral course, colonoscopy demonstrated partial healing of ulcerative defects and resolution of intestinal strictures; IHC revealed CMV antigen as pale-brown granules confined to isolated stromal cells, with no expression detected in glandular cells or the microvascular endothelium.

Statistical significance. Owing to the limited sample size (n=3), the dynamics presented in the table are reported on a qualitative basis; positive dynamics were observed across all clinical and morphological parameters. Confirmatory statistical testing (Wilcoxon signed-rank or McNemar test) in larger cohorts is recommended.

Abbreviations: CBC — complete blood count; CMV — cytomegalovirus; HIV — human immunodeficiency virus; IHC — immunohistochemistry; PCR — polymerase chain reaction.

Conclusions

Thus, refractoriness to diarrhea therapy in HIV-infected patients necessitates a search for the reasons for this lack of therapeutic effect, one of which may be cytomegalovirus infection. The identification of clinically significant cytomegalovirus infection in this patient population requires consideration of prescribing antiviral therapy (Ganciclovir) in combination with ART.

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