



Case Report

Perforated Duodenal Ulcer Associated with Nonsteroidal Anti-inflammatory Drug Administration in a Dairy Cow

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Abstract

A case report of perforated duodenal ulcer in a 4.5 year-old Holstein cow is presented. The cow was treated with an overdose of diclofenac sodium. Necropsy findings included diffuse fibrinous peritonitis and microscopically there was severe necrosis and acute inflammation of the duodenum at the margin of the ulcer. Although gastrointestinal ulcers are often associated with non-steroidal anti-inflammatory drugs in others species, it is rarely described in cattle.

Key Words: duodenal ulcer, diclofenac, bovine, NSAID.

Introduction

Although non-steroidal anti-inflammatory drugs (NSAIDs) are effective therapeutic agents with analgesic, anti-inflammatory and antipyretic properties, their use is associated with a significant incidence of side-effects, including gastrointestinal bleeding, ulceration and inhibition of platelet aggregation (12,14). Diclofenac is a NSAID widely prescribed for the treatment of arthritis, osteoarthritis and musculoskeletal injury (2). Several clinical and experimental studies have documented a propensity of diclofenac to cause small intestine injury (2,10,12,16). These side-effects of the NSAID are more often reported in small animals (7,11,15,19), horses (9,14), humans (4,12,14), and rats (2,14,17). Abomasal ulceration is common in cattle (1,3,5,6,13,16), however, it is rarely associated with the use of NSAID (6,16). Conversely, duodenal ulceration is rare (8,16,18,20). Some authors associate duodenal ulceration with a heavy grain intake, left and right abomasal displacements, stress due to parturition, onset of lactation (20), and chronic

inflammatory processes, such as mastitis by *Staphylococcus aureus* (18). Duodenal ulcer is rarely described in cattle associated with the use of NSAID (16). The toxicity of diclofenac in calves was investigated in India. Nine to 11 month-old calves received diclofenac sodium 3mg/kg twice daily orally for four days and were necropsied at the fifth day. Necropsy revealed large, deep and irregularly shaped ulcers in the abomasum and duodenum. In this study, a few ulcers were noted in the rumen (16).

Case Report

A 4.5 year-old Holstein cow died suddenly in a farm in the State of Minas Gerais, Brazil, with no previous perceptible clinical signs as reported by the owner. The herd was fed forage and a high concentrate ration. Diclofenac sodium (1mg/kg body weight, IV, each 12 hours for three days) was administered for treating chronic pododermatitis. The animal was found dead, and necropsy findings included diffuse fibrinous peritonitis, with fibrinous adhesions of

the duodenum (adjacent to the common bile duct) to the mesentery, liver, gallbladder, and diaphragm (Fig.1). In the segment of duodenal adhesion there was an acute perforated duodenal ulcer, with 1.0 cm in diameter, located approximately 4.0 cm aborally to the pylorus (Fig. 2). The cow also had approximately 2 liters of fluid in the thoracic cavity characterizing hydrothorax. Duodenum samples were fixed in 10% formalin, routinely processed for paraffin-embedding, and stained with hematoxylin and eosin. Microscopic lesions included marked necrosis and acute inflammation with fibrin deposition and an inflammatory infiltrate predominately neutrophilic in the duodenal wall. In some sections, necrotic debris, Brünner's glands of the duodenal submucosa (Fig. 3), and plant fibers were observed.

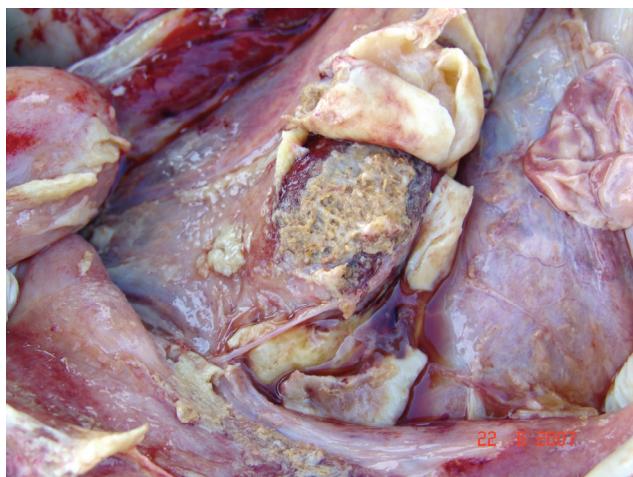


Figure 1 – Fibrinous peritonitis associated to duodenal perforated ulcer



Figure 2 – Mucosal of duodenum with perforated ulcer.

