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Churg-Strauss Syndrome with Perforating Ulcers of the Colon

We report a case of a 72-year-old woman with Churg-Strauss syndrome, who presented with intestinal perforation. She has had bronchial asthma with peripheral blood eosinophilia for 30 years. Gross findings of a resected colon showed multiple ulcers with perforation. Histologic findings demonstrated transmural inflammation infiltrated with large numbers of eosionophils, neutrophils and lymphoplasma cells, and characteristic extravascular granuloma in the subserosa. There were multifocally-distributed transmural vasculitis showing all stages of activity in medium and small-sized arteries and veins located in the submucosa, and proper muscle and subserosal layers of the colon, some of which revealed granulomatous inflammation. Histologic finding of liver showed chronic viral hepatitis B with mild inflammatory activity and macronodular cirrhosis. Immunohistochemical findings, acid fuschin orange G staining and electromicroscope found no evidence of hepatitis B virus infection contributing to the pathogenesis of this lesion.

Key Words: *Churg-Strauss Syndrome; Intestinal Perforation; Hepatitis B*

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INTRODUCTION

Churg-Strauss syndrome (CSS; allergic granulomatosis and angiitis) is an uncommon disorder characterized by hypereosinophilia, systemic vasculitis and extravascular granulomas occurring in individuals with asthma and allergic rhinitis (1, 2). The gastrointestinal tract is the third most common site in CSS cases, after the lung and skin (3, 4). However, the involvement of the intestine with perforation is a rare complication in CSS cases (3-5), and previous reports of CSS provide only a few details regarding the nature of the lesions in the gastrointestinal tract. Therefore, we report here a case of CSS in a patient with B viral hepatitis, who presented with multiple colon ulcers and perforation.

CASE REPORT

Clinical findings

A 72-year-old woman was admitted to Inha University Hospital because of severe abdominal pain and fever. She had a history of recurrent asthmatic attacks since she was in her forties. She also had a history of rhinitis and is a hepatitis B viral carrier. Two months earlier, she had complained of anorexia and abdominal pain without precipitating or aggravating factors. There was no history of constipation, diarrhea, hematemesis, melena, hematochezia or ingestion of unusual or undercooked food.

On admission, it was noted that the sound of her breathing had decreased and that there was a mild expiratory wheezing in the bilateral lung. Abdominal examination revealed distention with diminished bowel sounds and diffuse rebound tenderness. A computed tomographic (CT) scan of the abdomen showed a thickening of the bowel wall and free fluid in the pelvis, and the liver, gallbladder, pancreas, kidneys, adrenal glands and spleen appeared normal. Radiographs of the chest and paranasal sinuses were normal.

Peripheral white blood cell count was 6.6×10^9/L with 14% eosinophil, hemoglobin was 10.2 g/dL, and hematocrit was 30.4%. Platelet count was 159,000/μL. Liver function tests were normal, except for elevated levels of serum glucose (207 mg/dL) and alkaline phosphatase (211 IU/L). Thyroid function test, tests for antinuclear antibodies (ANA), and antineutrophilic cytoplasmic antibodies (ANCA) were negative. Radioimmunoassay for the hepatitis virus was positive for hepatitis B surface antigen (HBs Ag) and negative for both hepatitis B surface antibody (HBs Ab) and anti-hepatitis C virus in the serum. An emergency operation was performed and a segment

