Endoscopic Findings on Alimentary Lymphoma in 7 Dogs

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ABSTRACT. Alimentary lymphoma was evaluated endoscopically in 7 dogs and a histopathological examination was made to detect the origin of neoplastic lymphocytes in 5 dogs. A solitary mass in the rectum (1 case), irregular cobblestone appearance in the duodenum (4 cases) and a moderate irregular appearance resembling lymphocytic-plasmacytic enteritis (2 cases) were endoscopically detected. Endoscopic ultrasonography demonstrated increased thickness of the duodenal wall in 2 cases examined. Neoplastic lymphocytes of alimentary lymphoma proved to originate in T cells in all 5 cases examined by immunohistochemical analysis.

KEY WORDS: alimentary lymphoma, canine, endoscopy.

Lymphoma is a common neoplasm in dogs and cats, and is anatomically classified into multicentric, mediastinal, alimentary and extranodal forms. The alimentary form is common in cats [1, 5, 9, 10], but uncommon in dogs, accounting for only 5 to 7% of all lymphomas [2, 8]. It is generally believed that full thickness biopsy of the intestine is necessary to diagnose alimentary lymphoma as the lesions are usually deep-seated and invade the serosa. Since it is difficult to detect lesions deep in intestinal tissues, endoscopic biopsy specimens are frequently not enough for histopathological diagnosis. Nevertheless, endoscopic biopsy is clinically introduced as a rule to evaluate the pathology of alimentary lymphoma without discussing its endoscopic features in detail. In this study, alimentary lymphoma was endoscopically evaluated and histopathological examination was taken to detect the origin of the lymphoma cells.

The 7 dogs were diagnosed with alimentary lymphoma by histopathology of endoscopic biopsy specimens at Nihon University Animal Medical Center from September, 2001 to December, 2002. The breeds of these dogs were labrador retriever (n=2), golden retriever (n=2), great pyrenees (n=1), miniature dachshund (n=1) and beagle (n=1). Age at the time of examination ranged from 3 to 10 years [mean ± standard deviation (SD); 7.2 ± 2.4 years]. Four dogs were intact males and three were intact females. Before endoscopic evaluation, physical examination, complete blood count, serum biochemical analysis, fecal analysis and radiography were performed. Major clinical signs were weight loss (n=6; loss of total body weight 14–32%), diarrhea (n=5), vomiting (n=4) and anorexia (n=4). Abnormality on physical examination included an abdominal mass (n=3), which was confirmed by radiography. Fine-needle aspiration from the abdominal mass was performed for cytology to support the diagnosis. No enlargement of surface lymph nodes was observed. No parasites were found on fecal analysis in any of the dogs. In abdominal radiography, hepatomegaly and splenomegaly were not detected. In hematologic findings, none of the dogs was anemic. Leukocytosis due to neutrophilia was observed in three dogs and lymphocytosis in two dogs. Hypoproteinemia (n=3), hypoalbuminemia (n=5) and hypcholesterolemia (n=2) might be caused by disturbance of the digestive tract. No dog showed an increased serum level of lactate dehydrogenase (LDH) or hypercalcemia.

Table 1. Endoscopic findings of 7 cases with alimentary lymphoma

<table>
<thead>
<tr>
<th>Dogs No.</th>
<th>Breed</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Histopathology</th>
<th>Endoscopic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stomach</td>
<td>Duodenum</td>
</tr>
<tr>
<td>1</td>
<td>miniature dachshund</td>
<td>3</td>
<td>male</td>
<td>N.T.</td>
<td>N.T.</td>
</tr>
<tr>
<td>2</td>
<td>labrador retriever</td>
<td>10</td>
<td>female</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>beagle</td>
<td>8</td>
<td>male</td>
<td>N.T.</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>labrador retriever</td>
<td>10</td>
<td>male</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>golden retriever</td>
<td>6</td>
<td>female</td>
<td>N.T.</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>great pyrenees</td>
<td>7</td>
<td>female</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>golden retriever</td>
<td>7</td>
<td>male</td>
<td>N.T.</td>
<td>+</td>
</tr>
</tbody>
</table>

*: Neoplastic lymphocytes detected, -: Neoplastic lymphocytes not detected, N.T.: not tested.
Fig. 1. Typical endoscopic findings. (a) Rectum; dog No. 1. Solitary mass (arrow). (b) Duodenum; dog No. 5. Whitish and very friable mucosa. Remarkably irregular and cobblestone appearance in mucosal surface. (c) Duodenum; dog No. 6. Mild erythema and moderate irregularity resembled LPE.

Fig. 2. Endoscopic ultrasonography findings obtained from dog No. 5. Normal five-layered appearance and increased thickness of the duodenal wall.

Fig. 3. Immunohistochemical staining of biopsy specimen taken from dog No. 2. (a) Many neoplastic lymphocytes positively stained by T cell marker, CD3, × 100. (b) Few neoplastic lymphocytes stained by B cell marker, CD21, × 100.
Routine endoscopic examination was performed with a flexible video endoscope (VQ-8142A, Olympus, Japan) on the dogs after withholding food for 12–18 hr. General anesthesia was induced and maintained with isoflurane in oxygen. The endoscopic findings indicated a solitary mass in the rectum of dog No.1 (Fig. 1a). A remarkably irregular cobblestone appearance was detected in the mucosal surface of the duodenum in dogs No. 2, 3, 4 and 5 (Fig. 1b). In dogs No. 6 and 7, a moderate irregular appearance with patchy erythema was seen in the duodenal mucosa (Fig. 1c). This appearance resembled lymphocytic-plasmacytic enteritis (LPE).

