Introduction

The adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs) on the upper gastrointestinal tract and small intestine are well established. The effect of such therapy on the large intestine, the so-called NSAID colopathy, is less well described. Debenham reported the first case of NSAID-induced colonic damage in 1966, highlighting a case of cecal ulceration in a patient taking oxyphenbutazone for rheumatoid arthritis [1]. Since then, the association between NSAIDs and colonic damage has become well established, albeit less well recognized than NSAID-induced gastropathy and enteropathy. Isolated case reports of NSAID colopathy range from the more acute complication of inflammation and ulceration to the more chronic picture of fibrosis and stricture formation. Since literature data are scarce, the aim of this case report is to present the patients on chronic hemodialysis with NSAID colopathy.

Case Report

A 55-year-old patient had been on regular hemodialysis since 1996 (home hemodialysis since 2001) due to hypertensive nephrosclerosis. He was dialyzed for 5 hours, three times per week using high-flux polysilfone membranes. His co-morbid conditions included secondary hyperparathyroidism and peripheral vascular disease. Therefore, he underwent subtotal parathyroidectomy six years before and bilateral aorto-femoral bypass in January 2011. Two years later, his peripheral vascular disease deteriorated and he developed very painful and pronounced ischemic lesions of the legs. Unbeknownst he used over the counter (OTC) drugs (Diclofenac) in high doses for several months.

Corresponding Author: Prof. dr Nada Dimković, Kliničko-bolnički centar “Zvezdara”, 11000 Beograd, Dimitrija Tucovića 161, E-mail: bokna@eunet.rs

University of Belgrade, Faculty of Medicine, Belgrade
Zvezdara University Medical Centre, Belgrade
Clinical Department of Nephrology
Clinical Department of Gastroenterology and Hepatology

COLITIS AND “DIAPHRAGM DISEASE” OF THE COLON IN HEMODIALYSIS PATIENT DUE TO PROLONGED USE OF NON-STERoidal ANti-INFLAMMATory DRUG

KOLITIS I BOLEST DJIAGRAFME KOLONA KOD PACIJENTA NA HEMODIJALIZI ZBOG DUGOTRAJNE UPOTREBE NESTROIDNOG ANTIFLAMATORNOG LEKA

Nada DIMKOVIĆ, Danijela BOJIĆ, Petar SVORCAN, Aleksandar JANKOVIĆ, Petar ĐURIĆ and Jelena TOŠIĆ

Summary

Introduction. The use of non-steroidal anti-inflammatory drugs may lead to stricture of the small intestine and less frequently of the colon. Colonic strictures have not been described in patients on dialysis and the aim of this report is to show the case of dialysis patient who was followed for recurrent and prolonged diarrhea. Case Report. We present the patient on chronic dialysis for 15 years who used non-steroidal anti-inflammatory drugs due to chronic pain and who developed recurrent diarrhea. Diagnosis was made by endoscopy and confirmed by histology. Specific therapy was applied with a good response. Conclusion. Although not described in the literature, non-steroidal anti-inflammatory drug-induced colitis and/or diaphragm disease could be a potential reason for recurrent or prolonged diarrhea in dialysis patients. Key words: Colitis; Colonic Diseases; Anti-Inflammatory Agents; Non-Steroidal; Renal Dialysis; Diarrhea; Chronic Disease; Diagnosis; Therapeutics; Fibrosis; Colonoscopy; Morphological and Microscopic Findings

Sažetak

Uvod. Upotreba nesteroideh antiinflamatornih lekova može dovesti do striktura tankog creva, a i kolona. Striktura kolona navedene etiologije do sada nije opisana u literaturi kod bolesnika na dijalizi te je cilj ovoga prikaza bolesnik na dijalizi koji je praćen zbog dugotrajnih proliva. Prikaz slučaja. Prikazan je bolesnik lečen hroničnim dijalizama 15 godina koji je koristio nesteroide antiinflamatorne lekove usled hroničnog bola. Kod bolesnika su se razvili recidivanti i prolongirani prolivi; dijagnoza je postavljena endoskopski i potvrđena histološki. Primjena je specifična terapija sa dobrim ishodom. Zaključak. Iako do sada nisu opisivani u literaturi, kolitis i dijafragma kolona mogu biti uzrok recidivanti i prolongirani proliva zbog upotrebe nesteroideh antiinflamatornih lekova kod bolesnika na dijalizi. Ključne reči: Kolitis; Oboljenja kolona; Nesteroidni antiinflamatorni lekovi; Hemodijaliza; Dijareja; Hronično oboljenje; Dijagnoza; terapija; Fibroza; Kolonoskopija; Morfo- i mikroskopski nalazi

