

Case report

Salmonella colitis or inflammatory bowel disease? A case demonstrating overlapping of clinical, endoscopic and pathologic features

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SUMMARY

Inflammatory bowel disease and gastroenteritis secondary to Salmonella infection may manifest with overlapping clinical, endoscopic and histologic features. The case reported is of a 70-year-old woman who was admitted to hospital due to fever and diarrhea. Colonoscopic findings were suggestive of Crohn's disease, however pathologic examination when based on crypt architecture and presence of an acute neutrophilic inflammatory infiltrate in the lamina propria, was not diagnostic of either Crohn's disease or acute self limited colitis. Stool cultures were positive for Salmonella and treatment with antibiotics was begun, followed by the patient's clinical improvement. Repeat colonoscopy was performed a few days later and endoscopic findings demonstrated marked improvement. Pathologic examination of biopsies this time were compatible with Crohn's disease, particularly evaluating the formation of microgranulomas as well as basal lymphoid hyperplasia and basal lymphoid aggregates.

Key words: Inflammatory bowel disease, Salmonella infection, endoscopy, pathology

INTRODUCTION

Inflammatory bowel disease (IBD) and gastroenteritis due to Salmonella infection may present with over-

lapping clinical, endoscopic and histological features. Differential diagnosis may become extremely difficult in the setting of Salmonella infections, complicating undiagnosed IBD.^{1,2} We report the case of an elderly patient admitted to hospital due to acute enteritis secondary to Salmonella infection, complicating undiagnosed Crohn's disease (CD) and we highlight the diagnostic and therapeutic dilemmas tackled during her hospitalization.

CASE REPORT

A previously healthy 70-year-old white female was admitted to hospital due to fever and diarrhea of 9 days' duration; the patient reported 4-5 diarrheal defecations per day. The patient, a resident of a rural area close to the Athens district, had an unremarkable history. She reported no recent travel abroad and had no pets or other animals. She was not under any medication. Alcohol consumption was occasional.

On clinical examination her temperature was 38.4°C. Her blood pressure was 110/70 mmHg and her pulse rate was 95/min (in the supine position). She had orthostatic hypotension in the erect position (blood pressure 90/60 mmHg, pulse rate 120/min). There was diffuse abdominal tenderness on palpation, but no rebound or guarding. Rectal examination revealed the presence of diarrheal stools, without signs of blood or mucous.

Laboratory values revealed: hematocrit 33.2%, hemoglobin 11.5 g/dl, mean corpuscular volume 90.3 fl, mean corpuscular hemoglobin 31.3 pg, mean corpuscular hemoglobin concentration 34.6 g/dl, white blood count 1100 m³ (75% neutrophils, 7% lymphocytes, 17% monocytes), and normal platelets. The erythrocyte sedimentation rate was accelerated and C-reactive protein

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was elevated (78 mm/h and 21 mg/dl, respectively). Albumin was 3.3 g/dl (normal: 3.5-5.3), calcium was 7.1 mg/dl (normal: 8-10.3), phosphorus was 2.6 mg/dl (normal: 2.7-4.5), lactate dehydrogenase was 222 U/L (normal: 89-187). Other blood chemistry results, including glucose, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, γ -glutamyl-transferase, bilirubin, triglycerides, serum amylase and uric acid were normal. Coagulation studies were normal. The Widal reaction was negative. HbsAg, anti-HBs, anti-HBc, anti-HCV, anti-HIV, VDRL, c-antineutrophil cytoplasmic antibodies (ANCA) and p-ANCA were negative. Urinalysis was normal. An electrocardiogram and a chest x-ray were normal. Abdominal x-rays were unrevealing. Ultrasonography and computed tomography of the abdomen were normal.

