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TITLE OF CASE
Atypical tumour-like involvement of the colon in secondary systemic amyloidosis which vanished after one month of observation
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SUMMARY *Up to 150 words summarising the case presentation and outcome*

Amyloidosis occurs as a result of the extracellular deposition of protein fibrils in organs and tissues, thus causing mild to severe pathophysiological changes. The gastrointestinal tract is a common site of amyloid deposition. While intestinal amyloidosis frequently results in polypoid lesions, ulcerations, nodules and petechial mucosal haemorrhage, tumour-like lesions are rarely developed, and infrequently diagnosed before the resection because of the difficulty in differentiating them from colon cancer. We herein reported a case of intestinal AA amyloidosis with a complication of a tumour-like lesion endoscopically resembling a malignant lesion, which was completely diminished after one month of observation with bowel rest. Such conservative treatment is a feasible option to cure intestinal tumour-like lesions in patients with intestinal amyloidosis when no neoplastic change is histologically detected, possibly decreasing the need for surgery of the fragile mucosa.

BACKGROUND *Why you think this case is important – why you decided to write it up*

Amyloidosis is defined as an extracellular deposit of fibril proteins, P-components, or other glycoproteins in organs and tissues, thus causing mild to severe pathophysiological changes (1). Primary or light chain (L)-associated AL amyloidosis is the most common form of systemic amyloidosis, which is associated with plasma cell dyscrasia, which frequently co-exists with multiple myeloma (2). Conversely, secondary amyloidosis with acute-phase reactant serum amyloid A protein (AA amyloidosis) is associated with infectious, inflammatory and neoplastic disorders, particularly with rheumatoid arthritis (3). Several other forms have been found in a variety of clinical settings; including familial amyloidosis (ATTR amyloid), hemodialysis -

associated amyloidosis (A β 2 amyloid), and some localized amyloidoses. The GI tract is well known to be a common site of amyloid deposition, which clinically presents as dysmotility, gastrointestinal bleeding and malabsorption (4). The morphological features of intestinal amyloidosis include elevated lesions, ulcerations, nodules, or diffusely distributed petechial mucosal haemorrhage (5-7). However, tumour-like lesions rarely occur in patients with intestinal amyloidosis, and most of these lesions are diagnosed after their resection because of the complications including stricture and haemorrhage, or the difficulty in discriminating them from malignant lesions (8-12). We herein report a case of intestinal AA amyloidosis with a complication of intestinal stricture by a tumour-like lesion resembling a colon cancer or lymphoma, which was completely eliminated with just bowel rest for one month.

CASE PRESENTATION *Presenting features, medical/social/family history*

A 60-year-old female visited our hospital due to a 2-week history of abdominal pain and distention. She had suffered from rheumatoid arthritis and been receiving anti-inflammatory drugs for 15 years. A blood examination revealed a high number of white blood cells (18140/ μ l; 70.0% neutrophils, 18.1% lymphocytes, 9.1% monocytes, 0.3% basophils and 1.0% eosinophils), a high level of C reactive protein (9.15 mg/dl) and serum amyloid A protein (491.8 μ g/ml), and a low level of hemoglobin (8.2 g/dl). Tumor markers, including carcinoembryonic antigen and CA19-9, were within the normal ranges. Electrocardiography showed no abnormal findings. Computed tomography revealed a thickening of the colonic wall and ascites in the pelvis (Figures 1A, B). A colonoscopy was performed after obtaining the patient's written informed consent to determine the cause of the abdominal pain and distention. The examination detected edematous mucosa with small ulcerations in the ileum (Figure 2A) and a circumferential tumour-like lesion, which resembled colon cancer, with a stricture in the transverse colon (Figure 2B). Histological specimens obtained from the ileum and the tumour-like lesion revealed a thickening of the submucosal vascular wall and mild to moderate inflammatory change throughout the full thickness of the mucosa with the infiltration of neutrophils, eosinophils and lymphocytes. The specimen exhibited apple-green birefringence with polarized light after Congo red staining. Immunohistochemically, the deposit was positive for amyloid A and negative for κ and λ , thus suggesting that these lesions were formed by the deposition of the intestinal AA amyloidosis (Figure 3A-H). The findings for a proliferation of dysplastic glands and atypical lymphocytic infiltration were negative. Whereas a tumour component was not histologically detected, it was clinically difficult to determine whether a neoplastic component, such as malignant lymphoma or colon cancer, coexisted in the tumour-like lesion.

INVESTIGATIONS *If relevant*

DIFFERENTIAL DIAGNOSIS *If relevant*

The disorders that would be included in the differential diagnosis based on the atypical tumour-like lesion in this case would be: colonic neoplasms including malignant lymphoma, colon cancer and carcinoid and gastrointestinal stromal tumours.

