# A Case of Small Bowel Ulcer Caused by NSAIDs and Detected after Capsule Endoscope Retention

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**We recently detected an annular ulcer thought to have been caused by non-steroidal anti-inflammatory drugs (NSAIDs) when we performed small bowel capsule endoscopy on a patient with suspected small-bowel bleeding and a history of frequent use of oral NSAIDs. The patient was a 64-year-old woman who complained of bloody stools and abdominal pain. The annular ulcer showed concentric stenosis, which caused retention of the capsule endoscope. NSAIDs are some of the most frequently used anti-inflammatory analgesics, and even more frequent use can be expected with the aging of society. No reports to date appear to have described retention of a capsule endoscope due to annular ulceration caused by NSAIDs. We report herein our experience with a patient showing small-bowel ulcer caused by NSAIDs.**

**Key words: small-bowel bleeding, capsule enteroscopy, retention, NSAID-induced small-bowel ulcer**

## INTRODUCTION

In recent years, development of the small bowel capsule endoscope and balloon small bowel capsule enteroscope have allowed endoscopic observation of the entire small intestine. When used in combination with conventional test methods, these techniques enable the diagnosis and treatment of diseases of the small intestine in an efficient and minimally invasive manner. Hemorrhagic lesions, neoplastic lesions, inflammatory bowel disease, and other such conditions that had previously been diagnosed as digestive tract bleeding of unknown origin can now be readily diagnosed. We recently detected an annular ulcer thought to have been caused by non-steroidal anti-inflammatory drugs (NSAIDs) when we performed small bowel capsule endoscopy on a patient with suspected small-bowel bleeding and a history of frequent use of oral NSAIDs. The annular ulcer showed concentric stenosis, which caused retention of the capsule endoscope. Although capsule endoscopy is considered safe and minimally invasive, rare cases of serious accidents such as retention and aspiration have been reported. NSAIDs are some of the most frequently used anti-inflammatory analgesics, and even more frequent use can be expected with the aging of society. That, in turn, can be expected to lead to an increase in cases of small-bowel ulcers caused by NSAIDs. Some patients develop diaphragm-like strictures (annular ulcer scars) by the long term complications of NSAIDs. We report herein our experience with a patient showing small-bowel ulcer caused by NSAIDs, which was detected due to retention of a capsule endoscope.

## CASE REPORT

A 64-year-old woman with chronic renal failure was brought to our hospital on an emergency basis due to bloody stools on April 20, 2010. Hemoglobin level had decreased to 3.8 g/dl, and endoscopy of the upper and lower digestive tract was performed. No lesion likely to have been the source of bleeding was found, so small bowel capsule endoscopy was performed and revealed small bowel erosion and vascular ectasia. Hemorrhagic signs disappeared thereafter and the patient was discharged, to be monitored on an outpatient basis. The patient stopped visiting the hospital, but frequently ingested loxoprofen sodium to treat headaches. Beginning from November 18, 2010, the patient again experienced bloody stools and abdominal pain, which went untreated. On November 25, she was referred to our hospital by her primary care doctor and hospitalized for testing and treatment.

The patient had a history of kidney stones at 27 years old, acute hepatitis (details unclear) at 55 years old, radiotherapy for cervical cancer at 59 years old, and initiation of dialysis for chronic renal failure at 61 years old. Family history was unremarkable.

***Findings on hospitalization:*** Height, 153 cm; weight, 45.5 kg; lucid; blood pressure, 183/92 mmHg; heart rate, 68 beats/min; and body temperature, 37.1℃. Severe anemia was apparent, but no jaundice. Other than mild tenderness in the lower abdomen, no abnormal findings were identified.

