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Case Report

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Rectal Prolapse Associated with Recurrent Diarrhea in a Laboratory Cynomolgus Monkey (*Macaca fascicularis*)

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Rectal prolapse is a protrusion of one or more layers of the rectum through the anus. A 5-year-old laboratory cynomolgus monkey who had suffered from recurrent diarrhea died after surgical resection of a prolapsed rectum. On examination, the prolapsed rectum was a cylinder-shaped tissue whose surface was moist and dark red with a small amount of hemorrhage. Histologically, the rectum was characterized by a segmental to diffuse cellular infiltration in the submucosa and muscle layers. Inflammation in the rectum resulted in irritation of the myenteric plexus, which could cause hypermotility of the intestines, leading to chronic diarrhea. Rectal prolapse would result in economical loss or death of laboratory animals. However, rectal prolapse in the laboratory monkey could be easily overlooked because diarrhea or other symptoms resulting from rectal prolapse could be sometimes misunderstood as a primary problem. Therefore, researchers should suspect rectal prolapse if intestinal symptoms in the laboratory monkey are untreatable.

Key words: Rectal prolapse, laboratory cynomolgus monkey, recurrent diarrhea

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Rectal prolapse is defined as protrusion of one or more layers of the rectum through the anus. Rectal prolapse is subdivided into either complete or incomplete rectal prolapse, depending on whether it involves all layers of the rectum or just the rectal mucosa (Anderson and Miesner, 2008). Rectal prolapse is commonly associated with severe diarrhea and tenesmus in animals. Predisposing factors include parasites, rectal trauma, tail docking, neoplasia of the rectum or distal colon, urolithiasis, urethral obstruction, cystitis, and dystocia (Remfry, 1978). Prolapse of the rectum has been reported in many domestic and wild animals, including dogs, cats, cattle, horses, ewes, pigs, monkeys, hippopotami and rhinoceroses (Tribe, 1965; Greiner, 1973; Miller and Boever, 1983; Garden, 1988; DeBowes, 1991; Elker and Modransky, 1991; Popovitch *et al*., 1994; Bertelsen *et al*., 2004; Anderson and Miesner, 2008). However, cases of rectal prolapse in non-human primates are rarer than in other laboratory animals, including mice, rats, and dogs (Ediger *et al*., 1974; Romero *et al*., 1997; Kumar *et al*., 2004)

A 5-year-old, 2.7 kg, intact female, cynomolgus monkey was housed and maintained in the specific pathogen-free (SPF) facility at the National Primate Research Center (NPRC), according to Korea Research Institute of Bioscience and Biotechnology (KRIBB) Institutional Animal Care and Use Committee Guidelines (Approval No. KRIBB-AEC-10047). This monkey was kept in an indoor individual cage and was fed commercial monkey chow (Harlan, USA) supplemented daily with various fruits, and supplied water *ad libitum*. Environmental conditions were controlled to provide a temperature of 24±2°C, a relative humidity of 50±5%, 100% fresh air at a rate of ≥12 room changes per hour, and a 12:12 h light:dark cycle. The monkey was accidently found to have a prolapsed rectum. Surgical resection of the prolapsed rectum was performed immediately as follows: The monkey

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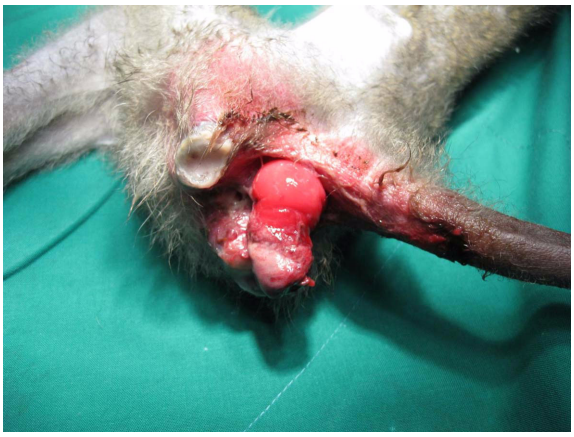

Figure 1. Rectal prolapse of the laboratory cynomolgus monkey. Cylinder-shaped prolapsed rectum was protruded through the anus. The surface of the prolapsed rectum is moist and dark red with a small amount of hemorrhage.

was premedicated intramuscularly with ketamine (10 mg/kg) and atropine (0.04 mg/kg). The animal was then intubated and maintained under general anesthesia using 1.5% isoflurane vaporized in 100% oxygen (West *et al.*, 2009). The prolapsed rectum was surgically removed and then a purse-string suture was placed in the anus.

