NOTE *Surgery*

Mesojejunoileac Liposarcoma with Intrahepatic Metastasis in a Dog

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ABSTRACT. We report a liposarcoma at the mesojejunoileum that was widely excised, and then the intrahepatic metastatic liposarcoma was found. The dog was treated by two single-agent chemotherapy separately. The patient was an 8-year-old, male Dachshund, and was referred to our hospital owing to the significant distention of the left abdomen. Neither radiography nor ultrasonography detected the actual association of the tumor with the abdominal viscera before surgery. A large-sized tumor mass that adhered to the mesojejunoileum was explored by laparatomy. Final diagnosis of a pleomorphic liposarcoma was made by the routine histology and further identified by Oil Red O stain. The two single-agent chemotherapy including doxorubicin followed by capecitabine, however, failed to cause remission of the intrahepatic metastatic lesions. The patient died 22 months after operation and the cause of death was supposed to be metastatic liposarcoma.

KEY WORDS: chemotherapy, liposarcoma, metastasis.

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Liposarcomas occurred primarily in appendicular or axial locations, and extracutaneous development of liposarcomas was rare in dogs [1, 3, 4, 10]. Liposarcoma tends to be aggressive, locally invasive and may metastasize to lung, liver, spleen and bone [1, 5]. They are locally invasive neoplasms that rarely metastasized, and wide excision is preferred to marginal excision [1]. However, the usefulness of chemotherapy in liposarcomas has rarely evaluated [7]. To our knowledge, liposarcoma developed in the mesojejunoileum has not been reported in veterinary literature.

A male Dachshund, eight-year-old, was referred to our hospital owing to enlargement of the abdomen, predominately on the left side. He was obese and weighed 11.6 kg. Two months earlier, both radiography and ultrasonography performed at an animal clinic and presumed a large-sized mass associated with the spleen. The patient had a history of gradual distention of the left abdomen, and the intermittent anorexia, vomiting, difficulty at defecation, and occasional listlessness. There was a palpable firmness and painless mass within the abdomen.

Lateral radiographs displayed that the mass was within ventrally cranial to middle abdomen, dorsal displacement of stomach and intestines, and caudal displacement of intestines. The ventrodorsal radiograph showed that this mass was located within the left abdomen, and superimposed on the left kidney, and that caused cranial displacement of stomach and medial displacement of intestines (Fig. 1). Distant metastatic lesions were not found by thoracic radiographs. Ultrasonography (USG) revealed that this tumor mass had a feature of a mixed echogenicity, which was within the left abdomen and located caudal to the liver and in front of urinary bladder, and enlarged regional lymph nodes were not found. The mass was measured as 12-cm in maximum diameter.

Routinely hematological examination revealed a moderate normocytic, normochromic anemia (hematocrit, 22.5% and hemoglobin, 7.2 g m/dL) with two nucleated RBC in

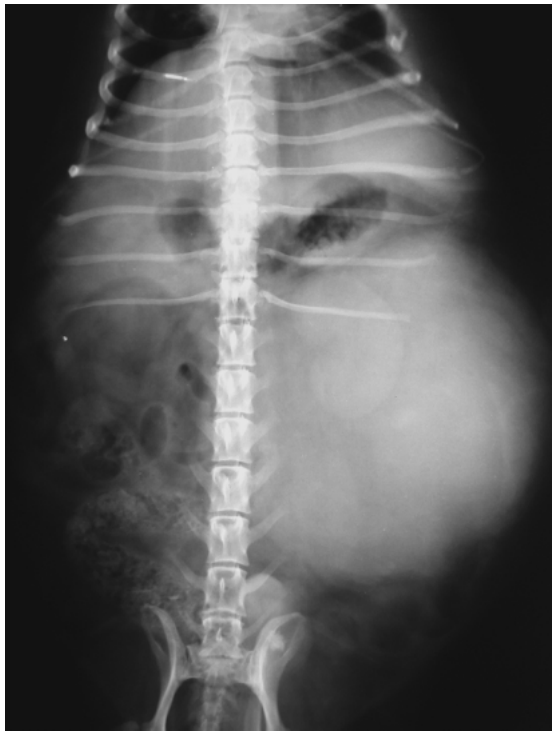

Fig. 1. A ventrodorsal radiograph showed that this enlarged mass was located on the left abdomen, and superimposed on the left kidney, and caused cranial displacement of stomach and medial displacement of intestines.