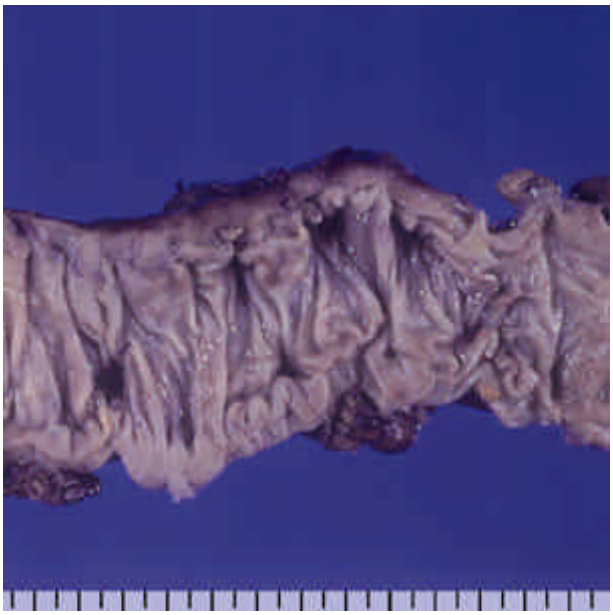

Fig. 1. Mucosa of the colon shows multiple ulcers accompanied by inflammation and intervening intact mucosa.

of the sigmoid colon was resected.

Pathologic findings

The resected colon measured 21 cm in length and 5.5 cm in circumference. Externally, an acute serosal inflammation, hemorrhage and marked adhesion with mesentery were noted. The mucosa showed multiple deep ulcers with intervening intact edematous areas, one of which was perforated (Fig. 1). Histologically, an ulceration with acute and chronic inflammation was noted, showing heavy infiltrations of eosinophils, neutrophils and lymphoplasma cells throughout all layers of the intestine (Fig. 2, 3). It was found that there was a reactive change in the surrounding mucosa close to the ulcers that revealed a preserved crypt architecture with a minimal degree of mucosal inflammation (Fig. 2).

There were multiple vasculitis in the submucosa, muscle proper and subserosa that involved medium and small-sized arteries and veins. The vasculitis showed transmural and granulomatous inflammation with large numbers of eosinophils, neutrophils and lymphoplasma cells, frequently accompanied by fibrinoid necrosis of the inner half of the vessel walls. In some of the vasculitis, the lumen was obstructed by fresh or organizing thrombi with disruption of the internal elastic lamina. In some vessels the thickened wall was replaced by fibroblastic proliferation (Fig. 4).

Extravascular granulomas are helpful in differentiating polyarteritis nodosa, and were identified in the subserosal space (Fig. 5). An eosinophilic microabscess was also noted in the surrounding tissue of the ulcer.

A wedge of the biopsied liver tissue showed a macronodular cirrhosis composed of uneven-sized regenerative nodules with fibrotic septae. There was a mild degree of lobular and periportal inflammatory activity infiltrated with mononuclear cells, attributed to the B viral hepatitis virus infection.

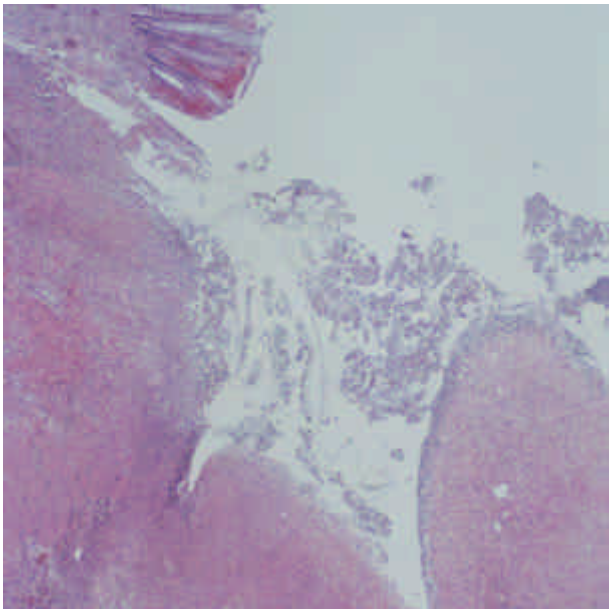

Fig. 2. Deep perforating ulcer with transmural, acute and chronic inflammation and intact crypt architecture in the surrounding mucosa (H&E, ×20).