***Test values on hospitalization:*** white blood cell

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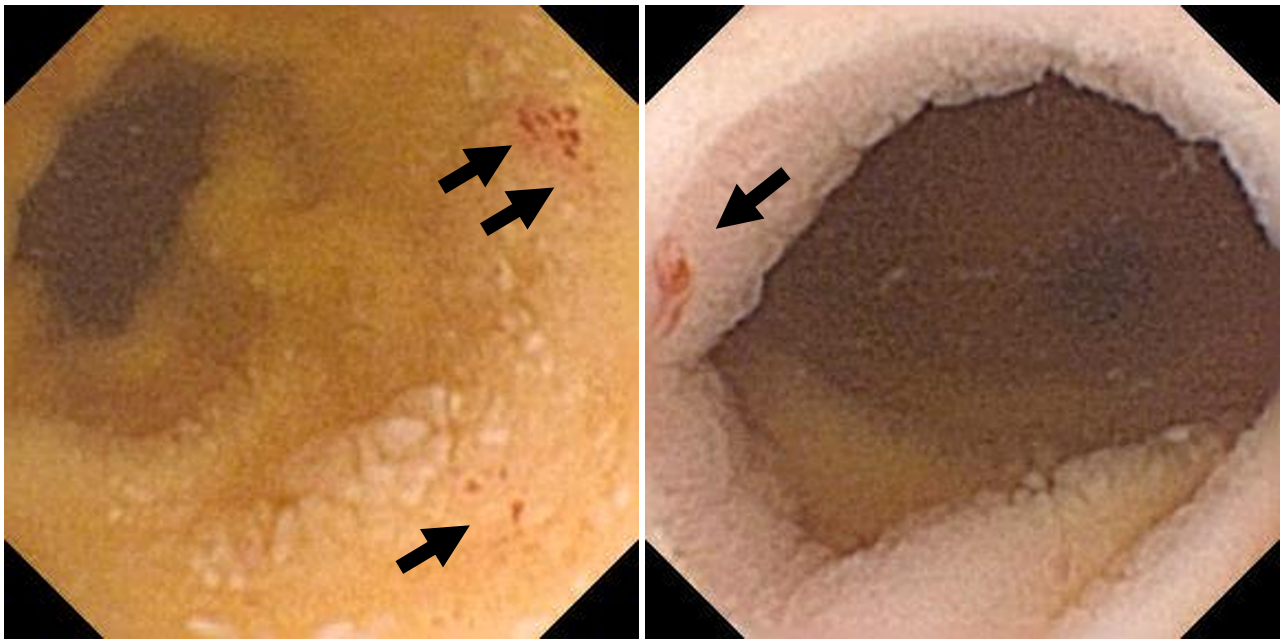

**Fig. 1** Small bowel capsule endoscopy performed in an attempt to identify the source of digestive tract bleeding of unknown cause (Dec 1, 2010). Scattered sites of erosion are seen in the central region of the small intestine (arrows).

