Ulcerative colitis or cytomegalovirus colitis in a patient with chronic kidney disease on hemodialysis: a diagnostic challenge

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ABSTRACT

Ulcerative colitis (UC) is a chronic inflammatory bowel disorder affecting the colon and rectum with pathogenesis associated with immune disorders and immunosuppression-based treatment. The immune system of patients on hemodialysis (HD) is suppressed by the uremic environment and the use of immunosuppressives drugs can lead to opportunistic infections such as cytomegalovirus (CMV). CMV infection can lead to relapse or alter the course of UC. This article reports the case of a 42-year-old male patient with chronic kidney disease (CKD) with no defined etiology, in HD for 6 years, without any clinical intercurrence until then, who presented with severe pancolitis, with initial endoscopic and histological diagnosis of UC. He evolved refractory to clinical treatment, being submitted to total colectomy and ileostomy. The microscopic analysis of the surgical specimen revealed in addition to a chronic inflammatory process the presence of atypical endothelial cells suggestive of CMV infection, confirmed by immunohistochemistry. There was a clinical improvement after treatment with ganciclovir. The findings of this patient emphasize the importance of considering the possibility of UC and CMV colitis as a differential diagnosis in patients with CKD in HD who present with fever and bloody diarrhea, especially in those who do not respond to the initial clinical treatment.

Keywords: ulcerative colitis; cytomegalovirus; chronic kidney disease; colectomy.

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INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory bowel disorder that primarily affects the colon and rectum and has pathogenesis associated with immunological disorders. The clinical picture of individuals with UC includes abdominal pain, diarrhea with blood, urgency and tenesmus and the clinical evolution is dependent on the disease activity[1].

Individuals with end-stage renal disease (ESRD) are rarely diagnosed with UC. The immunological suppression caused by the uremic environment could make them less susceptible to developing an association between these diseases[1]. This association, especially in those who are refractory to the clinical treatment of UC, can favor the emergence of opportunistic infections, such as the infection caused by the cytomegalovirus (CMV)[2]. On the other hand, differentiating between an outbreak of UC and an episode of true CMV colitis is a challenge in clinical practice[3].

The present paper aims to report a case of a patient with CKD undergoing hemodialysis therapy with an initial diagnosis of UC and subsequent diagnosis of colitis caused by CMV. Its importance is due to the rare description of these diseases association in the literature in patients with CKD, as well as the severity of the opening clinical condition.

CASE REPORT

Male, brown, 42-year-old patient with chronic kidney disease (CKD) undergoing hemodialysis (HD) for 6 years, with no defined etiology, admitted to our hospital due to persistent fever and bloody diarrhea that started three days before admission. The patient had been diagnosed with CKD six years earlier, having entered dialysis therapy at diagnosis. It evolved during this period without clinical complications, until the current situation. He was initially treated for a probable intestinal infection with oral antibiotic therapy (ciprofloxacin and metronidazole) and albendazole. After three days of taking the medications, he persisted with fever and worsening of the diarrheal condition, in addition to signs of septicemia, being transferred to an intensive care unit where blood and stool samples were collected for cultures and the antibiotic was changed to piperacillin-tazobactam.

The results of blood cultures and stool cultures were negative, as well as three samples of the parasitological examination of feces. Due to the persistence of diarrhea and clinical worsening, he underwent colonoscopy with characteristic findings of moderately active UR, pancolitis (Figure 1), whose biopsy specimens showed severe acute erosive chronic proctitis and cryptic microabscesses.

Faced with the endoscopic diagnosis of UC, he started using corticosteroids (intravenous) and mesalazine (oral and rectal), without clinical improvement, maintaining about 20 daily evacuations. Azathioprine was added, also without response. Due to pancolitis refractory to clinical management, 36 days after admission, he underwent surgical treatment with total colectomy and ileostomy.

