**NOTE** *Pathology*

# Jejunal Intussusception Associated with Lymphoma in a Horse

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ABSTRACT. A 2-year-old Thoroughbred horse presented with acute onset of colitis, and the intussuscepted jejunum was surgically resected. A transmural mass protruding into the lumen was found at the leading edge of the intussusceptum. Based on histological and immunohistochemical examinations, the mass was diagnosed as diffuse large B-cell lymphoma with metastasis to the mesenteric lymph nodes. Anatomical localization of the mass in the intussusception and absence of other obvious underlying diseases indicated that the intussusception had occurred in association with the mass. To our knowledge, this case is the first report of equine intussusception associated with focal intestinal lymphoma.

KEY WORDS: equine, intussusception, jejunum, lymphoma.

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An intussusception is an invagination of a segment of bowel (intussusceptum) into an adjacent aboral segment of bowel (intussuscipiens), which can cause stenosis or obstruction of the food passage and venous infarction of the invaginated segment [2, 8, 16]. In the veterinary medicine, intussusception is common in dogs, moderately common in lambs, calves and young horses and much less common in cats [4]. In dogs and cats, Ileocolic intussusceptions occur most frequently, and small intestine, cecum and colon may be involved in lambs and calves [4].

In horses, intussusception has been commonly reported in young horses of less than 3 years of age [8–10, 12, 13, 16, 19]. Ileocecal junctions are the most common sites [2, 8, 9], though any segments of the small and large intestines can be affected [3, 6, 8, 10–12, 18, 19]. Clinically, acute cases show severe abdominal pain, whereas symptoms in chronic cases include a poor general physical condition, intermittent or continual colic, weight loss, intermittent fever, depression, poor appetite and scant, soft feces [8–13, 16, 19].

Causes of intussusception are usually not apparent, though conditions which precipitate excessive peristalsis are considered to be important predisposing factors and, less frequently, the causes may be intramural lesions protruding into the lumen or foreign bodies [8]. In horses, causes of altered peristalsis include enteritis, heavy ascarid infestation, mesenteric arteritis and sudden dietary changes [8, 16]. Protruding lesions in the bowel wall have included granuloma, papilloma, polyp and intramural leiomyoma [3, 6, 8, 18]. *Anoplocephala perfoliata* has been associated with ileal, ileocecal, cecocecal or cecocolic intussusceptions [8, 10, 16]. In this report, we describe a case of jejunal intussusception associated with a focal intestinal lymphoma in a horse.

A 2-year-old, female, Thoroughbred horse presented with acute onset of abdominal pain. Administration of analgesia temporally reduced the pain. Ultrasound examination indicated a small intestinal intussusception with ileus. Surgically, the jejunal segment with intussusception, about 2.5 m in length, was resected, and an end-to-end anastomosis was performed between the cut ends (Fig. 1). Remaining intestinal tissue showed no significant gross changes. The surgically resected jejunum revealed a transmural mass protruding into the lumen, 5 × 4 × 1.4 cm in size, at the leading edge of the intussusceptum (Fig. 2). The mucosal surface of the returning layer of intussusceptum was severely congested. The resected tissue was fixed in formalin, embedded in paraffin wax, sectioned at 4 $\mu$m thickness and stained with hematoxylin and eosin.

Histologically, in the jejunal mass, neoplastic lymphoid cells proliferated massively in the submucosa and invaded the muscular and subserosal layers (Fig. 3). The luminal surface, i.e. mucosal epithelium to muscularis mucosae, was broadly necrohemorrhagic with dense infiltration of neutrophils. Aggregated lymphoid follicles were located in the submucosa, just adjacent to the neoplastic proliferation. Subserosal layer was focally broadened with proliferation of the neoplastic cells and background granulation tissue formation. The neoplastic lymphoid cells had a single nucleus 2 to 3 times the diameter of a red blood cell and lightly eosinophilic cytoplasm (Fig. 4). The nuclei were round with occasional shallow indentations and had a finely branched chromatin pattern and irregularly thickened nuclear membranes. Mitotic figures were frequently observed. The average number of mitosis in 10 high-power fields using 40-power objective was 12.2. The adjacent intestinal wall on the colonic side, i.e. the returning layer of the intussusceptum, was thickened with severe hemorrhage and edema, and fibrinohemorrhagic

