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lesson of the month (1)

Subacute small bowel obstruction due to diaphragm disease

Diaphragm disease occurs in 2% of chronic non-steroidal anti-inflammatory drug users and occasionally may cause subacute small bowel obstruction.

Lesson

A 52-year-old self-employed farm manager was seen in a gastrointestinal (GI) outpatient clinic with a four-week history of severe worsening upper abdominal pain and weight loss of $1\frac{1}{2}$ stone. He felt bloated before and after meals and had new onset low-grade constipation. He had vomited about six times over several weeks. When lying down at night he was getting reflux symptoms. Lansoprazole given for his pain by his general practitioner (GP) had been of no benefit, but Gaviscon® seemed to help.

Apart from cluster headaches and asthma, he was suffering from osteoarthritis for which he took non-steroidal anti-inflammatory drugs (NSAIDs) and had required a right knee replacement. According to the GP records, he had a nine-year history of intermittent prescriptions of diclofenac and ibuprofen for his arthritis and also self-medicated with ibuprofen bought over-the-counter. More recently he had been on low-dose aspirin and lansoprazole but he was not on any other medication. He was a smoker of 30 cigarettes per day.

On examination he appeared well. There was some epigastric discomfort on palpation but the rest of the exam was normal. Rectal examination and rigid sigmoidoscopy were both normal. There was no lymphadenopathy.

The patient's screening blood results did not reveal any significant abnormality that could be relevant to his symptoms: haemoglobin of 13.8 g/dl, white blood count 7.1, platelets 241, serum creatinine 110 μmol/l with an estimated glomerular filtration rate of 65 ml/min, albumin 40 g/l, C-reactive protein <2.0 mg/l; and normal liver function tests, thyroid function tests and lipid profile.

Oesophagogastroduodenoscopy was performed revealing food residue in the stomach, despite a 14-hour fast, and linear oesophagitis. Oesophageal brushings microscopically confirmed the presence of candida.

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Unenhanced abdominal computed tomography showed proximal small bowel dilatation with a rapid decrease in luminal diameter at the lower jejunum. No evidence of an extrinsic mass was seen (Fig 1).

A barium follow through demonstrated the same findings and, again, no obstructive mass was seen. The overall impression was of a benign obstructive lesion.

The patient underwent laparoscopically assisted small bowel resection under general anaesthetic. Laparoscopy revealed a dilated proximal jejunum down to a very short stricture of 1.5 cm in length beyond which the small bowel was collapsed. The stricture looked ischaemic, and there was no mass effect, lymphadenopathy or ascites. The more distal bowel, as well as the other viscera, looked normal. As the patient was also due to have his periumbilical hernia repaired, a small periumbilical incision was made to access the diseased loop of small bowel and resect it with proximal and distal division at 5 cm from the lesion.

The resected bowel specimen contained a 15-mm long strictured area with ulcerated mucosa (Fig 2). Histology of the stricture revealed focal ulceration and granulation tissue within the tips of the villi and abnormally thickened and hyperplastic muscularis mucosa with fibrous proliferation and submucosal oedema (Fig 3). Histology of the bowel adjacent to the stricture was unremarkable. These findings were consistent with diaphragm disease.

The patient has had no pain or vomiting since the operation. He continued to have loose stools for a few weeks but this eventually resolved, and at the last telephone encounter two weeks after his surgery he reported no symptoms. He was advised to stop his NSAIDs.

Comment

NSAIDs carry a significant potential for gut toxicity. Although upper GI (ie gastroduodenal) damage inflicted by NSAIDs is more readily appreciated by clinicians, small bowel disease caused by these drugs appears to be more common, as demonstrated by capsule enteroscopy.[1,2] Contrary to their name denoting an anti-inflammatory action, NSAIDs in reality give rise to an increased permeability and inflammation of the small bowel in 65% of patients taking these drugs long term.[3] It is thought that a number of mechanisms are involved, including an inhibitory action on cyclo-oxygenase (COX), which underlies the conventional pathway of blocking the synthesis of prostaglandins, and a topical effect of uncoupling of adenosine triphosphate synthesis in the mitochondria of enterocytes, the latter probably being more important for initiation of the small intestinal damage.[4] The exposure to NSAIDs results in a spectrum of intestinal disease. The most typical manifestations of NSAID enteropathy are occult GI bleeding and protein-losing

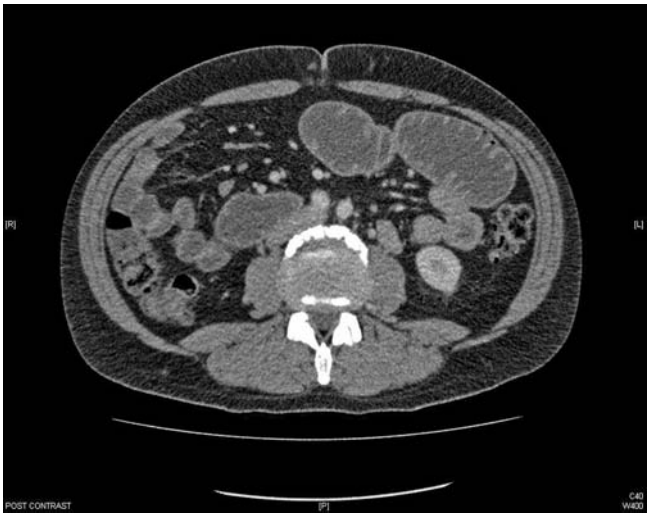

Fig 1. Dilated proximal small bowel seen on computed tomography.

