Nonsteroidal anti-inflammatory drugs: An unusual cause of multiple ileal perforations

Mohamed Ali Sheredi, Zakaur Rab Siddiqui

ABSTRACT

Introduction: In this case report, we describe a rare case of pneumoperitoneum with peritonitis due to multiple ileal perforations with a history of high doses of diclofenac sodium usage.

Case Report: A young adult male with recent history of high doses of Nonsteroidal anti-inflammatory drugs (NSAIDs) presented in emergency department with acute onset pain in right iliac fossa with high grade fever and tachycardia for 12 hours. Abdomen was tender in the right iliac fossa with guarding. X-ray of chest showed free gas under the diaphragm. Exploratory laparotomy was done and showed multiple ileal perforations. Resection and anastomosis of the affected segment was done, both ends brought as double barrel ileostomy which was reversed later on without any complication.

Conclusion: High doses of Nonsteriodal anti-inflammatory drugs can cause multiple ileal erosions and perforation and should be considered in the the differential diagnosis, if other possibilities are excluded.
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Introduction: In this case report, we describe a rare case of pneumoperitoneum with peritonitis due to multiple ileal perforations with a history of high doses of diclofenac sodium usage. Case Report: A young adult male with recent history of high doses of Nonsteroidal anti-inflammatory drugs (NSAIDs) presented in emergency department with acute onset pain in right iliac fossa with high grade fever and tachycardia for 12 hours. Abdomen was tender in the right iliac fossa with guarding. X-ray of chest showed free gas under the diaphragm. Exploratory laparotomy was done and showed multiple ileal perforations. Resection and anastomosis of the affected segment was done, both ends brought as double barrel ileostomy which was reversed later on without any complication. Conclusion: High doses of Nonsteroidal anti-inflammatory drugs can cause multiple ileal erosions and perforation and should be considered in the differential diagnosis, if other possibilities are excluded.

Keywords: Diclofenac sodium, Ileum, Intestinal perforation, Nonsteroidal anti-inflammatory drugs (NSAIDs)

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are known to have adverse effects on the upper gastrointestinal tract, however, its effect on the small intestine are not well described [1]. It is proven that NSAIDs can be harmful to the small intestine and can be associated with multiple complications, such as, small intestinal strictures, ulcerations, perforations, diarrhea, and villous atrophy. The NSAIDs can have adverse effects in any part of the gastrointestinal tract including, oesophagus, stomach, duodenum, small intestine, or colon [2, 3]. Risk is increased with age, in first three months of treatment, smoking, associated cardiovascular or respiratory disease, high dose and multiple NSAIDs, and concomitant use of anticoagulant or steroids [1, 3].

Herein, we report a case of NSAID-induced multiple small bowel erosions and perforations that involved the proximal as well as distal ileum. Furthermore, similar cases of NSAID-induced enteropathy described in literature are also reviewed, in which other causes were ruled out by obtaining biopsy specimens for histologic analysis.

CASE REPORT

A 31-years-old male, with no known co-morbidity, presented in emergency department with a history of severe right lower quadrant pain of more than 12 hours...
that was not responding to analgesics. There is associated intermittent high grade fever (up to 39.5°C), severe sore throat, and weight loss of 6 kg over 2 weeks, for which he received augmentin for a week and cefuroxime for another week with no improvement.

On physical examination in the emergency room the patient was tachycardiac, tachypneic, febrile and showed presence of severe follicular tonsillitis with oral ulcers. On further interrogation, the patient revealed that 16–20 tablets of diclofenac potassium per day for his pain for two weeks prior to the onset of his abdominal symptoms.

Systemic examination showed bilaterally equal air entry in the chest with regular heart sounds and no audible murmur. There was diffuse abdominal distention along with tenderness more in the lower abdomen. Although white cell count was high, however, all other laboratory tests including the Widal test were normal.

