

# Hemorrhagic Colitis as a Presenting Feature of Wegener Granulomatosis

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## Abstract

Wegener granulomatosis (WG) is an idiopathic small vessel vasculitis involving primarily airway and kidneys. Intestinal involvement of WG is rare and usually occurs after several years of WG and its treatment. We report a case of WG, presented initially as rapid-onset hemorrhagic pancolitis without any preexisting or concurrent illness or any medication use. A 79-year-old previously healthy woman presented with 2-day duration of bloody diarrhea. Colonoscopy showed pancolitis with numerous ulcers; the biopsy showed foci of inflammation, ulceration and hemorrhage in the lamina propria, without features of chronic inflammatory bowel disease. Her stool studies were negative for infection. She subsequently developed pulmonary hemorrhage and kidney dysfunction. Kidney biopsy showed pauci-immune necrotizing glomerulonephritis. She responded to a combination therapy of steroids, cyclophosphamide and plasmapheresis with resolution of intestinal and pulmonary symptoms and improvement of kidney function. This case represents the first known example of colitis as an initial presentation of WG without confounding etiologic factors. Hemorrhagic colitis, although uncommon, may be the major presenting feature of WG.

## Key words

Wegener granulomatosis – hemorrhagic colitis – pulmonary hemorrhage – pauci-immune glomerulonephritis.

## Introduction

Wegener granulomatosis (WG) is an idiopathic granulomatous small vessel vasculitis. Typical target organs

are the respiratory tract and kidneys. Although postmortem studies show occasional gastrointestinal involvement of WG [1], clinically significant intestinal symptoms in WG are rare. In the few reported cases, colitis occurred years after the disease onset and treatment [2-4] or in the context of active inflammatory illness [5-8]. Based on these reports, it has remained unclear as to whether colitis could truly be a manifestation of WG.

We report a WG patient who presented initially with rapid-onset hemorrhagic pancolitis without any preexisting or concurrent illness, nor any medication use. The colitis was followed by characteristic airway and kidney involvement of WG and responded to immunosuppressive treatment. This case provides strong evidence indicating that colitis can be a presenting manifestation of WG.

## Case report

A 79-year-old woman with no medical history and not on any medication presented to the local emergency department for a 2-day duration of bloody diarrhea. She recalled that it started with a sudden urge for bowel movement while watching TV after a home-cooked meal. She noted bright red blood in the toilet. She subsequently had multiple bloody stools including three episodes at night. Apart from mild abdominal discomfort, she denied feeling ill or having fever, chill, skin rash, nose bleed, cough or weight loss, and there had been no history of gastrointestinal disease. She did have a 25 pack-year smoking history and quit 7 years ago. Evaluation revealed normal vital signs and mild abdominal tenderness. Laboratory studies showed hemoglobin 11.4 g/dl and leukocytes  $11.8 \times 10^9/L$ . The serum electrolytes were normal, and the serum creatinine 0.8 mg/dL.

She was admitted to the hospital. A colonoscopy showed pancolitis with numerous ulcers of varying sizes, ranging from 0.5 to 2.0 cm. The ulcers had erythematous and edematous borders with white exudative base. Histologically, colonic mucosa evidenced foci of ulceration, inflammation and hemorrhage within the lamina propria (Fig. 1). Neither features of chronic inflammatory bowel disease nor evidence of granulomas were found.