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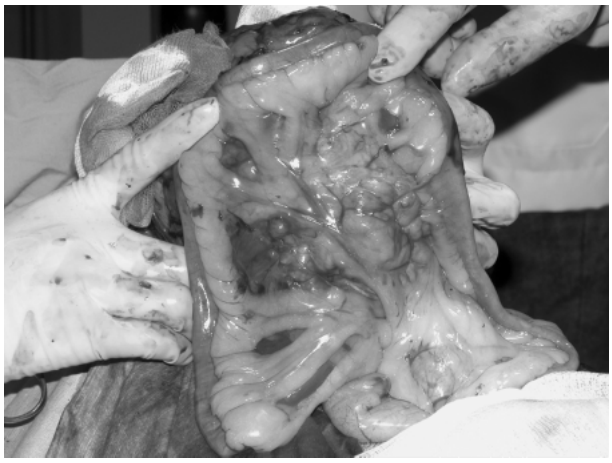

Fig. 2. An intraoperative photograph of liposarcoma with the mesojejunoileum present on the bottom aspect.

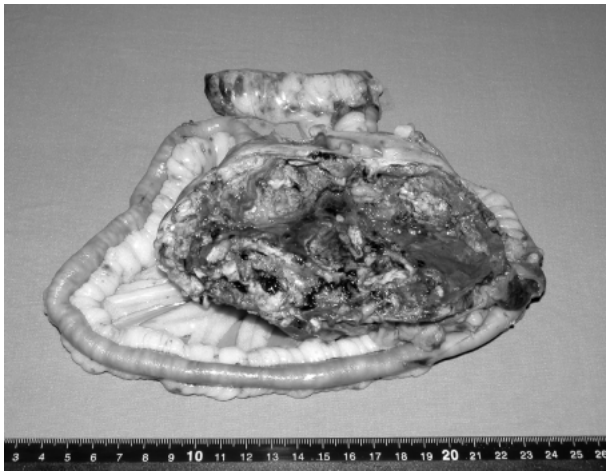

Fig. 3. On cut surface, liposarcoma showed greasy, fragile, multilobulated grayish-white masses with large amount of scattered necrotic area in straw color and full with light-yellow agar-like material.

100 WBC, and leukocytosis (52745/mm^3) consisting a mature neutrophilia (44833/mm^3). The serum chemistry profile present a mild hypoproteinemia (5.12 g/dL) and increased the ratio of albumin/globulin, highly elevated activities of asparagine aminotransferase (AST, 768 U/L), alanine aminotransferase (ALT, 971 U/L), lactate dehydrogenase (LDH, 627 U/L), creatine kinase (CK, 456 U/L) and alkaline phosphatase (ALP, 120 U/L). Results indicated the patient had a moderate anemia that might be due to the tumor-induced chronic blood loss. The moderate anemia was remarkably improved after oral administration of compound drugs containing amoxillin, ferrous sulfate, thiamine mononitrate, cyanocobalamine (B12) and riboflavin (B2) prior to surgery.

Intraoperatively, the tumor mass was found adherent to the mesojejunoileum (Fig. 2). Tumor was overlay and adhered by a large amount of greater omentum with the noticeable superficial vasculature. The affected area including ileum near ileocecal valve was found and therefore approximately 45-cm length of intestinal resection and anastomosis associated with tumor excision was conducted. Then through the entire abdominal inspection, we did not find any abnormality in lymph nodes, especially mesenteric, or other viscera. Grossly, the tumor was firm on palpation and measured as 12 × 10 × 8 cm in size. On cut surface, it showed greasy, fragile, multilobulated gray-white masses contained with large amounts of scattered necrotic area in straw color and full with light-yellow agar-like materials (Fig. 3). Foul smell was also noticed. Microscopic examination showed that the intestine was not infiltrated by tumor cells. At low magnification, the tumor was encapsulated and showed an image of "starry sky". The tumor was mainly composed of round to polygonal cells arranged in sheets, with little fine fibrovascular tissue. The tumor cells exhibited pleomorphic, round or ovoid nuclei in various size, and usually had prominent single or two nucleoli surrounded by marginated chromatin (Fig. 4). Other tumor cells resembled adipocytes with a single clear vacuole and a peripheral nucleus. A few bizarre multinucleated cells and mitotic figures were seen. Several areas of tumor mass showed hemorrhagic with deposition of hemosiderin. The majority of tumor cells had abundant cytoplasm that contained variably sized lipid droplets and positively stained by Oil Red O dye. Finally, a diagnosis of pleomorphic liposarcoma was concluded.