Urgent ultrasound of abdomen done which revealed free fluid in the abdomen. A chest X-ray showed free air under the diaphragm on the right side and an emergency laparotomy was performed for suspected peritonitis associated with intestinal perforation. Peroperatively, there were multiple small bowel perforation in the terminal ileum each approximately 5 mm in size along with a few impending perforations (Figure 1).

Approximately 15 cm of the ileum was resected due to very close and tinny perforations in which suturing was impossible, ileostomy was done with planned scheduled relook laparotomy through the laparostomy (mesh and VAC used).

Three relook laparotomies were performed and showed new perforations with impending perforations which were fixed by either primary repair or burying it inside.

Workup was done for the etiology including stool analysis for *Clostridium difficile* and found to be negative. Serum markers for vasculitis were also negative.

Histopathology report showed nonspecific inflammation and excluded inflammatory bowel disease, vasculitis, and vascular thrombosis. Only positive history found was ingestion of high dose nonsteroidal anti-inflammatory analgesics.

Patient recovered slowly but well and discharged after two weeks of hospital stay. After six weeks ileostomy reversal was done without any complications and remained healthy till now (six months postoperatively)

**DISCUSSION**

The differential diagnosis of nonspecific erosions, ulcerations and perforation of the small intestine includes Crohn’s disease, Typhoid fever trauma (from ingested toothpicks or bones), infection (cytomegalovirus, tuberculosis, or *Yersinia*), Vasculitides (such as lupus, rheumatoid, or periarteritis nodosa) postradiation therapy, ischemia, and various medications (like enteric-coated potassium). In certain case reports, rheumatoid vasculitis and other collagen vascular diseases are supposed to be responsible for described intestinal strictures and inflammation, therefore, patients suffering from such diseases should be thoroughly examined, as NSAIDs are usually mainstay to treat these disorders [3, 4].

In contrast to the previously accepted belief, recently, it is documented that NSAID-induced gastrointestinal injury occurs more frequently in the small bowel than in the stomach [4, 5]. (NSAID) induced enteropathy may manifest acutely as well as after chronic use, being five patients described in one study after use of medication for less than 4 weeks [6, 7]. Likewise, the development of enteropathy does not seem to be related to the route of administration of NSAIDs, because, use of Osmosin, a now obsolete indomethacin rectal suppository, was also associated with ileal perforations [8]. However, the effect of intravenous route has yet to be established. Furthermore, in another study, majority of patients with NSAID-induced enteropathy were taking either indomethacin or piroxicam preparations for more than a month. Among these patients, 40% had intestinal obstruction, 40% had ulceration and anemia, and 12% had intestinal perforation, suggesting the NSAIDs as a possible cause. In a separate autopsy series, undiagnosed
small bowel perforations was found to be the cause of death in three patients who had received long-term Aspirin therapy, that is, for six months or more [9]. In the study described previously, most of the patient underwent intestinal resection while in about one-fifth of them, the only treatment was discontinuation of use of NSAIDs [9]. Considering that, if the disease is suspected and treated early, it may preclude the need of surgery, thus, considerably reducing the associated morbidity and mortality.

In the case described here, the patient high doses of diclofenac sodium orally for two weeks. The subsequent laboratory and histopathologic findings were unable to identify any etiology for his ileal perforations other than NSAID-induced enteropathy, including inflammatory bowel disease, trauma, typhoid, tuberculosis and amoebiasis. Therefore, a diagnosis of diclofenac sodium-induced multiple ileal perforation was reached.

In another retrospective study, it is noted that those patients who were taking NSAIDs were twice as likely to have small and large bowel perforations or hemorrhage in comparison with control patients [10], further supporting our presumption in this case.

CONCLUSION

High doses of nonsteroidal anti-inflammatory drugs can cause multiple ileal erosions and perforation and should be considered in the differential diagnosis, if other possibilities are excluded. Early suspicion and timely intervention may reduce the associated morbidity and mortality.

Author Contributions
Mohamed Ali Sheredi – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data,Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Zakaur Rab Siddiqui – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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