Discussion

In the present report, we presumptively inferred that duodenal ulceration was due to NSAID overdosing. The therapeutic dose of the diclofenac sodium is 1 mg/Kg body weight per day by intramuscular or intravenous route. Although a rich concentrate feeding may be considered a predisposing factor, due to production of high

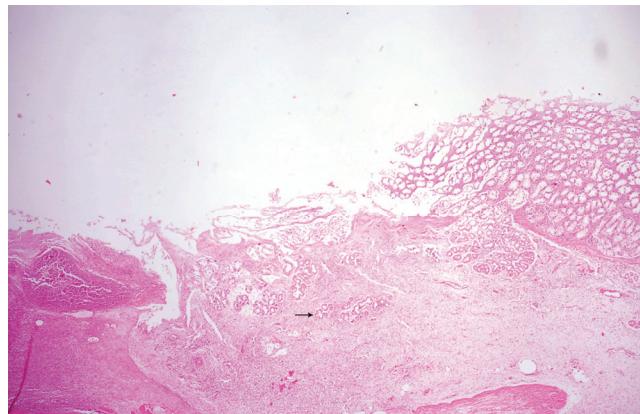


Figure 3 – Microscopic aspect of the duodenal ulcer. Note necrotic debris and Brünner's glands in the duodenum submucosa (arrow). H.E. X10

concentrations of volatile fatty acids, which may cause damage to mucosa of the digestive system (6), all cattle in this herd were exposed to the same conditions, but only the one that was treated with NSAID developed ulceration. Stress caused by the chronic pododermatitis may have contributed for the lesion in this cow. Stress results in release of glucocorticoids that increases the levels of hydrochloric acid in the abomasum, which may result in injury to the gastrointestinal mucosa (6). Although pododermatitis is a frequent disease affecting dairy cows, there are no reports of gastrointestinal ulcerations associated with this condition. The work about the occurrence a gastroduodenal ulcer associated with the induced stress by a chronic mastitis (18) is synthetic and there are no comments about therapeutic treatments used in such animal. We hypothesize that cattle might be more resistant to the intestinal ulcers associated with the use of NSAID, and that many of the non perforated ulcers may heal spontaneously.

References

1. ATKINSON, D.R., SCHAEFER, W.D. Abomasal ulceration and surgical correction. *Can. Vet. Jour.* 1970, 11, 34-35.
2. ATCHISON, C.R., WEST, A.B., BALAKUMARAN, A., HARGUS, S.J., POHL, L.R., DAIKER, D.H., ARONSON, J.F., HOFFMANN, W.E., SHIPP, B.K., TREINEN-MOSLEN, M. Drug enterocyte adducts: possible causal factor for diclofenac enteropathy in rats. *Gastroenterology*. 2000, 119, 1537-1547.
3. BORGES, J.R.J., CUNHA, P.H.J., MOSCARDINI, A.R.C., TORTELLY, R., FRANCO, G.L., SILVA, L.A.F. Compactação de abomaso em bovinos leiteiros: descrição de cinco casos. *Clínica Animal Brasileira*. 2007, 8, 859-864.
4. CASELLI, M., LACORTE, R., DeCARLO, L., ALEOTTI, A., TREVISANI, L., RUINA, M., TROTTA, F., ALVISI, V. Histological findings in gastric mucosa in patients treated with non-steroidal