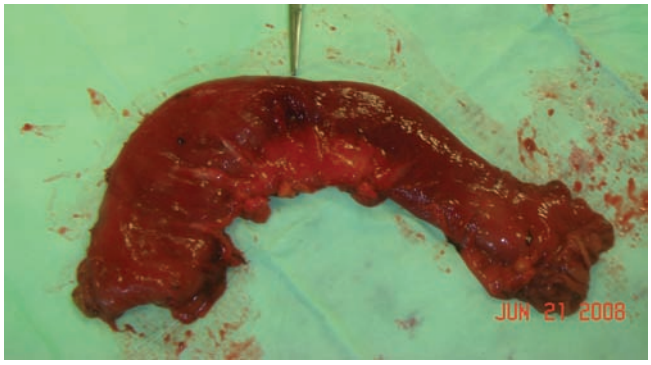

Fig 2. Resected small bowel with stricture visible as a local narrowing in the external diameter.

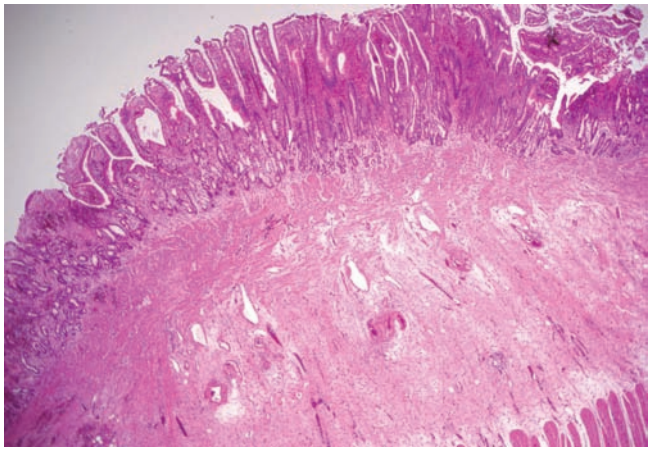

Fig 3. Thickened muscularis mucosae with splaying of the muscle fibres and fibrotic submucosa. The muscularis propria is seen in the bottom right corner (Haematoxylin and eosin, ×20).

enteropathy leading to iron deficiency anaemia and low serum albumin, respectively. Common symptoms include chronic diarrhoea and weight loss. More serious and life-threatening adverse reactions have also been described, such as acute intestinal bleeding and perforation. In the colon, NSAIDs may trigger colitis, ulceration and attacks of diverticulitis in individuals with pre-existing colonic diverticula.[5]

Less commonly, NSAIDs are able to cause fibrotic diaphragm-like strictures in the small bowel, the prevalence of which in one capsule endoscopy study on chronic NSAID users was reported as 2%.[2] The term 'diaphragm disease' (DD) was first introduced, and its histopathology findings described, by Lang *et al* in 1988; however, this description was not comprehensive enough.[6] A more recent review of 10 clinical cases observed at a single institution concluded that DD comprises a wide range of histological findings, and these included thickening and chaotic arrangement of muscular bundles in the muscularis mucosae, fibrosis of the lamina propriae, invariable mucosal ulceration at the apex of the diaphragm, numerous vessels, ganglion cells, nerve fibers and eosinophils in the mucosa.[7] An identical histology has also been reported in the condition called neuromuscular and vascular hamartoma, which is much rarer than NSAID-induced DD and commonly presents as small bowel obstruction.[8,9] It is not known currently whether the two described conditions actually belong to the same nosological spectrum.[8,9] Diaphragms occur throughout the small bowel but are most common in the ileum. Radiological confirmation is difficult as small bowel studies with luminal contrast are neither sensitive nor specific for the detection of diaphragms. Endoscopic techniques are more useful, and capsule enteroscopy nowadays has the key role in pre-operative diagnosis. Unfortunately, in those developing serious complications, eg severe bleeding or obstruction, the only route to definitive diagnosis is surgical intervention assisted by intraoperative bowel palpation and enteroscopy, which allow detection of the diaphragms.[10] Surgical treatment in patients with obstructing tall diaphragms includes small bowel resection with primary anastomosis. Discontinuation of the offending NSAID is strongly advised.

The degree of bowel stricturing by diaphragms varies and sometimes is quite striking, narrowing the lumen to the size of a pinhole. Despite this, obstructive symptoms requiring surgery in this disease appear to be surprisingly rare. There are multiple case reports of DD in the literature but we have found only 15 cases of subacute small bowel obstruction caused by this pathology published in Medline since 1988, when DD was identified as a separate entity. The case described above clearly represents a very rare example of clinically significant bowel obstruction due to DD.

NSAIDs have been extensively used for many painful conditions (eg arthritis) in recent years, and the prevalance of DD in the population has, therefore, probably been on the rise. Gastroduodenal NSAID toxicity is generally well remembered by clinicians in their daily practice, but there is good evidence that NSAID-related enteropathy comprising intestinal mucosal inflammation with increased permeability and formation of

highly characteristic diaphragm-like structures within the small bowel is, in fact, more common. A history of prolonged NSAID usage should be documented in every patient presenting with subacute bowel obstruction and strongly considered as a clue to the potential aetiology, even though clinically significant obstruction due to DD appears to be quite rare. If small bowel diaphragms are ultimately identified as the cause of obstruction, surgical resection can be successfully performed, and the prospects of cure from the disabling symptoms are excellent.

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