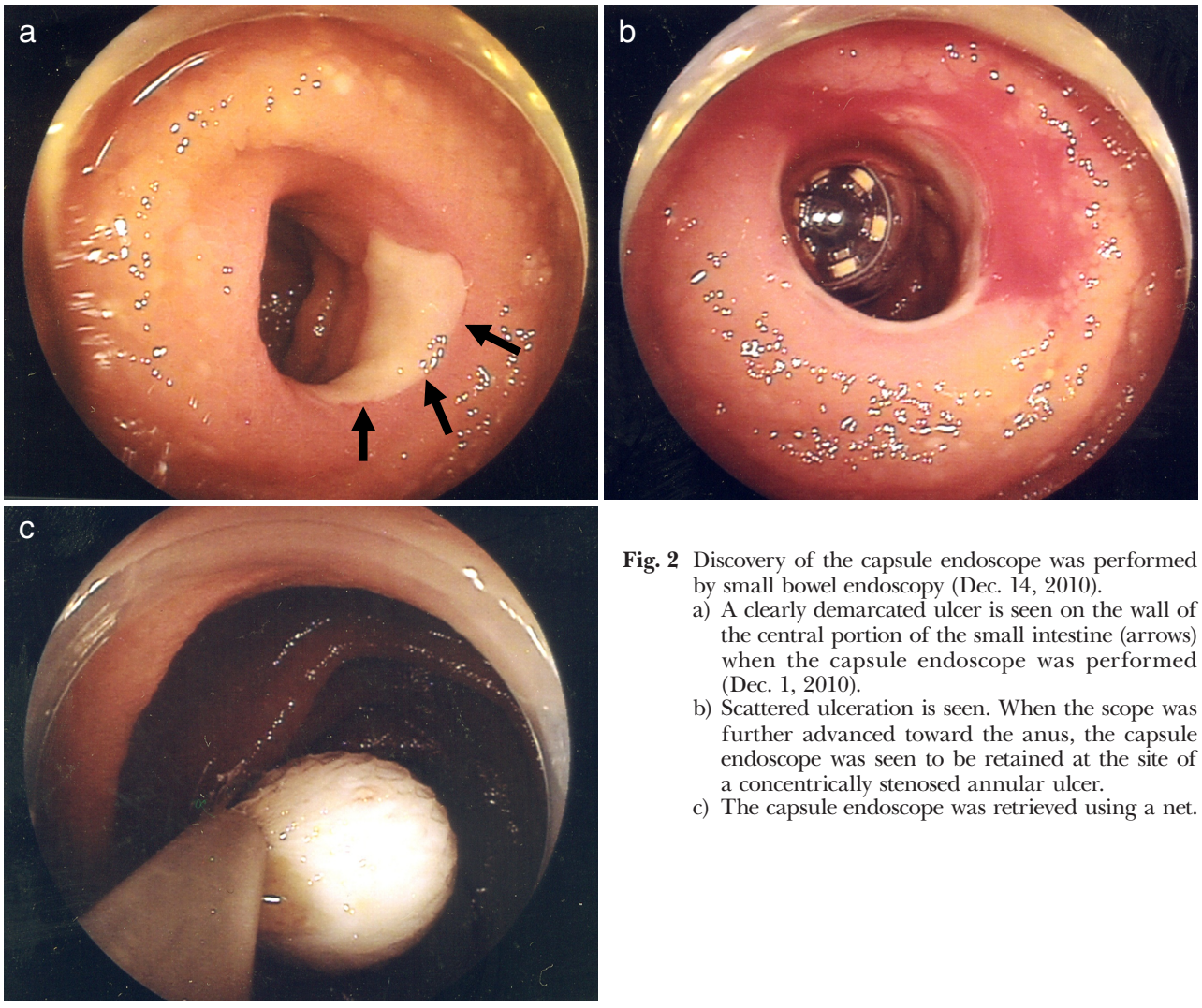


**Fig. 2** Discovery of the capsule endoscope was performed by small bowel endoscopy (Dec. 14, 2010).
a) A clearly demarcated ulcer is seen on the wall of the central portion of the small intestine (arrows) when the capsule endoscope was performed (Dec. 1, 2010).
b) Scattered ulceration is seen. When the scope was further advanced toward the anus, the capsule endoscope was seen to be retained at the site of a concentrically stenosed annular ulcer.
c) The capsule endoscope was retrieved using a net.

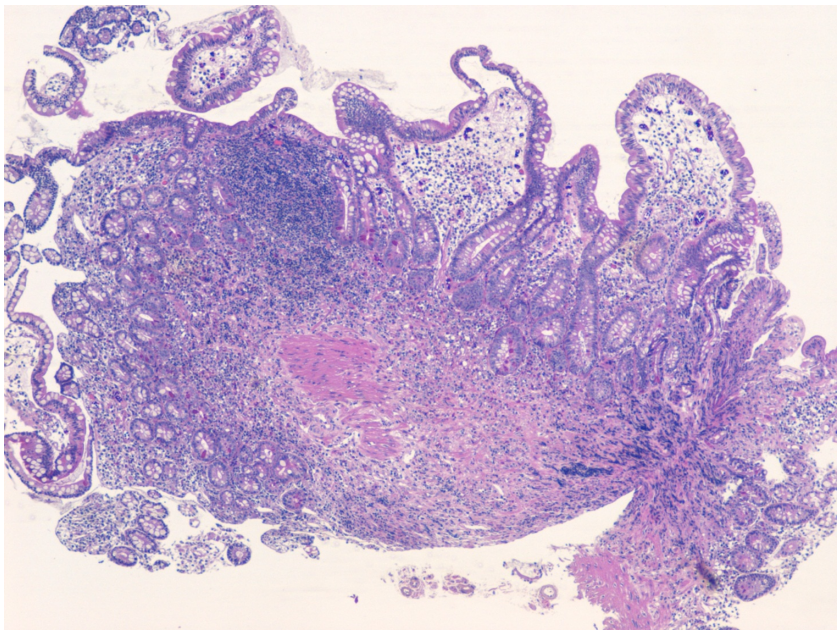

**Fig. 3** Histopathological findings (hematoxylin and eosin staining). Infiltration of the mucosal layer by chronic inflammatory cells is seen, but no findings indicate the presence of malignant cells.

