Case Reports

Diaphragm disease of the jejunum

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ABSTRACT

تسبب العقاقير المضاده للالتهابات غير الستيرودية (NSAIDs) حدوث مرض الحجاب في الأمعاء. نستعرض في هذا التقرير حالة مريض يبلغ من العمر 73 عاما أصيب بهذا المرض بعد عامين من استخدام العقاقير المضادة للالتهابات (NSAIDs). الشكوى التي تقدم بها المريض تشمل وجود ضعف عام، وغشيان بالإضافة للتغوط الأسود لفترة قصيرة. خلال عملية شق البطن الاستقصائي تم الكشف عن وجود تخصر متعدد في الأجزاء القريبة من المعي الصائم. الفحص المجمل والفحص المجهري أكدا الإصابة بهذا المرض، وقد تمت مراجعة المقالات المنشورة سابقا حول هذا المرض.

Non-steroidal anti-inflammatory drugs (NSAIDs) are associated with the development of diaphragm disease. We report a 73-year-old male patient with this condition who had used NSAIDs for 2 years. He presented with general weakness, syncopal attacks, and a short history of melena. At laparotomy, multiple areas of constricted bowel were found in the resected proximal jejunum. Gross and microscopic examination confirmed diaphragm disease. The relevant literature is reviewed.

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of musculoskeletal conditions. Their major side effect is gastrointestinal epithelial toxicity, which is not confined to the stomach and proximal duodenum but extends also to the rest of the small bowel, colon, and rectum.[1] Asymptomatic enteropathy is reported in 60-70% of patients and is characterized by increased intestinal permeability and inflammation,[2] the remainder of patients may have symptoms including abdominal pain, diarrhea, bloating, heartburn, and gastric upset.[3] Chronic occult bleeding, and protein loss may result in iron-deficiency anemia associated with intestinal erosions and ulcers, and in hypo-albuminemia.[4,5] Diaphragm disease is a rare condition seen in patients on long-term NSAIDs characterized by multiple (3-70) thin (2-4 mm) diaphragm-like septa narrowing the lumen to a pinhole resulting in luminal occlusion.[6,7] The objective of our study is to report a case of diaphragm disease of the jejunum caused by diclofenac with unusual clinical presentation.

Case Report. A 73-year-old man presented in March 2007 to the emergency department with general weakness, syncopal attacks, vomiting, and a short history of melena. He had a 2-year history of diclofenac sodium intake for chronic low back pain associated with lumbar disc prolapse, for which indomethacin was added for the last few months prior to his presentation. On examination, he was pale. He showed no abdominal distension or other signs of intestinal obstruction. Plain abdominal x-ray revealed no abnormality. Abnormal laboratory results included: hemoglobin level, 9.6 g/dl (11-18); urea, 18 mmol/l (2.5-7.7); total protein, 55 g/l (60-80), and albumin 33 g/l (35-50). Upper and lower gastrointestinal endoscopy was normal except for a few small sessile polyps in the ascending colon, which were resected. The endoscopist gave the impression that the bleeding was most likely from the small intestine, suggesting CT angiography, or nuclear medicine scan with Tc99m red blood cell labeling. The latter was performed and revealed the presence of early linear

focal increased uptake in the left upper quadrant of the abdomen, increasing in size, changing its shape, moving downwards and medially with time, and highly consistent with acute gastrointestinal bleeding in the small intestine, likely in the jejunum. Exploratory laparotomy was performed with the discovery of multiple areas of constricted bowel in the proximal segment of the jejunum. The involved portion was resected and sent for pathological examination.

Gross examination. The specimen received for surgical pathological assessment was a segment of small intestine measuring 30 cm in length. Upon sectioning, the luminal surface exhibited multiple prominent mucosal folds (circumferential ridges), measuring 2 - 3 mm in width (**Figure 1**). Pinpoint hemorrhages were demonstrated at the tips of these folds. No masses were identified.

Microscopic examination. Histologically, the multiple folds were composed of mucosa and submucosa, protruding into the lumen. The muscularis propria was uninvolved (**Figure 2a**). Additional findings were mild inflammation in the lamina propria, focal erosion of the surface epithelium lining the tips of the folds and submucosal fibrosis extending to the interface with the uninvolved muscularis propria (**Figure 2b**). No evidence of Crohn's disease, vascular disease, amyloidosis, tuberculosis, or malignancy was seen. Based on the clinical history and morphological findings, this case was diagnosed as NSAID-associated diaphragm disease of the jejunum. Patient consent was obtained in the beginning of this study. He was contacted many times during the study for clarifying some points in the clinical history for follow up. He showed good clinical recovery after surgery and now, 18 months following the presentation, is doing well with no similar complaints.

Discussion. Ring strictures of the small intestine were described in 1971 by Bilbao et al.[8] The term diaphragm disease, however, was first used in 1988 by Lang et al.[6] In their report, they described 7 cases of the disease associated with NSAID and discussed the possible mechanisms. Since that time, over 100 cases have been reported in the literature, most of which are located in the small intestine.[3] Most of these are linked to NSAIDs. The NSAIDs are known to cause hemorrhage and ulceration in the upper gastrointestinal tract. In addition, they have been reported to cause small intestinal inflammation in up to 70% of patients.[9] In the small intestine, these medications have been linked to perforation, bleeding, stricture, enteropathy, and diaphragm disease. In the colon, they can cause colitis, bleeding, perforation, and strictures.[10] The latter manifestations have more recently been reported and linked to slow-releasing or enteric-coated NSAID forms.[3] The NSAIDs known to be associated with this

