



## NSAID (Diclofenac) induced apoptotic colitis-A case report and review of literature

### KEYWORDS

Drug induced colitis, Apoptosis, NSAID, Diarrhea

### Dr. Vikash

Junior Resident, Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, UP-221005

### Dr. Neeraj Dhameja

Assistant Prof., Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, UP-221005

### Dr. V.K Dixit

Professor, Department of Gastroenterology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, UP-221005

**ABSTRACT** Colon can be involved by a variety of etiological agents like infection (bacterial or viral), parasitic (entamoeba), idiopathic (Inflammatory bowel disease - Crohn's disease or ulcerative colitis), ischemic colitis and various drugs. The patient usually presents with pain abdomen, bleeding per rectum and diarrhea.

Here we describe one such case of drug (NSAID) induced colitis.

**Methods:-** A 75 year old female presented with diarrhea and bleeding per rectum for last one year. On colonoscopy there were multiple ulcers present in left colon.

Histopathological examination showed multiple colonic fragments with maintained crypt architecture. The lamina propria showed dense mixed inflammation rich in eosinophils with focal areas of hyalinisation. In addition many crypts showed apoptosis with cytoplasmic and nuclear remnants.

**Results:-** Finally, a diagnosis of diclofenac induced apoptotic colitis was made based on clinical and histopathological findings.

**Conclusion:-** Biopsy sampling is mandatory in cases of colitis and we should always take history of drug intake in patients presented with colitis having unusual morphological features on biopsy. Because rapid therapeutic response can be achieved on discontinuation of NSAID.

### Introduction

Colon can be involved by a variety of etiological agents like infection (bacterial or viral), parasitic (entamoeba), idiopathic (Inflammatory bowel disease - Crohn's disease or ulcerative colitis), ischemic colitis and various drugs.

The patient usually presents with pain abdomen, bleeding per rectum and diarrhea.

Colonoscopic examination shows erosions, ulceration and strictures involving the colon and colonic biopsies are usually taken for histopathological diagnosis.

Sometimes histopathological findings may show unusual morphological findings which may help in making a diagnosis.

Here we describe one such case of drug (NSAID) induced colitis.

### Methods

A 75 year old female presented with diarrhea and bleeding per rectum for last one year. On colonoscopy there were multiple ulcers present in left colon.

Histopathological examination showed multiple colonic fragments with maintained crypt architecture (Fig.1). The lamina propria showed dense mixed inflammation rich in eosinophils with focal areas of hyalinization (Fig. 2,3). Some of the crypts showed partial loss of lining epithelium and some showed flattening of epithelium. In addition

many crypts showed apoptosis with cytoplasmic and nuclear remnants (Fig. 4). The crypts showed reactive atypia with mitotic figures. Crypt abscesses were also seen. No basal plasmacytosis, crypt distortion, crypt branching, granuloma or infectious organisms seen.

### Results

Based on these histopathological findings a detailed clinical history was taken including drug intake. She was suffering from osteoarthritis for last 5 years and was taking NSAIDs (Diclofenac) since last three years. No history of organ transplantation was present.

Finally, a diagnosis of diclofenac induced apoptotic colitis was made based on clinical and histopathological findings.

### Discussion

Colon can be affected by variety of drugs which may cause colitis. The drugs commonly cause colitis includes mycophenolate, antimetabolites, TNF-inhibitors,

colchicine, taxane, NSAIDs etc. These drugs can produce different pattern of injuries like focal active colitis, chronic colitis, apoptotic excess, dilated damaged crypts, erosions, stenosis, epithelial atypia, increased mitosis and malakoplakia etc<sup>4</sup>.

The presence of increased apoptotic bodies (normal <1 per 20 crypts) should always raise the possibility of apoptotic colitis which is commonly associated with graft versus host disease or mycophenolate mofetil, an immu-

nosuppressive drug used in organ transplantation. Rarely, NSAIDs can cause increased crypt apoptosis resulting in apoptotic colitis. A study by Lee et al<sup>1</sup> showed increased apoptosis in NSAID induced colitis. Also in this biopsy, there was focus of lamina propria hyalinization and withered appearance of the crypts, suggestive of ischemic etiology. This could be related to vasoconstriction by NSAIDs because of inhibition of prostaglandin synthesis.