Microscopic analysis of the surgical specimen revealed an acute chronic inflammatory process associated with atypia in endothelial cells suggestive of viral infection by cytomegalovirus (CMV) and immunohistochemical analysis confirmed the viral infection (Figure 2). Serological examination for CMV was performed, detecting positive IgG and negative IgM. Quantitative blood testing for CMV by PCR (polymerase chain reaction) revealed 180 copies/mL of the virus. He used the antiviral drug ganciclovir intravenously, evolving with an improvement in his clinical condition. During the entire hospital stay, he presented progressive weight loss of more than 20 kg, characterizing severe malnutrition. He started a total parenteral diet that reached 58% of his nutritional needs and later a mixed diet (parenteral plus oral) plus nutritional supplementation, with good clinical and nutritional evolution.

DISCUSSION

We report a clinical case of a 42-year-old male patient with CKD of no defined etiology, undergoing dialysis for 06 years, without any clinical complications so far, who presented a severe and refractory condition of pancolitis, receiving an initial diagnosis of UC. The UC is a chronic and idiopathic inflammatory bowel disease (IBD) characterized by periods of relapse and remission, which involves the rectum mucosa in 95% of cases and can be extended continuously and circumferentially to proximal segments of the colon. The peak age for its development is between 30 and 40 years old and there is no gender predominance. The incidence rate

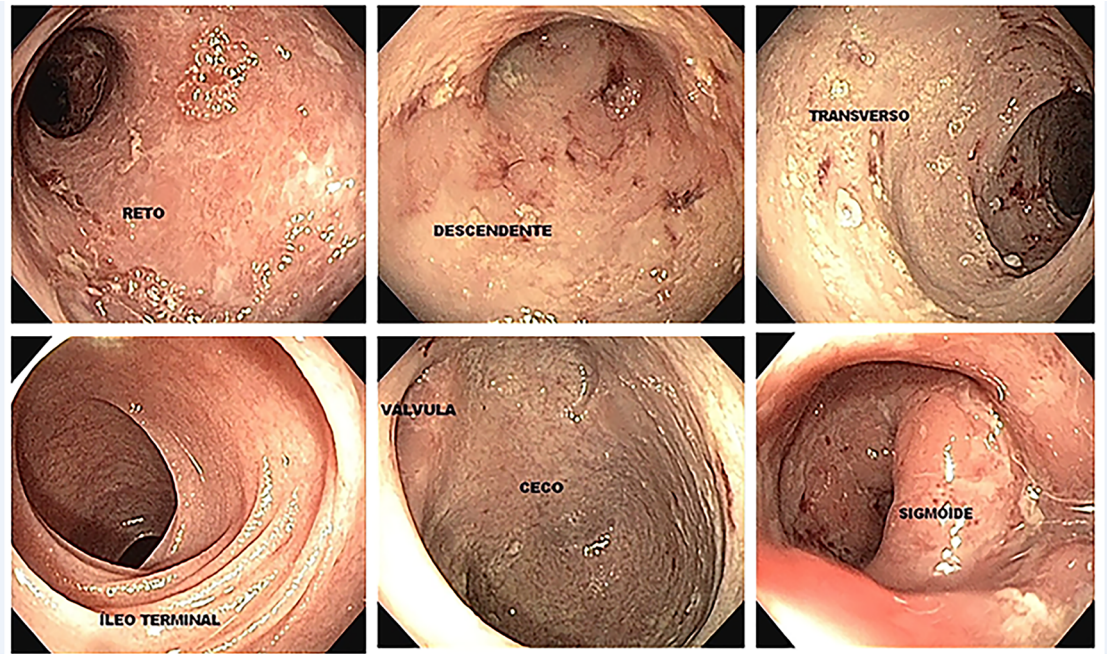

Figure 1 videocolonoscopy images showing enanthematous and edematous mucosa of the colon and rectum, with increased granularity and decreased visualization of submucosal vascularization. Presence of shallow ulcerations covered by fibrin and reduced haustraction, giving a tubular appearance to the colon.