<p>TREATMENT <i>If relevant</i></p>
<p>OUTCOME AND FOLLOW-UP</p> <p>To determine the diagnosis of the tumour-like lesion after relieving the inflammatory change, she was observed under a conservative treatment with bowel rest and total parental nutrition. Her abdominal symptoms immediately and almost completely disappeared. One month after initiating conservative treatment, a colonoscopic examination detected edematous mucosa and small ulcerations which were typical lesions of intestinal amyloidosis, however, the tumour-like lesion at the transverse colon had completely vanished (Figure 4A). Thereafter, no relapse of the abdominal symptoms or tumour-like lesion was observed during the three years follow-up period, although the presence of amyloid deposits was positive in a follow-up biopsy.</p>
<p>DISCUSSION <i>including very brief review of similar published cases (how many similar cases have been published?)</i></p> <p>This report presents a rare case of intestinal amyloidosis which later developed a tumour-like lesion resembling either colon cancer or lymphoma in the transverse colon. It is worth noting that the tumour-like lesion was eliminated with bowel rest and total parental nutrition, thereby suggesting that conservative treatment without either a resection or intensification of anti-inflammatory therapy can cure such tumour-like intestinal amyloidosis with intestinal obstruction and/or haemorrhage. The previously reported cases and our present case of a tumour-like lesion in the colon of patients with amyloidosis are summarized in Table 1 (8-12). The age of the patients with tumour-like lesions ranged from 52 to 73, and two patients were female, while the others were male. The locations of the tumour-like lesions were the transverse colon in 4 cases and sigmoid colon in 2 cases. Abdominal symptoms, including pain and distention, were present in all cases, hematochezia was noted in 3 cases, and anemia in 1 case. Circumferential stenosis was endoscopically detected in 5 cases, thus indicating that the tumour-like lesions in the colon of the amyloidosis patients frequently cause intestinal obstruction. In most of the cases, except our case, the tumour-like lesions were resected by open surgery or via endoscopic mucosal resection to</p>

prevent the intestinal obstruction and determine the diagnosis of the lesion. In our case, we chose the conservative therapy for the intestinal amyloidosis to relieve the intestinal inflammation and determine whether the tumour-like lesion contained a malignant component. Fortunately, the tumour-like lesion vanished within a month, and surgery was avoided in this case. This is the first case in which a tumour-like lesion in the colon of the patient with amyloidosis was cured by conservative therapy with no resection. It is well known that the intestinal wall with amyloid deposits is fragile and tends to bleed, which can cause suture failure after the intestinal surgery (13). Therefore, conservative therapy including a temporary bowel rest and total parental nutrition is a feasible option to determine the diagnosis and, at least in our case, to cure such tumour-like lesions in the colon of the patients with amyloidosis, when no neoplastic change is histologically detected.

Although the mechanism underlying the development of such tumour-like lesions is unclear, the involvement of the amyloid deposit in the vascular wall appears to lead to ischemic changes that possibly lead to the development of the dark red and nodular elevation resembling colon neoplasms. It has also been reported that such vascular involvement of the amyloid deposits leads to a solid nodular deposition in mucosal and submucosal layers, forming the submucosal tumour-like elevation (9). Further analysis with a larger number of the tumour-like intestinal amyloidosis lesions will be helpful for determining the mechanism underlying the development of such amyloid tumours in the colon.

In summary, the present case with AA amyloidosis exhibited a tumour-like lesion in the colon, which vanished after treatment with a bowel rest and total parental nutrition. This therapeutic strategy successfully diagnosed and cured the tumour-like lesion using no surgical or endoscopic resection. Such conservative treatment is a favorable option for diagnosing and curing amyloid tumours in the colon, and is expected to decrease the need for performing surgery on the fragile mucosa, which tends to bleed and thus show an increased risk of suture failure.

LEARNING POINTS/TAKE HOME MESSAGES 3 to 5 bullet points

- In the patients with the systemic amyloidosis, tumor-like lesions are possibly developed in the colon due to the involvement of amyloid deposits in the intestinal wall.
- Such tumor-like lesions cause the abdominal pain, distention and bleeding. Therefore, when

the patients with infectious, inflammatory and neoplastic disorders, particularly with rheumatoid arthritis, complained such abdominal symptoms, physicians should consider the secondary amyloidosis with tumor-like lesions in the colon.

- A conservative treatment is a feasible option to cure such tumor-like lesions in the patients with intestinal amyloidosis, possibly avoiding the unnecessary surgery for the fragile mucosa.

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Figure captions

Figure 1. A computed tomography image.

Computed tomography revealed thickening of the colonic wall in the transverse colon (A) and ascites in the pelvis (B).

Figure 2. A colonoscopic image in the small and large intestine.

Colonoscopy detected edematous mucosa with small erosions in the ileum (A) and a circumferential tumour-like lesion resembling colon cancer and associated with stricture in the transverse colon (B).

Figure 3. Histological findings in the colonic lesions.

The infiltrations of neutrophils, eosinophils and lymphocytes were observed in the biopsied specimen obtained from the ileum (A, x200) and the transverse colon (B, x200), with a thickening of submucosal vascular wall (C, x400). The specimen exhibited apple-green birefringence with polarized light after Congo red staining (D, E x400). Immunohistochemically those areas were positive for amyloid A (F), but negative for κ (G) and λ (H), thus indicating that the lesions were intestinal AA amyloidosis.