She was treated by fluid administration. On the 2nd day of hospitalization colonoscopy was performed, revealing numerous ulcerations in the transverse and the ascending colon and the cecum. The bowel mucosa between these ulcerations revealed normal parts as well as erythematous and edematous segments (Fig. 1, Panel A). The terminal ileum revealed several ulcerations and an edematous mucosa (Fig. 1, Panel B). Endoscopic features strongly resembled those of CD. Microscopic pathology of the biopsies taken was unable to definitely attribute the lesions to an infective agent or to CD. Fissures and "aphthous"-type ulcers could be microscopically postulated in the examined biopsy material and formation of well-vascularized granulation tissue covered by fibrinous inflammatory exudate could be observed. Non-ulcerated mucosa was infiltrated by dense inflammatory elements (lymphocytes, eosinophils and polymorphonuclear leukocytes). However, the pathologist's impression was mostly in favor of infectious colitis due to absence of crypt distortion and dense polymorphonuclear infiltrates (though not pure ones). Upper gastrointestinal endoscopy was then performed revealing mild gastritis of the antrum. At that point, stool cultures taken at admission were found positive for Salmonella group E sensitive to ciprofloxacin. Treatment was initiated, resulting in rapid improvement of the patient's symptoms. However, despite the decrease in the number of bowel movements to 2-3 per day, diarrhea persisted. Repeat stool cultures were negative for Salmonella. Repeat colonoscopy was performed on the 11th hospital day, revealing scattered erosions in the transverse and the ascending colon and the cecum (Fig. 2, Panel A). The terminal ileum also demonstrated mucosal edema (Fig. 2, Panel B). Pathologic examination of the biopsies taken, revealed a comparative improvement of the lesions' activity, this time

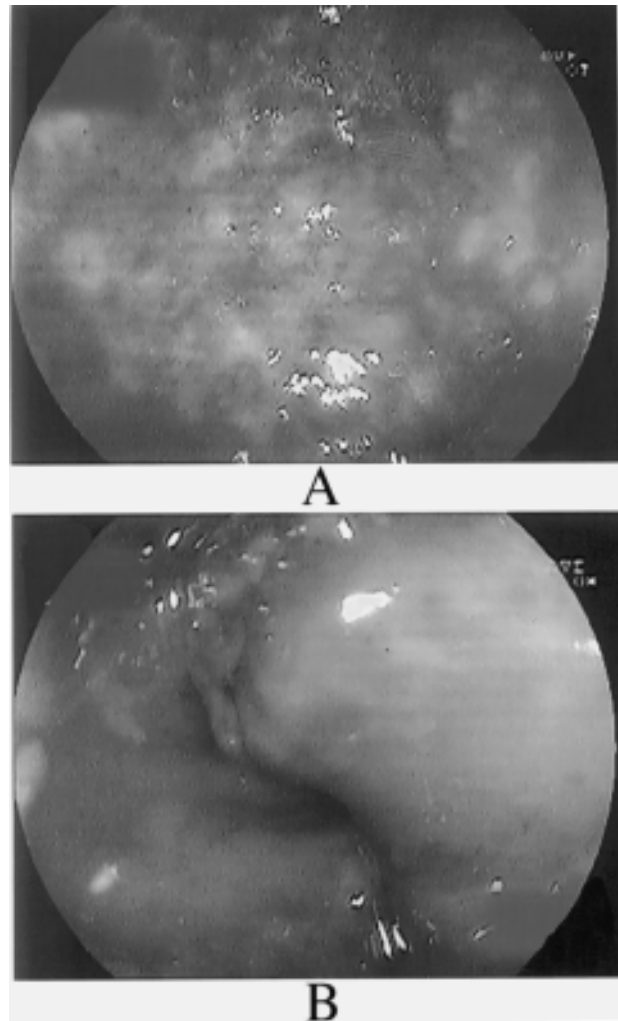


Figure 1. Colonoscopy, revealing ulcerations in the colon. Note normal bowel mucosa as well as erythematous and edematous segments (Panel A). Ulcerations and mucosal edema throughout the terminal ileum (Panel B).

demonstrating focally dense chronic mucosal inflammation extending into the (superficial) submucosa (Fig. 3) (which was available for examination in the biopsies) with formation of microgranulomas, consistent with the diagnosis of CD. Antibiotics were discontinued after the completion of 5 days' treatment. The patient was discharged and therapy with prednisone and 5-aminosalicylic acid was started. The symptoms gradually resolved completely. She has remained well without evidence of recurrence of symptoms during a 6-month follow-up period.

