Histopathology of Colitis X in the Horse

Takashi UMEMURA, Hideo OHISHI1), Yasuo IKEMOTO1), Hiroshi SATOH and Yutaka FUJIMOTO

Department of Comparative Pathology, Faculty of Veterinary Medicine, Hokkaido University, Kita 18-Nishi 9, Kita, Sapporo 060
and 1)The Hidaka Agricultural Mutual Relief Association, 200 Higashihorai, Mitsuishi, Hokkaido 059-31

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ABSTRACT. Histopathological examination was conducted on 16 horses affected with colitis X. Characteristic lesions of the disease were exfoliation of the mucosal epithelial cells and hemorrhagic necrosis of the ceco-colonic mucosa, fibrin thrombus formation of the capillary and venules, especially in the intestinal mucosa, congestive edema of the lungs, and widespread necrosis of tubular epithelial cells with hyalin casts in the kidneys. These lesions support the morphological ground to the hypothesis that endotoxin shock is immediate cause of colitis X. As one of a possible predisposing events to the shock, involvement of systemic infectious disease, especially viral infection was suggested by interstitial pneumonia observed in 15 cases and reticulum cell proliferation with occasional formation of multinucleated giant cell in the lymphoid follicles of the large intestine, spleen, and lymph nodes in most cases.

Since the first report of colitis X in the horse [16], several authors have described similar diarrheal diseases in the horse such as colitis X [7–10, 12, 20], exhaustion shock [15, 17], post-stress diarrhea [13], endotoxemia [4], and diarrhea [2, 5]. They were sporadic, peracute, highly fatal diseases of unknown cause in horses and colts, characterized by the sudden onset of severe diarrhea and signs of toxemia. Many workers [3, 4, 7, 9, 12, 15–17] seem to agree with endotoxin shock as a primary cause of the condition, and some of them proclaimed successful reproduction of the disease by intravenous administration of bacterial endotoxin [3, 4, 16] or oxytetracycline [1, 5].

The colitis X have been diagnosed based on clinical and macroscopical findings [6–8, 14, 15, 20]. It seems sometimes difficult to differentiate colitis X from the other enteric diseases [6, 14, 17] and to confirm the successful experimental reproduction of the disease [1, 3, 4] because histopathological entity of the colitis X was not well established. This may be partially caused from relatively few cases of the disease reported and rapid post-mortem autolysis of the affected intestinal mucosa which impede the detailed analysis of the lesions.

Present report describes histopathological changes of 16 horses including one obtained from a mass outbreak of colitis X. Possible pathogenesis of the disease is discussed from the morphological point of view.

MATERIALS AND METHODS

The horses examined were collected from Hidaka-district (13 cases), Iburi-district (2 cases), and Sapporo (1 case) in Hokkaido from 1961 to 1978. Among the 16 horses, 10 were male, 6 were female, 12 were within one year old, and the other 4 were 1 to 6 years old.

All 16 cases suddenly exhibited watery or bloody diarrhea and/or colicky pains. Eleven cases died within one day, 3 within 2 days and one within 3 days after onset of the clinical signs. The remain-
ing one case was killed and autopsied at moribound condition one day after onset of the diarrhea. Fifteen cases occurred sporadically, but the other one was obtained from a mass outbreak of the sudden bloody diarrhea involving 16 horses in the same stall. Other clinical signs commonly observed were marked depression, anorexia, muddy congested or cyanotic mucous membranes, cold extremities, and rapid thready pulse. Hematological examination revealed mild or severe hemocytopenia in 5 cases and slight or severe leukopenia in 3 cases. Aerobic incubation of the intestinal contents from 2 cases yielded large amounts of lactose-fermenting Escherichia coli. Nine cases showed pneumonia or pneumonia-like symptoms from 1 week to 2 months before death. Tetacycline treatment before onset of the clinical signs was recorded in 10 cases, but the other 6 cases were not treated with antibiotics. Two cases were affected with equine incoordination or polyuria when they exhibited the diarrhea. Another one case was at the terminal stage of pregnancy.

After autopsy, tissue samples were collected from all of the organs and tissues, except for 9 cases in which some organs were not available for histological examination. The tissue samples were fixed with 10% formalin and were embedded in paraffin. The paraffin sections were stained with hematoxylin and eosin. Special staining used were Periodic acid-Schiff reaction, Mallory-Heidenhein's Azan stain, and Watanabe's silver impregnation.

RESULTS

Characteristic macroscopical changes of the disease were as follows;

1. Retention of dark, tarry and nonclotting blood in the subcutaneous tissues and visceral organs (16 cases).

2. Petechiae or diffuse hemorrhages with marked congestion in the mucosa of the large intestine, especially in the cecum and large colon (16 cases). The mucosa of these intestine was partially covered with pseudomembranes (3 cases). Lymphoid follicles of the cecum and colon were invariably flat, enlarged, and increased in number (16 cases). The contents of the large intestine were muddy or watery, brown or dark red (6 cases), and had irritant foul-smelling (3 cases).