Endoscopic ultrasonography (EUS) demonstrated the structure of the intestinal tract wall and extra-tract features in dogs No.4 and 5. EUS was performed by the water repletion method with an ultrasonic probe (UM-S20-20R, Olympus, Japan). The five-layered appearances were normal (Fig. 2). The reference range of duodenal wall thickness determined at the descending duodenal wall of 5 healthy beagles was 4.4 ± 0.2 mm (mean ± SD). In a previous study, normal values for small intestinal wall thickness measured by transabdominal ultrasonography were reported to be between 2 and 3 mm [6]. The descending duodenal wall thickness of dogs No. 4 and 5 was confirmed to increase to 5.7 mm and 5.3 mm, respectively.

Each moiety of multiple samples collected with biopsy forceps (ø1.8 mm) was placed in 10% neutral-buffered formalin for histopathologic examination and the others were snap-frozen in optimal cutting temperature (OCT) medium over the vapor phase of liquid nitrogen for immunophenotypic analysis. Neoplastic lymphocytes were detected in biopsy specimens of all 7 cases (Table 1).

Immunophenotypic analysis with antibodies to canine T cell (anti human CD3, CD3–12; Serotec, U.K.) and canine B cell (anti canine CD21, CA2.1D6; Serotec, U.K.) was performed, and revealed that the majority of neoplastic lymphocytes were positive for CD3 and negative for CD21 in all 5 dogs (Fig. 3).

Six of 7 dogs were treated with chemotherapy including some or all of the following: L-asparaginase, vincristine, cyclophosphamide, doxorubicin, cytarabine and prednisolone. Follow-up information was available for 6 dogs. Of the 6 dogs treated with chemotherapy, 3 dogs (dogs No. 4, 5 and 6) responded poorly and died within 8 weeks from the first administration though there was temporary amelioration of symptoms. The remaining 3 dogs obtained remission. Dog No. 2 died after 211 days and dog No. 3 was euthanized after 193 days from the time when alimentary lymphoma was diagnosed. Dog No. 1 was still alive 356 days from the initial diagnosis at the time of the last follow-up. Dog No. 7 was symptomatically treated.

In endoscopic examination, 4 dogs showed characteristic findings of remarkably irregular cobblestone appearance on the mucosa of the duodenum. The mucosal surface had many protrusions and fissures; it looked like cobblestone appearance as in human cases. The color of the mucosa varied from white to pink. Poor distensibility and elasticity of the duodenal wall was found whenever air was insufflated.

The thickness of the descending duodenal wall proved to be increased in dogs with alimentary lymphoma by EUS, which could disclose the intestinal wall structure more clearly than transabdominal ultrasonography because it was not affected by the gas inside the intestine.

When alimentary lymphoma is suspected from the endoscopic feature of a cobblestone appearance but is not diagnosed histopathologically, the response to treatment should be carefully evaluated. Biopsy specimens are occasionally insufficient to differentiate lymphoma from LPE histopathologically. Multiple biopsy specimens should be taken as deep in the tissues of the lamina propria as possible for accurate diagnosis in the histopathologic examination.

It was widely believed that the lymphocyte phenotype of alimentary lymphoma was probably of B cell origin based on cell morphology and tumor architecture [4], but 2 previous reports characterized the lymphocyte phenotype involved in canine alimentary lymphoma by means of immunohistochemistry [3, 7], indicating it to be of T cell origin in 3 of 5 cases. In this report 5 dogs with alimentary lymphoma examined by immunophenotypic analysis were all confirmed to have the disease originate in T cells.

Of the 6 dogs treated with chemotherapy, one dog (No. 1), which had only a solitary mass at the rectum, was still alive. Three dogs (No. 4, 5 and 6) which died within 8 weeks from the first admission, endoscopically showed a cobblestone appearance or moderate irregular appearance with protuberances in the mucosal surface of the duodenum. Two dogs (No. 2 and 3) with remission over 6 months had a cobblestone appearance in endoscopic features. Thoracic and abdominal parenchyma was submitted for postmortem examination in dog No. 6, and the diagnosis was confirmed to be alimentary lymphoma.

In conclusion, alimentary lymphoma in dogs was endoscopically detected as a solitary mass in the rectum (1 case) or as an irregular cobblestone appearance in the duodenum (4 cases). Alimentary lymphoma could be strongly suspected when a solitary mass or cobblestone appearance were detected in endoscopic findings. The moderate irregular appearance resembling LPE was also shown as endoscopic features in 2 cases, which were histopathologically diagnosed as lymphoma. Moreover, neoplastic cells of alimentary lymphoma were confirmed to be of T cell origin by immunohistochemical analysis. These findings indicated that the endoscopic examination including EUS would be helpful in the diagnosis of alimentary lymphoma in dogs.

REFERENCES