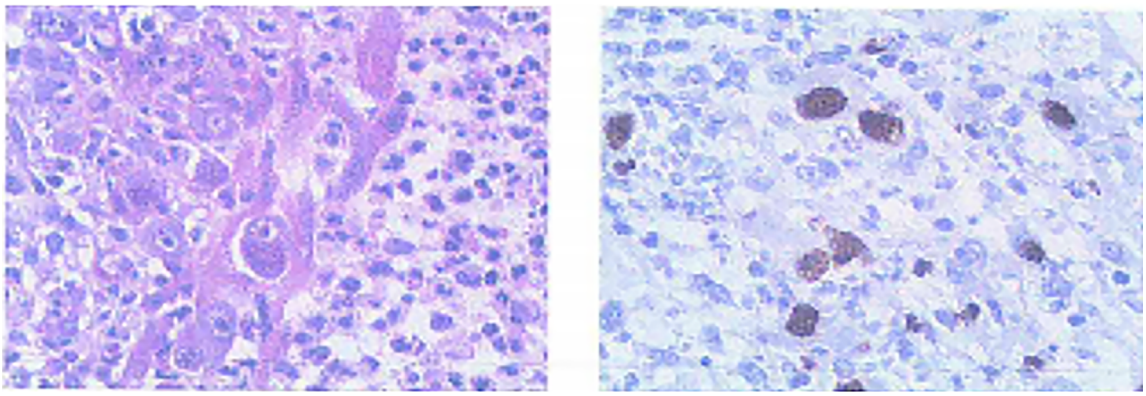

Figure 2 Positive immunohistochemistry for cytomegalovirus in colon specimens.

of UC can range from 0,5 to 31,5 per 100.000 people each year, depending on the studied population. Given the observed incidence profile, it is important to consider the influence of environmental factors on the course of the disease[4,5].

The signs and symptoms of UC are diarrhea, resulting from colonic dysfunction in relation to the absorption of water and minerals, with severity depending on the course of the disease, mucous bloody stools, tenesmus, abdominal pain, fever, fatigue, anorexia and body mass loss[6]. The nutritional status of the patient is directly influenced by the clinical condition of the disease[7]. The diagnosis of UC is based on clinical, laboratory, endoscopic and histological characteristics[8].

UC is an intestinal disorder that is rarely present in patients with dialysis CKD[9,10]. The immune system of individuals undergoing hemodialysis is constantly affected by the uremic environment. Thus, as the immune response of the dialysis population is attenuated, the UC activity is potentially suppressed, which, in turn, may justify the unusual association between these diseases[11].

In this context, when CKD is associated with diseases whose treatment consists of immunosuppressive therapies, such as UC, it makes the individual more susceptible to the development of opportunistic infections, since the immune response will be imminently compromised. CMV infection is an example of an opportunistic infection that can arise[1]. Although there is a high prevalence of CMV in CKD patients, CMV disease in these patients is rarely reported[12].

The first report of the association between CMV and UC was described in 1961 by Powell *et al* [13]. Since then, the role of CMV in these patients remains uncertain, in the sense that viral infection may exacerbate established IBD or whether it is a result of reactivation as a result of IBD activity and its treatment[14]. The prevalence of CMV in IBD ranges from 1,5 to 4,5%. Among patients with IBD, CMV is found more commonly in UC than in Crohn's disease, especially during episodes of severe acute colitis, with a prevalence of up to 40%[15].

CMV reactivation is frequent in UC severe or resistant to corticosteroid therapy. Increased cell proliferation in inflamed and ulcerated colonic tissue with active UC exerts a positive tropism for CMV, attracting it to the site; the reduction in the activity of "natural killer" T lymphocytes in individuals with UC, as well as the use of immunosuppressive drugs, appear as crucial factors in the process of reactivation of CMV infection in patients with UC[14].

