

Case Report

NSAID Induced Small Bowel Strictures

Kalpita Hatti^{*#}, Vincent Giuliano[#]

Division of Clinical Rheumatology, University of Virginia, USA
#Both are contributed equally.

***Corresponding author**

Kalpita Hatti, Vincent Giuliano, Division of Clinical Rheumatology, University of Virginia, 450 Ray C Hunt Dr, Charlottesville, VA 22908; Tel: 585- 978 -1508; Fax: 434- 243-9143; Email: kh6jy@virginia.edu

Submitted: 13 February 2014

Accepted: 28 February 2014

Published: 02 March 2014

Copyright

© 2014 Hatti et al.

OPEN ACCESS**Keywords**

- NSAIDs
- Diaphragm disease
- Small bowel strictures

Abstract

Strictures of the small bowel resulting from ingestion of non steroidal anti inflammatory drugs (NSAIDs), also known as small bowel diaphragm disease, were first described by Lang et al. in 1988. NSAIDs are the most commonly prescribed drugs in the world and, although their adverse effects on the upper gastrointestinal tract are widely recognized, their effects on the small bowel are under-reported.

We present a case of a 58-year-old man who presented with multiple strictures of the small bowel, initially suspected to be due to inflammatory bowel disease (IBD) who, after partial small bowel resection, developed recurrent strictures due to ongoing NSAID use.

INTRODUCTION

Strictures of the small bowel resulting from administration of non steroidal anti inflammatory drugs (NSAIDs), also known as small bowel diaphragm disease (DD), was first described by Lang et al. in 1988 [1]. NSAIDs are the most commonly prescribed drugs in the world and, although their adverse effects on the upper gastrointestinal tract are widely recognized, their effects on the small bowel are under-reported. Most of the case reports and case series have been published in surgical and gastroenterology journals. Primary care physicians, internists, pain specialists and rheumatologists may be confronted with a patient presenting with small bowel obstruction and not be aware of the potential relationship of this to the patient's long term NSAID use. Most of the patients described in the medical literature have presented with partial small bowel obstruction, iron deficiency anemia, GI bleeding or an abdominal mass. These lesions rarely are detected with standard endoscopy of the upper or lower GI tract and most often; the diagnosis is established only during surgery. Capsule endoscopy is a novel method that permits the endoscopic examination of the mucosa of the entire small intestine, which can typically reveal concentric strictures beyond which the capsule does not pass. Histologic examination of the mucosa may reveal superficial annular or longitudinal ulcers. There is widening of the submucosa, creating annular constriction of the lumen, and it is filled with disorganized fascicles of smooth muscles [2], which assumes the shape of a diaphragmatic barrier. Because diaphragm disease (DD) is so difficult to identify, the diagnosis is frequently made after an extensive workup that yields normal findings. Most often, documented DD of the small bowel has been treated with resection. Discontinuation of the offending NSAID is the mainstay of empirical treatment. We present a case of a 58-year-old man who presented with multiple strictures of the

small bowel, initially suspected to be due to inflammatory bowel disease (IBD) who, after partial small bowel resection, developed recurrent strictures due to ongoing NSAID use.

CASE PRESENTATION

A 58-year-old man with a long history of lower spinal degenerative disc disease presented to an outside hospital with nausea, vomiting, and diffuse abdominal pain with distension. He had been taking meloxicam 15 mg daily for seven years as well as omeprazole 20 mg daily. Laboratory data revealed microcytic anemia. Colonoscopy did not visualize an obstruction. Therefore, a barium small bowel follow through study was performed which identified multiple concentric strictures in the distal ileum. An ileo-cecal resection was performed at that time. Microscopic pathology demonstrated a rare focus of chronic inflammation within the muscularis propria, but no evidence of active inflammatory bowel disease. He was discharged from the hospital and he continued to take Meloxicam for chronic pain. Four months later he started complaining of abdominal pain and a CT enterography showed partial small bowel obstruction with a zone of transition in the distal ileum 20-30 cm proximal to the ileocolic anastomosis, which was treated conservatively. Six months after the surgery he presented again, to our hospital with abdominal obstructive symptoms and small bowel follow through revealed four new strictures proximal to the ileo colic anastomosis (Figure 1 and 2). Multiple attempts were made to perform push enteroscopy during his colonoscopy, but this procedure was unsuccessful due to angulation of the anastomosis and the stricture just proximal to the anastomosis. A full blood panel for IBD serologic and genetic markers was negative. He underwent another laparotomy with resection of the strictures. The surgeon identified typical diaphragmatic lesions as seen in

NSAID enteropathy. Biopsy from the second resection showed no pathologic abnormality except for dense sub mucosal fibrosis (Figure 3). He has been followed up in clinic for two years now. He has remained off NSAID therapy and has had no further recurrences.

DISCUSSION

Diaphragm disease is now considered part of the spectrum of diseases associated with NSAID-induced injury to the GI tract, but it remains an under recognized problem. The development of "diaphragm like strictures" is a pathogonomic feature and these lesions rarely, if ever, regress spontaneously. More cases have been reported over the last decade with the advent of capsule endoscopy and balloon enteroscopy allowing direct visualization



Figure 1 Small bowel follow through study showing multiple concentric strictures shown by the red arrows.