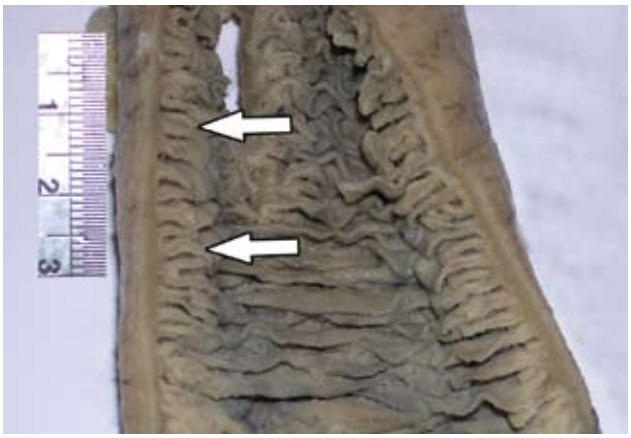

Figure 1 - Gross photograph: mucosal surface shows multiple mucosal folds measuring 2 to 3 mm in width (arrows).

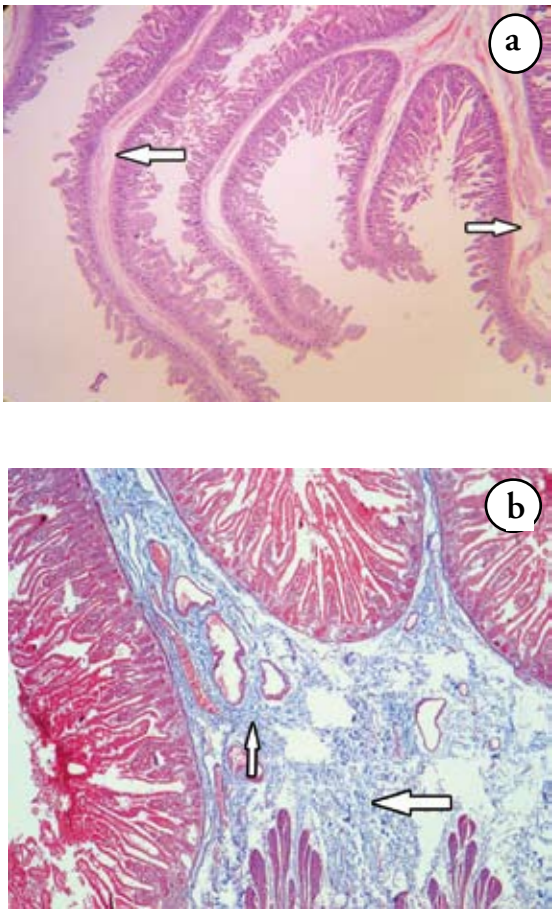

Figure 2 - Microscopic photographs showing **a)** prominent mucosal folds (arrows) forming diaphragm-like strictures (Hematoxylin and eosin, x20). **b)** Submucosal fibrosis (thin arrow) extending to the interface with the muscularis propria (thick arrow), (Masson trichrome, x40).

disease include indomethacin[6,11] and diclofenac.[12] Our case was one of those cases associated with diclofenac. It was taken for 2 years. The patient added indomethacin over the last few months prior to presentation; therefore, we think it played only a minor role, if any, in the disease process. Two hypotheses have been postulated for the mechanism of intestinal injury caused by NSAIDs. The first, proposed by Lang et al,[6] suggests the role of NSAIDs in cyclooxygenase inhibition with subsequently decreased synthesis of prostaglandins, which in turn affects mucosal integrity with increased vulnerability of the mucosa to bacteria and toxins. Eventually, mucosal damage and focal submucosal fibrosis may affect the flexibility of the plicae circularis, producing a permanent fold.[6] The second explanation, suggested by Going et al[11] in 1993, was that of the role of circumferential ulceration; which in the healing phase shows formation of contracting rings of scar tissue that ultimately form diaphragms by acting as drawstrings across the bowel lumen. Microscopically, the classic mucosal diaphragms show patchily fibrosed submucosa, mildly inflamed mucosa, ulceration, atrophic villi, and irregular surface. More extensive fibrosis in the submucosa is identified in the broad-based stenotic lesions.[6,7] Our case showed similar changes; however, the fibrosis was extending to the interface with the uninvolved muscularis propria, and no broad-based changes were seen. Most cases are asymptomatic until presenting with acute or subacute intestinal obstruction. Other modes of presentation include weight loss, diarrhea, anemia, hypoalbuminemia and other features of malabsorption.[7] Our patient came with an uncommon presentation of general weakness and syncopal attacks with no symptoms or signs of obstruction. His complaints were related to sudden drop of hemoglobin level that might be attributed to hemorrhage from the eroded surface epithelium over the mucosal folds. In addition, he had mild hypoalbuminemia and hypoproteinemia. Diagnosis of diaphragm disease by conventional investigations is difficult, as these fail to demonstrate the diaphragms. In 90% of cases, diagnosis is made at laparotomy and subsequent histology.[7] Differential diagnoses include Crohn's disease, radiation enteritis, potassium-induced ulceration, celiac disease, ischemic bowel disease, and tuberculous strictures.[6,7] These diagnoses should be excluded first before making a diagnosis of diaphragm disease. Following surgical resection, recurrence may occur in 50% of patients. This is attributable to incomplete resection at the initial operation or continued use of NSAIDs.[6]

Diaphragm disease is an infrequent but recognized NSAID-associated gastrointestinal complication, the diagnosis of which needs a high index of suspicion. The physician and patient should be aware of the possible recurrence, especially if the patient continues to use NSAIDs. We report a patient with diaphragm disease of the jejunum caused by diclofenac with unusual presentation of anemia-related general weakness and syncopal attacks, but without intestinal obstruction.

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