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ORIGINAL ARTICLE

Endoscopic and Clinical Features of Cytomegalovirus Colitis in Critically Ill Patients: A Retrospective Review

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Background: Patients with cytomegalovirus (CMV) colitis have increasingly been recognized among critically ill patients, yet few specific clinical and endoscopic features are known. In this study, we investigated the common clinical and endoscopic features of CMV colitis in critically ill patients.
Methods: From January 1, 2000 to February 28, 2014, patients with a histopathological diagnosis of CMV colitis were retrospectively reviewed. We reviewed and analyzed the clinical presentation, primary diseases, serum CMV antibody, treatment, mortality, and endoscopic features of these patients.
Results: Eighteen patients were diagnosed as having CMV colitis and 15 CMV colitis patients were included in this study. The mean age was 65.7 years (range 42–92 years). Bloody diarrhea and persistent diarrhea were the most common initial presentations of CMV, and sepsis was the most common co-morbidity found. CMV-IgM was positive in three (17%) patients, and CMV-IgG was positive in 14 (93.3%) patients. All patients received ganciclovir and 11 patients clinically improved. Four (26.6%) patients died and two patients had colon perforation. According to the severity of the diseases, endoscopic presentation of CMV colitis ranged from colonic mucosa edema, loss of vasculature, subepithelial hemorrhage, and circular or geographic ulcers to perforation. Ten (66.7%) patients had multiple ulcers and five (33.3%) patients had a single ulcer. Eleven (73.3%) patients had colitis involving distal to splenic flexure, and four (26.6%) patients had colitis involving the whole colon.
Conclusion: Critically ill patients who present with bloody stool or persistent diarrhea should be considered for the diagnosis of CMV colitis. The endoscopic presentation of CMV colitis is highly variable. We suggest that the endoscopic manifestation of CMV colitis can be divided into three stages: non-ulcerative inflammatory stage, simple ulcerative stage, and complicated ulcerative stage.

1. Introduction

A high incidence of active cytomegalovirus (CMV) infection (36%) has been found among critically ill patients.[1] The most commonly involved organ is the gastrointestinal tract, especially the colon.[2] Critically ill patients with active CMV infection are associated with higher morbidity and mortality.[3,4] Diagnosing CMV colitis relies largely on colonoscopic and pathological studies. Early detection and prompt treatment of CMV colitis can lessen the morbidity and mortality rates. Endoscopic features of CMV colitis among patients with human immunodeficiency virus (HIV), post-transplantation, or with inflammatory bowel disease have been reported previously.[5] However, well-recognized clinical and endoscopic features of CMV colitis among critically ill patients are lacking. In this study, we investigated the clinical and endoscopic features of CMV colitis of patients at our center, to facilitate early detection and treatment with an antiviral agent.

2. Methods

From January 1, 2000 to February 28, 2014, we retrospectively reviewed the medical records of patients with a histopathological diagnosis of CMV colitis. We used the keywords “cytomegalovirus” and “CMV” to search for cases with a histological diagnosis of CMV colitis in the electronic medical records of the pathology laboratory. CMV colitis was diagnosed histologically using the identification of true cytomegalic viral inclusion on hematoxylin and eosin staining, and subsequently confirmed immunohistochemically using a specific antibody against CMV antigen and by noting the presence of

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focal owl-eye intranuclear inclusions. We identified 18 patients that were diagnosed as having CMV colitis in the study period. Three patients were excluded because one patient was infected with HIV, and two patients did not have colonoscopic images. We eventually selected 15 patients with CMV colitis.

Endoscopic images and descriptions were documented in 15 CMV colitis patients. We recorded and analyzed the clinical history, primary diagnosis, laboratory data, treatment, and mortality of these patients. The Taipei Medical University-joint institutional review board approved the protocol of this study without the need to obtain consent from the patients.

3. Results

Table 1 shows the demographic and clinical information of these 15 patients.

The mean age of the patients was 65.7 years (range 42–92 years). The most common primary diseases included cerebral vascular accident on bed-ridden status (47%), followed by end stage renal disease (35%) and type 2 diabetes mellitus (35%). Fourteen (93.3%) patients had a history of sepsis treated with extended (>10 days) broad-spectrum antibiotics, and eight patients developed septic shock. The most common indications for colonoscopy were bloody stool (60%) and persistent diarrhea (40%). Clinically, none of the above were diagnosed as having CMV colitis before receiving their endoscopic examination. All patients received testing for CMV antibody status; CMV-IgM was positive in three (17%) patients, and CMV-IgG was positive in 14 (93.3%) patients. All patients received treatment with ganciclovir, and colitis clinically improved in 11 (73.3%) patients. Four (26.6%) patients died, of whom, one patient died of colon perforation and three patients died of their comorbidities.