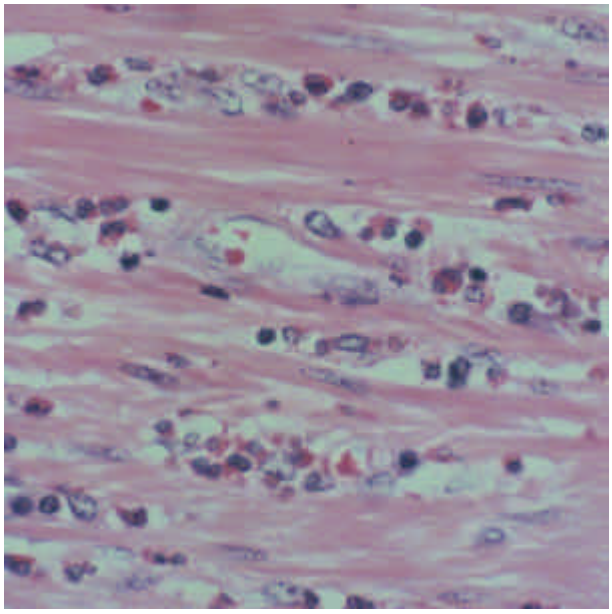

Fig. 3. Marked infiltration of eosinophils in the proper muscle layer (H&E, ×400).

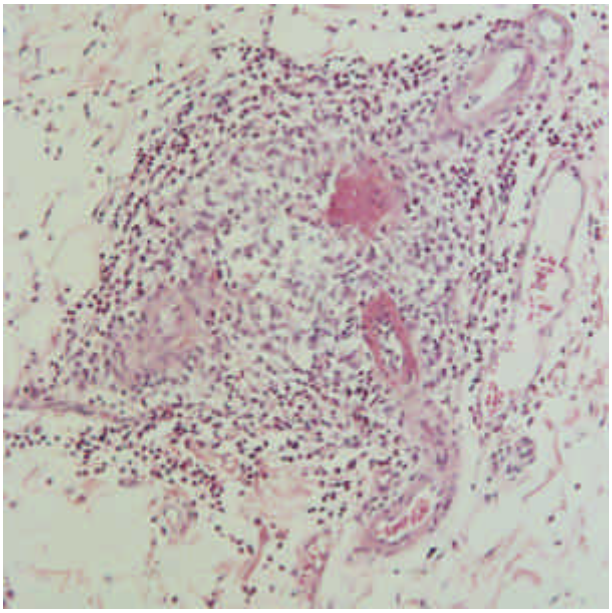

Fig. 4. Granulomatous vasculitis with mixed inflammatory cell infiltration, including large numbers of eosinophils and fibrinoid necrosis in medium sized vessels (H&E, ×100).

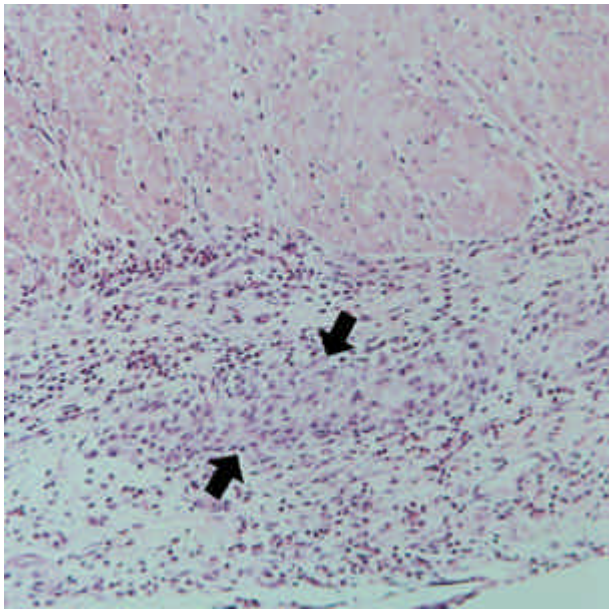

Fig. 5. An extravascular granuloma (arrows) with heavy infiltration of eosinophils in the subserosal space (H&E, ×100).

