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CYTOMEGALOVIRUS COLITIS IN INFLAMMATORY BOWEL DISEASE: RISK FACTORS FOR CLINICALLY SIGNIFICANT COLITIS AND COLECTOMY

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ABSTRACT

Introduction: Cytomegalovirus (CMV) is a frequent cause of infection in patients with inflammatory bowel disease (IBD) that has been linked with a poor prognosis. Its diagnosis is currently made by immunohistochemistry staining or polymerase chain reaction (PCR) of intestinal tissue samples. **Material and Methods:** Retrospective study of patients with IBD and confirmed CMV-colitis, diagnosed from January-2010 to June-2019 at the Costa del Sol Hospital. Risk factors associated to clinically significant colitis (CSC) and colectomy were evaluated. **Results:** Thirty patients (median of age 49 years), 29 with ulcerative colitis (UC) and one with Crohn´s disease (CD), were included. Most of our patients were immunocompromised (83,3%) due to the use of immunosuppressive medication, and 56,7% showed a steroid-refractory colitis. In 23 out of 30 patients (75.9%) the established criterion for clinically significant colitis was met. Of all patients with CMV-colitis, 89,3% resolved the infection and 7,1% relapsed. At the end of study follow-up, 5 patients (16,7%) required an emergency or scheduled colectomy. Male gender (p = 0.030) and the severe endoscopic activity (p = 0.032) were risk factors for CSC, while malnutrition was the single risk factor related to colectomy (p = 0,003). **Conclusions:** In our study some patients presented with severe colitis needing antiviral treatment and in others CMV did not seem to have an important prognostic role. Male sex and the endoscopic inflammatory activity were risk factors of CSC. Malnutrition was the only risk factor related to colectomy.

KEYWORDS: Cytomegalovirus, Inflammatory Bowel Disease, Risk Factors, Clinically significant colitis.

INTRODUCTION

Cytomegalovirus (CMV) is a double stranded DNA virus from the *Herpesviridae* family. It causes an infection that is quite common in the general population and usually leads to an asymptomatic or mild upper respiratory tract infection in immunocompetent patients. After the primary infection, the virus remains latent on hematopoietic progenitor cells and myeloid cells (monocytes CD14+)[1-3] leading to a chronic latent infection, which is controlled by the immune system.[4] Therefore, throughout the life of the patient, under any circumstance that destabilizes this balance, the virus could be reactivated. In immunocompromised patients such as patients with primary or secondary immunodeficiencies (infection by human immunodeficiency virus or hematological cancers), patients treated with immunosuppressive therapy (transplanted, immunomodulators, biological treatments ...), hemodialysis or premature newborns, the control of infection by the immune system may not be satisfactory and precipitate a new peak of viral replication[5]. In these patients the infection is usually clinically significant and with end-organ damage, mainly lungs, retina or colon. Colonic involvement rarely occurs in immunocompetent patients, but it may be seen in immunosuppressed patients or in the context of an exacerbation of inflammatory bowel disease (IBD).

The prevalence of CMV infection in patients with IBD is similar to the prevalence in the general population, which is described in 58,9-83%.[6-7] In Spain, based upon positive IgG serology, the prevalence has been described up to 61-76% of healthy controls and patients with IBD[8]. However, it is known that patients with IBD are a population at risk of CMV reactivation. In patients with IBD, CMV prevalence has been described up to 32,9-36%,[9-11] although this percentage is reduced to 8,3% when clinically relevant disease is considered.[12]

According to the ECCO consensus (European Crohn´s and Colitis Organization), there is currently no optimal

detection method for the diagnosis of clinically relevant CMV infection. Currently, the most recommended diagnostic tests include anatomopathological and immunohistochemistry study of intestinal biopsy, using monoclonal antibodies against an early CMV antigen or tissue CMV-DNA detection by polymerase chain reaction (PCR) with a cut-off level to be considered as significant >250copies/mg.[13] The main problem is, that to obtain a diagnosis we need a colonoscopy, with a delay of 3-5 days to obtain the confirmation of the infection and the beginning of the antiviral therapy.[11]