Cecal intubation was successful in 10 (66.6%) patients, and terminal ileum had been examined in three patients. One patient was intubated up to the ascending colon, two patients up to the transverse colon, and two patients up to the sigmoid colon. Table 2 describes the endoscopic features of the 15 patients. Colitis involved distal to splenic flexure in 11 (73.3%) patients, and involved the whole colon in four (26.6%) patients. Two of three patients with successful terminal ileum intubation had proven CMV involvement of the ileum. Only one patient had CMV colitis involving solely the proximal to transverse colon without the involvement of the distal part of the colon. Two patients had colon perforation occurring at the sigmoid colon.

Ten (66.7%) patients had multiple ulcers and these ulcerative lesions were skipping lesions. Five (33.3%) patients had a single ulcer, which was predominantly located at the rectum or sigmoid colon. The earliest endoscopic features of CMV colitis presented as colonic mucosa edema, loss of vasculature, and scattered subepithelial hemorrhage (Figure 1A). Twelve (80%) patients had scattering subepithelial ecchymosis at the base or adjacent to the ulcers (Figure 1B). Extended subepithelial hemorrhage turned purplish in color, and was followed by mucosa necrosis leading to necrotic mucosa debris and ulcer formation (Figure 1C and D). Ulcer morphology was either circular (Figure 1E) or geographic (Figure 1F) in shape, and no longitudinal ulcers were found in our series. Eleven (73.3%) patients had an ulcer greater than 2 cm in diameter or exceeding one-third of the circumference (Figure 1G). Giant and deep ulcers were mostly observed in advanced disease with polypoid lesion formation and the presence of necrotic tissue (Figure 1H).

Table 2 Endoscopic features of cytomegalovirus (CMV) colitis

Patient no.	Location	No. of lesions	Size (cm)	Ulcer morphology	Subepithelial ecchymosis	Perforation
1	R to A	Multiple	>2	C and G	Yes	+ sigmoid
2	R to ileum	Multiple	>2	C and G	Yes	—
3	R	Single	>2	C	Yes	—
4	R	Single	>2	C	Yes	—
5	S to D	Multiple	1–2	G	Yes	—
6	R to S	Multiple	1–2	G	No	—
7	T to Ileum	Multiple	1–2	C	Yes	—
8	S	Multiple	>2	G	No	—
9	R to A	Multiple	>2	C and G	Yes	—
10	R	Single	>2	G	Yes	—
11	R	Single	>2	G	No	—
12	R to S	Multiple	>2	G	Yes	—
13	S to D	Multiple	<1	G	Yes	—
14	S	Single	>2	C	Yes	+ sigmoid
15	R to D	Multiple	>2	C and G	Yes	—

A = ascending; C = circular; D = descending; G = geographic; R = rectum; S = sigmoid; T = transverse.

4. Discussion

In this study, we described the clinical and endoscopic features of CMV colitis in 15 critically ill patients from January 1, 2001 to February 28, 2014 at Wan Fang Medical Center. Of all 15 patients, we found that both bloody stool and persistent diarrhea were the most common clinical presentations (Table 1), with an increased rate among critically ill patients with extended intensive care unit stays. We also found that most of our patients had severe sepsis or septic shock and were treated with extended broad-spectrum antibiotics

Table 1 Demographic data of the patients

Patient no.	Age (y)	Sex (M/F)	Comorbidity			Initial presentation	Serum CMV Ab (IgM/IgG)	Survival
1	42	M	ICH	CRF	Sepsis	Diarrhea	+/−	+
2	72	M	Amyloidosis	ESRD	Sepsis	Bloody stool	+/+	Expired
3	81	M	CVA	CRF	Sepsis	Bloody stool	−/+	+
4	81	M	COPD	CRF	Sepsis	Bloody stool	−/+	Expired
5	75	F	C-S injury	CRF	Sepsis	Bloody stool	−/+	+
6	85	M	CVA	sepsis		Diarrhea	−/+	+
7	55	M	ESRD	ICH	Sepsis	Diarrhea	−/+	+
8	64	F	ESRD	CAD	Sepsis	Bloody stool	−/+	+
9	65	M	ESRD	T2DM	Sepsis	Diarrhea	−/+	+
10	78	M	Prostate cancer	ICH	Sepsis	Bloody stool	−/+	+
11	92	M	CVA	T2DM	Sepsis	Bloody stool	−/+	+
12	69	M	ESRD	T2DM	Sepsis	Diarrhea	−/+	+
13	43	F	ESRD			Diarrhea	−/+	+
14	81	F	COPD	T2DM	Sepsis	Bloody stool	−/+	Expired
15	86	F	Lung cancer	CAD	Sepsis	Bloody stool	+/+	Expired

C-S = cervical spine; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CRF = chronic respiratory failure; CVA = cerebrovascular accident; ESRD = end stage renal disease; ICH = intracranial hemorrage; T2DM = type 2 diabetes mellitus; F = female; M = male.