CASE REPORT

Small bowel diaphragm disease mimicking malignancy

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SUMMARY

Non-steroidal anti-inflammatory drugs (NSAIDs) can produce diaphragm disease where multiple strictures develop in the small bowel. This typically presents with anaemia and symptoms of small bowel obstruction. The strictures develop as a result of circumferential mucosal ulceration with subsequent contraction of rings of scar tissue. We report a case of a 47-year-old woman with a 6-month history of NSAIDs abuse who presented with subacute small bowel obstruction 1 year after stopping NSAIDs. CT and MRI showed multiple ileal strictures with florid locoregional lymphadenopathy. A malignant diagnosis such as lymphoma was considered likely as florid mesenteric lymphadenopathy has not been previously reported in diaphragm disease. Laparotomy with small bowel resection was therefore performed. Histology showed diaphragm disease with the enlarged mesenteric nodes having reactive features. Gross locoregional lymphadenopathy should not deter a diagnosis of diaphragm disease in cases of multiple small bowel strictures where there is a strong history of NSAIDs use.

BACKGROUND

It is not uncommon for patients to present to surgical and gastroenterology clinics with anaemia and symptoms of subacute small bowel obstruction such as colicky abdominal pain, often precipitated by eating, borborygmi and weight loss. The differential diagnosis includes Crohn's disease, lymphoma, small bowel adenocarcinoma, neuroendocrine tumour and gastrointestinal stromal tumour (GIST). Investigations include haematological and biochemical analysis, gastroscopy, colonoscopy, abdominal CT scan, small bowel MRI, capsule endoscopy and double balloon endoscopy. A strong history of non-steroidal anti-inflammatory drugs (NSAIDs) use makes diaphragm disease a strong contender in the differential diagnosis if small bowel strictures are found. In our case, investigations showed marked locoregional lymphadenopathy in association with ileal strictures. The lymphadenopathy suggested a malignant diagnosis, as florid mesenteric lymphadenopathy has not been previously reported in diaphragm disease. Laparotomy with resection of the ileal strictures was performed. Histology showed diaphragm disease. The enlarged mesenteric nodes, up to 5 cm×3 cm in size, showed reactive hyperplasia with markedly expanded lymphoid follicles with large germinal centres. We wrote up this case to raise awareness that diaphragm disease can cause

florid locoregional lymphadenopathy mimicking malignancy.

CASE PRESENTATION

A 47-year-old woman was referred to the gastroenterology clinic with a 5-month history of abdominal pain exacerbated by eating, weight loss and iron deficiency anaemia. She had become frightened to eat. She had previously undergone laparotomy and drainage of a right tubo-ovarian abscess caused by actinomycosis. She had starting taking Nurofen plus (ibuprofen 200 mg and codeine phosphate 12.8 mg) 18 months before presentation because of sciatica and had become addicted to them, taking up to 30 tablets per day over a 6-month period of time. Reading that these could cause major health problems such as peptic ulceration, she had discontinued them 7 months before her symptoms began.

INVESTIGATIONS

Haematological and biochemical investigations were haemoglobin 86 g/L (115–165), mean corpuscular volume 77 fL (79–97), ferritin 5 µg/L (10–290) and albumin 40 g/L (35–50). Gastroscopy was normal and duodenal biopsies showed no evidence of coeliac disease. The oral bowel preparation for colonoscopy caused vomiting, and colonoscopic views were limited to the descending colon due to faecal residue. A small bowel MRI showed areas of narrowing and thickening, within the mid and distal

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Figure 1 MRI showing ileal strictures (arrows).