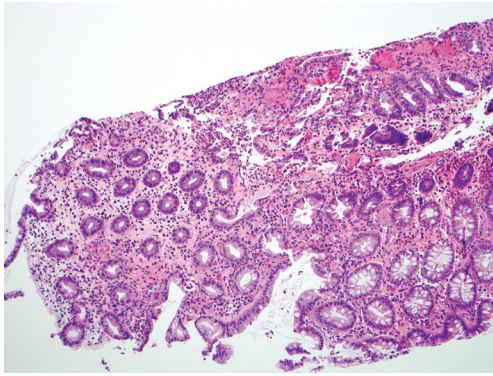
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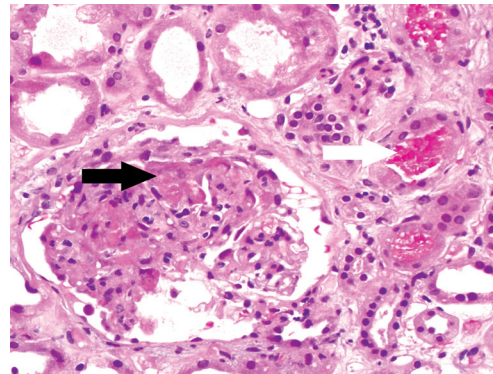
**Fig 1.** Colonic mucosa from the biopsy shows areas of ulceration, acute inflammation and hemorrhage (H&E x 10).

The patient's stool studies were negative for infection. Her hematochezia lessened with supportive care. Three days later, she developed a mild dry cough, without fever. Chest x-ray showed a new left upper lobe infiltrate (Fig. 2A, B), which, in retrospect represented pulmonary hemorrhage, but was considered as hospital-acquired pneumonia. She was discharged on antibiotics on hospital day 6 with a diagnosis of acute inflammatory colitis of unclear etiology.

One week later, she was re-admitted to the intensive care unit (ICU) for respiratory distress and kidney dysfunction. Apparently, she had had frequent bloody stools since the hospital discharge. Her cough had gradually worsened and was associated with bloody sputum and dyspnea. She denied having fever or other constitutional symptoms. Physical examination showed respiratory rate 24/minute, oxygen saturation 90% with 70% oxygen facemask, blood pressure 147/49 mmHg, pulse 89/minute, diffuse crackles in bilateral lung fields, and a non-tender abdomen. No oral, nasal, or pharyngeal ulcers or skin rash were noted. Laboratory results included hemoglobin 9.1 g/dL, leukocyte count  $19.5 \times 10^9/L$ , and creatinine 2.0 mg/dL. Urine microscopy showed  $>100$  RBCs/HPF with  $>25\%$  dysmorphic RBCs. A chest x-ray evidenced new alveolar hemorrhage (Fig. 2C).

She was provisionally diagnosed with acute vasculitis with a pulmonary-renal syndrome. Pulse-dose steroids were initiated, along with further diagnostic investigation. Serological studies showed a positive cANCA at 1:16 and

PR3 antibody of 0.9 units (positive  $> 0.9$  units; equivocal, 0.4-0.9 units). P-ANCA and MPO antibody were negative. Serum C3 and C4 were normal, as were the rest of the serological studies. The kidney biopsy revealed necrotizing and crescentic glomerulonephritis (Fig. 3). Six of the 17 viable glomeruli showed necrosis of the glomerular tuft and cellular or fibrocellular crescents. There was mild interstitial fibrosis with focal inflammatory cell infiltrates. Immunofluorescence studies showed a pauci-immune pattern.



**Fig 3.** A representative glomerulus on the kidney biopsy shows segmental necrosis of the glomerular tuft (black arrow). Red blood cells are seen within some tubular lumens (white arrow) (H&E x 20).

Plasmapheresis and cyclophosphamide were added on day 2 of the ICU admission. Her bowel symptoms subsided within three days of the treatment. Serum creatinine peaked at 3.0 mg/dL and then improved to 2.2 mg/dL at 12 days of the treatment. She completed a 2-week course of plasmapheresis, continued with cyclophosphamide therapy (planned for three months), tapering dosage of prednisone, and trimethoprim/sulfamethoxazole, and was followed as an outpatient.

