NOTE

Histopathological Characteristics as Diagnostic Indicators in Canine Parvoviral Enteritis

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ABSTRACT. Eleven dogs from several veterinary hospitals which died of spontaneous parvoviral enteritis were studied histopathologically to determine pathognomonic lesions which may serve as diagnostic indicators in this disease. Giant epithelial cells with bizarre nuclei and intracellular microcysts suggesting dysplastic regeneration were often observed in the affected mucosa of the small intestine in all cases.—KEY WORDS: atypical giant cell, canine parvoviral enteritis, microcyst.

Canine parvoviral disease has spread throughout the world since 1978. Many workers have since reported clinical, virological and epidemiological findings. Histopathological lesions in naturally occurring or experimentally induced disease have been described in the heart, lymphatic organs, bone marrow, and, especially, in the intestinal tract [1, 3–5, 7–9, 11, 13, 14]. These changes reported include formation of inclusion bodies in cardiac fibers [3, 5, 13] and intestinal epithelial cells [1, 4, 8], decreased number of lymphocytes [8, 11, 14] or bone marrow cells [14] and degeneration of these host cells. However, it is not always easy to diagnose parvoviral enteritis histologically because of the severe loss of intestinal epithelial cells in which nuclear inclusion bodies might be formed and of the similarity of lesions to post mortem autolysis.

In this study, typical lesions of canine parvoviral enteritis are described along with pathognomonic changes to confirm histological diagnosis in naturally occurring cases.

Eleven dogs were necropsied for the study. They were finally diagnosed as canine parvoviral enteritis on the basis of histopathology. The age of these dogs ranged from 2 months to 2 years. There were four crossbred, two Shibas, and one each of various breeds (Shetland, Maltese, Chihuahua, Pomeranian and Yorkshire terrier). All cases had been diagnosed or suspected as canine parvoviral enteritis by attending clinicians from a history of sudden onset of diarrhea.

At necropsy, the entire length of the small intestine was most frequently affected. The mucosal surface was dark red to purple in color because of severe congestion and hemorrhage. The mucosal thickness was reduced, and the mucosal surface of the affected intestine was smooth, resembling the appearance of an intact aorta. In addition, there was mild or severe atrophy of Peyer’s patches in the small intestine. The large intestine was less frequently involved, and only slight hemorrhagic or focal congestion was observed in half of the cases.

Formalin-fixed intestinal tissue samples were obtained from the grossly affected parts: 3 other samples representing the duodenum, jejunum and ileum of the small intestine; and 2 from the cecum and colon of the large intestine. These tissue samples were embedded in paraffin, sectioned at 5 μ
m, and stained with hematoxylin and eosin (HE).

Histopathologically, the lesions in the small intestine consisted of degeneration, necrosis and desquamation of mucosal epithelium or regeneration of epithelial cells. In only one case were considerable numbers of degenerated epithelial cells preserved in the duodenal crypts, which desquamated cells accumulated in the lumen. This case which was considered to have died at an early stage of viral infection was easily diagnosed because of frequent inclusion bodies in the epithelial cells of the duodenal mucosa. However, desquamation of the epithelial cells was more severe through the whole length of the small intestine in the other cases, with only a few epithelial cells remaining in the mucosa. The affected mucosa showed severe villous atrophy with collapse of intestinal crypts and confirmation of diagnosis was difficult because of the
absence of definite inclusion bodies in these cases.

Large bizarre or distorted epithelial cells measuring up to 34 μm in cell length and 32 μm in width, suggesting dysplastic regeneration of epithelium, were often observed in the affected mucosa of all cases (Figs. 1–3). These cells had large nuclei and clear vesicular cytoplasm. Some large cells showed prominent microvilli on their free surface (Figs. 2, 3). In some cases, only a few cells lined some crypts (Fig. 3), but a large number of large cells often covered entire crypts and the surface of villi in other cases (Fig. 2). Frequently, they had one or more microcysts (also called cytoplasmic cysts) in their cytoplasm (Figs. 4, 5). Internal surface of the microcysts was covered with prominent microvilli. Some microcysts were empty and others contained eosinophilic amorphous substance (Fig. 5).

Degenerative change in the large intestine was milder than in the small intestine and many intranuclear inclusion bodies were detected mainly in desquamated cells in the crypts (Fig. 6). Moreover, no regenerative hyperplasia of the epithelium and microcyst formation were observed except in one case.

The main histological feature of affected mucosa in the most cases was severe loss of epithelial cells, and in such a case, the confirmation of the diagnosis by detection of inclusion bodies was often difficult. These mucosal changes were often indistinguishable from post mortem autolysis in cases which could not be necropsied immediately after death.

It is suggested that histological examination of the large intestine is more adequate than the examination of severely affected small intestine to confirm a diagnosis of parvoviral enteritis; the mucosal epithelium of the large intestine is more intact in cases of the disease and many inclusion bodies are easily detectable. The difference in histological appearance between the small and large intestines might be attributable to the different turnover time of epithelial cells; it is generally longer in the large intestine than in the small intestine [6, 16]. Also, viral replication and consequent death of host cells by the infection with parvovirus might depend on the proliferation rate of host cells [2, 4].
Regenerative changes in the small intestine characterized by the giant epithelial cells with bizarre nuclei were similar to those seen in the small intestine in feline panleukopenia [15]. These were reported to be constant findings in canine parovirial enteritis [4, 7-9, 11] and were described as a hyperplastic regeneration [7] or hyperplastic change [9]. However, the significance of this peculiar appearance of abnormally large cells with bizarre nuclei has not been discussed in previous studies.

Intracellular microcysts have been observed in a wide variety of tumor cells, including gastric carcinoma, granular cell adenocarcinoma of the kidney, mesothelioma, adenomatoid tumor, thymoma and pituitary adenoma [10, 12, 17]. They have been regarded as an expression of lost surface polarity and formation of surface structures inside the cytoplasm of epithelial cells, which have the potential of forming microvilli on the cell surface, caused by the neoplastic transformation of the progenitor cells [10, 12]. Frequent microcysts in the regenerating epithelial cells in this study may suggest the atypical differentiation of these cells under abnormal transformation, which might be caused by viral infection of intestinal stem cells. Canine parovirus is known to have great tropism for an intestinal stem cell [4, 5, 9], and this predilection might make it possible to distinguish paroviral enteritis from coronaviral disease. In this sense, intracellular microcysts, indicative of the viral infection of stem cells, are considered to be a specific pathognomonic change in canine paroviral enteritis, like the inclusion bodies in enterocytes. These atypical epithelial cells will be more easily detectable in the sections undergoing autolysis.

REFERENCES


要 約

犬バールボウィルス性腸炎の診断的指標としての病理組織学的特徴（短報）：三浦浩二・土谷稔・奈良関功（株）生物科学技術研究所――自然発生バールボウィルス性腸炎による死亡例の消化管について病理組織学的に探索した。小腸では著しい粘膜上皮の脱落のため封入体の検出は困難であったが、大腸では顕著に封入体が検出された。小腸において珍味な形態を呈する再生上皮が多数例においてしばしば観察され、パルボウィルス感染の病理組織学的診断の指標として有用であることが論議された。