Cecocecal intussusception after administration of imidocarb dipropionate in horse – case report

[*Intussuscepção cecocecal após administração do dipropionato de imidocarb em equino - relato de caso*]

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ABSTRACT

The intussusception of the large intestine in adult horses has been poorly reported. The aim of this study is to report a case of an acute abdomen due to cecocolic intussusception in a Brazilian Sport Horse mare, aged eight, after the administration of imidocarb dipropionate. The drug used for the treatment of piroplasmosis caused a state of dysmotility in the large intestine and subsequent abdominal discomfort. Surgical intervention was necessary, performed through a median celiotomy, opting for partial typhlectomy due to tissue and circulatory compromise. The postoperative evolution was satisfactory and without serious complications, with a good short- and long-term prognosis, as the patient continued to perform its athletic functions.

Keywords: partial typhlectomy, cecal amputation, equine

RESUMO

A intussuscepção do intestino grosso em cavalos adultos tem sido pouco relatada. O objetivo deste estudo é relatar um caso de abdome agudo devido à intussuscepção cecocólica em uma égua da raça Sport Horse brasileira, com oito anos de idade, após a administração de dipropionato de imidocarb. O medicamento usado para o tratamento da piroplasmose causou um estado de dismotilidade no intestino grosso e subsequente desconforto abdominal. Foi necessária intervenção cirúrgica, realizada por celiotomia mediana, e optou-se pela tiflectomia parcial devido ao comprometimento tecidual e circulatório. A evolução pós-operatória foi satisfatória e sem complicações graves, com bom prognóstico a curto e longo prazo, já que o paciente continua exercendo suas funções atléticas.

Palavras-chave: Tiflectomia parcial, amputação cecal, equino

INTRODUCTION

Cecal motility disorders can lead to alterations that manifest as anorexia or loss of appetite, abdominal distension, hypomotility, or atony. Cecocolic intussusception is also a cause of an acute abdomen in equines, involving the invagination of the apex of the cecum into the body or base of the cecum. Even currently, the pathophysiology is not entirely elucidated, and the literature associates its occurrence with dysfunctions in intestinal motility caused by the presence of endoparasites, changes in diet or management, exercise routines, infectious agents, intoxications, or the use of parasympathomimetic drugs (Bell and Textor, 2010; Blikslager *et al.*, 2017; Moore and Hardy, 2017). The literature describes that cecocolic and cecocaecal intussusceptions occur in young horses under three years of age (Paulussen *et al.*, 2017; Gough *et al.*, 2019). However, there are

case reports of cecocecal and cecocolic intussusception in adults. The former occurs in animals over six years of age, and the latter varies between eight and 12 years (Bell and Textor, 2010; Gratwinck *et al.*, 2017).

Among the various hypotheses explaining intussusceptions, one involves the utilization of parasympathomimetic medications. The release of acetylcholine or the presence of other parasympathomimetic drugs, such as bethanechol, can enhance the myoelectric activity of the duodenum, jejunum, cecum, and pelvic flexure in horses (Marti *et al.*, 2005).

Similarly, imidocarb dipropionate also exhibits a parasympathomimetic effect due to its reversible inhibition capability on the acetylcholinesterase enzyme. The adverse effects of its use for the treatment of piroplasmosis are documented in the literature:: a significant increase in defecation frequency, fecal production, and fecal water content, in addition to inducing abdominal discomfort and intestinal hypermotility (Mair, 2020; Kutscha *et al.*, 2012; Donnellan *et al.*, 2013). The objective of this study is to report a case of acute abdomen due to ectopia of loops associated with cecocolic intussusception in an eight-year-old mare following the administration of imidocarb dipropionate.