3. Mild or moderate enlargement of the cecocolic and mesenteric lymph nodes with blood absorption (8 cases).

4. Mild or moderate mucosal hemorrhages in the stomach and small intestine (9 cases).

5. Verminous endoarteritis or mild verminous aneurysm in the anterior mesenteric and ileocecal arteries (2 cases). Except these 2 cases, no remarkable changes due to Strongyulus vulgaris were noted in the anterior mesenteric arteries and their branches in all cases.

Histologically, all the visceral organs were more or less congested and the congestion was most prominent in the mucosa of the large intestine in all cases. Fresh, focal or diffuse hemorrhages were found frequently in the adrenals, endocardium and lymph nodes as well as the large intestine.

Large intestine: Main lesions were confined to the mucosa and submucosa except several cases in which the muscularis and serosa as well showed severe congestion and hemorrhages. The mucosal lesions varied considerably in severity depending upon the cases and locations within the intestine. Mild lesions were exfoliation of the mucosal epithelial cells (Fig. 1) with or without congestion (Fig. 2), lymph stagnation, and edema of the intestinal wall. The crypts were occasionally dilated containing many exfoliated epithelial cells. Epithelial cells lining these crypts were frequently cuboidal with basophilic cytoplasm and round, vesicular nuclei. These mild mucosal lesions were noted diffusely or confined to limited areas of the large intestine in 10 cases. In the other cases and areas, epithelial changes were overwhelmed with hemorrhages, fibrinous exudation and neutrophilic infiltration in the mucosa. The most advanced mucosal lesions were found
in 8 cases and showed collapse of mucosal structure due to extensive hemorrhagic necrosis with marked dilatation of the capillaries and venules in the lamina propria and submucosa (Fig. 3). Multiple fibrin thrombi were noted in these blood vessels of 13 cases. Lymphoid follicles invariably showed lymphocytic depletion and reticulum cell proliferation. The follicles often contained a few or many multinucleated giant cells in 15 cases (Fig. 4) or encapsulated with thickened fibrous connective tissues in 7 cases respectively (Fig. 5).

Small intestine: Mild exfoliation of epithelial cells was found in the jejun-ileal mucosa of 2 cases. Lymphoid follicles were commonly enlarged and some of them from 5 cases exhibited lymphocytic depletion and proliferation of reticulum cell with occasional formation of multinucleated giant cells.

Lymph nodes: Number and location of the lymph nodes histologically examined were variable in each cases, but they consistently exhibited blood absorption, sinus catarrh, and lymphocytic degeneration in variable degree. Proliferation of reticulum cell was found in the reaction centers of 11 cases. A few multinucleated giant cells of presumably reticulum cell origin were noted in the cortex and sinus of several lymph nodes in 9 cases.

Spleen: The red pulp were severely congested in 5 cases. Lymphoid follicles were rather atrophic and lymphocytes in the follicles were degenerated or depleted. Severe proliferation (Fig. 6) of reticulum cell was seen in the follicles of 13 cases. Encapsulation of the follicles with thickened fibrous connective tissue was noted in 7 cases, and the central arteries of these follicles were located within the fibrous capsules.

Lungs: Eight cases showed mild or severe congestive edema. Focal or diffuse interstitial pneumonia was noted in 15 of 16 cases. The alveolar walls of the affected areas were thickened mainly by infiltration of mononuclear cells and proliferation of alveolar lining epithelial cells. The alveoli were slightly atelectatic and sometimes contained a large number of macrophages with or without neutrophils. The inner surface of these alveoli was covered with cuboidal epithelial cells (Fig. 7). Multinucleated giant cells were occasionally found within the alveoli (Fig. 8). Proliferation of reticulum cell was observed in the peribronchial lymphoid tissues in 6 cases.

Besides the fibrin thrombi in the large intestine, a few, similar thrombi were found in the lungs, liver, spleen, small intestine, stomach, and pancreas in order of frequency in 6 cases. Notable histological changes in the other organs were multiple focal necrosis and mild proliferation of the interlobular bile ducts in the liver in 1 and 5 cases respectively, widespread necrosis of tubular epithelial cells with hyalin casts formation in the kidneys in 7 cases, hemorrhages with solitary or focal cortical cell necrosis in the adrenals in 2 cases.

DISCUSSION

Clinical findings commonly described by previous workers were sudden onset of the severe diarrhea and/or colic, peracute and highly fatal clinical course [7, 9, 10, 12, 14–17, 20], dehydration and hemoconcentration [8, 14–17], occasional leukopenia [15–17], and toxemic appearances such as depression [8, 12, 15–17, 20], discoloration mucous membrane [7, 10, 14–17, 20], and tarry rapid pulse [9, 14–17]. Characteristic macroscopic findings commonly reported were dark, tarry, nonclotting blood in the subcutaneous engorged blood vessels [8, 10, 12, 14–16], and hyperemia, petechiae and ecchymosis in
the various organs and tissues [10, 12, 14-17, 20]. The mucosal lesions of the cecum and colonic varied in intensity from hyperemia with petechiae to marked hemorrhagic necrosis with watery, sometimes bloodtinged ingesta [7-10, 12, 14-17, 20]. The cecocolic lymph nodes were hyperemic and edematous [7, 9, 10, 12, 14-16]. It seemed approvable that the present 16 cases were affected with colitis X, because they exhibited almost all of those clinical and macroscopical findings.