In the last years, due to the need to accelerate this process and achieve an early diagnosis, several studies have been promoted to find a faster and non-invasively diagnosis of the CMV infection in these patients. With this purpose, blood antigenemia based on monoclonal antibodies to detect the early pp65 protein of the tegument and quantitative PCR of serum CMV-DNA in blood have been used. However, the problem with these techniques is their low diagnostic sensitivity in patients with IBD (39-44% and 47-60% respectively), which means that currently they cannot substitute yet the pathological and immunohistochemical study or tissue CMV-PCR.[14-16]

On the other hand, some studies have attempted to identify risk factors for CMV infection by combining a series of clinical, endoscopic and pharmacological parameters. Nowacki, et al. published in 2018 a retrospective analysis of clinical histories of patients with IBD, identifying 6 risk factors for CMV-colitis: the duration of the disease, endoscopic Mayo Subscore, dose of corticosteroids, use of an anti-TNF alpha and the extension of the ulcerative colitis (UC). Subsequently, based on these predictors, they developed a risk score for CMV-colitis in patients with UC, with a negative predictive value (NPV) of 90% and positive predictive value (PPV) of 72%, proving to be a good score to rule out CMV.[17] The advantage of this score is that the items are easily found in any clinical history of a patient with IBD and its result can be obtained immediately after the colonoscopy, at the beginning of the diagnostic process. As an inconvenience, it is not possible to identify patients at greatest risk of clinically significant disease, which are those who will benefit most from an early treatment. Attempts have also been made to identify endoscopic features that make CMV infection more likely. The presence of deep ulcers, irregular or with a cobbled appearance is more frequent in patients with CMV-colitis than those without it (60% versus 20%. P <0.05), with a described 52% diagnostic sensitivity.[16,18]

In this context, our study is carried out with the aim to register the cases of infection/reactivation of CMV in patients with IBD in our hospital and assessing the possible risk factors that make this reactivation more likely, in order to identify and treat these patients as early as possible and reduce complications, as well as to prevent, as far as possible, future reactivations.

MATERIAL AND METHODS

We carried out a retrospective study in all patients with IBD who had confirmed CMV infection/reactivation in our institution from January-2010 to June-2019. All patients with Crohn´s disease (CD) or ulcerative colitis (UC) in whom CMV infection/reactivation was diagnosed by histopathological and immunohistochemical study and/or CMV-PCR of colon tissue samples were included. Patients without evidence of IBD were excluded.

Demographic data such as age at the time of diagnosis, gender and comorbidities (arterial hypertension, diabetes mellitus, hypercholesterolemia, chronic lung disease, chronic heart disease, chronic liver disease and chronic kidney disease) were recorded as independent variables. As a dependent variable we considered baseline immunosuppression status in patients with a prior HIV infection, organ transplantation, known hematological disease or drug-induced immunosuppression whenever on stable treatment with immunomodulators or biological drugs or with corticosteroids at a dose greater than 20mg/day for the last 2 weeks prior to diagnosis. The diagnostic methods by which CMV infection was established included blood CMV-PCR (threshold ≥1500 copies/mL), tissue pathological exam (hematoxylin-eosin staining and specific immunohistochemical study) and CMV-PCR in tissue samples (threshold level ≥250 copies/mg). We also recorded the degree of endoscopic inflammatory activity (mild, moderate or severe) according to the Mayo Clinic Disease Activity Index endoscopic subscore, the extension of the disease by means of Montreal classification of IBD, serum levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) as well as fecal calprotectin at diagnosis. Nutritional status was also recorded using the body mass index (BMI). Those with confirmed *Clostridioides difficile* infection were excluded from the analysis. Finally, the antiviral treatment used (Ganciclovir, Valganciclovir or a combination of both) and the duration of the antiviral therapy were valued as well as the clinical outcome of the infection, defined as resolution, persistence or recurrence of CMV infection. With this information, the patient was classified into clinically significant colitis (CSC) when he received antiviral treatment and non-clinically significant colitis when the CMV infection did not receive antiviral treatment. This decision was made by the doctor in charge in each case. Colectomy rate at 6 and 12 months was also evaluated.