Figure 4. Colonoscopic findings of the ileum and colon after one month of observation.

One month later, the tumour-like lesion at the transverse colon had completely vanished, while the edematous mucosa and small ulcerations typical of the intestinal amyloidosis were still observed (A).

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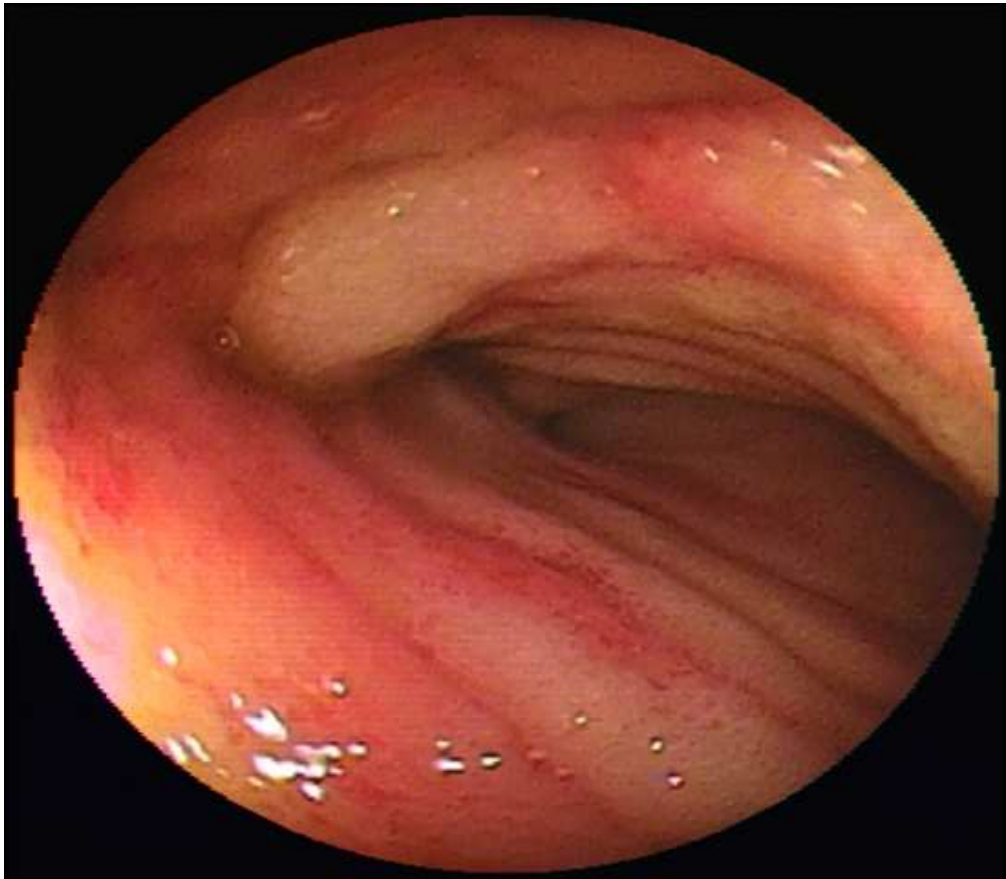
