Stomach Lesions of Gray Diarrhea in Mink

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Abstract. Hematologic and pathologic examination on thirty-five mink, clinically affected with gray diarrhea, were carried out. Four had other recognizable diseases. Twenty-two had microscopic stomach lesions, not described in other mink diseases. The lesions were multifocal and consisted of loss of the middle and basal layers of the mucosa, with neutrophil and mononuclear cell infiltration. Fibrosis was observed in the stomach lesions of some. Direct and indirect fluorescent antibody techniques, utilizing sera from affected mink, failed to demonstrate an autoantibody in them. Hematologic responses of affected mink varied widely.

Gray diarrhea is a syndrome of mink characterized by severe diarrhea and marked weight loss coupled with a normal or increased appetite. The feces are soft and gray, containing nonassimilated fat, which gives them a rancid odor. The disease is rarely fatal, but results in emaciated, undersized mink with poor fur. It usually occurs in mink over 14 months old. While the malady occurs wherever mink are raised, the cause is obscure. Genetic predisposition, pancreatic dysfunction, viral etiology, and a primary malabsorption syndrome have all been proposed as primary causes [11]. Palarski [11] reported that nitrofurazone was effective, but this finding has not been confirmed by others [4].

The purpose of this study was to delineate the pathologic and hematologic values of the naturally occurring disease, and to emphasize stomach lesions. Possible etiologies and relationships to other syndromes in man and animals are discussed.

Materials and Methods

Thirty-five affected mink from a farm near Newport, Washington, USA, were examined in three groups. All had clinical signs of gray diarrhea.

Group 1. Thirteen mink representing several genotypes were killed with cyanide, and gross and microscopic examinations were conducted after pelting. Hematoxylin and eosin (HE) staining was utilized for general histologic observation. Luxol fast blue-periodic acid-Schiff (LFB-PAS) stain was used for observing stomach structure.

Group 2. Five chronically affected pastel females were exsanguinated and necropsied. The blood was used for hematologic examination by routine methods. Histological examination emphasized the
Table 1. Hematology and stomach lesions in clinically affected gray diarrhea in mink

<table>
<thead>
<tr>
<th>Group</th>
<th>Mink #</th>
<th>Hemato-</th>
<th>Hemoglobin</th>
<th>RBC × 10^6</th>
<th>WBC</th>
<th>Differential WBC count</th>
<th>Reticulo-</th>
<th>Gamma</th>
<th>Stomach</th>
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<tr>
<td></td>
<td></td>
<td>crit %</td>
<td>Gm %</td>
<td>per cmn</td>
<td></td>
<td>per cmn</td>
<td>cytocytes</td>
<td>globulin</td>
<td>lesions</td>
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<td>13.2</td>
<td>5.6</td>
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<td>7.3</td>
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<td>8,800</td>
<td>15 83 0 0 2 36 6.7</td>
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</table>

* Cases examined with fluorescence microscopy.

gastrointestinal tract. One tissue block was made of the pancreas and 5 to 7 tissue blocks were prepared from the whole stomach of individual mink. Ten to 12 blocks were made from the intestinal tract at approximately 10 cm intervals. The length of the tract from the beginning of the duodenum to the end of the rectum was about 100 to 120 cm after formalin fixation. HE staining and LFB-PAS stain were used for histologic observation.

Group 3. Seventeen pastel females were studied by the same procedures as described in Group 2. Sera from 5 of the mink were examined by direct and indirect fluorescence microscopy [7]. Cryostat sections of the digestive tracts of normal mink as well as stomach lesions from diseased mink were prepared and incubated with sera of diseased mink stained with rabbit anti-mink gammaglobulin conjugated with fluorescein isothiocyanate (FITC). Direct fluorescence microscopy was accomplished by staining cryostat sections of stomach lesions from diseased mink with FITC-labeled sera of diseased mink.

Results

Hematological examination: Findings from 17 mink examined hematologically from Group 2 and 3 are shown in Table 1. Samples varied considerably. A red blood cell count of less than 7 million per cmn was observed in 7 mink. These mink had an increased reticuloocyte count. White blood cell counts ranged from 5,000 to 15,000 per cmn, although most were in the normal range. Gammaglobulin levels were within the normal range in all instances. The sera of 5 mink in Group 3 were used for fluorescence microscopy. Red blood cell counts of these mink ranged from 5.3 to 7.3 million.

Necropsy findings: No gross changes were detected except in a few mink that died during clinical observation after their arrival at our laboratory. One of these had characteristic lesions of Aleutian disease in the kidney and liver.

Microscopic findings: In most animals examined, the stomach was the only organ with significant microscopic lesions. In general, the thickness of the mucosa was increased over that of normal mink, measuring about 0.6-0.9 mm [2]. Lesions were most predominant in the fundus, but were observed in all areas of the stomach.
Table 2. Lesions in clinically affected gray diarrhea mink

<table>
<thead>
<tr>
<th>Group</th>
<th>Total number of affected mink</th>
<th>Number of cases with stomach lesions</th>
<th>Number of cases with no lesions</th>
<th>Other lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>6*</td>
<td>6</td>
<td>1 Bronchopneumonia</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>1 Ulcerative esophagitis</td>
</tr>
<tr>
<td>3</td>
<td>17</td>
<td>14</td>
<td>1</td>
<td>1 Liver abscess 1 Aleutian disease</td>
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</table>

* Two had diffuse parietal cell degeneration.