However, the monkey was found dead the next day. The monkey had suffered from recurrent watery diarrhea for about four-months and had been treated unsuccessfully with antibiotics and showed severe emaciation with inappetence two weeks before death. On examination, the monkey was pale and coarse-haired. The animal had developed a prolapsed rectum with approximately 5 cm×2.5 cm of cylinder-shaped tissue exposed through the anal sphincter prior to surgery (Figure 1). The surface was moist and dark red with a small amount of hemorrhage. At necropsy, the rectum had a thickened edematous wall and congested mucosa. However, the small intestine, cecum, and colon appeared normal. The content of the small intestine was watery, becoming mucoid and paste-like distally in the colon and rectum. The mesentery lymph nodes showed moderate enlargement. No other organs had obvious macroscopic lesions. Tissues were resected and fixed in 10% neutral buffered formalin, processed routinely, and embedded in paraffin. Tissue sections, 3 μm in thickness, were cut and stained with hematoxlin and eosin (H&E). Fecal analysis was performed for detection of bacteria, as described previously (Marjani *et al.*, 2009).

Histologically, the intestinal lesion was confined to the rectum. Compared to other tissues, the rectum showed marked necrotic change. A segmental to diffuse cellular infiltration was observed in the submucosa and muscle layers of the rectum (Figure 2A). Epithelial cells lining the mucosa were

