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SHORT COMMUNICATION

Clinical Case Report

Post-chemotherapy intestinal fibrotic stricture in a cat with high-grade intestinal lymphoma: a case report

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Abstract

A 3-year-old castrated male cat was presented with lethargy, anorexia, and melena. A complete blood count revealed regenerative anemia. Abdominal ultrasonography revealed a layer-disrupted intestinal mass at the ileocecal junction. Fine needle aspiration performed on the mass revealed large lymphocytes, suggesting lymphoma. The patient was treated with CHOP-based chemotherapy but admitted for emergency care with vomiting and depression during the CHOP protocol. Abdominal ultrasonography suggested annular intestinal stricture at the site of lymphoma. The patient underwent ileocecectomy, which resolved the small intestinal obstruction. Histopathologic examination of the resected specimen demonstrated transmural enterotyphilitis with prominent fibrosis. The patient remained stable without relapse. To our knowledge, this is the first case of intestinal stricture occurring during chemotherapy for feline high-grade intestinal lymphoma.

Key Words: chemotherapy, feline lymphoma, gastrointestinal obstruction

Intestinal lymphoma is a commonly diagnosed intestinal tumor in cats, and chemotherapy is often used for treatment³⁾. While performing

multiagent chemotherapy, such as COP or CHOP-based protocol, low-grade hematologic and gastrointestinal toxicosis is common^{7,9)}. This case

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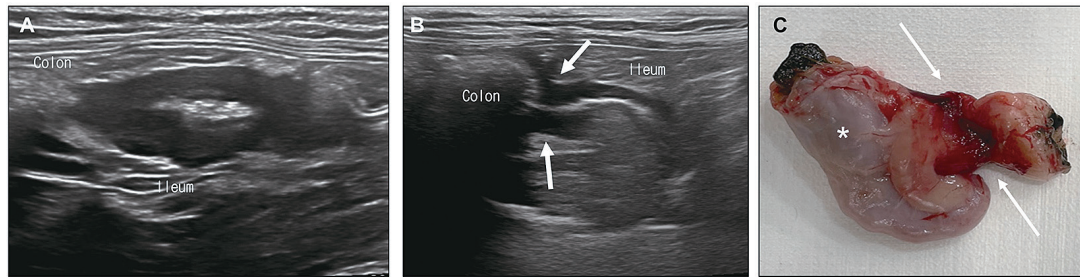


Fig. 1. Ultrasonographic image of the ileocecal region at the first presentation (A). Annular ileocecal stricture on ultrasonography (B) and in the resected specimen (C). The stricture (arrows) is narrow, with marked dilation of the proximal intestine.

reports a rare complication following CHOP-based chemotherapy in feline high-grade intestinal lymphoma patients.

A 3-year-old, 4.67 kg, castrated male, domestic short-hair cat was presented to Western Referral Animal Medical Center (Seoul, South Korea) with lethargy, anorexia, and melena for 2 days. Complete blood count (CBC) revealed regenerative anemia (hematocrit (HCT), 11.8%, reference interval (RI), 27.7–46.8%; reticulocyte count, $131.5 \times 10^3/\mu\text{L}$, RI, $15.0\text{--}81.0 \times 10^3/\mu\text{L}$). The biochemical profile was normal. Abdominal radiography revealed a large, round, soft tissue opaque mass in the center of the abdomen. Abdominal ultrasonography revealed that the small intestinal mass (6×3.5 cm in long and short axes, respectively) was hypoechoic and the mass was found to disrupt the normal intestinal wall layering (Figure 1A). Ultrasound-guided, fine-needle aspiration of the abdominal mass revealed high cellularity with medium to large lymphocytes. Based on aspirate cytology, high-grade intestinal lymphoma (HGIL) was diagnosed. Polymerase chain reaction for antigen receptor rearrangements, performed using the cells aspirated from the intestinal mass, revealed monoclonality of T-cell lineage. The results of feline immunodeficiency virus antibody and feline leukemia virus antigen tests were all negative. No other lymph node enlargements were detected on physical examination or thoracic radiographs.

The patient passed melena during

hospitalization, and the serum total bilirubin level slightly increased (0.23 mg/dL, RI, 0–0.2 mg/dL). The serum color was within normal limits. Blood smear examination found no intra and extravascular hemolytic evidence, such as spherocytes, ghost cells, or red blood cells with Heinz bodies. In addition, there was no evidence of extrahepatic biliary tract obstruction. Since the patient experienced melena during hospitalization, intestinal hemorrhage was considered the cause of regenerative anemia. The patient received a blood transfusion. In-house blood typing was performed, and the patient was classified as type A. 40 ml of packed red blood cells were transfused. The patient also received nasogastric tube feeding, oxygen supplementation, and antibiotics, including cefotaxime (Pharmgen Cefotaxime Sodium Inj.; 30 mg/kg, twice a day, intravenous; Pharmgenscience Pharmaceutical, Korea) and metronidazole (Metrinal Inj.; 15 mg/kg, twice a day, intravenous; Daihan Pharmaceutical, Korea). Gastrointestinal protectants and antiemetic drugs, including famotidine (Gaster Inj.; 0.5 mg/kg, twice a day, intravenous; Donga-st Pharmaceutical, Korea), sodium alginate (Algid solution; 100 mg/cat, twice a day, per os; SCD Pharmaceutical, Korea), and maropitant (Cerenia; 1 mg/kg, once a day, per os; Zoetis, US) were administered to the patient. Ferric Hydroxide Polymaltose complex (Ferromax solution; 200 mg/cat, once daily, per os; Hanmi Pharmaceutical, Korea) was also provided.