DISCUSSION

Differential diagnosis of the various clinical, endoscopic and histologic features of IBD and infectious gas-

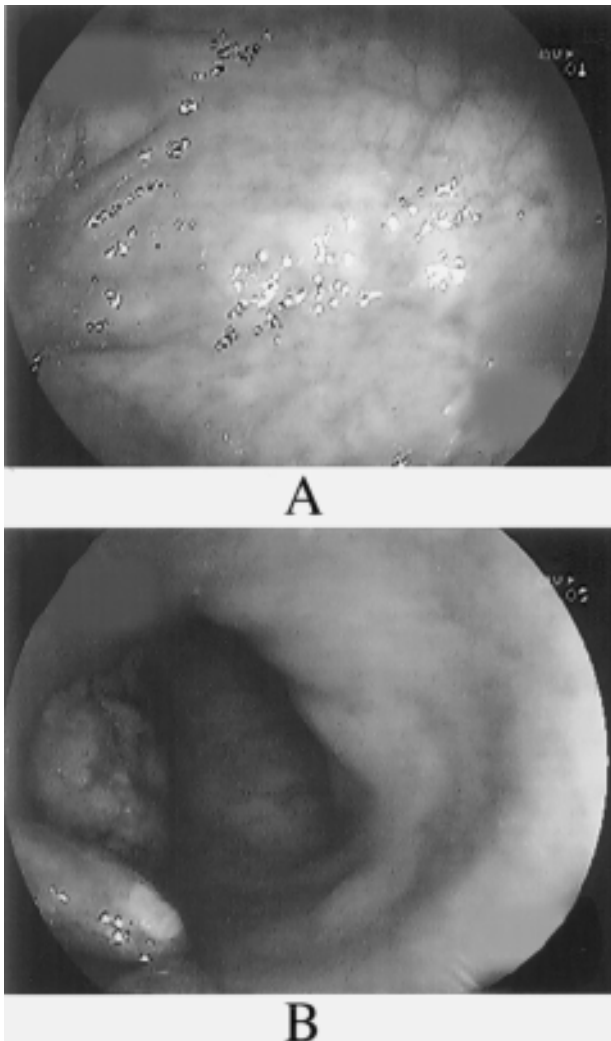


Figure 2. Repeat colonoscopy 9 days later, demonstrating improvement of lesions. Note the presence of scattered erosions in the colon (Panel A) and the mucosal edema in the terminal ileum (Fig. 2, Panel B).

troenteritis may sometimes become extremely difficult. These difficulties may become even greater when dealing with a case of undiagnosed IBD complicated by infectious gastroenteritis.^{1,2}

Salmonella infections are an important health problem and represent a very frequent cause of food-borne outbreaks of gastroenteritis. The very young, the elderly and immunosuppressed individuals are at risk of invasive infections.^{3,4} Endoscopy is usually unnecessary, as the diagnosis may be based on non-invasive methods such as stool cultures. However, severe cases may justify colonoscopy to rule out other diagnoses, since Salmonella gastroenteritis is usually an acute, self-limited disease, char-

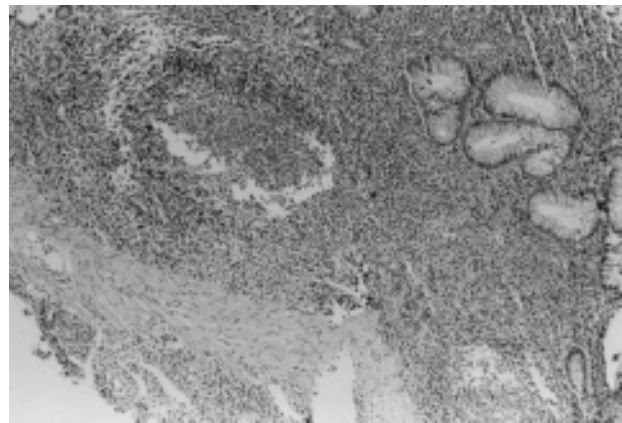


Figure 3. Dense infiltration of lymphoid cells with a well-marked follicular arrangement extending through the thickened muscularis mucosae (Hematoxylin-Eosin, x100).