Hence, a drug history (NSAID ingestion) should always be considered in the differential diagnosis of colitis in patients who present with lower intestinal symptoms (diarrhea, abdominal pain, anemia etc) with or without radiologically demonstrable lesions.

### Conclusion

Biopsy sampling is mandatory in cases of colitis and we should always take history of drug intake in patients presented with colitis having unusual morphological features on biopsy. Because rapid therapeutic response can be achieved on discontinuation of NSAID.

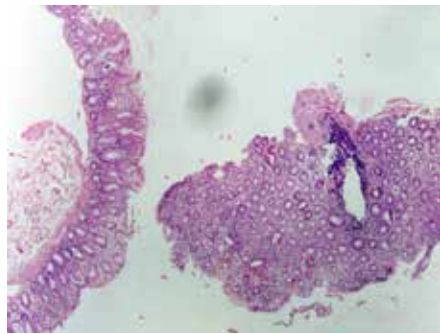


Fig 1.H&E stain showing preserved crypt architecture 4X

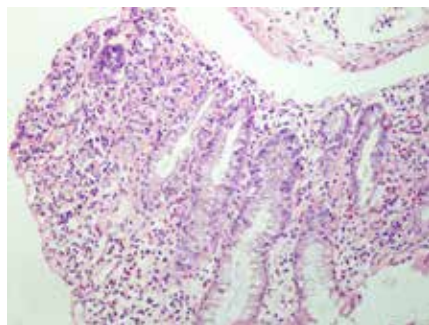


Fig 2. H&E stain showing increase intraepithelial lymphocyte, eosinophils 20x

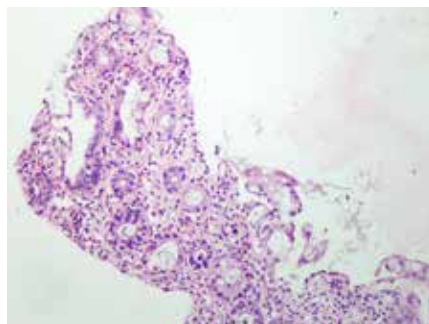


Fig. 3 H&E showing withered crypts with hyalinization 20X

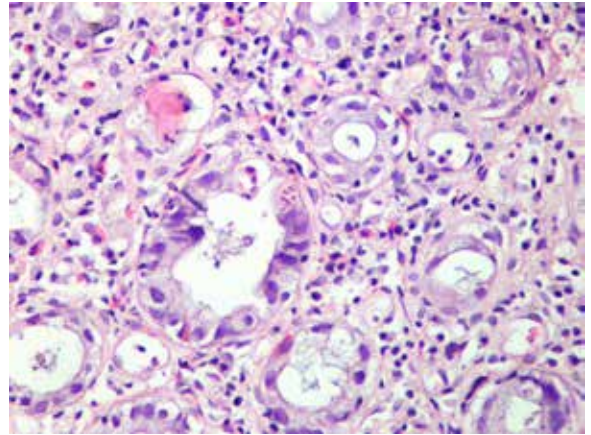


Fig. 4 H&E stain showing multiple apoptotic bodies

### References

1. Lee FD et al. Importance of apoptosis in the histopathology of drug related lesions in the large intestine. *J clin Path* 1993;118-122
2. Madhok R, McKenzie JF, Lee FD, Bruckner FE, Terry TR, Sturrock RD. Small bowel ulceration in patients receiving non-steroidal anti-inflammatory drugs for rheumatoid arthritis. *Q J Med* 1986;58:53-8
3. J L Faucheron, R.Pare. Non-Steroidal anti-inflammatory drug induced colitis. *Int J Colorect Dis*(1996)11;99-101
4. Aoife J McCarthy, Gregory Y Lauwers, Kieran Sheahan. Iatrogenic pathology of the intestines. *Histopathology* 2015, 66, 15-28