For the statistical analysis we used measures of central tendency: median and interquartile range for quantitative variables and frequency distribution for qualitative variables. For the comparison of subgroups of prognostic variables, Mann-Whitney U-test was used for quantitative variables while Fisher's exact test was used for qualitative variables. Statistical significance was established at p <0.05.

RESULTS

Baseline characteristics of the study population

62 patients were diagnosed of CMV-colitis from January 2010 to June 2019. 32 out of 62 were excluded as CMV-colitis occurred in the absence of IBD. Of the remaining 30 patients with CMV-colitis and IBD, twenty-nine had UC for one with CD. Twenty patients were men (66,7%) and 10 women (33,3%), with a median age of 49 years (22-77 years). Baseline characteristics of our patients are described in **Table 1**.

Disease status at diagnosis of CMV-colitis

At the time of the diagnosis 25 patients (83,3%) were drug-induced immunocompromised: 24% with thiopurines immunomodulators, 32% with biological treatment, 12% with combined immunomodulator-biologics and 32% with high doses of corticosteroids. 40% of those patients on biological therapy received infliximab or adalimumab (2 patients with infliximab and another 2 patients with adalimumab), while another 2 patients (20%) were on vedolizumab. In 5 patients (16,7%) CMV-colitis occurred at the diagnosis of the UC. At least half of the patients (56,7%) were receiving corticosteroid treatment at the moment of the diagnosis. Six of them with a dose of corticosteroids ≥20mg/day (20%) and eleven patients with a dose of corticosteroids ≥40mg/day (36,7%). In 3 of those patients, CMV-colitis was cyclosporine-refractory.

Clinical presentation of CMV-colitis was severe in 10 patients (33,3%), moderate in 17 (56,7%) and mild in 3 patients (10%). In the cases with UC, the extent at the presentation was pancolitis in 15 patients (51,7%), left-sided colitis in 11 (37,9%) and proctitis in 3 patients (10,3%). For the patient with CD the disease involved the colon.

Diagnosis and course of the disease

In all patients the diagnosis was stablished by colon biopsies. In 53,3% of the patients the diagnosis was based upon typical findings by hematoxylin-eosin and immunohistochemistry staining for CMV. In the remaining 46,7%, the histological study was non-conclusive and the tissue CMV-PCR was done resulting positive, with a median of 11.154 copies/mg (IQR: 788-386.819 copies/mg).

Within the analytical inflammatory parameters, we observed a mean CRP of 8,57mg/dL (range: 0,02-339,80), a mean ESR of 3,5mg/dL (range: 3-4) and a mean fecal calprotectin of 423ug/g (range: 35-3.690). Nineteen out of 30 patients were nutritionally assessed. Of them, the median BMI was 24 (range: 18-33). We observed malnutrition in 5 patients out of 19, two with moderate malnutrition (10,5%) and three with severe malnutrition (15,8%).

With respect to the antiviral treatment used, only 23 patients received antivirals (75,9%). 8 of them (26,7%) were treated with consecutive intravenous Ganciclovir and thereafter per-oral Valganciclovir, 10 with Valganciclovir (34,5%) and 1 patient just with Ganciclovir (3,4%).

The outcome was satisfactory in the majority of cases (89,3%), 2 patients subsequently reactivated CMV (7.1%), and in 1 patient CMV-colitis persisted despite several courses of treatment with Ganciclovir, Valganciclovir and even Foscarnet. Confirmation of CMV infection resolution was stablished in 67,9% of the cases (19 patients) by tissue pathological and microbiological studies, while in the remaining 32,1% CMV infection resolution was considered after a favorable clinical outcome. Fourteen patients (46,4%) required a change in the baseline maintenance treatment, 9 of them at 6 months after the acute episode and 5 at 12 months. At the six months outcome check-up, 3 patients (10,7%) required a colectomy, two of them during the acute episode due to the development of megacolon and the other one during the next 12 months after the acute episode.