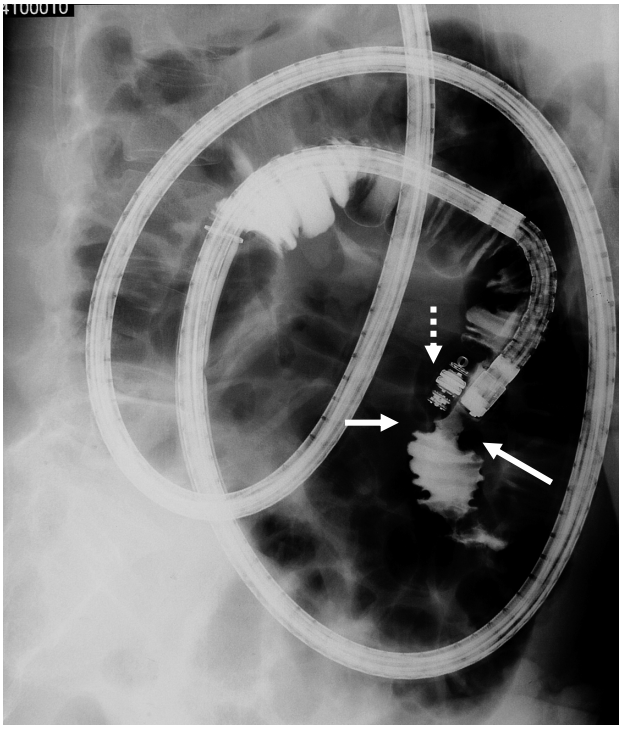

**Fig. 4** Small bowel contrast imaging was performed using Gastrografin™ at the time of capsule endoscope recovery (Dec 14, 2010). Stenosis (arrows) is seen all around the ulcer in the central portion of the small intestine, causing retention of the capsule (dotted line). Contrast imaging was performed at the same site, but no clearly abnormal findings were seen on the anal side of that site.

count, 4300/μl; red blood cell count, 82 × $10^4$/μl; hemoglobin, 2.2 g/dl; platelets, 15.1 × $10^4$/μl; mean corpuscular volume, 86.6 $\mu l^3$; Fe, 16 μg/dl; TIBC (Total Iron Binding Capacity), 283 μg/dl; and ferritin, 8 ng/ml. No abnormalities were evident in other biochemical or tumor markers (including carcinoembryonic antigen and carbohydrate antigen 19-9).

***Course of treatment:*** Blood transfusion was performed for severe anemia, and use of loxoprofen sodium was discontinued. Endoscopy of the upper and lower digestive tracts was again performed and revealed scattered diverticula in the lower digestive tract but, again, no other lesions likely to have been the source of bleeding. Small bowel capsule endoscopy was performed on December 1 and revealed scattered sites of erosion in the central portion of the small intestine (Fig. 1) and an annular ulcer on the anal side of the erosion (Fig. 2a). The annular ulcer caused concentric stenosis, and the capsule was unable to advance beyond that site, resulting in retention. For that reason, the capsule was retrieved on December 14 (Fig. 2b-c). Biopsy of the annular ulcer showed chronic cellular infiltration of the mucosa, but no indication of malignancy (Fig. 3). Bacterial culture and culture for mycobacteria were also performed, but the results were negative. In addition, contrast imaging was performed using Gastrografin™ (Bayer, Osaka, Japan), but no findings suggestive of multiple ulcers or malignant tumor were evident in the vicinity of the annular ulcer (Fig. 4). We initially considered performing endoscopic balloon dilatation at the time of capsule discovery, but in the end we decided against that option for the fol-

**Table 1** Diagnostic criteria of Nishimura *et al.* [4] for small bowel mucosal damage caused by NSAIDs.

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| 1) | History of NSAID use. |
| 2) | Endoscopy reveals ulceration, erosion and typical membranous stenosis. |
| 3) | Improvement in clinical symptoms or endoscopic findings following discontinuation of NSAIDs. |
| 4) | Malignant lymphoma, inflammatory bowel disease and infection are able to be ruled out. |

lowing reasons: the annular ulcer was located in the central portion of the small intestine and deep, while the curvature was sharp and intense peristalsis was present. Following capsule removal, no signs of bleeding were seen, and we intended to perform treatment at a later date. However, the patient strongly requested that she be monitored on an outpatient basis, and so was discharged from the hospital on December 23 without undergoing any treatment.

## DISCUSSION

We performed upper and lower gastrointestinal tract endoscopy on this Japanese woman who had experienced persistent bloody stool, abdominal pain and severe anemia, but the examinations did not reveal any obvious lesions that could be considered as the source of bleeding. In general, causes of bleeding appear unclear in approximately 5% of all cases of digestive tract bleeding [1]. We considered the present patient also represented a case of digestive tract bleeding of unknown cause, as in the previous admission, and performed small-bowel capsule endoscopy on December 14. Examination did not reveal residual clots or bloody intestinal fluid in the small intestine, but scattered sites of erosion were seen in the central portion of the small intestine. In addition, an annular ulcer with white moss and a clear margin on the anal side of the erosion was seen. No blood vessel ends or adherent blood clots were seen, but the ulcer was suspected as the lesion responsible for the intestinal bleeding. Moreover, the ulcer showed concentric stenosis around the entire circumference of the intestine, and this was considered as the reason for the retention of the capsule.