Immunohistochemical, histochemical and electromicroscopic findings for the vessel

Immunohistochemical staining using HBs Ag and HBc Ag was performed to evaluate whether the hepatitis B virus infection contributes to the pathogenesis of this lesion. Regardless of the pathologic process, there was no evidence of HBs Ag or HBc Ab in the vessel wall, including the basement membrane of the arteries or veins located in the colon. In addition, no immune complex was identified in the vessel wall using acid fuschin orange G (AFOG) staining.

DISCUSSION

Since the initial description by Churg and Strauss in 1951 (1), several cases of CSS have been reported in the literature. CSS is closely related to classic polyarteritis nodosa (PAN), and is one of the three syndromes in the PAN group (6). Lanham et al. proposed three diagnostic criteria based on clinical findings: (a) asthma, (b) peak peripheral blood eosinophil count in excess of 1.5×10^9/L, and (c) systemic vasculitits involving two or more extrapulmonary organs (2). Vasculitis of the gastrointestinal tract is also known to occur as part of a systemic process that includes polyparteritis nodosa, Henoch-Schönlein purpura, rheumatoid arteritis, Kawasaki disease, small vessel vasculitis, systemic lupus erythematosus or CSS (7, 8). The case described in this study satisfied the above-stated critiera in that bronchial asthma and high eosinophilia were included. However, systemic vasculitis was not found in any organ other than the gastrointestinal tract.

The clinical manifestations of CSS usually consisted of abdominal pain, ileus, ischemic bowel disease, bleeding ulcers, and bloody diarrhea, and they are nonspecific (4, 5, 8-9). The primary clinical features of this patient at the time of admission were acute onset abdominal pain with rigidity, which was too nonspecific to make a correct diagnosis.

The exact etiology of CSS is not known, but most noninfectious vasculitis, especially PAN, appear to be initiated by one of several immunologic mechanisms, to include viral infections and B viral hepatitis in particular (10, 11). Although several reports exist stating that the hepatitis B viral infection is associated with CSS, it has not been widely accepted (10, 11). This patient had B viral hepatitis, but there was no evidence of infection by hepatitis B virus or its immune complex in gastrointestinal tract. It should be concluded that this lesion is not supposed to be associated with hepatitis B virus infection, but rather CSS and hepatitis were coincidental lesions.

CSS with gastrointestinal involvement have been reported to occur in approximately 50% of patients with CSS (3, 4). Pathologic findings include multiple ulcerations of the intestine with or without perforation, ischemic change, intestinal obstruction and ileus (4, 5, 8, 9). The gastrointestinal involvement of vasculopathy including CSS does not show ischemic change because the

blood vessels located in the gastrointestinal tract have rich collateral circulation and vascular involvement by the pathologic process is multifocal. Therefore, intestinal perforation has been reported as a rare complication of CSS (3-5, 8). In Korea, CSS with gastrointestinal tract involvement is very rare and only two cases are reported in literature. The pathologic findings of intestine were multiple, small ulcerations and ischemic change without perforation (12, 13). However, for unknown reasons, a perforation of the gastrointestinal tract is commonly reported in the Japanese literature, and the small intestine is the most common site (14). In our case, the surrounding mucosa adjacent to the ulcerations and perforation did not reveal a definite mucosal ischemic change or transmural infarction. However, a suppurative inflammation and eosinophilic abscess were noted in those areas, so the cause of perforation was probably due to secondary infection at the site of mucosal damage induced by ischemia.

Histologically, CSS is difficult to differentiate from PAN because both show a transmural vasculitis with fibrinoid necrosis in medium-sized arteries (7-9). However, extravascular granulomas and heavy infiltration of eosinophils in the small and medium-sized vessels noted in this case were helpful in making a distinction between the two (8, 14). In addition, differential diagnosis of CSS and eosinophilic gastroenteritis might be a problem in the initial diagnostic process because nonspecific gastrointestinal complaints and peripheral hypereosinophilia are noted in both syndromes (8, 15, 16). However, the term eosinophilic gastroenteritis should be reserved for cases that lack vasculitis in the histologic findings (8, 15, 16).