Analysis of risk factors

We analyzed suitable risk factors that may influence in the course of CMV-colitis. In our study, male sex is a risk factor for presenting clinically significant CMV-colitis ($p = 0,030$). Even though previous immunosuppression state was more prevalent in CSC patients (79,2% of patients with previous immunosuppression for 60% of those without it), this difference did not reach statistical significance ($p = 0,569$). Similarly, no relevant differences were observed regarding the type of baseline treatment at the time of diagnosis of CMV-colitis nor presence of refractory disease to corticosteroids.

Within the diagnostic tests, those patients with severe endoscopic inflammatory activity were associated with a CSC ($p = 0,032$). In our patients, we observed that the higher the endoscopic inflammatory activity, the higher the risk for CSC, as shows that colitis was clinically significant in 90% of severe colitis, 76,5% in those with moderate colitis and none of those with a mild degree of inflammatory activity. Regarding the extension of the disease, no relevant differences were observed between the different locations.

With respect to the possible relationship between mucosal CMV viral load and CSC, even by establishing a high cut-off level of 2.000 copies/mg, we did not observe that there was a statistically significant difference in CSC risk between those with a high (≥2.000 copies/mg) or low viral load ($p = 0,152$). Moreover, no differences were observed in laboratory parameters of inflammation (CRP, ESR or fecal Calprotectin). The analysis of the risk factors is described in **Table 2**.

With respect to risk factors for colectomy, we observed that the most relevant risk factor was the nutritional

status. In 3 patients with severe malnutrition all of them required a colectomy (p = 0,003). Both the extent of the disease and the severity of the colitis at diagnosis showed a trend for higher colectomy risk, but not reaching statistically significant difference. 26,7% of patients with an extensive colitis required a colectomy for only 9,1% of those with left-sided colitis and no one with proctitis (p = 0,550). The 20% of patients with severe colitis required a colectomy, for the 17,6% of those with a moderate activity and no one with mild disease (p = 0,278). Plasmatic levels of CRP or fecal calprotectin levels were either associated to a higher statistical risk of colectomy (p = 0,219 and p = 0,245 respectively). Finally, no relationship was demonstrated between prior immunosuppression status and risk of colectomy or baseline treatment at the time of diagnosis, corticosteroid refractoriness, corticosteroid doses or tissue viral load. The analysis of the colectomy risk factors is summarized in **Table 3**.

Table 1: Demographic characteristics of the patients included in the sample.

	Frequency	Percentage
Sex		
Male	20	66,7%
Woman	10	33,3%
Arterial hypertension	4	13,3%
Diabetes	3	10,0%
Dyslipemia	4	13,3%
Chronic lung disease	1	3,3%
Heart disease	1	3,3%
Chronic kidney disease	1	3,3%
Chronic liver disease	1	3,3%
Previous immunosuppression	24	80%

Table 2: Risk factors for presenting clinically significant colitis.