CASUISTRY

An eight-year-old mare of the Brazilian Sport Horse breed, weighing 400kg, underwent clinical evaluation by a veterinary team. The mare displayed yellowed oral and conjunctival mucous membranes, along with a condition of hyperthermia and extreme apathy. The veterinary team conducted a clinical diagnosis of piroplasmosis and for treatment administered imidocarb dipropionate at a dose of 2.4mg/kg intramuscularly (IM). Approximately 30 minutes after administration, the mare began to show signs of abdominal discomfort, attempts to lie down and roll over in the stall, and profuse, foul-smelling diarrhea. Clinical manifestations notpreviously observed. As a result, intravenous fluid therapy was initiated using a total volume of 15L of lactated Ringer's crystalloid solution on first day, flunixin meglumine (1.1mg/kg IV single dose), procaine penicillin (30,000 IU/kg IM), and 10% gentamicin sulfate (6.6mg/kg IV) was administered daily for four days due to the

enteritis condition and mild, intermittent pain. Thus, intravenous fluid therapy was initiated using lactated Ringer's solution with a total volume of 15L, flunixin meglumine (1.1mg/kg intravenous/IV, single dose/SID), procaine penicillin (30.000 IU/kg IM SID), and 10mg/mL gentamicin sulfate solution (6.6mg/kg IV SID) for four days due to the presentation of enteritis and a mild, intermittent pain condition. After two days of treatment, there was an improvement in clinical signs of colic syndrome, with fluid therapy implemented based on the assessment of dehydration.

However, on the fourth day of treatment, the animal exhibited anorexia, absence of feces in the stall, and a new episode of pain unresponsive to analgesia with flunixin meglumine (1.1mg/kg IV). The veterinarian administered 1% detomidine hydrochloride at a dose of 0.02 mg/kg intravenously. With the need for new treatments, they referred her to the Medical and Surgical Clinic for Large Animals at the Veterinary Hospital of the Federal University of Minas Gerais (HV UFMG). Upon arrival at HV UFMG, the patient presented with controlled pain under the effects of sedation, moderate tachycardia (heart rate of 55 beats per minute), tachypnea (respiratory rate of 40 breaths per minute), a three-second capillary refill time, reddish pink and dry oral mucosa, along with a cyanotic border around the incisors. The initial laboratory tests demonstrated a hematocrit level of 35% and a total plasma protein (TPP) of 5.78g/dL, suggesting an estimated dehydration ranging from 5 to 7%. Atony noted upon abdominal auscultation in all four quadrants, with tympanic resonance upon simultaneous percussion in the right quadrants. No spontaneous reflux during the passage of the nasogastric tube; however, the gastric content were alkaline, foul-smelling, and darkly colored. On transrectal palpation, there were hard, dark-colored stools in the rectal ampulla and dislocated intestinal, including a loop projecting from the right to the left, showing signs of gas distention. A tense ventral band and mass were detected in the cecal region.. The examiner stopped palpating due to pain. The peritoneal fluid showed clear appearance, light yellow color, RBC count of 4,450/mm^3, total nucleated cell counts of 8,300/mm^3, and total protein of 3g/dL (<3,000/mm^3 and 0.8 to 1.2g/dL, respectively, as per Blikslager *et al.*, 2017).

Cytology indicated mostly neutrophils (over 75%), followed by lymphocytes (below 25%), classifying it as an exudate (normal ratio is 2:1 of neutrophils to mononuclear cells; Blikslager *et al.*, 2017).

The blood count collected after beginning dehydration correction revealed mild leukopenia (5,100/mm^3; reference range: 5,500 to 12,550/mm^3), with neutrophils at 54% (2,754/mm^3; reference range: 2,700 to 6,700/mm^3), lymphocytes at 40% (2,040/mm^3; reference range: 1,500 to 5,500/mm^3), and 6% monocytes (306/mm^3; reference range: 0 to 800/mm^3).

The remaining hematological parameters were within the reference values for the species. The biochemical test revealed a slight increase in alanine aminotransferase (ALT 23.8U/L; reference range: 3 to 23U/L) and aspartate aminotransferase (AST 406.4 U/L; reference range: 226 to 366U/L), hyperglycemia (167.86mg/dL; reference range: 75 to 155mg/dL), and a slight decrease in plasma protein (TPP 5.78g/dL, albumin 3.3g/dL, and globulin 2.8 g/dL; reference ranges: 5.2 to 7.9g/dL, 2.6 to 3.7g/dL, 2.6 to 4.0g/dL, respectively). The reference values for hematological and biochemical parameters are based on Thrall *et al.* (2014).