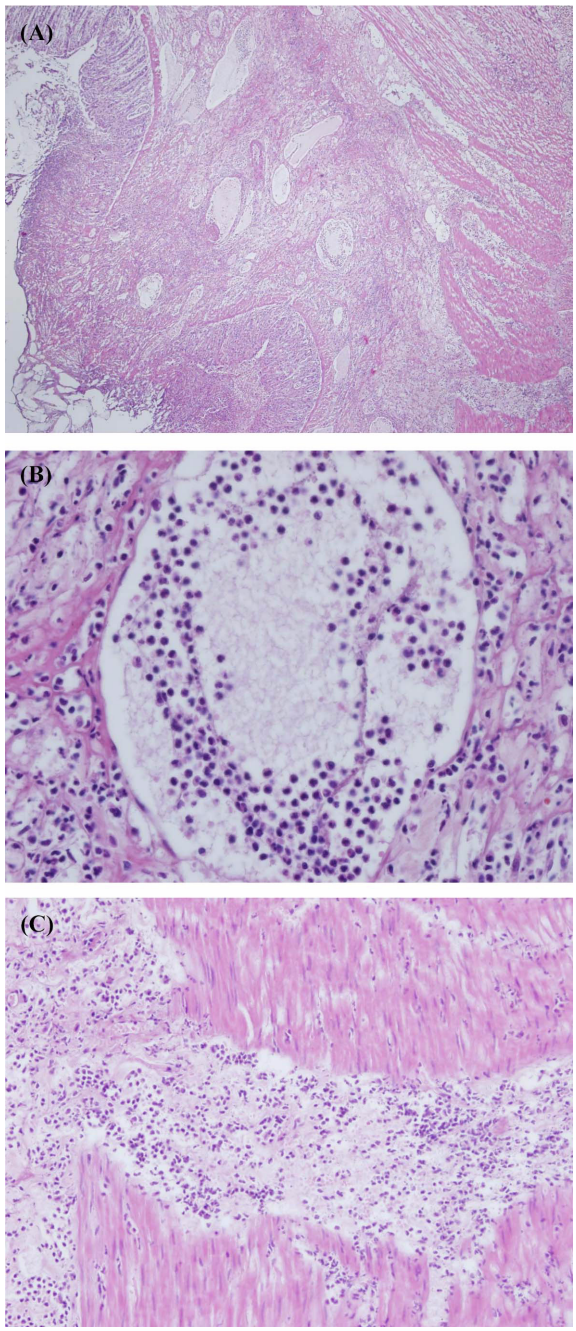

Figure 2. Histological findings of the prolapsed rectum of the laboratory cynomolgus monkey. (A) The rectum is characterized by a segmental to diffuse cellular infiltration in the submucosa and muscle layers. H&E stain (×40). (B) In the submucosa, the lymphatic vessels were markedly dilated and contain a number of neutrophils admixed with a few number of monocytes and lymphocyte and abundant amount of fibrin (×400). (C) Numerous neutrophils with a few lymphocyte in the submucosa penetrated into muscle layers (×200).

sloughed off. The intestinal lumen contained necrotic cells. The lamina propria contained no infiltrate. The submucosa was prominently thickened and multifocally infiltrated by

numerous neutrophils, a few lymophocytes, and necrotic cells. Collagenous fibers in the submucosa were necrotic and dilated by eosinophilic fibrinous exudate. Lymphatic vessels in the submucosa showed marked dilation and contained a number of neutrophils admixed with a small number of monocytes and lymphocytes and an abundance of fibrin (Figure 2B). Interspacing of necrotic myofibers in the muscle layer showed marked widening. Inflammatory cells consisting of numerous neutrophils and a few lymphocytes showed multifocal penetration into deep muscle layers (Figure 2C). Most myofibers were hypercontracted, fragmented, and diffusely infiltrated with a moderate number of neutrophils and a few lymphocytes. However, no microorganisms were detected in H&E staining and bacterial examination.

In humans, the precise cause of rectal prolapse is not clear. However, rectal prolapse is reportedly involved with a number of associated abnormalities and conditions. Main causes are longstanding constipation with chronic straining. Other causes include elevated intraabdominal pressure, weakness of the pelvic floor, a deep pouch of Douglas, neurological disorders, decreased resting anal sphincter pressure, and some parasitic infections (Andrews and Jones, 1992). However, previously reported cases in non-human primates, particularly those of rhesus monkeys and mountain gorillas, have not usually been associated with these causes, except for infections (Tribe, 1965; Kalema-Zikusoka and Lowenstine, 2001).

In our case, dubious lesions of diarrhea were not confirmed in other intestines, except for the rectum, and causative agents were not detected in feces collected during necropsy. The histopathological examination provided evidence that to some extent, the monkey, who had been treated with antibiotics (Amoxicillin, 11 mg/kg), was recovering from inflammation, because drainage of inflammatory cells into the lymphatic duct was observed. Based on bacterial examination, it is likely that long term-treatment with antibiotics prevents isolation of causative agents from rectal tissue and other tissues. In our opinion, movements of laboratory monkeys in a confined cage increase the probability of a traumatic wound in the anus, whose wounds may cause proctitis or proctocolitis, leading to rectal prolapse. Traumatic rectal prolapse has also been described in other reports (Shakespeare, 2000; Olivier *et al*., 2001). In this case, irritation of the myenteric plexus *due to* inflammation in the rectum could have caused hypermotility of the intestines, leading to chronic diarrhea, which resulted in emaciation with inappetence, followed by death, because histopathological examination revealed evidence that inflammatory cells in the submucosa penetrated into deep muscle layer in the rectum compared to intact mucosa of the intestines and fecal analysis doesn't detect any causative agent related to chronic diarrhea.

Rectal prolapse would result in economical loss or death of laboratory animals, as well as domestic animals and wild animals. However, rectal prolapse in the laboratory monkey could be easily overlooked because diarrhea or other symptoms caused by rectal prolapse could be sometimes misunderstood as a primary problem. Thus, researchers should suspect rectal prolapse in laboratory monkeys who are suffering from untreatable intestinal problems.