REFERENCES

1. Churg J, Strauss L. *Allergic granulomatosis and granulomatous-vascular syndrome. Ann Allergy 1951; 27: 277-301.*
2. Lanham JG, Elken KB, Pursey CD, Hughes GR. *Systemic vasculitis with asthma and eosinophilia: a clinical approach to the Churg-Strauss syndrome. Medicine (Baltimore) 1984; 63: 65-81.*
3. Chumbley LC, Harrison EG Jr, DeRemee RA. *Allergic granulomatosis and angiitis (Churg-Strauss syndrome). Report and analysis of 30 cases. Mayo Clin Proc 1977; 52: 477-84.*
4. Kurita M, Niwa Y, Hamada E, Hata Y, Oshima M, Mutoh H, Shiina S, Nakata R, Ota S, Terano A, Sugimoto T, Ono M, Sawada T, Mori M, Niki T, Oka T. *Churg-Strauss syndrome (allergic granulomatous angiitis) with multiple perforating ulcers of the small intestine, multiple ulcers of the colon, and mononeuritis multiplex. J Gastroenterol 1994; 29: 208-13.*
5. Sharma MC, Safaya R, Sidhu BS. *Perforation of small intestine caused by Churg-Strauss syndrome. J Clin Gastroenterol 1996; 23: 232-5.*
6. Fauci AS, Hayres BF, Katz P. *The spectrum of vasculitis: clinical, pathologic, immunologic, and therapeutic considerations. Ann Intern Med 1978; 89: 660-71.*
7. Fauci AS. *Vasculitis. J Allergy Clin Immunol 1983; 72: 211-23.*
8. Burke AP, Sobin LH, Virmani R. *Localized vasculitis of the gastrointestinal tract. Am J Surg Pathol 1995; 19: 338-49.*
9. Kaneki T, Kawashima A, Hayano T, Honda T, Kubo K, Koizumi T, Sekiguchi M, Ichikawa H, Matsuzawa K, Katsuyama T. *Churg-Strauss syndrome (allergic granulomatous angiitis) presenting with ileus caused by ischemic ileal ulcer. J Gastroenterol 1994; 29: 208-13.*
10. Lee WM. *Hepatitis B virus infection. N Engl J Med 1997; 337: 1733-45.*
11. Guillevin L, Ronco P, Verroust P. *Circulating immune complexes in systemic necrotizing vasculitis of the polyarteritis nodosa group. Comparison of HBV-related polyarteritis nodosa and Churg-Strauss angiitis. J Autoimmun 1990; 3: 789-92.*
12. Kim KK, Oh YC, Joo NY, Lim OJ, Kim MJ, Youn SH, Woo JG. *A case of Churg-Strauss syndrome with the lung and gastrointestinal tract. J Korean Soc Allergy 1995; 15: 658-64.*
13. Jung S-H, Kim K-H, Nam SM, Park HC, Chu HK, Whang IS, Kim JH, Jun HS. *A case of Churg-Strauss syndrome with manifestations of esophageal ulcer, acute acalculous cholecystitis and ischemic colitis. Korean J Med 1993; 45: 369-75.*
14. Shimamoto C, Hirata I, Ohshiba S, Fujiwara S. *Churg-Strauss syndrome (allergic granulomatous angiitis) with peculiar muliple colonic ulcers. Am J Gastroenterol 1990; 85: 316-9.*
15. Owen DB, Kelly JK. *Eosinophilic gastroenteritis. In: Atlas of gastrointestinal pathology. 1st ed. W.B. Saunders Company, 1994; 201-2.*
16. Suen KC, Burton JD. *The spectrum of eosinophilic infiltration of the gastrointestinal tract and its relationship to other disorders of angiitis and granulomatosis. Hum Pathol 1979; 10: 31-43.*