Due to the difficulty in maintaining analgesia and considering the clinical-laboratory findings, the choice was made to conduct an exploratory celiotomy using a pre-umbilical midline approach. During the surgical intervention, we observed retroflexion of the colon and cecal ectopia.Exposing the cecum was not possible.

After exposing the large colon, we performed enterotomy in the pelvic flexure region, followed by colon evacuation and enterorrhaphy closed in double-layer, with continuous simple and Cushing pattern, using No. 2-0 absorbable suture (polyglecaprone 25).

Upon exposing the cecum, we identified a cecocolic intussusception, where the apex folded into the distal portion of the cecal body. We then performed manual reduction maneuvers, involving external massage (Fig. 1A) and gentle traction of the cecal apex. The affected segment, we observed devitalized areas (necrosis),

hemorrhagic points, and compromised vascular perfusion from the apex to the body region were observed (Fig. 1B, 1C, and 1D).

The severity of the inflammatory involvement was decisive in the decision to perform a partial typhlectomy. Isolating the abdomen with a sterile plastic field, we conducted a typhlectomy spanning approximately eight centimeters between the lateral and ventral band. Subsequently, the cecum was emptied through retrograde lavage. The medial and lateral cecal vessels are each double ligated using absorbable suture No. 0 (poliglecaprone 25) proximal to the intended typhlectomy site. Positioning the Doyen intestinal forceps, we proceeded to cut the cecum, was cut, removing the compromised portion. The double-layer pattern, continuous simple and Cushing, with No. 1 and 0 absorbable suture (polygalactin 910).

In the absence of other complications, the exposed structures were repositioned within the abdominal cavity. A three-layer closure technique was adopted for the procedure: the muscular layers sutured with using No. 6 absorbable sutures (polyglycolic acid) in a simple continuous pattern, incorporating interruptions every ten centimeters for added security. The subcutaneous layer was approximatedusing No. 2-0 absorbable sutures (poliglecaprone) in a continuous pattern, firmly anchored to the underlying muscular layer. Finally, the skin was sutured using No. 2-0 non-absorbable sutures (mononylon), once again utilizing a simple continuous pattern for wound closure.

The postoperative care involved daily intensive measures: cryotherapy for 48 hours in a horse stock, parenteral fluid therapy with lactated Ringer's solution for rehydration and maintenance, along with a bolus (1.3mg/kg in 15 minutes) and continuous infusion of lidocaine hydrochloride (0.05mg/kg/min) for 6 hours, flunixin meglumine (1.1mg/kg IV for the first two days, followed by an adjusted dose of 0.25mg/kg IV every six hours for an additional four days), gentamicin sulfate (6.6mg/kg IV once daily for three more days), and procaine penicillin (30,000IU/kg IM once daily for seven days). Additionally, sodium heparin (30 IU/kg SC every eight hours for five days) and omeprazole (4mg/kg orally for seven days)