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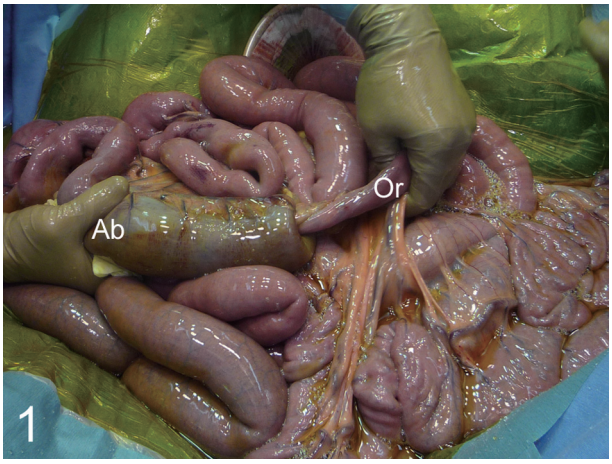


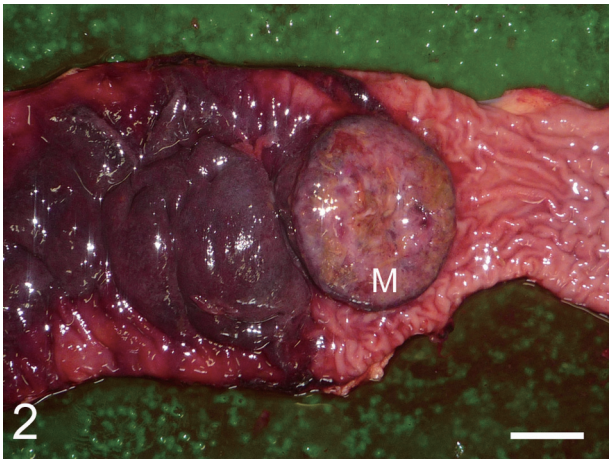


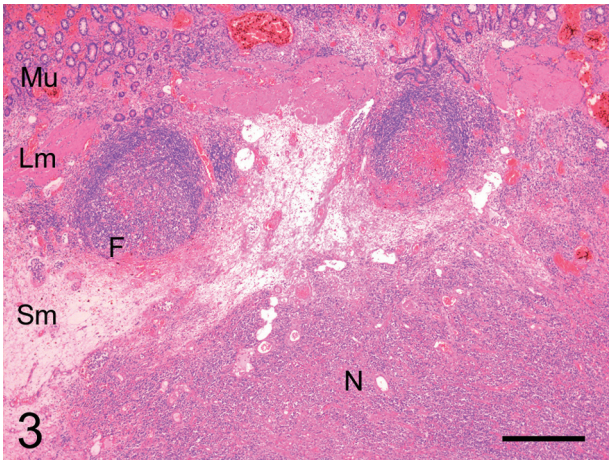


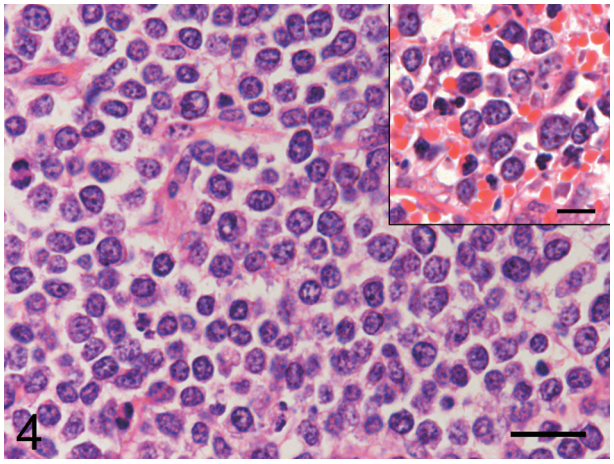


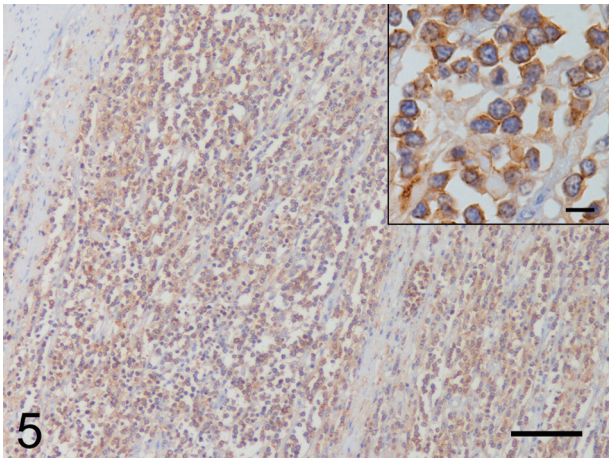


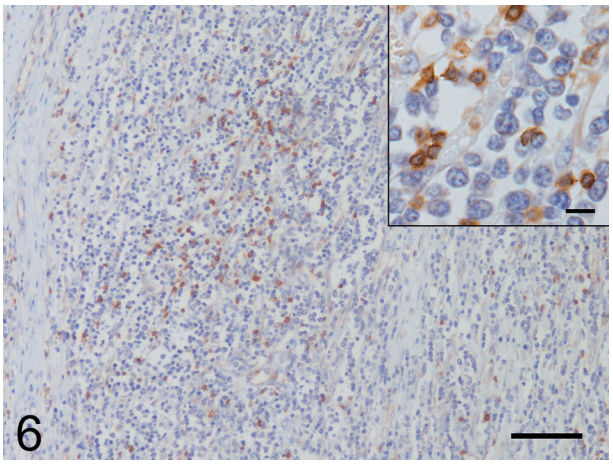


Fig. 1. Gross photograph of jejunal intussusception in a horse. Segment of the jejunum invaginates into the adjacent aboral segment. Or: oral side, Ab: aboral side.

Fig. 2. A mass (M) protruding into the lumen in surgically resected jejunum from a horse with intussusception. Aboral intestinal wall (left to the mass) is thickened with congestion and edema. Bar=2 cm.

Fig. 3. Neoplastic cells (N) proliferating in the submucosa (Sm) and adjacently located lymphoid follicles (F). Overlying mucosa (Mu) is severely congested. Lm: lamina muscularis mucosae. HE. Bar=200 $\mu$m.

Fig. 4. Higher magnification of neoplastic lymphoid cells in the jejunal mass. The cells have a round nucleus with occasional shallow indentations, finely branched chromatin pattern and irregularly thickened nuclear membrane and scant cytoplasm. Several mitotic figures are detected. HE. Bar=20 $\mu$m. (Inset) The neoplastic lymphoid cells had a single nucleus 2 to 3 times the diameter of a red blood cell. HE. Bar=10 $\mu$m.

exudate adhered to the mucosa. These changes were considered to result from a congestion due to intussusception. Neither inflammatory nor necrotic change suggestive of a preexisting bacterial infection was detected.

Immunohistochemical examination was performed by the avidin-biotin-peroxidase complex method (Vectastain Elite ABC Kit; Vector Laboratories, Burlingame, CA, U.S.A.) using a monoclonal antibody against human CD79a (clone HM57; Dako, Glostrup, Denmark) and polyclonal antibodies against human CD3 (Dako), human CD20 (LabVision, Fremont, CA, U.S.A.) and human lambda light chains (Dako). Most of lymphoid neoplastic cells in the jejunal mass were positively stained for CD79a (Fig. 5) and CD20, but negative for CD3 or lambda light chains. Among these cells, scattered smaller lymphoid cells were stained for CD3 (Fig. 6). From these findings, the mass in the intussuscepted jejunum was diagnosed as diffuse large B-cell lymphoma. Granulation tissue in the mass indicated that the mass had been formed in the chronic process.

