Diaphragm disease associated with nonsteroidal anti-inflammatory drugs mimicking intestinal tumor: A case report

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1. Introduction

Most clinicians are familiar with the effects of nonsteroidal anti-inflammatory drugs (NSAIDs) on the gastroduodenal epithelium, and there is an increasing evidence of their effects on the distal intestine [1], since video capsule endoscopy and balloon enteroscopy are available for the detection of small intestinal lesion [2–4].

Stenotic lesion was first reported as a diaphragm disease in 1988 [5]. Diaphragm disease is pathognomonic of NSAIDs-induced enteropathy, and is rare.

The term ‘diaphragm’ describes the rings of collagenous scar tissue, which are positioned like a drawstring across the bowel lumen, inducing the obstruction [6].

Herein, we report a case of small bowel resection for diaphragm disease.

2. Presentation of case

A 73-year-old man presented with persistent nausea and vomiting. He had been regularly administering loxoprofen sodium hydrate for years for hip pain.

On admission, he was systemically well with a soft, undistended abdomen and mild tenderness. His routine blood tests were normal except for mild anemia (WBC, 7300/μl; Hb, 10.0 g/dl; Plt, 29.8/μl; Lac, 1.6 mmol/l). Abdominal ultrasound scan revealed the small intestine as dilated and showed areas of narrowing and thickening (Fig. 1). Computed tomography revealed a terminal ileal obstruction with edematous loops (Fig. 2).

An incomplete initial diagnosis of small bowel obstruction from intussusception with ileal lymphoma or multiple ileal tumors was made. Thereafter, laparoscopy was performed. Reddening of the serous membrane and dilatation of the proximal small intestine were observed in the distal ileum, 15 cm from the terminal ileum. The remaining small intestine was normal. Twenty-centimeters of ileum was resected by primary ileo-ileal anastomosis. The patient had a favorable recovery after surgery and was discharged 8 days later.
On macroscopic examination, the resected ileum contained a 10 cm long stricture with ulcerated mucosa (Fig. 3).

Stricture histology revealed focal ulceration and numerous inflammatory cells and fibrosis of the submucosa (Fig. 4). Some apoptotic bodies were also observed in the crypts (Fig. 5).

The patient remained well and asymptomatic at a 3-year follow-up.

3. Discussion

Studies have demonstrated that more than 50% of patients on NSAIDs experience some mucosal damage in the small intestine [7]. Diaphragm disease is estimated to occur in 2% of chronic NSAIDs users and may cause subacute bowel obstruction in a small subset of patients who have undergone spiral endoscopy [8].

The pathogenesis of mucosal damage has two hypotheses. First, the NSAIDs-induced decrease in prostaglandin production is considered as the cause of small bowel injuries [9–13]. Second, NSAIDs solubilize lipids of the phospholipids on the mucosal surface, such that the epithelial mitochondria are directly damaged. Thereafter, the mitochondrial damage depletes intercellular energy leading to calcium efflux and induction of free radicals, a disruption of the intercellular junctions occurs, and mucosal permeability increases in the small intestinal mucosa. Finally, the mucosal barrier becomes weakened, such that bile acid, proteolytic enzymes, intestinal bacteria, or toxins easily penetrate the epithelial cells, resulting in mucosal injury [13]. In the preparation of the ulcer, fibrosis of the mucosal and submucosal layers forms a diaphragm or mucosal web, with luminal narrowing, consequently, leading to obstruction [14].

Hayashi et al. defined the criteria of NSAIDs-induced small intestinal injuries as (1) history of NSAID use; (2) endoscopic findings of erosion and/or ulcer and/or typical diaphragm-like strictures; (3) improvement in clinical findings (signs and symptoms) and/or endoscopic findings by the cessation of NSAIDs, except for diaphragm disease; and (4) exclusion of other causes (e.g., malignant tumor, inflammatory bowel disease, and infectious disease) [15].

Preoperative diagnosis of diaphragm disease is sometimes challenging due to its uncharacteristic manifestations; moreover, the radiological findings are usually indefinite and distinctive.

Consequently, diaphragm disease is most often diagnosed by exploratory laparotomy followed by histopathological examination of the resected bowel [14]. Additionally, the history of NSAIDs use is required.

We considered nonspecific multiple small bowel ulcerations, Behcet’s disease and Crohn’s diseases, that were ruled out because the patient was relatively old, and had no symptoms of inflammatory bowel disease or extraintestinal diseases. The pathology examination did not reveal noncaseating granulomas or tumor cells; therefore, intestinal tuberculosis, ileal lymphoma, multiple ileal carcinomas, or neuroendocrine tumor were ruled out. He had a long history of NSAID medication for his hip pain. These findings were consistent with the criteria (1) and (4) of NSAIDs-induced small intestinal disease.

Treatment of strictures must include surgery and withdrawal of the offending NSAID.

The following drugs considerably inhibited small bowel injuries: lansoprazole, rabeprazole, lafutidine, roxatidine, teprenone, rebamipide, irsogladine, and misoprostol. However, drugs that did
not inhibit the injuries were omeprazole, famotidine, cimetidine, ecabet sodium, and sucralfate [7].

Additionally, diaphragm disease can be treated with endoscopic balloon dilation to prevent surgery. This is because fibrotic strictures that occur may be limited only to the submucosal layer and, therefore, dilating the bowel may give some relief. Alternatively, patients may be required to undergo surgery and if the patient presents with severe symptoms, this may require an emergency laparotomy [16,17].

In this case, small bowel stenosis due to tumor was suspected at first, and the long-term NSAID use caused inflammation in the deepest part of the intestine to spread to the subserous layer, such that surgery was appropriate.
4. Conclusion

A case of laparoscopic small bowel resection for small bowel ulcers and scar stenosis caused by NSAIDs. Currently, the main treatment is surgery. However, determining the course of treatment based on the accumulation of small bowel endoscopic dilatation is advisable for cases in the future.

Declarations of Competing Interest

The authors report no declarations of interest.

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Ethical approval

This case report was approved by the Kobe City Medical Center General Hospital Review Board (#zn200704).

Consent

The consent to publish this case report was obtained from the patient.

Author’s contribution

AM drafted the manuscript, and HH revised the manuscript critically. DY and TY revised the histopathological findings. All authors contributed to study concept or design at this submission and approved the final manuscripts.

Registration of research studies

N/A.