The large intestine exhibited edema in the lamina propria and submucosa, marked congestion of capillaries and veins [7, 9, 10, 12], and necrosis of mucosal epithelial cells in various extent [15-17]. Lymphocytic necrosis was prominent in the lymphoid follicles of the large intestine, spleen, and lymph nodes [9, 10, 12, 16, 17]. Besides these histological changes, the following findings were frequently observed in the present cases:

1. Reticulum cell proliferation with occasional giant cell formation in the lymphoid follicles of the large intestine (16 cases), small intestine (5 cases), spleen (13 cases), and lymph nodes (11 cases). Some of the follicles were encapsulated with thickened fibrous connective tissues.

2. Capillary and venular fibrin thrombi in the large intestine (13 cases) and other organs (6 cases).

3. Focal or diffuse interstitial pneumonia (15 cases) and congestive edema of the lungs (8 cases).

4. Widespread necrosis of tubular epithelial cells with hyalin casts formation in the kidneys (7 cases).

Detailed histological examination on the large intestine of present cases revealed desquamation of mucosal epithelial cells and hemorrhages in the lamina propria preceded pseudomembranous and suppura-tive changes and subsequent hemorrhagic necrosis of the mucosa. These mucosal changes as well as multiple fibrin thrombi in the intestinal mucosa, widespread necrosis of tubular epithelium with thylain casts formation in the kidneys, and congestive edema of the lungs coincide well with the histological changes of shock [11, 18, 21], and these changes seem to support the morphological ground to the hypothesis that endotoxin shock is immediate cause of colitis X.

The precipitating events of the shock appeared in the literatures are tetracycline treatment [2, 5, 13] and various stress factors such as transportation [2, 16], surgery [5, 20], respiratory disease [11, 16], advanced pregnancy [9], and unfavorable circumstances [9]. Among the clinical histories of the present cases, tetracycline treatment (10 cases), respiratory distress (9 cases), and transportation (1 case) were recorded before onset of the diarrhea and colic, but 3 cases had no records of such predisposing factors. The histological changes attracted much of our attention were interstitial pneumonia which was highly suggestive of viral pneumonia [19] and proliferation of reticulum cells with occasional formation of multinucleated giant cells and proliferation of collagenous fibers in the lymphoid follicles. All of these changes could not be consequences of the shock state which lasted a few hours to 3 days before death, but suggested the involvement of certain precipitated events, especially systemic viral infection. Although etiological agent of the pneumonia could not be demonstrated in this study, involvement of systemic infection was suggested as one of a possible predisposing events to the shock except tetracycline treatment and other various stress factors.
HISTOPATHOLOGY OF COLITIS X

REFERENCES


EXPLANATION OF FIGURES

Fig. 1. The mucosa of the large intestine. Exfoliation of the mucosal epithelial cells and slight dilatation of the crypts. Hematoxylin-Eosin stain (H-E), ×280.

Fig. 2. The mucosa of the large intestine. Congestion and edema of the mucosa. H-E, ×70.

Fig. 3. The mucosa of the large intestine. Hemorrhagic necrosis of the mucosa. Dilated blood vessels contain fibrin thrombi in the lamina propria. H-E, ×170.

Fig. 4. Lymphoid follicle of the large intestine. Degenerated lymphocytes and many multinucleated giant cells. H-E, ×280.

Fig. 5. Lymphoid follicle of the large intestine. Proliferation of reticular fibers. The follicle is encapsulated with thickened fibrous connective tissue. Watanabe’s silver stain, ×170.

Fig. 6. Lymphoid follicle of the spleen. Depletion of lymphocytes and proliferation of reticulum cells. H-E, ×280.

Fig. 7. The lung. Interstitial pneumonia. Marked swelling and proliferation of alveolar epithelial cells are demonstrated. H-E, ×280.

Fig. 8. The lung. Interstitial pneumonia. Proliferation and desquamation of alveolar epithelial cell with occasional formation of multinucleated giant cells. H-E, ×280.
要約

大腸炎罹患馬の病理組織像：梅村孝司，大石秀夫①，池本安夫①，佐藤 搏，藤本 胖（北海道大学総医学部比較病理学教室，①日高地区農業共済組合）——大腸炎罹患馬16例を病理組織学的に検索した。特徴的な病変は腸粘膜の出血性壊死にいたる粘膜上皮剥離，腸粘膜における毛細血管性および静脈性線維素血栓形成，肺のうっ血水腫，および腎尿細管尿細胞の著しい障害と尿円柱形成であった。これらは所見は大腸炎の直接的機序が菌体内毒素によるショックであるという仮説を病理学的に支持するものと考えられた。さらに，間質性肺炎が15例に，細網状細胞増殖が多数例の大腸，脾膵，およびリンパ節のリンパ濁胞に観察され，リンパ濁胞内では多核巨細胞形成をともなうものもあった。これらの所見から，全身感染症，特にウィルス感染症がショックの誘発に関与している可能性が示唆された。