## Discussion

In this patient, acute hemorrhagic colitis was the presenting feature of what turned out to be a classic



**Fig 2.** Serial chest x-rays of the patient show (A) no infiltration prior to her illness; (B) acute alveolar infiltrate in the left upper lobe consistent with hemorrhage; (C) a new area of alveolar infiltrate in the right upper lobe upon ICU admission, consistent with a migratory pattern of the pulmonary hemorrhage; and (D) improvement in the bilateral pulmonary hemorrhage after one week of treatment. Notably, a central venous catheter was placed for plasmapheresis.

case of WG with pulmonary-renal syndrome. Wegener granulomatosis often starts with rhinorrhea, nasal mucosal ulceration, cough and renal impairment. Chest X-rays show nodular and cavitary lesions and/or migratory infiltrates, and kidney biopsy shows pauci-immune necrotizing and crescentic glomerulonephritis. Serologic tests for cANCA/PR3 antibody are strongly associated with WG; however, these studies may be negative in the minority of WG patients. Thus, diagnosis of WG relies on clinical presentation, tissue biopsy, and exclusion of other causes [9].

Intestinal involvement is rare in WG. About 20 cases of colitis have been reported [2, 3]. The key issue raised in these reports is whether colitis can be a manifestation of WG. It remains uncertain because in the majority of the reports, the colitis developed up to several years after WG diagnosis and treatment, so that the colitis could potentially be related to either the underlying WG activity or the treatment. In rare cases in which colitis preceded the characteristic pulmonary and kidney manifestations, there were many accompanying and potentially confounding illnesses and treatments. For instance, in one patient, small bowel colitis was preceded by a 3-week duration of small joint polyarthropathy which was treated with NSAIDs and analgetics and an ovary abscess of unknown duration [10]. In another case, the colitis occurred in the context of inflammatory arthritis and sinusitis of unclear duration and treatment [6]. In other cases, colitis was preceded by an array of manifestations including sinusitis, deafness, mouth ulcers, joint pain, and weight loss [5, 8]; treatment of these antecedent illnesses was not sufficiently documented. Small vessel vasculitis can also be caused by drugs, infections, and immune complex deposition in a variety of autoimmune diseases [11]. Thus, in the context of other systemic illnesses and their treatments as in these cases, a directly connection of colitis and WG can not be drawn with certainty. Our case is unique in that the patient had no antecedent medical illness or any medication intake prior to the onset of colitis. This case clearly indicates that hemorrhagic colitis can indeed be a manifestation of WG.

The histological features of the kidney biopsy in our patient are typical of WG. The colonic biopsy showed mucosal ulcerations with foci of acute inflammation and hemorrhage. Colitis associated with small vessel vasculitis typically presents as inflammation and ulceration; however, histological findings may not be specific [11]. In our case, even though the sampled colonic specimen did not show granulomas, the absence of characteristic features of chronic inflammatory bowel disease (Crohn's disease or ulcerative colitis) or an infectious agent, the temporal association with pulmonary and kidney manifestations, and the responsiveness to the immunosuppressive treatment support colitis as a manifestation of WG.

Current treatment for WG associated with pulmonary hemorrhage and necrotizing glomerulonephritis consists of prednisone, cyclophosphamide, and plasmapheresis. This

treatment has been shown to induce a rapid improvement in pulmonary hemorrhage and stabilization or improvement of renal function. In our patient the symptoms of colitis also resolved within several days of the treatment, as did the alveolar hemorrhage. Likewise, her kidney function stabilized in three days and gradually improved in 12 days.

This case has important clinical implications. Wegener granulomatosis can rapidly progress and be fatal if left untreated or if treatment is delayed. The recognition that hemorrhagic colitis may be a sole presenting feature of WG can increase alertness of this diagnostic possibility, leading to an early diagnosis and treatment, thereby avoiding permanent organ damage and potential mortality.

In **conclusion**, this case represents the first known example of colitis as an initial presentation of WG unrelated to any other intercurrent illness or medication intake. It is prudent to consider WG in patients with acute colitis of unclear etiology.

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