Figure 2 CT scan showing ileal stricture (long arrow) with prestenotic dilation of the ileum (short arrow).

ileum (figure 1). The terminal ileum, duodenum and jejunal loops were normal. A CT enterogram showed concentric thickening within the mid and distal ileal loops involving multiple short segments with associated prestenotic dilation of the ileum up to 4.2 cm in diameter (figure 2). A 5 cm dominant stricture was present in the mid ileum with associated multiple large locoregional lymph nodes (figure 3).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included ileal lymphoma, fibrostenotic Crohn's disease, multiple ileal adenocarcinomas, neuroendocrine tumours and GIST tumours. Although the combination of NSAIDs intake and small bowel strictures raised the possibility of diaphragm disease, this was discounted because of the findings of large locoregional lymph nodes. These have not been previously reported in diaphragm disease.

TREATMENT

As the florid locoregional lymphadenopathy suggested malignancy, laparotomy and small bowel resection was considered mandatory so as to obtain histological diagnosis and to cure the patient's obstructive symptoms. At laparotomy, the proximal 258 cm of small bowel was normal. The next 120 cm of ileum contained 13 strictures (figure 4) and there was florid lymphadenopathy in the adjacent small bowel mesentery with lymph nodes up to 5 cm×3 cm in size (figure 5). The final 108 cm of

Figure 3 CT scan showing concentric thickening of a 5 cm segment of ileum (long arrow) with enlarged locoregional nodes (short arrows).

Figure 4 Operative photograph showing 3 ileal strictures indicated by haemostats.

terminal ileum was normal. The 120 cm of ileum containing the strictures was resected with a primary ileoileal anastomosis. The patient made a good recovery from surgery and went home 5 days later.

OUTCOME AND FOLLOW-UP

The patient was reviewed in outpatient clinic 6 weeks after discharge. She was eating normally and had gained weight. Her symptoms of abdominal pain and borborygmi had been cured. Histological examination of the resected ileum showed 13 small bowel strictures with normal mucosa between. Each stricture had a raw circumferential raised erythematous mucosal surface. Some showed evidence of ulceration and fibrin covering the surface. The strictured areas showed underlying oedema and smooth muscle proliferation, together with neuromuscular and vascular hamartoma-like lesions. There was no evidence of vasculitis, fissure ulcers, granuloma formation, dysplasia or invasive malignancy. The enlarged mesenteric lymph nodes showed reactive changes with markedly expanded lymphoid follicles containing large germinal centres. The histological diagnosis was of small bowel diaphragm disease caused by NSAIDs use.

DISCUSSION

NSAIDs are a diverse group of commonly prescribed drugs. They all inhibit an enzyme called cyclooxygenase (COX) in

Figure 5 Operative photograph showing a 7 cm×3.5 cm lymph node conglomerate in the ileal mesentery (arrows).

many tissues reducing prostaglandin levels at these sites. One role of prostaglandin is in the production of inflammation. COX inhibition by NSAIDs reduces inflammation and, therefore, pain. It is well documented that some patients can become dependent on NSAIDs, leading to NSAIDs abuse.¹ Although it is widely known that NSAIDs can cause gastrointestinal ulceration and haemorrhage, their ability to produce small bowel strictures is less well known. Diaphragm disease was first described by Lang *et al*² in 1988. He reported seven patients who had been taking NSAIDs, who had developed small bowel strictures resembling perforated diaphragms. Since this description, diaphragm disease has become a well recognised though relatively rare complication of NSAIDs use.^{3–5} The most common presentation of diaphragm disease is with anaemia in combination with obstructive symptoms including abdominal pain, distention, vomiting and weight loss. The mechanism of small bowel injury by NSAIDs is believed to be a microvascular injury causing a reduction in villous circulation leading to epithelial cell damage. This allows luminal aggressors, enteric bacteria, their products and bile to gain access to the mucosa, causing inflammation.⁶ Circumferential mucosal ulcers develop. Scar tissue and submucosal fibrosis then develops and subsequent contraction of the rings of scar tissue cause diaphragm-like strictures in the small bowel. The histological features of diaphragm disease are submucosal fibrosis, irregular thickening of the muscularis mucosa with a disorganised arrangement of neural, vascular and smooth muscle elements, resembling hamartoma.⁶