	Cinically significant colitis	Subclinical reactivation / infection	P value
Sex			
Male	17 (89,5%)	2 (10,5%)	0,030
Woman	5 (50%)	5 (50%)	
Previous immunosuppression status			
No	3 (60%)	2 (40%)	
Yes	19 (79,2%)	5 (20,8%)	0,056
Maintenance treatment			
5ASA	5 (62,5%)	3 (37,5%)	
Immunosuppressor	5 (83,3%)	1 (16,7%)	
Biological treatment	7 (87,5%)	1 (12,5%)	
Combined	2 (66,7%)	1 (33,3%)	0,078
No treatment	3 (75%)	1 (25%)	
Refractory to corticosteroids	13 (76,5%)	4 (23,5%)	1,000
Rescue with cyclosporine	3 (100%)	0 (0%)	0,550
Endoscopy Activity index			
Leve	0 (0%)	2 (100%)	
Moderada	13 (76,5%)	4 (23,5%)	0,032
Grave	9 (90%)	1 (10%)	
Extent of the disease			
Proctitis	2 (66,7%)	1 (33,3%)	
Left	7 (70%)	3 (30%)	0,802
Pancolitis	12 (80%)	3 (20%)	
Viral load			
<2.000 copies/mg	3 (60%)	2 (40%)	0,150
≥2.000 copies/mg	7 (100%)	0 (0%)	
Nutricional status			
Without nutritional risk	11 (84,6%)	2 (15,4%)	
Moderate malnutrition	2 (100%)	0 (0%)	0,498
Severe malnutrition	3 (100%)	0 (0%)	

Table 3: Risk factors of ending up needing a colectomy.

	Colectomy	Surgery free evolution	P value
Sex			
Male	4 (20%)	16 (80%)	0,640
Woman	9 (90%)	1 (10%)	
Previous immunosuppression status			
No	1 (16,7%)	5 (83,3%)	
Yes	4 (16,7%)	20 (83,3%)	1,000
Maintenance treatment			
5ASA	0 (0%)	8 (100%)	
Immunosuppressor	0 (0%)	6 (100%)	
Biological treatment	3 (37,5%)	5 (62,5%)	
Combined	0 (0%)	3 (100%)	0,045
No treatment	2 (40%)	3 (60%)	
Refractory to corticosteroids	2 (11,8%)	5 (88,2%)	0,628
Rescue with cyclosporine	2 (66,7%)	1 (33,3%)	0,433
Endoscopy Activity index			
Leve	0 (0%)	3 (100%)	
Moderada	3 (17,6%)	14 (82,3%)	0,055
Grave	2 (20%)	8 (80%)	
Extent of the disease			
Proctitis	0 (0%)	3 (100%)	
Left	1 (9,1%)	10 (90,9%)	0,278
Pancolitis	4 (26,7%)	11 (73,3%)	
Viral load			
<2.000 copies/mg	1 (20%)	4 (80%)	1,000
≥2.000 copies/mg	1 (14,3%)	6 (85,7%)	
Nutricional status			
Without nutritional risk	1 (7,1%)	13 (92,9%)	
Moderate malnutrition	1 (50%)	1 (50%)	0,003
Severe malnutrition	3 (100%)	0 (0%)	

DISCUSSION

In our study, a heterogeneous distribution of CMV infection was observed. In some cases, CMV was associated with a serious disease, with the need for rescue treatments or even a colectomy, while in other cases the infection seemed to have no relevance in the course of the disease and it was rather the control of the IBD flare-up that determined the patient's clinical outcome. In the last years, this topic has been widely debated. Some authors argue that CMV is frequently present in patients with IBD but it does not have a clear role in the course of the disease or in the response to treatments, so it does not always need to be treated.[9-10,19-22] In the study by Criscouli et al. they prospectively collected 42 patients with IBD that were hospitalized and observed that 33% of the patients with a corticosteroids refractory colitis had CMV in the colon specimens and only the 10% of the patients with a good response to corticosteroids had the CMV. In this study only 3 patients with corticosteroid-refractory colitis and one with a good response to corticosteroids were treated with antivirals, with no clinical differences observed between treated and untreated patients.[10] In a more recent study, involving 110 patients retrospectively, that were hospitalized for IBD with presence of CMV infection diagnosed by PCR in blood or tissue, only 68% of patients received antiviral treatment and no differences were observed between treated and untreated patients in terms of severity, clinical response, CRP levels, hospital stay or colectomy rate in the first 3 months after admission.[22] Finally, it has also been observed that, during treatment with immunomodulators, the detection of slight replication peaks in the blood are frequent without any clinical relevance.[19] That is why the research of CMV infection is not routinely recommended in this context and only if the patient has a corticosteroid-refractory colitis or a poor clinical course.[13]