After the surgery, the mare was administered cefalothin sodium, flunixin meglumine and continuous infusion of lidocaine hydrochloride. The mare showed pyrexia of 40°C, watery diarrhea, dehydration and severe colic, and the general condition was deteriorated in spite of additional supportive care. A fecal sample was sent to a commercial laboratory for bacteriological tests, and *Clostridium difficile* was isolated. The horse died one week after the surgery, and necropsy was performed.

At necropsy, the small and large intestinal walls were diffusely edematous and thickened, and multifocal pseudomembranous fibrin adhesion was detected on the mucosa of the right dorsal and small colon. The lungs showed diffuse edema. Histologically, neoplastic lymphoid cells similar to those in the jejunal mass were found in the cortical sinuses of the cranial mesenteric lymph nodes. Deterioration in clinical condition after the surgery, bacterial isolation of *Clostridium difficile* from the feces and intestinal edema with multifocal fibrinonecrotic colitis found at necropsy were consistent with antibiotic-associated and *Clostridium difficile*-associated colitis [4, 14].

Classification of equine lymphoma based on anatomic distribution is as follows: multicentric, generalized, alimentary/intestinal, splenic, mediastinal/thymic and cutaneous forms [1]. Lymphoma is the most common neoplasia of the intestinal tract in horses and is considered to arise from the lymphocytes of the lamina propria (gut associated lymph tissue) [1, 25]. Equine intestinal lymphoma can manifest as follows: diffuse or segmental thickening of the intestinal wall, focal masses or scattered crater-like ulcers with raised margins [1]. Mass-forming lymphoma can be single or multiple and can spread to organs, such as the liver, spleen, kidneys and mesenteric and other lymph nodes [22–26]. Histological classification of equine lymphoma has been studied by several authors [7, 15, 20]. In our case, neoplastic lymphoid cells expressed B-cell markers, and the number of CD3-immunoreactive lymphocytes was not high. Moreover, the mitotic index was high. These findings favored the diagnosis of diffuse large B-cell lymphoma rather than T cell-rich large B-cell lymphoma [7, 15, 20]. According to these classifications, the present case was considered to be alimentary/intestinal diffuse large B-cell of focal mass-forming type.

Intramural lesions protruding into the lumen can be a predisposing factor for development of intestinal intussusception [8, 9, 16]. In dogs and cats, although most of cases were considered idiopathic, neoplastic masses including focal intestinal lymphoma were observed as underlying diseases in relatively large number of cases with intussusception [5, 17, 21]. In horses, protruding cryptococcal granuloma, papilloma, polyp and intramural leiomyoma have been reported to be associated with intussusception [3, 6, 8, 18]. The masses were correlated with development of intussusception based on the anatomical localization of them in the intussusception. In our case, the focal lymphoma localized at the leading edge of the intussusceptum, corresponding to the previous cases. From the anatomical localization of the mass and absence of other obvious underlying intestinal problems, the jejunal intussusception in our case could have occurred in association with the focal lymphoma. Localized narrowing of the lumen and associated changes in peristalsis may have triggered the development of intussusception in the present case.

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Fig. 5. Most of neoplastic cells proliferating in the muscular layer are positively stained for CD79a. Bar=100 $\mu$m. (Inset) Higher magnification. The immunoreactive cells have a round nucleus with shallow indentations. Bar=10 $\mu$m. Immunohistochemistry for human CD79a counterstained with hematoxylin.

Fig. 6. A few, scattered cells in the muscular layer are positively stained for CD3. Serial section to Fig. 5. Bar=100 $\mu$m. (Inset) Higher magnification. The immunoreactive cells are smaller lymphoid cells. Bar=10 $\mu$m. Immunohistochemistry for human CD3 counterstained with hematoxylin.

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