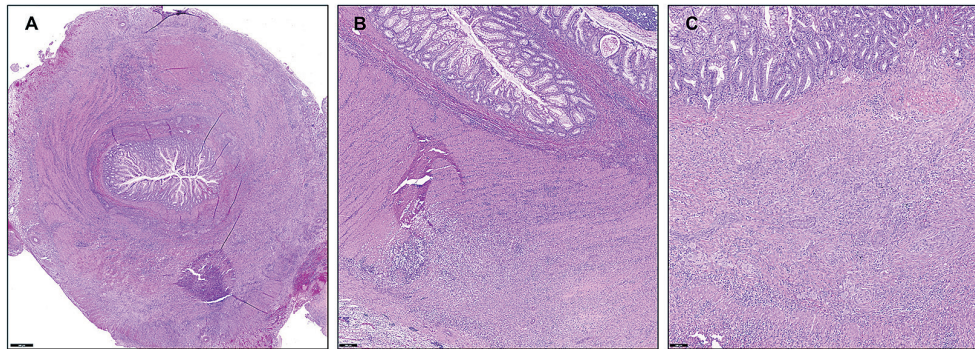


Fig. 2. Histological section of an annular stricture. Circumferential inflammation and fibrosis (A). Mucosa and muscular tunics with inflammatory infiltrate (B). Submucosa with fibrosis (C). H&E stain. Scale bars = 500 μ m (A), 200 μ m (B), 100 μ m (C).

The patient was treated with a CHOP-based chemotherapy protocol given that feline HGIL has shown a robust response to the treatment²⁾. When the first vincristine intravenous injection was administered, the patient was severely anemic (HCT 14.9%, reticulocyte count $80.7 \times 10^3/\mu\text{L}$). After 5 days of the first dose of cyclophosphamide (Alkyloxan, JW Pharmaceutical) at 200 mg/m^2 per oral, the patient presented with vomiting. Maropitant (Cerenia, Zoetis) 1 mg/kg once a day per oral was re-prescribed as supportive therapy. Next, vincristine (Vincran, REYON Pharmaceutical) 0.6 mg/m^2 was infused intravenously as scheduled. Two days later, the patient was admitted for emergency care due to vomiting and depression. CBC revealed regenerative anemia (HCT, 25.9%, reticulocyte count, $211.2 \times 10^3/\mu\text{L}$). There was a mild increase in the activity of alkaline phosphatase (82 U/L, RI, 9–53 U/L). Blood urea nitrogen and creatinine concentrations were within normal limits. The intestinal mass decreased in size ($2.4 \times 0.7 \text{ cm}$) as observed using abdominal ultrasonography, and the patient showed partial remission of HGIL based on response evaluation for nodal lymphoma in dogs¹²⁾. Segmental intestinal dilation that was abruptly kinked at the original site of lymphoma (Figures 1B and 1C) was observed, suggesting an annular intestinal stricture and indicating the need for surgical intervention. Ileocelectomy and end-to-side anastomosis were performed during the surgery.

The histopathology of the resected specimen revealed ulceration and transmural histiocytic and lymphocytic enterotyphilitis with fibroplasia/fibrosis and fibrinous peritonitis at the ileocecal junction (Figure 2). During the entire course of chemotherapy, laboratory screening for tumor lysis syndrome (such as hyperphosphatemia, hyperkalemia, and hypocalcemia) did not reveal any abnormalities in this patient¹¹⁾. Nine months after completing CHOP-based chemotherapy, the patient remains in remission.

Our case is the first to describe that the CHOP protocol applied to feline HGIL resulted in an intestinal stricture. Though intestinal stricture is an unreported complication of chemotherapy in veterinary medicine, in humans, it is regarded as a major complication that may occur during or after chemotherapy for gastrointestinal lymphomas⁶⁾. Fibrosis secondary to tumor cell death, inflammation, necrosis, and scarring of adjacent tissue during chemotherapy is a common complication of chemotherapy and is considered indicative of healing^{1,8,10,13)}.

Mechanisms underlying post-CHOP intestinal fibrotic stricture are multifactorial^{1,8,10,13)}. In a previous study, two cats with non-neoplastic intestinal stricture had attenuated vasculature at the stricture site⁵⁾; thus, intestinal ischemia could be an underlying factor of intestinal stricture in cats. In humans, inflammation accelerates intestinal fibrosis¹⁴⁾. In addition, a hypoxic tumor microenvironment or extensive production

of reactive oxygen species results in the development of fibrosis^{4,15}). In our case, the patient was severely anemic when the first vincristine intravenous injection was administered. The patient was discharged from the oxygen cage the same evening; thus, the patient might have suffered from poor tissue perfusion to the affected intestine. Histopathologic examination confirmed mixed inflammatory infiltrates and diffuse fibrosis in the patient. Therefore, the post-CHOP intestinal fibrotic stricture of our patient could have been attributed to the cumulative effects of severe anemia-induced ischemia, inflammation, and oxidative stress during chemotherapy.

To the best of our knowledge, this is the first reported feline case of intestinal fibrotic stricture occurring during CHOP-based chemotherapy for HGIL. Among the clinical manifestations of intestinal strictures (such as anorexia), vomiting resembles a sign of gastrointestinal toxicosis following chemotherapy. Intestinal stricture should be considered as a differential diagnosis when HGIL patients present with gastrointestinal dysfunction post-chemotherapy.

Conflict of Interest Statement

The authors declare no conflict of interest concerning the publication of this manuscript.

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