- anti-inflammatory drugs. *J. Clin. Path.* 1995, 48, 553-555.
- 5. COSTA, L.R.R., GILL, M.J., WILLIAMS, J., JOHNSON, A.J., ANGEL, K.L., MIRZA, M.H. Abomasal ulceration and abomaso-pleural fistula in a 11-month-old beefmaster bull. *Can. Vet. J.* 2002, 43, 217-219.
 - 6. DIRKSEN, G., GRÜNDER, H.D., STÖBER, M. Medicina Interna y Cirugía del Bovino. 4ed., Buenos Aires: Inter-Médica. 2005. 632p.
 - 7. DUERR, FM., CARR, AP., BEBCHUK, TN., POPPLE, NC. Challenging diagnosis – Icterus associated with a single perforating duodenal ulcer after long-term nonsteroidal anti-inflammatory drug administration in a dog. *Can. Vet. J.* 2004, 45, 507-510.
 - 8. FATIMAH, I.; BUTLER, DG.; PHYSICK-SHEARD, PW. Perforated Duodenal Ulcer in a Cow. *Journal of Canadian Veterinary*, 1982, 23,173-5.
 - 9. GELBERG, H. B. Alimentary System. In: McGAVIN, M.D, ZACHARY, J.F Eds. *Pathologic Basis of Veterinary Disease*. 4a. ed. St. Louis: Mosby Elsevier, 2007, 301-91.
 - 10. HAMID, S., YAKOOB, J., JAFRI, W., ISLAM, S., ABID, S., ISLAM, M. Frequency of NSAID induced peptic ulcer disease. *J. Pak., Med. Assoc.* 2006, 56, 218-222.
 - 11. NARITA, T., OKABE, N., HANE, M., YAMAMOTO, Y., TANI, K., NAITO, Y., HARA, S. Nonsteroidal anti-inflammatory drugs induce hypermotilinemia and disturbance of interdigestive migration contractions in instrumented dogs. *J. Vet. Pharmacol. Therap.* 2006, 29, 569-77.
 - 12. PAVELKA, K., RECKER, D.P., VERBURG, K.M. Valdecoxib is a effective as diclofenac in the management of rheumatoid arthritis with a lower incidence of gastroduodenal ulcers: results of a 26-week trial. *Rheumatology*. 2003, 42, 1207-15.
 - 13. POPET, D.C., BENNETTI, J.B. Abomasal ulceration in a Jersey cow. *Can. Vet. Jour.* 1961, 2, 189-191.
 - 14. RADI, Z.A., KHAN, N.K. Effects of cyclooxygenase inhibition on the gastrointestinal tract. *Experimental and Toxicologic Pathology*. 2006, 58, 163-173.
 - 15. REED, S. Nonsteroidal anti-inflammatory drug-induced duodenal ulceration and perforation in a mature rottweiler. *Can Vet. J.* 2002, 43, 971-2.
 - 16. SHRIDAR, N.B., NARAYANAN, K. Toxicity study of diclofenac in calves. *Indian Vet. J.*, 2007, 84, 141-143.
 - 17. SOMASUNDARAM, S., RAFI, S., HAYLLAR, J., SIGTHORSSON, G., JACOB, M., PRICE, A.B., MACPHERSON, A., MAHMOD, T., SCOTT, D., WRIGGLESWORTH, J.M., BJARNASON, I. Mitochondrial damage: a possible mechanism of the “topical” phase of NSAID induced injury to the rat intestine. *Gut*. 1997.41, 344-353.
 - 18. SZAZADOS I., KADAS, I.. Duodenal stress ulceration in a cow, leading to emergency slaughter. *Deutsche Tierarztliche Wochenschrift*. 1979. 86, 153.
 - 19. TAYLOR, PM., WINNARD, JG., JEFFERIES, R. LEES, P. Flunixin in the cat: a pharmacodynamic, pharmacokinetic and toxicological study. *Br. Vet. J.* 1994. 150, 253-62.
 - 20. WEST, H.J.; BAKER, JR. Duodenal ulceration in a cow associated with left displacement of the abomasum. *The Veterinary Record*, 1991, 129, 196-7.