Rheumatoid Arthritis Accompanied by Colonic Lesions

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Abstract

A 69-year-old woman with a 6-year history of rheumatoid arthritis treated solely with an orally administered NSAID had slowly progressing persistent mild abdominal pain and diarrhea, accompanied with marked signs of inflammation as well as hypoproteinemia due to protein-losing gastroenteropathy. Examinations of the large intestine revealed variously shaped ulcerative lesions, centered around the left hemicolon, as well as luminal narrowing. The course of the disease and the shape of the lesions strongly suggested involvement of rheumatoid vasculitis; oral administration of prednisolone was effective.

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Key words: colonic ulcer, vasculitis, protein-losing gastroenteropathy, corticosteroids

Introduction

While the major manifestation of rheumatoid arthritis (RA) is polyarthritis, it is known that the heart, lungs, skin and nerves may also be affected by vasculitis. Enteritis associated with the use of anti-rheumatoid drugs, as well as gastrointestinal lesions resulting from secondary amyloidosis, are well known gastrointestinal complications resulting from RA. However, the incidence of gastrointestinal complications resulting from rheumatoid vasculitis, such as intestinal perforation, infarction and ulceration is low, and to date few reports have been published (1-7).

In the present report, we present a RA patient with an insufficiency of vasculitis findings, but in whom the clinical course and morphology of the lesions strongly suggested RA associated colonic lesions, and indeed the symptoms improved after administering corticosteroids alone.

Case Report

The patient was a 69-year-old woman diagnosed as having RA (stage I, class II) in 1990 and who had taken loxoprofen until 1995. Since 1995, the patient has not received any RA medication. The patient consulted our department in June 1996 because of the development of a slowly progressing persistent mild abdominal pain and mucous stools. Colonoscopy and barium enema revealed abnormal findings and the patient was admitted to our hospital. Although the patient had a history of cardiac infarction and hypertension, physical examination revealed only an elevated temperature (38.5°C) and slight, symmetrical swelling of the digital PIP joints. There were no abnormalities of the chest, abdomen or skin on examination.

On admission, findings on laboratory examinations revealed a sedimentation rate of 86 mm/h and a serum C-reactive protein (CRP) level of 16.5 mg/dl which suggested severe inflammation. There was also anemia (hemoglobin 9.6 g/dl) and hypoproteinemia (total protein 5.4 mg/dl). Although immunological examinations indicated positivity for antinuclear antibodies at a low titer (80 mg/dl), levels of rheumatoid factor, complement and immune complex as well as a lupus erythematosus test were all normal. Alpha-1 antitrypsin clearance was 33 mg/dl, suggesting protein-losing gastroenteropathy. Frequent stool cultures and culturing of biopsies from large intestinal mucosa revealed no significant bacteria. Blood cytomegalovirus antibody and ameba antibody examinations were all negative. Therefore, infectious enteritis was excluded.

Findings on a barium enema done on admission showed ulcerative lesions accompanied by surrounding ridges in the rectum (Fig. 1). Multiple niches suggestive of ulcers with a strong undermining tendency were also detected in the sigmoid colon (Fig. 2). Rough mucosa with luminal narrowing was noted between the descending and transverse colon together with diffuse small ulcers (Fig. 3). There was a clear demarcation between affected and normal mucosa in the transverse colon near the hepatic flexure but there were no abnormalities seen in the ascending colon or cecum.

Colonoscopy findings on admission showed that large, easily bleeding ulcers with a white coating and surrounding wall

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were observed in the distal rectum (Fig. 4). There were scattered round and deep ulcers in the non-inflamed sigmoid colon (Fig. 5). Broad linear ulcers with unclear margins accompanied by multiple inflammatory polyps were noted in the descending colon and diffuse redness and erosions were observed in the descending and transverse colons (Fig. 6). The intervening mucosa between the lesions was normal in the rectum and sigmoid colon, suggesting skip lesions. These findings ruled

Contrast enema findings on admission (Fig. 1, 2, 3).
Figure 1. Ulcerative lesions accompanied by surrounding ridges were observed in the distal rectum.
Figure 2. Multiple niches were detected in the sigmoid colon.
Figure 3. Segmental narrowing with rough mucosa was noted between the descending and transverse colon together with diffuse small ulcers.

Colonoscopic findings on admission (Fig. 4, 5, 6).
Figure 4. Large ulcers with white coating and surrounding walls were observed in the rectum.
Figure 5. There were scattered deep round ulcers in the sigmoid colon, although the intervening mucosa between the ulcers was normal.
Figure 6. Serpigenous ulcers with unclear margins were noted in the descending and transverse colon.
out the possibility of ulcerative colitis. No particular abnormalities were observed in the ascending colon or cecum.

Moreover, upper gastrointestinal endoscopy and double contrast examination of the small intestine showed no abnormal findings. *Helicobacter pylori* infection was not examined.