Underlying diseases that can display annular ulceration include small bowel ulcers caused by NSAIDs and intestinal tuberculosis. In addition, annular ulcers have also been seen in some cases of ischemic colitis, nonspecific multiple small intestinal ulceration and Crohn's disease [2]. Adhesion of mucus and border irregularity are reportedly seen in active intestinal tuberculosis [3], but we were able to rule out this possibility on the basis of histopathological and endoscopic findings. We also tried contrast imaging using Gastrografin™. However, no findings showed a longitudinal ulcer extending along the long axis of the intestine, which is said to be characteristic of ischemic colitis. Similarly, there were no findings of multiple ulcers that would lead to suspicion of nonspecific multiple small intestinal ulcers or a protruding or depressed lesion that would be suggestive of malignant tumor.

We therefore concluded that, based on the diagnostic criteria of Nishimura *et al.* [4] (Table 1), the annular ulcer of the small bowel detected in this patient was most likely caused by NSAID use. The reasons were as follows: 1) the patient had a history of frequent use of oral NSAIDs to treat headaches; 2) a clearly demarcated ulcer on the wall of the small intestine is considered characteristic of NSAID ulcers [5]; 3) symptoms improved after NSAIDs were discontinued following hospitalization; and 4) inflammatory bowel disease and infection were able to be ruled out on the basis of the histopathological findings.

NSAIDs are thought to cause small bowel lesions through an immunological disorder caused by inhibition of cyclooxygenase 2 or infiltration by intestinal bacteria that accompanies increased permeability of the mucosa due to the drugs, and the disorder in turn causes tissue damage. Lesion disappearance and recovery after discontinuation of NSAIDs serve as the basis for definitive diagnosis [6].

In the present patient, we were able to identify the lesion responsible for the intestinal bleeding by capsule endoscopy, but the capsule was incidentally retained in the bowel. Retention of the capsule during capsule endoscopy is generally defined as when the capsule remains in the intestinal tract for 2 weeks or more. At present, the incidence of such retention in cases with capsule endoscopy performed to investigate digestive tract bleeding of indeterminate cause has been reported to be about 1–2% [7, 8]. Retention thus represents a rare complication of the procedure. On the other hand, Matsumoto *et al.* [9], in a study of small bowel ulcers, reported finding non-specific ulcerative lesions in 51% (31/61 patients) of patients who ingested NSAIDs, and thus documented a high prevalence of small bowel ulcers in NSAID users. Our search of the published literature found no previous reports of capsule retention due to an annular ulcer caused by ingestion of NSAIDs.

Matsumoto *et al.* [10] also investigated annular ulcer incidence in 21 cases of NSAID-induced small bowel ulcer, finding annular ulcers in 12 cases, 4 of which also presented with advanced stenosis. These findings suggest that the incidence of NSAID ulcer progression to annular ulcer formation and stenosis, as exhibited in the present patient, is comparatively rare.

Capsule endoscopy is a minimally invasive technique in comparison with other methods of endoscopic examination, and places little physical burden on the

patient while tending to be easy to perform. However, use of oral NSAIDs appears likely to increase further with the aging of society, and an accompanying increase in the prevalence of small bowel ulcers due to NSAIDs may be expected. In that context, an increase may be anticipated in reports of capsule retention due to NSAID ulcers, such as seen in the present patient. For that reason, when considering capsule endoscopy, the disease history and physical examination findings of the patient should be fully established, and imaging examinations using contrast imaging of the small bowel may be needed in some cases.

The present patient was discharged from the hospital without being treated, with retrieval of the capsule was the only action taken. That was because the annular ulcer was located in the central portion of the small intestine and deep, where the curvature was sharp, and intense peristalsis was present. The course of this patient will be carefully monitored on an outpatient basis to determine whether there are signs of recurrence of small bowel bleeding and the patient should also continue to avoid using NSAIDs.

Although comparatively rare, severe stenosis associated with annular ulcer should be considered when performing small bowel capsule endoscopy on patients with suspected NSAID-induced small bowel ulcer due to symptoms of bloody stool and anemia and a history of NSAID use.

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