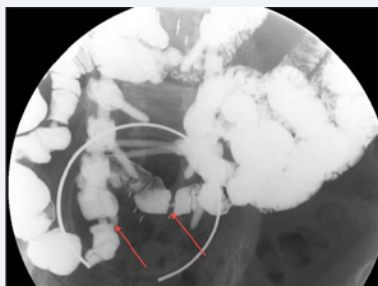


Figure 2 Small bowel follow through study showing multiple concentric strictures shown by the red arrows.

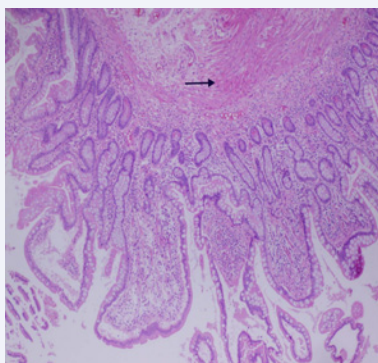


Figure 3 Microscopic cross section of mucosal diaphragm shows chronic inflammation with some submucosal fibrosis (shown by black arrow).

of the small intestines [3]. The pathogenesis of these lesions is not fully understood. One hypothesis is that a reduction in the mucosal synthesis of prostaglandins induced by NSAIDs disrupts mucosal integrity which results in bacterial invasion. NSAIDs also may modulate COX-independent signal transduction pathways, such as nuclear factor- κ B and peroxisome proliferator-activated receptor, which may contribute to the anti-inflammatory activity of these medications. Other proposed mechanisms include the production of increased intestinal permeability and the uncoupling of mitochondrial oxidative phosphorylation. These mechanisms may work alone or in combination to facilitate invasion by toxins and bacteria. Moreover, they decrease leukocyte migration and adhesion that aid the clearance of toxins. The enterohepatic circulation of NSAIDs and their concentration in bile have also been shown to correlate with mucosal injury [4]. The pathogenesis of DD may be related to a combination of these factors, but why some patients are more susceptible than others is unknown. Experimental studies have demonstrated that enterobacteria play a crucial role in small intestinal damage. Although proton pump inhibitors have been traditionally used to protect the gastric mucosa and animal studies have shown their protective effect in Indomethacin induced rat enteritis [5], there is some evidence which shows that acid suppressants allow enterobacteria to thrive resulting in aggravation of NSAID induced enteropathy. Hence the use of proton pump inhibitors and H2 blockers are independent risk factors for the development of small bowel strictures [6,7]. NSAID induced DD is a diagnosis of exclusion and it would be prudent to rule out inflammatory bowel disease, malignancy, radiation enteritis and infections. Video capsule endoscopy and balloon enteroscopy are becoming increasingly popular for the detection of small intestinal lesions. Typically endoscopic images reveal mucosal breaks, erythema, diaphragm like strictures and scarring [8]. The mainstay of treatment is discontinuation of NSAIDs. Endoscopic balloon dilation therapy could be an alternative to surgical intervention, when plausible for diaphragm disease.

CONCLUSION

NSAID induced small bowel strictures should be considered as a potential etiology for small bowel obstruction in a patient taking long term NSAIDs. It is essential to recognize this problem and discontinue NSAIDs in a timely manner.

REFERENCES

1. Lang J1, Price AB, Levi AJ, Burke M, Gumpel JM, Bjarnason I. Diaphragm disease: pathology of disease of the small intestine induced by non-steroidal anti-inflammatory drugs. *J Clin Pathol.* 1988; 41: 516-526.
2. Yousfi MM, De Petris G, Leighton JA, Sharma VK, Pockaj BA, Jaroszewski DE, et al. Diaphragm disease after use of nonsteroidal anti-inflammatory agents: first report of diagnosis with capsule endoscopy. *J Clin Gastroenterol.* 2004; 38: 686-691.
3. Hershfield NB. Endoscopic demonstration of non-steroidal anti-inflammatory drug-induced small intestinal strictures. *Gastrointest Endosc.* 1992; 38: 388-390.
4. Kelly ME, McMahon LE, Jaroszewski DE, Yousfi MM, De Petris G, Swain JM, et al. Small-bowel diaphragm disease: seven surgical cases. *Arch Surg.* 2005; 140: 1162-1166.
5. Kuroda M, Yoshida N, Ichikawa H, Takagi T, Okuda T, Naito Y, et

- al. Lansoprazole, a proton pump inhibitor, reduces the severity of indomethacin-induced rat enteritis. *Int J Mol Med*. 2006; 17: 89-93.
6. Watanabe T, Tanigawa T, Nadatani Y, Nagami Y, Sugimori S, Okazaki H, et al. Risk factors for severe nonsteroidal anti-inflammatory drug-induced small intestinal damage. *Dig Liver Dis*. 2013; 45: 390-395.
7. Wallace JL, Syer S, Denou E, de Palma G, Vong L, McKnight W, et al. Proton pump inhibitors exacerbate NSAID-induced small intestinal injury by inducing dysbiosis. *Gastroenterology*. 2011; 141: 1314-1322.
8. Higuchi K, Umegaki E, Watanabe T, Yoda Y, Morita E, Murano M, et al. Present status and strategy of NSAIDs-induced small bowel injury. *J Gastroenterol*. 2009; 44: 878-888.

Cite this article

Hatti K, Giuliano V (2014) NSAID Induced Small Bowel Strictures. *Ann Orthop Rheumatol* 2(1): 1011.