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References

Anderson, D.E. and Miesner, M.D. (2008) Rectal prolapse. *Vet. Clin. North Am. Food Anim. Pract*. 24, 403-408.

Andrews, N.J. and Jones, D.J. (1992) ABC of colorectal diseases: Rectal prolapse and associated conditions. *BMJ* 305, 243-246.

Bertelsen, M.F., Olberg, R.A., Mehren, K.G., Smith, D.A. and Crawshaw, G.J. (2004) Surgical management of rectal prolapse in an Indian rhinoceros (*Rhinoceros unicornis*). *J. Zoo Wildl. Med*. 35, 245-247.

DeBowes, R.M. (1991) Standing rectal and tail surgery. *Vet. Clin. North Am. Equine Pract*. 7, 649-667.

Ediger, R.D., Kovatch, R.M. and Rabstein, M.M. (1974) Colitis in mice with a high incidence of rectal prolapse. *Lab. Anim. Sci*. 24, 88-94.

Elker, B. and Modransky, P. (1991) Rectal prolapse in food animals. Part 1. Cause and conservative management. *Comp. Cont. Educ. Pract*. 13, 1869-1873.

Garden, S. (1988) Rectal prolapse in pigs. *Vet. Rec*. 123, 654.

Greiner, T.P. (1973) Surgery of the rectum and anus. *Vet. Clin. North Am*. 2, 167-180.

Kalema-Zikusoka, G. and Lowenstine, L. (2001) Rectal prolapse in a free-ranging mountain gorilla (gorilla beringei beringei): Clinical presentation and surgical management. *J. Zoo Wildl. Med*. 32, 509-513.

Kumar, M.J.M., Nagarajan, P., Venkatesan, R. and Juyal, R.C. (2004) Case Report and Short Communication: Rectal prolapse associated with an unusual combination of pinworms and citrobacter species infection in FVB mice colony. *Scand. J. Lab. Anim. Sci*. 31, 221-223.

Marjani, M., Selk, G.M. and Moosakhani, F. (2009) Rectal prolapse secondary to antibiotic-associated colitis in a dog. *Clin. Pathol*. 18, 473-475.

Miller, R.E. and Boever, W.J. (1983) Repair of rectal stricuture and prolapse in a pygmy hippopotamus (*Choeropsis liberiensis*). *J. Zoo Wildl. Med*. 14, 63-66.

Olivier, A., Lane, E., Volkmann, D.H., Hofmeyr, M. and Stegmann, G.F. (2001) Rectal prolapse associated with a healed pelvic fracture in a pregnant free-ranging African black rhinoceros (*Diceros bicornis*). Part 2: Surgery and necropsy. *J. S. Afr. Vet. Assoc*. 72, 242-244.

Popovitch, C.A., Holt, D. and Bright, R. (1994) Colopexy as a treatment for rectal prolapse in dogs and cats: a retrospective study of 14 cases. *Vet. Surg*. 23, 115-118.

Remfry, J. (1978) The incidence, pathogenesis and treatment of

helminth infections in rhesus monkeys (*Macaca mulatta*). *Lab. Anim.* 12, 213-218.
Romero, A., Grau, M.T., Villamayor, F., Sacristán, A. and Ortiz, J.A. (1997) Subacute toxicity of ebrotidine in rats and dogs. *Arzneimittelforschung* 47, 492-497.
Shakespeare, A. (2000) Intussusception as a complication of rectal prolapse replacement in a ewe. *Vet. Rec.* 147, 78-79.
Tribe, G.W. (1965) Rectal prolapse in a *Macaca mulatta* monkey. *Vet. Rec.* 77, 551.
West, G.A., Golshani, K.J., Doyle, K.P., Lessov, N.S., Hobbs, T.R., Kohama, S.G., Pike, M.M., Kroenke, C.D., Grafe, M.R., Spector, M.D., Tobar, E.T., Simon, R.P. and Stenzel-Poore, M.P. (2009) A New model of cortical stroke in the rhesus macaque. *J. Cereb. Blood Flow Metab.* 29, 1175-1186.