The differential diagnosis of the symptoms caused by diaphragm disease, anaemia and subacute small bowel obstruction, includes gastroduodenal ulceration, coeliac disease, Crohn's disease, small bowel lymphoma, small bowel adenocarcinoma, neuroendocrine tumours and GIST tumours. Investigations for these symptoms include haematological and biochemical analysis, gastroscopy, duodenal biopsy, colonoscopy with terminal ileal biopsies, abdominal CT scan and small bowel MRI scan. Capsule endoscopy should be used with caution as the capsule may become impacted in diaphragm disease necessitating surgery.⁷ The diagnosis of diaphragm disease is largely dependent on a strong history of NSAIDs use together with the finding of multiple small bowel strictures. Diaphragm disease usually affects the ileum and can produce bowel involvement ranging from multiple diaphragm-like strictures to longer broad small bowel strictures. The terminal ileum is usually not involved. Although jejunal strictures can be assessed, biopsied and dilated using double balloon endoscopy,⁸ the ileal strictures in our case started 258 cm from the duodenojejunal flexure and were probably not accessible using this technique.

A definitive preoperative diagnosis of diaphragm disease is extremely difficult to make. However, if there is a high suspicion of diaphragm disease, then conservative treatment with withdrawal of the NSAIDs can be adopted,⁹ though if narrow or long fibrostenotic strictures have become established, then surgical resection may be inevitable, as once fibrous scar tissue has matured, removal of the cause of injury is unlikely to allow resolution. In medically fit patients with severe obstructive symptoms, surgery is usually performed to relieve the obstruction and obtain a definitive histological diagnosis. At laparotomy, the strictures may be difficult to detect externally and manoeuvres such as the use of an intraluminal ballbearing or small bowel CO₂ insufflation have been used to help identify them.¹⁰ Surgery usually involves resection of all the small bowel containing the strictures, however, in order to preserve intestinal

length, a combination of resection and stricturoplasty can be used. The combination of resection of the small bowel strictures and discontinuation of NSAIDs is usually curative.

In our case the radiological finding of florid locoregional lymphadenopathy in relation to the ileal strictures raised the possibility of malignancy. This made surgery mandatory, as florid locoregional lymphadenopathy has not been previously described in diaphragm disease.^{6–11} There has been one previous report of diaphragm disease being misdiagnosed with malignancy, however, in this patient there was ongoing treatment for malignancy and imaging showed only minor mesenteric lymph node enlargement.¹² The diagnosis of diaphragm disease largely rests on a history of NSAIDs use, anaemia, symptoms of small bowel obstruction and the finding of small bowel strictures on imaging. Our case illustrates two important features, that diaphragm disease can present with obstructive symptoms more than 6 months after stopping NSAIDs use, and that it can produce florid locoregional lymphadenopathy mimicking malignancy.

This case report highlights an important condition, small bowel diaphragm disease, which will become more prevalent with the continued and widespread use of NSAIDs. A history of long NSAIDs use and the presence of anaemia should lead clinicians to consider diaphragm disease in the differential diagnosis, particularly when oesophagogastroduodenoscopy and colonoscopy are negative.

Learning points

- ▶ Diaphragm disease is caused by non-steroidal anti-inflammatory drugs (NSAIDs) use and presents with anaemia and symptoms of subacute small bowel obstruction including abdominal pain, weight loss and borborygmi.
- ▶ Diaphragm disease is diagnosed by the finding of multiple small bowel strictures on CT or MRI where there is a strong history of NSAIDs use.
- ▶ Diaphragm disease can present more than 6 months after stopping NSAIDs use.
- ▶ In patients with severe obstructive symptoms caused by diaphragm disease, surgical resection of the diseased small bowel is diagnostic and usually curative.
- ▶ Florid mesenteric lymphadenopathy can occur in diaphragm disease, mimicking malignancy.

Competing interests None declared.

Patient consent Obtained.

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