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After he complained of diarrhea that was treated as antibiotic colitis but without clinical improvement. At that time he refused suggested colonoscopy. During 2013, the patient attended outpatient clinic repeatedly complaining of recurrent episodes of diarrhea. Laboratory analyses revealed low serum albumin (30 g/L) and iron (6.2 umol/L) levels in addition to positive inflammatory syndrome (CRP 180 mg/dl). Colonoscopy was performed in February 2014 and it confirmed a small (5 mm) polyp in the rectum, scarce inflammation of the colonic mucosa and circumferential stricture of the ascending colon (close to hepatic flexure), with a couple of small shallow ulcerations at the inner brim and surface of the stricture (Figure 1).

Histology confirmed colitis and “diaphragm disease” (i.e. diaphragm-like stricture) of the colon. The presence of edema with moderate chronic inflammatory infiltrate in the centre of the lesion, without vasculitis changes can be seen (Figure 2).

The patient was treated with oral mesalazine 3g/day for 3 months with a good clinical response. Diarrhea stopped within 10 days and hypoalbuminemia improved to 34 g/L two weeks later.

Discussion

A spectrum of symptoms within NSAID colopathy is a relevant differential diagnosis when encountering a patient presenting with classical symptoms of colon cancer or an inflammatory bowel disease. Although the effect of NSAIDs is not likely to be dose related, our patients were taking doses between 50 mg to 150mg daily for several months and it is possible that the duration of treatment was highly significant demonstrating a temporal relationship between drug administration and the spectrum of endoscopic findings. Colonic strictures are more frequent in the right colon [2], as was the case in our patient.

Pathophysiology and factors predisposing the location of such colonic strictures are not entirely elucidated. The use of NSAID affects the metabolism of arachidonic acid in favor of proinflammatory prostaglandin production, which then induces mucosal damage (usually in terminal ileum and colon). It triggers an inflammatory chain reaction by attracting the neutrophils in the mucosa and submucosa with the consequent erosions and/or ulcerations [3]. As submucosal inflammation matures into collagenous tissue, strictures develop at the sites of healed ulcers. Colonic ulceration is thought to be one of the early stages of stricture formation [4]. Ulceration and stricture formation predominate within the ascending colon, and are thought to be due to the increased use of slow-release formulations of NSAID [5, 6], designed for absorption in the distal parts of digestive tube, thus avoiding NSAID-related damage of the stomach and duodenum. The reports on rectal bleeding, ulceration and local stenosis due to the use of NSAID suppository preparations support the direct/topical mode of action [7].

Through systemic action, NSAIDS can increase the permeability of bowel mucosa [8, 9] (confirmed by scintigraphy with radioactive marker) as well, which induces increased protein losing into the bowel. This
often results in clinically overt diarrhea with a decreased serum albumin level, which was the case with our patient. It is hypothesized that NSAIDs induce subtle intracellular events, such as increased fragility of lysosomes and decreased oxidative phosphorylation, resulting in accelerated apoptosis [10]. This contributes to increased local irritation of bowel mucosa and subsequent local and systemic NSAID adverse events.

NSAID related colitis is not a common finding in patients on hemodialysis. They are prone to digestive bleeding and these drugs are avoided. Perhaps this is the reason why NSAIDs colitis is rarely described in the nephrology literature. This case can remind doctors that NSAIDs may be the cause of chronic diarrhea in patients on hemodialysis thus shortening the precious time needed for making diagnosis.

Treatment recommendation is to stop NSAID use (if necessary switch to cyclooxygenase-2 (COX-2) inhibitors) and to start oral mesalazine 3 g/day for 3 months in patients with diarrhea (as we did in our patient) or steroids p.o. for 3 weeks [11, 12]. In case of bowel occlusion due to diaphragm, balloon dilatation or surgery is indicated [12]. Fortunately, our patients had a good response to mesalazine.

Conclusion

When a patient on chronic hemodyalisis program and on prolonged non-steroidal anti-inflammatory drug therapy presents with chronic or recurrent diarrhea, it is useful to think of non-steroidal anti-inflammatory drug colitis and/or diaphragm disease as a possible differential diagnosis. With the increasing use of enteric coated and sustained release non-steroidal anti-inflammatory drug preparations this condition is likely to become more frequent. Increasing awareness of its clinical presentation and of its spectrum of endoscopic findings facilitates a more prompt diagnosis and appropriate treatment to be established, thus avoiding potential toxic effects of other treatments.

References