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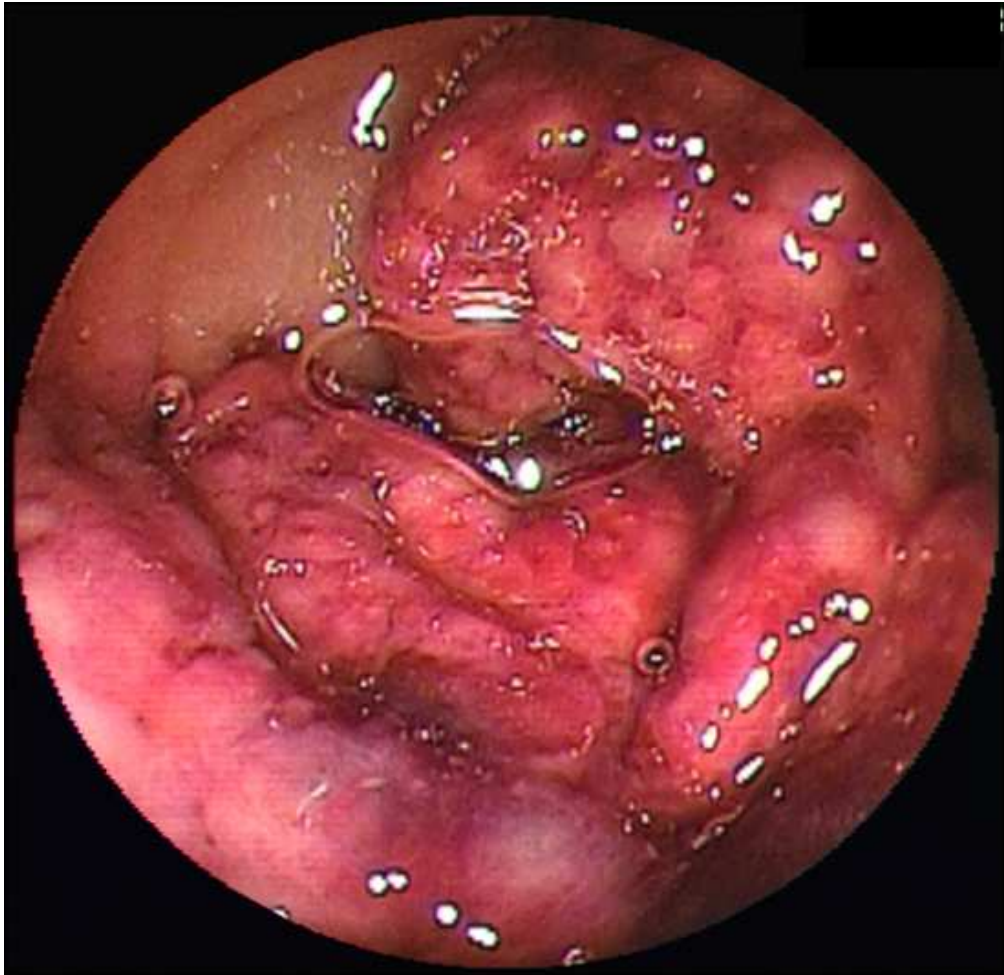
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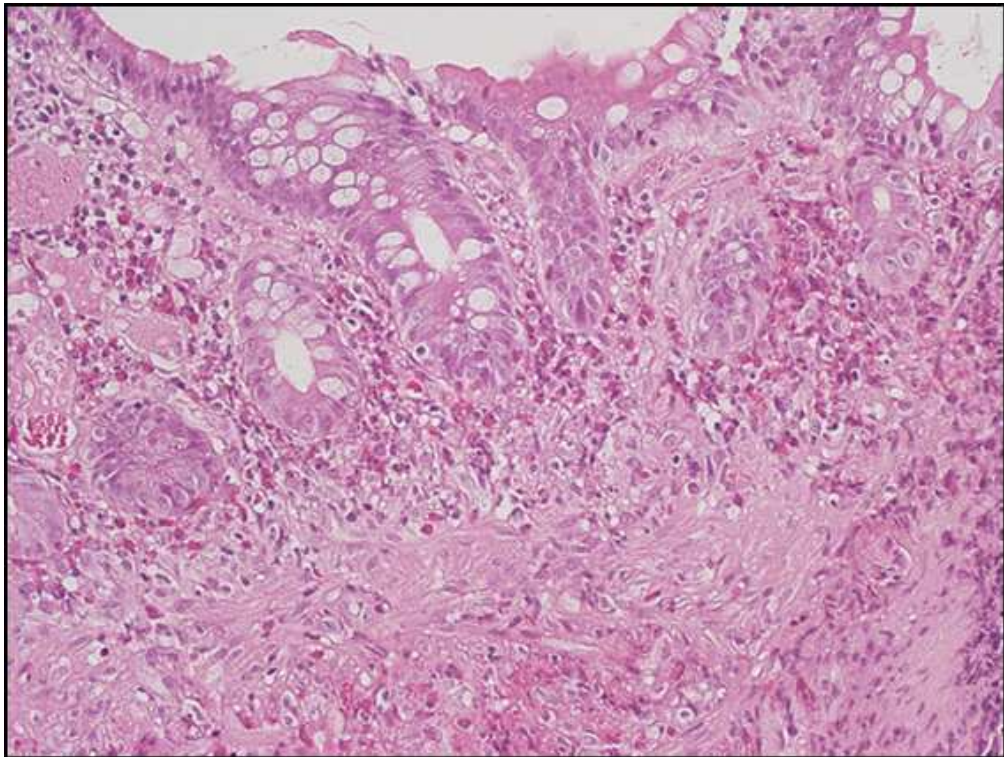
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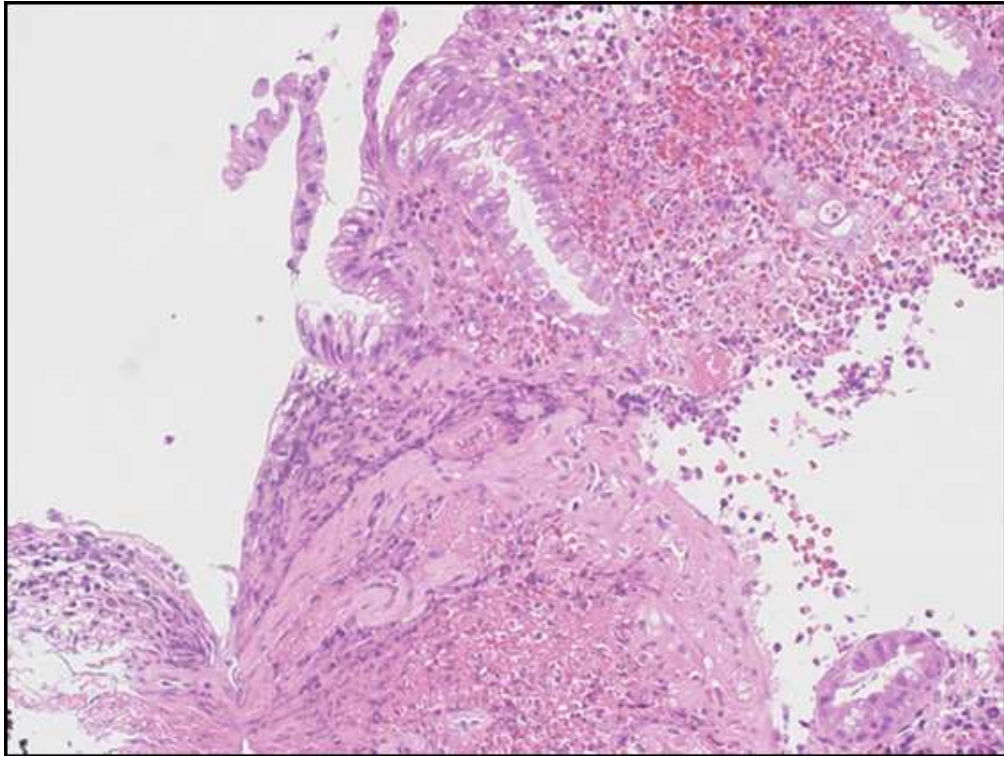
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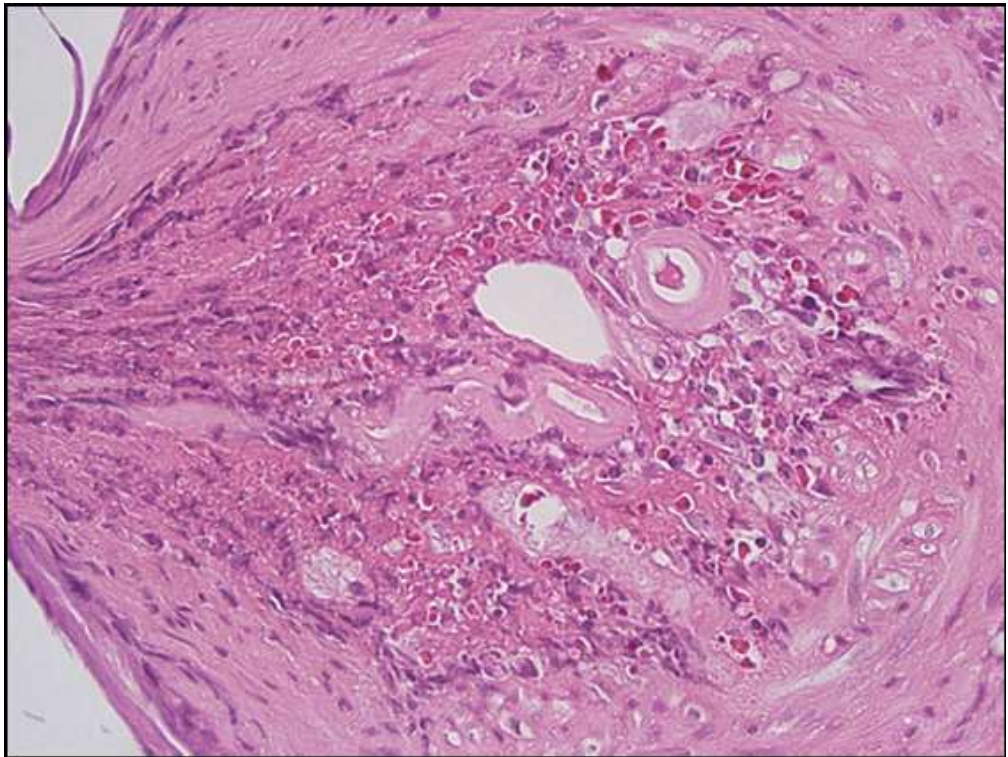