acterized by a short duration.^{1,4} The fact that mere isolation of Salmonella in stool does not necessarily attribute the patient's syndrome to an infection⁴ further justifies colonoscopy in cases such as the one presented. The principle site affected in human salmonellosis is generally considered to be the small intestine. However, colonic involvement may be seen, especially in nontyphoid salmonellosis.^{5,6} Common salmonellae usually cause diffuse colitis. Therefore, endoscopic and radiographic features usually mimic ulcerative colitis. Endoscopic findings suggestive of CD are uncommon in Salmonella infections.⁵⁻⁷ On the other hand, histology may prove to be insufficient to differentiate Salmonella colitis from IBD, especially in acute cases of IBD, despite pathologists' attempts to provide adequate histopathologic diagnostic criteria.^{1,2,8} In general, severe cases of Salmonella infection show prominent neutrophilic infiltrates in degenerating crypts, more intensely in the lamina propria. On the other hand, areas of hemorrhage and ulceration, reminiscent of CD, are also present. In detail, there may be extensive areas of mucosal necrosis and hemorrhage with punched-out mucosal ulcerations or erosions with elevated borders, as in the present case and extensive mucosal and submucosal necrosis and hemorrhage. These changes differ from IBD by the relative scarcity of chronic inflammatory cells, not observed in our case. It is of interest that in severe cases of Salmonella colitis, giant cells may populate the infected tissues, which, if transmural inflammation is present, might suggest the presence of CD. The giant cells do not form compact granulomas, as seen in CD. However, inconspicuous microgranulomas may be seen in Salmonella infection. Occasionally, patients with Salmonella colitis may show mild crypt dis-

tortion and branching, especially those patients with persistent diarrhea, as the presented patient.⁹ Nevertheless, we must bear in mind that Salmonellosis and IBD may also coincide. Large studies have been performed to establish whether salmonellosis is more common in patients with IBD, but opinions vary.² In any case, prompt recognition and proper treatment is mandatory, since delays seem to increase the severity of the diseases.² It has therefore been suggested that colitis due to *Salmonella* infection may perhaps be another indication for antibiotic treatment.² On the other hand, treatment of IBD is essential in controlling the disease's symptoms and the clinician often faces various diagnostic and therapeutic dilemmas. The duration of the evolution of the disease after treatment may help in making the proper decisions.^{1,2,4,5}

Our patient was an elderly woman with no significant previous medical history, who was admitted due to severe acute enteritis. Her general condition was bad; she was dehydrated, resulting in orthostatic hypotension. The severity of her symptoms, in combination with the fact that the results of stool cultures were unavailable at the time, mandated colonoscopy. Colonoscopic findings were consistent with CD. On the other hand, the pathologist's impression was in favor of infectious colitis. By then, the results of stool cultures were also available and found positive for *Salmonella*. This was a surprise to our endoscopic department, as infectious and especially *Salmonella* colitis is usually diffuse and its endoscopic features usually mimic ulcerative colitis, but it justified our reluctance to initiate corticosteroid therapy for CD before we had the results of both the histologic and stool culture examinations. The combination of the patient's age, clinical features, positive stool cultures and the pathologist's impression that the lesions were mostly attributable to an infectious agent, justified initiation of antibiotic treatment. Following antibiotic treatment, the patient's symptoms improved, but did not totally resolve. However, *Salmonella* colitis (as well as most forms of infectious colitis) is usually acute, self-limited and characterized by a short duration.¹⁰ Thus, the fact that the patient did not totally recover necessitated repeat colonoscopy. Repeat colonoscopy and histologic examination provided the diagnosis of an underlying CD. After a 5-day antibiotic treatment and in view of the findings of the repeat colonoscopy and biopsies, corticosteroids were finally administered. This resulted in the patient's complete recovery. On the other hand, recent evidence suggests a favorable impact of antibiotic treatment on CD.¹¹ However, it is questionable whether antibiotics can induce such an impressive clinical, endoscopic and histo-

logic improvement of CD in a few days, as in our patient. Therefore, we consider that the impressive improvement of the endoscopic features during repeat colonoscopy, followed by analogous changes in the patient's symptoms and histology, provide solid proof that some part of the clinical, histologic and endoscopic findings should be attributed directly to the salmonellosis.

In conclusion, IBD and gastroenteritis secondary to *Salmonella* infection may present with similar clinical, endoscopic and histological features and may sometimes coincide. Differential diagnosis may then become extremely difficult especially if IBD is undiagnosed. Awareness of this possibility and timely recognition may help avoid diagnostic and therapeutic errors.

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