In other studies, and with a tendency in recent years towards this position, it is argued that CMV have a real role as a poor prognostic factor in IBD with worse long-term outcomes. It has been seen that in the context of moderate-severe colitis, the presence of CMV leads to an increased risk of presenting corticosteroid-refractory colitis,[11-12, 23-24] a lower response rate to Infliximab,[25] as well as an increased risk of colectomy in the short or long term.[12,15,24,26] The prospective study by Kim et al, with 72 patients, of whom 31 had CMV infection diagnosed by positive IgM serology or positive histological study, showed a lower clinical remission rate ($p = 0,048$) and a higher accumulated rate of colectomy ($p = 0,025$)[26] in patients with positive CMV with respect to those without CMV. Recently, Schenk et al. studied

prospectively 108 patients with corticosteroid-refractory colitis and exhibited a shorter time to colectomy in the group with positive CMV-PCR in tissue, compared to those with negative CMV, with an average of 501 days until colectomy in the CMV positive group versus 958 days in the CMV negative group (p <0,001).[24]

When analyzing long-term follow-up, it has also been seen that treatment with Ganciclovir seems to increase the rate of CMV clearance in tissue and it is associated with a better outcome free of surgery.[11,23,26-29] In addition, after the acute episode, patients have a greater predisposition to develop a state of corticosteroid-dependency, requiring a change in the maintenance treatment, with a higher risk in those who have not been treated with antivirals.[26-27]

The main problem of all these studies is their heterogeneity, including patients with both CD and UC, with different treatments at the time of CMV diagnosis, different clinical presentation and different ways of diagnosing CMV. Furthermore, these studies include a small number of patients and many of them are retrospective. There are also no differences between acute CMV infection or its reactivation, which could perhaps explain the different outcomes of these patients. In our study, this differentiation was not performed either, since IgG serology for CMV is not routinely determined and the previous situation of our patients was not known.

Regarding the risk factors for clinically significant CMV infection, we have observed, in agreement with previous studies, that male sex and the degree of endoscopic activity constitute a risk factor. We also observed, although not statistically significant, an increased risk in the context of corticosteroid treatment at doses ≥40mg/day.[12,17,20-21,23,30] Leveque et al. studied retrospectively 72 specimens from the colon in patients with IBD and observed that patients with positive CMV-PCR in colon biopsies, were older (p = 0,047), predominantly males (RR 4,48) and more frequently treated with corticosteroids (RR 3,2) or azathioprine (RR 3,17). They also observed that the lesions during colonoscopy were usually more extensive and usually more severe in these patients (RR 3.3)[20] Roblin et al, published another study, with 42 hospitalized patients with moderate-severe colitis on intravenous corticosteroid treatment, suggesting that patients with positive CMV in colon biopsies developed more frequently refractoriness to corticosteroids. In this study, samples were taken from both healthy and affected colon and it was observed that in patients with positive CMV, the biopsies from the healthy mucosa did not show CMV in the tissue study, suggesting that the damage caused by the activity of the IBD also had a role in predisposing for CMV superinfection or reactivation at this level.[23]