Primary CMV infection in an immunocompetent host has an asymptomatic course, however, in immunocompromised patients, such as those with HIV or chronic diseases, transplanted, undergoing chemotherapy or immunosuppressive therapies, it can progress with severe systemic manifestations affecting the gastrointestinal tract, lung, retina and liver[3]. The main risk factors for the association between CMV and UC in patients with CKD include individuals over the age of 30 years, with the presence of ulcer visualized at endoscopy and in recent therapy and mainly refractory to corticosteroids and/or immunomodulators[2].

The patient in our case did not respond to clinical treatment with high doses of corticosteroids and azathioprine, and had to undergo surgical treatment. Case reports and retrospective series suggest that CMV infection can trigger an outbreak of UC refractory to corticosteroid use and worsen disease prognosis, associated with increased risk of toxic megacolon and surgical intervention[14].

A colectomy is a surgical procedure required by up to 15% of individuals with UC[5]. Population studies in Stockholm and Copenhagen reported 10-year cumulative colectomy rates of 28% and 24% respectively. The need for hospitalization during the disease predicts a more aggressive condition; studies demonstrated that patients with UC who required hospitalization were five times more likely to need colectomy. The risk of hospitalization is greater in patients with extensive UC observed within the first 90 days of diagnosis, as well as in those with an early need for the use of corticosteroids[16].

The diagnosis of CMV colitis in the patient was only made after colectomy through histological findings of the surgical specimen (hematoxylin-eosin and immunohistochemistry) and subsequent viral screening in blood using PCR. The diagnosis of CMV is classically based on the histopathological identification of cells infected with CMV virus or antigens in tissues biopsied using hematoxylin-eosin or immunohistochemistry[14]. The gold standard method for diagnosing CMV intestinal infection is screening for the virus from intestinal biopsies using PCR[17]. PCR performed on the colonic mucosa has high sensitivity (93% to 96,7%) and specificity (93% to 98,7%), being useful in the diagnosis of CMV infection in suspected cases that have presented negative histochemical staining, in addition, a positive result may be associated with a worse prognosis of the disease[14,18].

The differential diagnosis between UC and CMV colitis is a challenge in clinical practice. Both share similar clinical characteristics, including fever, malaise, diarrhea, hematochezia, abdominal pain, and weight loss. Although some endoscopic findings are more common in patients with CMV colitis, such as perforated ulcers, there are no reliable pathognomonic characteristics on endoscopy that can distinguish between the two conditions[3]. The possibility that our patient had severe acute CMV colitis that was not diagnosed and treated early is plausible, however, typical findings of CMV colitis were not identified in the histological evaluation of specimens obtained through colonoscopy performed at the beginning of the condition, combined with the fact that the prevalence of CMV colitis is high during episodes of severe acute colitis of the UC[15] and the prevalence of CMV colitis in patients with chronic kidney disease is low[12].

Our patient had an expressive weight loss of about 30% of his body weight. He used a total parenteral diet and had good postoperative nutritional recovery despite having undergone total colectomy and having chronic kidney disease on dialysis. The timing of emergency surgery is crucial for patients with UC, as the delay can lead to worsening of the patients general condition and nutritional status. In addition, emergency surgery in anemic, nutritionally compromised, immunosuppressed and inflamed patients have high morbidity and mortality[19]. Aggressive nutritional therapy and correction of metabolic disorders combined with strict clinical follow-up should be instituted[20]. The need for surgery must be evaluated in advance and early surgery is recommended in case of failure in clinical treatment[21].

CONCLUSION

Despite the rare association of UC and chronic kidney disease, this diagnosis should be remembered in patients who present with persistent mucobloody diarrhea, which can be severe in the initial presentation, requiring surgical treatment. In addition, and since this patient is immunosuppressed by dialysis kidney disease itself, CMV colitis should be included in the differential diagnosis, and may occur alone or in association with ulcerative colitis, particularly in cases requiring high doses of corticosteroids. Thus, a high index of suspicion of UC and CMV colitis is necessary and, once the diagnosis is made, treatment must be instituted as early as possible to improve the outcome of these patients.

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