administered. Lesser amounts of feeding were provided (wet hay every two hours and Tifton grass). The surgical wound cleansed daily using 2% chlorhexidine gluconate and 0.5% hydroalcoholic chlorhexidine, with a sterile compress in contact with the wound and a compression bandage.
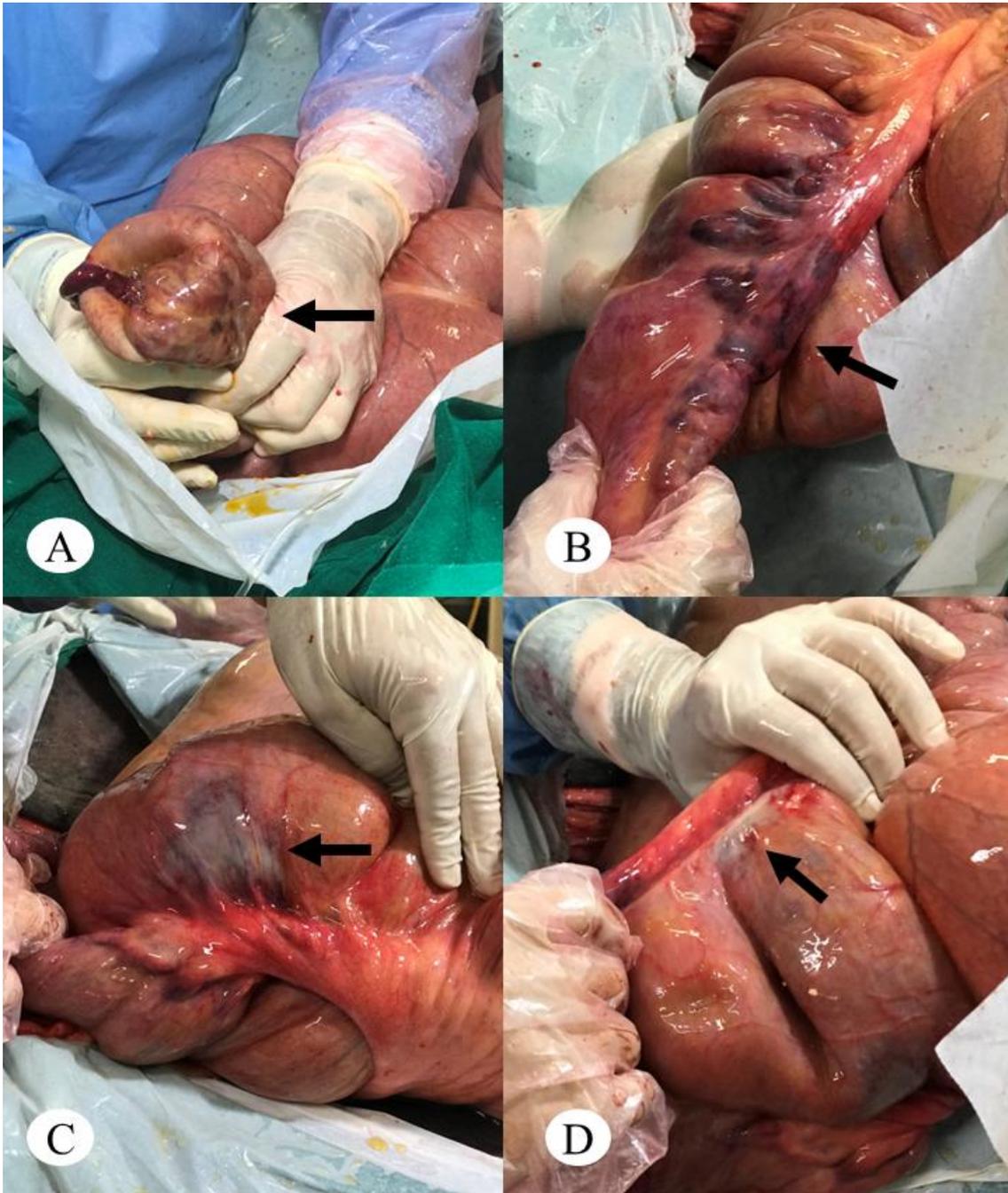

Figure 1. (A) Cecocecal intussusception with involvement of the cecal apex during reduction maneuver. (B) Impairment of vascular perfusion in the medial band of the cecum. (C) Area of devitalization with a grayish appearance and irregular edges on the lateral aspect, and (D) on the dorsal aspect of the cecum.

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Four days after the surgical procedure, blood laboratory tests were repeated: elevated ALT (43.6U/L) and AST (786.8U/L), decreased protein levels (PTT 5.42g/dL, albumin 2.81g/dL, and globulin 2.61g/dL); erythrogram showed a slight reduction in hematocrit (30%), hemoglobin (10.7%), and mean corpuscular hemoglobin (MCH); thrombocytosis (27,600/mm^3), and hyperfibrinogenemia (1,200mg/dL). To facilitate recovery, we introduced amino acid and multivitamin supplement using a commercial formula, administered once a day (SID) orally (PO), following the manufacturer's recommended dosage. As necessary and according to daily clinical and physical assessments, we administer fluid therapy. In the absence of clinical signs of abdominal discomfort, grass, hay, and mineral salts were provided *ad libitum*. On the 10th day after the surgical procedure, the sutures we removed from the surgical wound. By the 14th day, with improved clinical signs, the animal patient was discharged from the hospital, with a prescription of omeprazole (4mg/kg orally once daily) and mineral and vitamin supplementation for an additional 15 days. One year after the surgical procedure, the animal resumed its athletic function, and after two years following the procedure, it continues to perform its normal sporting activities without any further episodes of severe abdominal discomfort.