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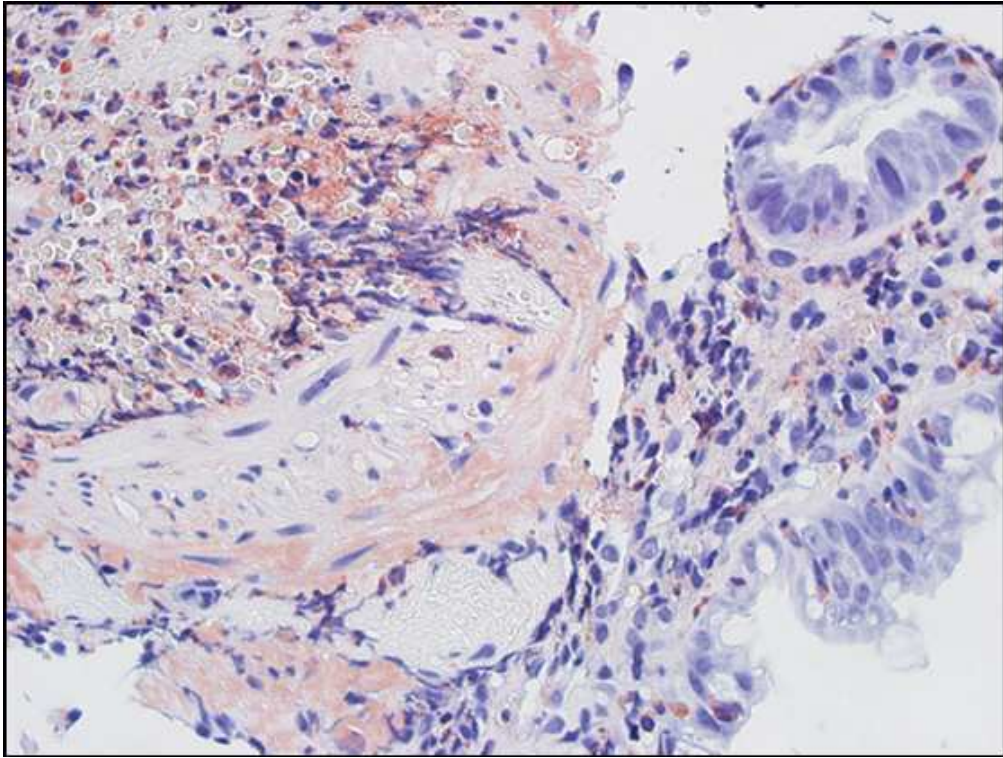
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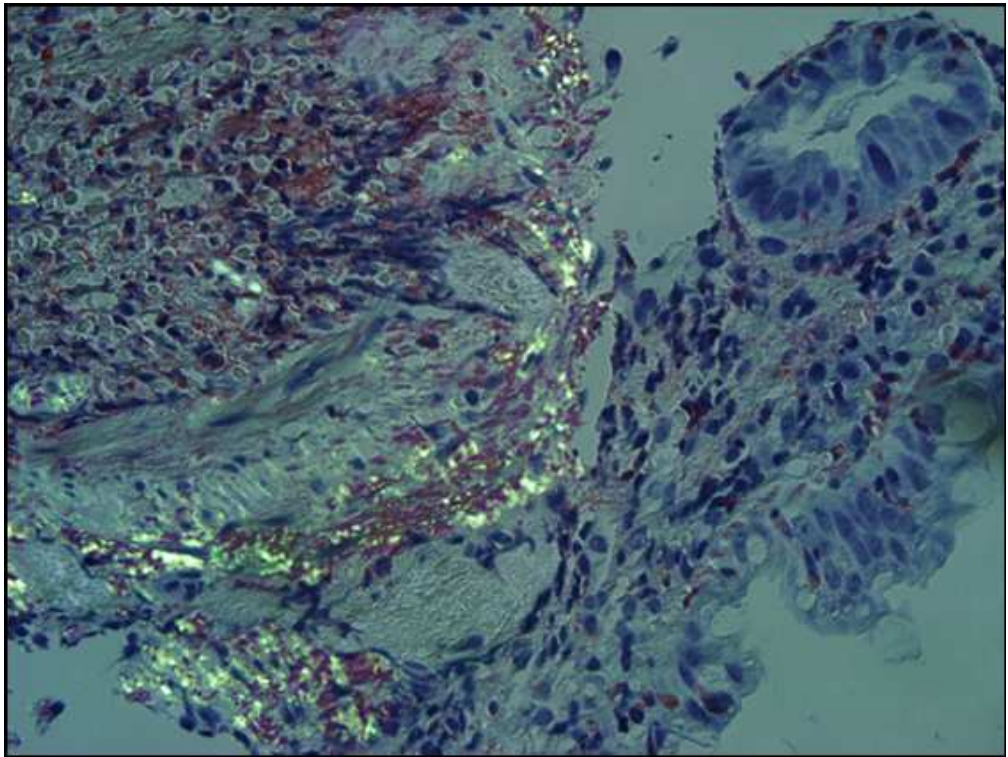
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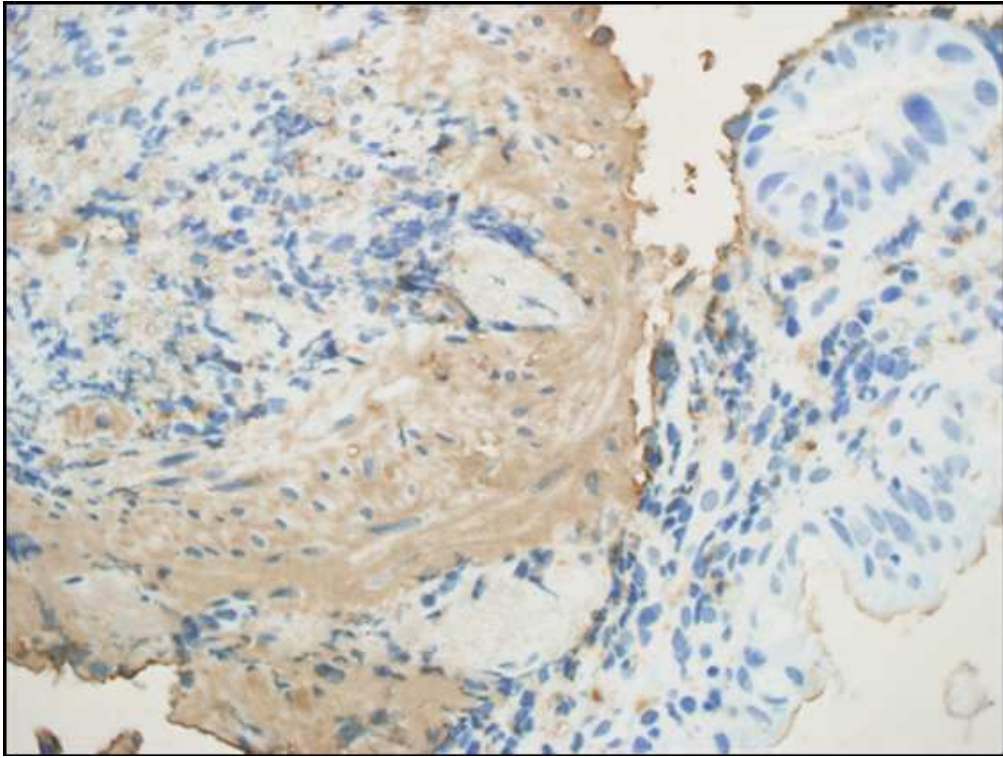
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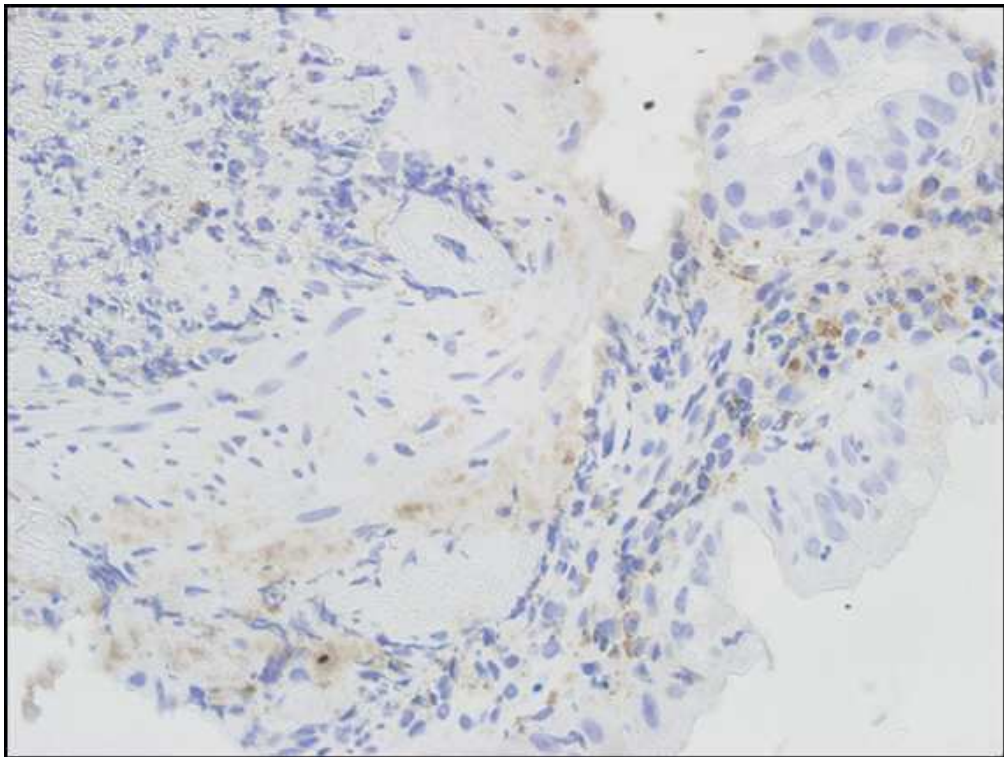