Patients´ immunosuppression status, although not statistically significant in our study, also seems to have a role in the acute CMV infection. There are multiple studies that link immunomodulatory treatment with CMV infection or reactivation.[17,20,31-32] A recent metanalysis published in 2017 showed that both corticosteroids or azathioprine treatment, are risk factors for CMV reactivation, with an OR of 2,05 (95% CI 1,40-2,99) and 1,56 (95% CI 1,01-2,39) respectively. Anti-TNF treatment did not show an increased risk of CMV reactivation (OR of 1,44-95% CI 0,93-2,24)[32] However, despite of the frequent use of these drugs, IBD patients do not have a clear systemic immunosuppression that predisposes them to systemic reactivation of CMV, which is usually presented as a colitis. This is why the predisposition that may trigger immunomodulatory treatment and its relationship with the colonic mucosa is still a matter under study. Dimitroulia et al. prospectively assayed blood and tissue CMV-PCR levels in patients with IBD and healthy controls, and observed that colonic CMV-PCR was positive much more frequently than in blood, which suggested that there was an alteration of the immune response at the mucosa and not a systemic immune alteration.[9] This is also the reason why diagnostic blood tests do not usually have a good sensitivity for the diagnosis of CMV reactivation in IBD.[14] Furthermore, in a meta-analysis of databases of genome wide association studies (GWAS), they observed several loci involved in both UC and CD, related to the interaction of the host with bacteria. Mainly locis related to the production of IL17 (NOD2 and the TNFRSF18 receptor) and to macrophages (NOD2, IL10 and CARD9). They concluded that perhaps in IBD there is an alteration in the relationship of the immune response, both innate and adaptive, with microorganisms both at the epithelial cells and in the intestinal lumen, leading to a pathological relationship instead of a symbiosis with intestinal microbiota.[33] This could explain that under certain circumstances (active colitis and/or by treatments used to control it) the relationship with the CMV in the bowel changes and develops its reactivation.

Hence it is possible to think that the greater load of CMV in tissue the more severe colitis. In our study we observed that patients with a high viral load in tissue (≥2.000 copies/mg) had a greater tendency to have clinically significant colitis, although it did not reach statistical significance, probably due to the small sample size. In the study of Clos-Parals et al, they evaluated the number of viral inclusions by immunohistochemistry in patients with UC and CMV reactivation and found that in patients who finally required a colectomy had more than 2 positive cells/biopsy.[34]

Finally, regarding the risk of colectomy after CMV colitis, we only observed malnutrition as a risk factor in our study. Generally, in IBD most of the attention for nutrition has been for CD, although in recent years an increase in the malnutrition rate of 67% has been also observed in UC patients who finally required surgery. It has been argued that this may be related to the implementation of biological treatments, which in non-

responders lengthen the time to colectomy and that the nutritional status of the patients deteriorates progressively.[35] Little is known about preoperative malnutrition in the context of UC with acute CMV infection, although it has been observed that both sarcopenia and hypoalbuminemia are related to a worse outcome of patients with IBD, as well as an increased risk of complications after colon surgery.[36-38] In the study by Zhang et al. where 99 patients with UC, 108 with CD and 60 controls were included, it was observed that during the outbreak of the IBD, changes in body composition (skeletal muscle area and skeletal muscle index) and sarcopenia were related to the activity of the disease, both in UC and CD. So that, those patients with greater inflammatory activity had a higher prevalence of sarcopenia and a lower skeletal muscle density (p <0,001) as well as an increased risk of colectomy.[35] Furthermore, sarcopenia and preoperative hypoalbuminemia are associated with an increased risk of complications after abdominal surgery: postoperative infections and sepsis, longer hospital stay, higher rate of deep vein thrombosis, as well as a higher risk of admission to the critical care unit and a higher mortality 30 days after surgery, with maximum significance in patients younger than 40 years.[37-38]

Among the limitations of our study, the small size of the sample does not allow to draw definitive conclusions and more studies are needed in this regard. Our study is also retrospective and the classification of the patient in CMV infection with clinical relevance or not, was determined by the physician on charge at the time of diagnosis according to the severity of the colitis, including as significant those patients who had been treated with antivirals for the CMV. It was not possible to differentiate between acute infection or reactivation, since there was no prior CMV serology and the baseline situation of CMV infection in our patients was unknown.

CONCLUSIONS

We can conclude that the distribution of the CMV-colitis in our population was heterogeneous. Some patients presented with severe colitis needing antiviral treatment and in others CMV did not seem to have an important prognostic role and it was the control of the ulcerative colitis which determined the outcome of the patient. Male sex and endoscopic inflammatory activity at the time of the acute CMV infection are risk factors for CSC and malnutrition was the only risk factor for colectomy in these patients.

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