Although many biopsies were taken from the ulcerative lesions in the rectum and the descending and transverse colon, only findings of chronic inflammation and sporadic crypt abscesses were observed, and there were no specific findings of vasculitis, amyloid or granulomas. Accordingly, there were no histological findings suggestive of ulcerative colitis or Crohn's disease. In addition, completely normal architecture was preserved in the intervening mucosa.

A clinical course of infectious enteritis could not be ruled out as the patient complained of fever in addition to slight abdominal pain and mucous stools. An antibiotic was therefore administered, but the symptoms did not improve. Total parenteral nutrition (TPN) was started in combination with Mesalazine. After 5 days Mesalazine was discontinued because of a generalized erythema, compatible with drug eruption. The general symptoms had continued signs those of inflammation (blood sedimentation and CRP levels) had not improved. As the patient had a 6-year history of RA, vasculitis was suspected as a cause of the colonic lesions and administration of corticosteroids was initiated. Two days after administering 30 mg prednisolone per day, subjective symptoms including fever and abdominal pain were relieved and the inflammatory signs and nutritional state markedly improved. Thereafter, the patient started normal food intake and the dose of prednisolone was tapered. There was no exacerbation of intestinal lesions, and the patient was discharged from the hospital. The dose of prednisolone was further decreased and finally discontinued under outpatient clinic supervision. The patient has been followed up and at present her condition is satisfactory without prednisolone administration. Colonoscopy performed approximately 5 months after starting the treatment showed that all of the colonic lesion were replaced by scar tissue (Figs. 7, 8).

**Discussion**

Most previously reported cases of gastrointestinal lesions resulting from rheumatoid vasculitis have been serious cases (1–7) and were classified as malignant RA because of their severity. Colonic manifestations included infarction and perforation and patients presented with acute and severe abdominal pain. The prognosis was bad in most cases.

However, there have been few reports of cases as observed here, presenting with slowly progressing diarrhea and mild abdominal pain, with only colonic ulcerations that appeared to be chronic on follow up, and showed a good prognosis (8, 9). The lesions were characterized by various ulcerative lesions including multiple round ulcers, irregular-shaped ulcers, longitudinal ulcers and aphthoid ulcers (10, 11) with a predilection for the left hemicolon, particularly the sigmoid colon, and the cecum (9, 12). Furthermore, the lesions sometimes showed a similarity to those of ulcerative colitis, such as diffuse rough mucosa (8), redness, erosions and easy bleeding (10). There were no consistent relationships between the development of intestinal lesions and the duration, the stage or the activity of the RA, with drug use (9). Some cases of RA have been reported in which joint symptoms were relieved with the development of other symptoms (11, 12). These reported cases were treated by prednisolone or Salazosulfapyridine with TPN, and the colonic lesions improved. A definite diagnosis of vasculitis is rarely established by biopsies and even at autopsy the diagnosis may be difficult (13, 14). Thus, for diagnosis, it is important to combine macroscopic findings of characteristic morphology with the history of RA.

(Fig. 7, 8) All of the colonic lesions were replaced by scar tissue.

Figure 7. Transverse colon.

Figure 8. Rectum.
In this patient, joint symptoms and findings on immunological blood examinations on admission suggested minor activity of the RA but a definite pathologic diagnosis of vasculitis could not be obtained and indeed was difficult. Although it is well known that long-term usage of NSAIDs provokes diverse morphological lesions in the gut (15), we did not consider that the lesions of our patient were caused by NSAIDs as the colonic symptoms were started and progressed a long time after the cessation of loxoprofen. However, other diseases that should be included in the differential diagnosis, such as ischemic enteritis, drug-induced enteritis, Crohn’s disease, ulcerative colitis and infectious enteritis were not likely because of the morphology of the intestinal lesions and the clinical course. Indeterminate colitis, which has both features of Crohn’s disease and ulcerative colitis, was not likely because the colitis of the present case did not have any features suggesting Crohn’s disease or ulcerative colitis. The various morphologies of the ulcerations were consistent with those of the previously reported cases of intestinal lesions resulting from RA (8, 9). Moreover, the remarkable healing of the intestinal lesions and improved protein-losing enteropathy, after the administration of corticosteroids, supported the diagnosis in this patient. Therefore, the protein-losing enteropathy in our patient seemed to be caused by the extensive colitis which accelerated permeability of the gut.

Localized vasculitis does not always correspond to the activity of rheumatoid arthritis (16). Therefore, if RA patients complain of gastrointestinal symptoms, the possibility of intestinal lesions should be taken into consideration and accordingly examined and treated. Most of the previously reported cases of malignant RA were severe cases with intestinal perforation or infarction with poor prognosis. Based on the present case, it seems necessary also to assess milder cases with good prognosis and undergoing conservative treatment, as herein, in order to evaluate the full extent to which rheumatoid arthritis can affect the gastrointestinal tract.

References