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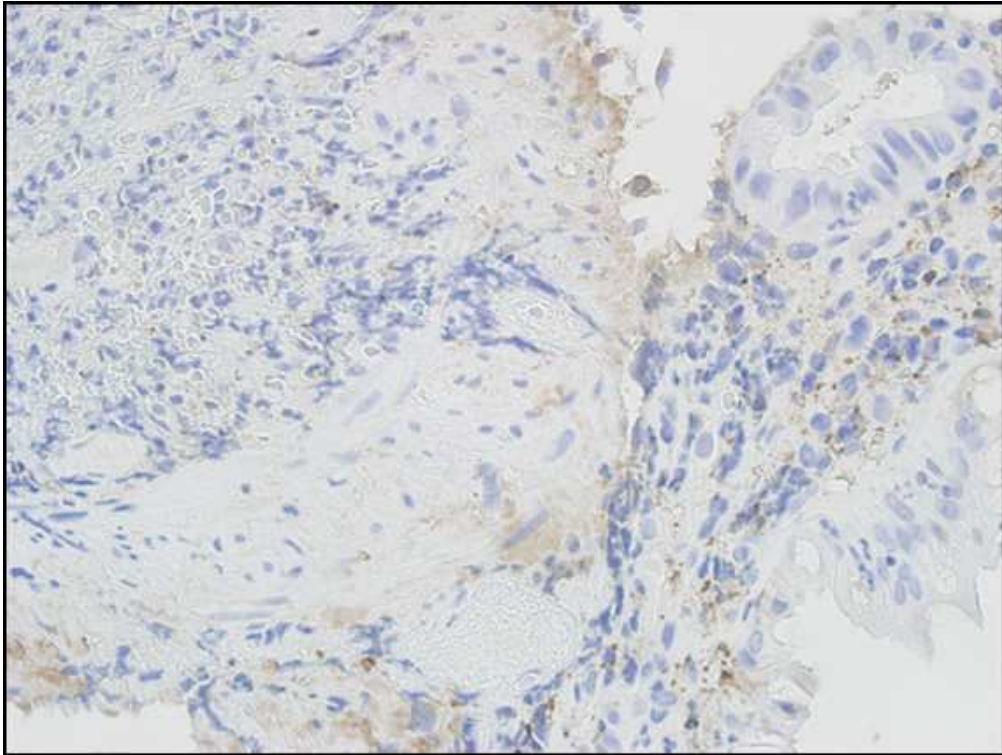
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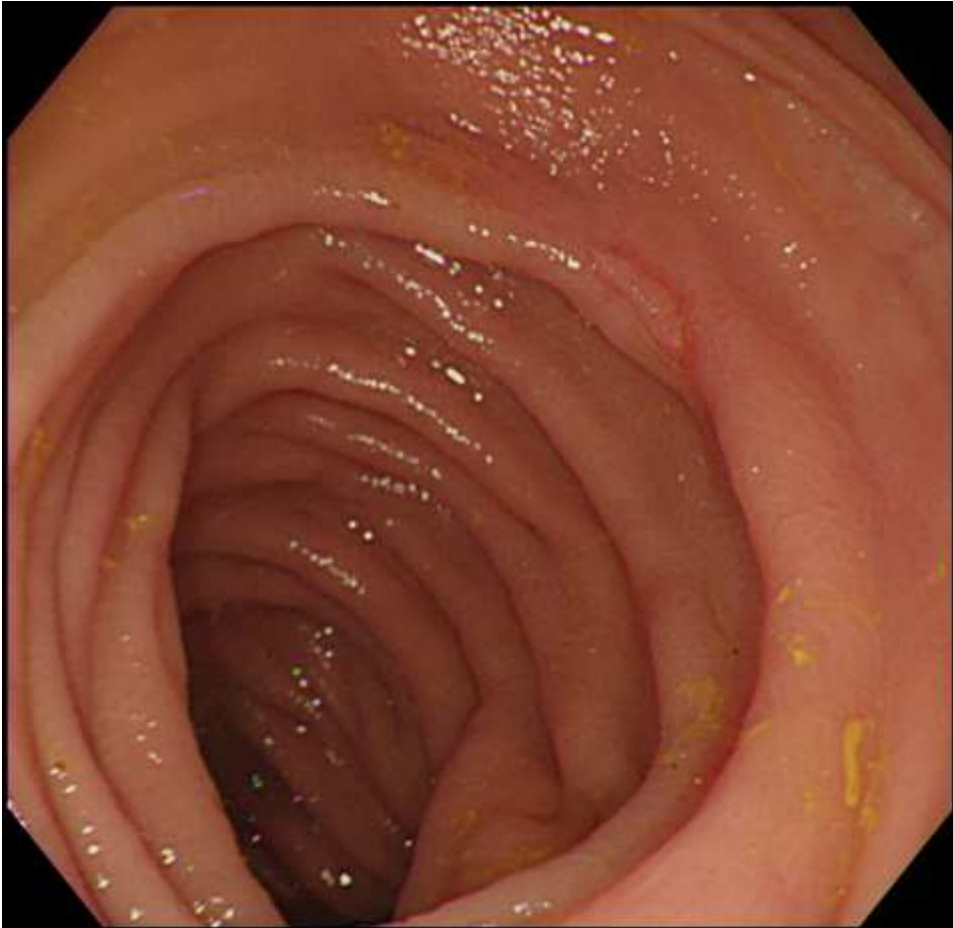
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Age	Gender	Location	Endoscopic findings	Symptoms	Type	Complication	Treatment	Reference
65	M	Sigmoid colon	Circumferential stenosis	Abdominal pain	AL	None	surgery	8
63	M	Transverse colon	SMT	Abdominal pain, hematochezia	AL	None	Endoscopic mucosal resection	9
78	M	Transverse colon	Circumferential stenosis	Abdominal pain, hematochezia	AL	None	surgery	10
52	M	Transverse colon	A circumferential stenosis with a small ulceration	Abdominal pain, hematochezia	Not described	None	surgery	11
73	F	Sigmoid colon	Circumferential stenosis	Abdominal pain, hematochezia	AA	Multiple myeloma	surgery	12
67	F	Transverse colon	A tumor-like lesion with a circumferential stenosis	Abdominal pain, anemia	AA	Rheumatoid arthritis	Total parental nutrition	Present case

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