Lesions were multifocal and did not spread diffusely into wide areas. There was cellular infiltration of neutrophils, lymphocytes, plasma cells, and histocytes. Some foci contained only mononuclear cells. In such lesions the upper isthmus layer extended into the middle and basal layers (Fig. 1). Occasionally an edematous albuminoid substance was deposited in the lamina propria. Epithelial cells were pyknotic and desquamated in some lesions but generally rather well preserved. Occasionally, the gastric pits penetrated to the base of the mucosa and formed cystic structures lined by isthmus epithelial cells (Fig. 2). The LFB-PAS stains revealed that no parietal cells and only a few chief cells were present in the lesions; the number of PAS-positive isthmus cells was increased. In advanced lesions, epithelial cells were desquamated and fibrosis was observed in the lamina propria (Fig. 3).

Of 13 affected mink in Group 1, 6 had stomach lesions, including 2 with diffuse parietal cell degeneration (Table 2). The cells stained deeply acidophilic and were pyknotic. Catarrhal lesions in the intestinal tract were observed in only 2 mink. No significant changes were observed in the other 7. One of these mink died of a bronchopneumonia.

In Group 2, 2 out of 5 mink had stomach lesions; one had ulcerative esophagitis and the other 2 were normal.

Stomach lesions were detected in 14 of 17 mink in Group 3. It was not unusual to find more than 30 focal lesions in the stomach sections of one mink. The 3 remaining mink included one without any lesions, one with a liver abscess and cholangitis, and another with lesions of Aleutian disease.

Fluorescence microscopy: No fluorescence was detected on stained sections of the stomach, duodenum, jejunum, ileum or rectum after indirect fluorescence microscopy. No fluorescence was in stomach lesions when the direct and indirect techniques were utilized.

**Discussion**

The salient clinical observations are diarrhea and malabsorption. Many diseases in human medicine have similar features [1, 3, 8, 13]. Some are disorders of the digestive tract per se, and others are associated with malfunction of other organ systems.

In 1965, Kaneko et al. reported 3 cases of malabsorption syndrome in the dog [6]. Histologically, intestinal lesions in these were associated with lesions in the gastric mucosa, pancreas, adrenal glands and lymph nodes. Similar cases, reported by Kallfelz et al. [5] and by Vernon [12], showed intestinal and pancreatic lesions. The fact that the cat may have the malabsorption syndrome was recorded by Wilkinson [14].

Our studies disclosed that only stomach lesions were in mink with gray diarrhea. The criteria of diagnosis of the disease were based on continued diarrhea and malnutrition. Accordingly, it would be not surprising if the syndrome had several causes. Bronchopneumonia, ulcerative esophagitis, liver abscess with cholangitis and Aleutian disease should be excluded from the gray
diarrhea group. Therefore, 22 of 31 mink (71%) had stomach lesions; in Group 3 where the cases were well developed, 93% had stomach lesions. The number of smaller lesions in Groups 1 and 2 was probably due to the fact that the whole stomach was not examined in Group 1 and that mink were killed early in the disease in Group 2.

More than 30 lesions were frequently detected in the stomach sections of a single mink, and the actual number of lesions would be considerably greater since only a portion of the organ was actually examined. In our laboratory, approximately 200 normal control mink have been examined histologically, and gastric lesions were rarely detected. Although much attention was given to stomach lesions, the relationship of these lesions to the syndrome is still obscure. It is difficult to explain the diarrhea on the basis of the stomach lesions noted. However, the loss of parietal cells and possibly an accompanying functional disability could cause achlorhydria with resulting physiological disturbance. The possibility of functional pancreatic abnormalities must be considered, although no lesions were observed.

Anemia was noted in several pastel mink in Groups 2 and 3. Pernicious anemia with chronic gastric mucosal atrophy has been recognized as an autoimmune disease in human medicine, and a family predisposition is associated with the disease [9]. Human pernicious anemia and gray diarrhea of mink may be similar, although characteristics of the stomach lesions are somewhat different. Autoantibodies in sera of affected mink were not demonstrated against both stomach lesions and normal tissues by direct or indirect fluorescence microscopy. Marsh and Gorham reported that vitamin B$_{12}$, which is effective for human pernicious anemia [9], was not effective in treating gray diarrhea in mink [10].

References


Explanation of Figures

Fig. 1. Focal cellular infiltration in the gastric lamina propria. The upper isthmus layer projects into the middle and basal layers. HE Stain. ×75

Fig. 2. Cystic arrangement of the isthmus with cellular debris, cellular infiltration and disappearance of both middle and basal layers.

HE Stain. ×120

Fig. 3. Focal erosion of the gastric mucosa. Cystic arrangements of the isthmus with calcium deposition, cellular infiltration and proliferation of fibrous tissue are seen in later lesions. HE Stain. ×120