DISCUSSION

The literature describes that cecocolic intussusception occurs in animals under three years of age (Bell and Textor, 2010; Gratwinck *et al.*, 2017; Paulussen *et al.*, 2017). However, the case reported here differs in this aspect as it involves an eight-year-old mare, like the case reported by Gratwinck *et al.* (2017), who described four cases of cecocolic intussusception in adult animals. The absence of visible endoparasites in the feces and in the intestinal contents obtained during pelvic flexure enterotomy and typhlotomy does not rule out parasitic infection but suggests that there was no severe macroscopic infestation. Given the implementation history of an anthelmintic protocol as reported by the owner, no parasitological analysis of the feces was conducted. This suggested that there was no direct correlation between endoparasites and

intussusception, in accordance with Gough *et al.* (2019) and Gratwick *et al.* (2017).

In this case, it is possible that the imidocarb dipropionate, a parasympathomimetic drug, administered before the initial signs of colic, may have caused dysmotility of the large intestine or segmental hypermotility, starting with diarrhea and subsequently leading to cecocolic intussusception. The relationship between intussusception and imidocarb dipropionate suggested because as other parasympathomimetic drugs have been associated with an increased myoelectric activity and transit rate in the large intestine (Marti *et al.*, 2005; Kutscha *et al.*, 2012; Donnellan *et al.*, 2013; Mair, 2020).

Prior to the administration of imidocarb dipropionate, neither the owner nor the veterinarian had mentioned the occurrence of diarrhea. Therefore, there is an assumption that this medication may have influenced an increase in the rate of intestinal transit, potentially leading to the development of a microbial imbalance disorder in the intestine and intestinal tract inflammation. It is important to emphasize that in this reported case, before using imidocarb dipropionate, do not administer anticholinergic medications. Cecal intussusceptions can present in diverse manners, encompassing acute, subacute, or chronic manifestations, leading to episodes of pain that vary from intense to sporadic (Martin Jr *et al.*, 1999). In the case presented, it can be inferred that a subacute nature of intussusception was being exhibited. In this scenario, the persistence of clinical symptoms over a four-day period was observed, culminating in the development of severe pain, which did not yield a satisfactory response to analgesics. The development of clinical symptoms was attributed to circulatory and ischemic manifestations that impacted the cecum.

The inflammatory process did not initiate changes in the peritoneal fluid consistent with the clinical presentation, as reported in the case by Gough *et al.* (2019). However, the analysis of peritoneal fluid alone does not indicate the diagnosis of intussusception, as in these cases, ischemic lesions do not spread into the peritoneal cavity (Bell and Textor, 2010). Animals experiencing acute abdominal conditions may

exhibit laboratory abnormalities due to intestinal alterations, which include fluid sequestration into a third space, dehydration, metabolic disturbances, inflammatory or ischemic gastrointestinal injuries, and infectious conditions.

The criteria for assessing intestinal viability adopted in this case were precise and resulted in a favorable final prognosis. Additionally, previous studies have shown satisfactory outcomes and a good survival rate for cases of cecocecal intussusception with associated manual reduction and partial typhlectomy (Bell and Textor, 2010). Therefore, survival will depend on complications and postoperative management. In this case report, the patient progressed without serious alterations, with a promising short and long-term prognosis, surpassing one year of survival without complications and returning to regular sporting activities.

CONCLUSIONS

The administration of imidocarb dipropionate may have favored the occurrence of cecocolic intussusception. Despite the limited number of reports in the literature, parasympathomimetic drugs cause intestinal dysmotility, such as hypermotility and inflammation of the segments involved in intussusceptions. However, to establish a direct correlation between imidocarb and the occurrence of intussusceptions, researchers must conduct controlled studies..

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