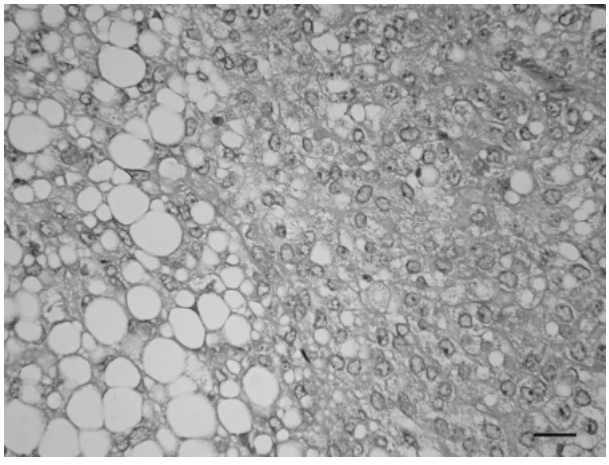

Fig. 4. The tumor cells exhibited pleomorphic, round or ovoid nuclei in various size, and usually had prominent single or two nucleoli surrounded by marginated chromatin. Other tumor cells resembled adipocytes with a single clear vacuole and a peripheral nucleus (left side). (Bar=25 μm, original magnification: × 400, HE stain.)

Follow-up examinations including radiography and USG were initiated since two weeks postoperation. Three months after surgery, a spherical mass, measured as 30.6 × 30.6 mm in size by a built-in caliber in ultrasound machine, with a higher echogenicity in the right lobe of liver was first

noticed. Subsequently, a percutaneous fine-needle aspiration of the mass in the liver lobe was conducted for cytologic examination. The smears were prepared from the aspirates and stained by Diff-Quik and Oil Red O techniques, respectively. Microscopic examination showed the tumor cells containing neutral lipid droplets in varied sizes. Therefore, the intrahepatic metastasis of liposarcoma was identified. We suggested a partial hepatic lobectomy but were not accepted by the owner. The intrahepatic lesion displayed gradually enlargement under a continuous USG examination. Chemotherapy was initiated with doxorubicin (30 mg/m^2, IV slowly more than 30 min) at the time of six months postoperation to treat the metastatic intrahepatic lesion. At that time, the intrahepatic tumor was measured as 45.0 × 41.0 mm in size through a saggital plane by USG. USG was performed each two-week interval for monitoring the response of tumor to chemotherapy. However, the intrahepatic tumor did not show remision and still enlarged to reach 51.9 × 40.7 mm, and 56.8 × 40.4 mm, respectively, in the following examination. Chemotherapeutic agent was changed to capecitabine (Xeloda®, Hoffmann-La Roche Inc, U.S.A.) at a dosage of 750 mg/m^2 (approximately 25 mg/kg) per orally daily for two weeks and ceased one week, as one cycle of therapy. This regimen was continued for eight cycles and then was ceased. Follow-up examination was always continued, just at the last cycle of capecitabine treatment, the tumor mass appeared 81.4 × 55.7 mm in size at 13 months postoperation . The last date of follow up was 15 months after surgery and the mass was 110 × 87.1 mm in size. Overall survival time for the patient was 22 months after surgery, and the time from the first recognition of tumor to death was two years.

Liposarcomas, by histological criteria, can be divided into well-differentiated and anaplastic tumors (also called pleomorphic) [4]. In the present case the pleomorphic liposarcoma was confirmed because of showing highly variable morphological features with large bizarre multinucleated cells. Pleomorphic liposarcoma is different from the well-differentiated variant that showed majority of cells resembling normal adipocytes [4]. Clinical signs the patient showed typical gastrointestinal symptoms associated with tumor's pressure.

The liposarcoma in our patient was underwent wide excision with the lesion and the adjacent intestine. Postoperative follow-up examination revealed a metastatic lesion in the liver, which was not found in preoperative examination by ultrasonography. The invasion and metastasis of visceral liposarcomas was rarely documented. Most of liposarcomas were locally invasive neoplasms and some had evidence of splenic, hepatic or pulmonary metastases; a single case of metastasis of splenic liposarcoma to the liver was reported [1]. In the present case, it was not found any related swelling of adjacent lymph nodes through intraoperative examination and postoperative follow-up examinations. A previous report revealed the evidence of invasive lesions to lymph nodes in a patient had an axillary liposarcoma with pulmonary metastasis [2]. Therefore, liposarcomas with metastasis by the routes of lymphatic or blood vessels might be possible. In this case, the detection of the metastastic lesion in liver was not found immediately after operation. It might be small size of the solitary metastastic lesion was not easily detected by using ultrasonography.

For the liposarcoma treatment, a wide surgical excision is the first choice of treatment, and may be combined with radiation therapy and chemotherapy to control recurrence. Although it was reported that one out of two liposarcomas revealed complete remission after giving two doses of doxorubicin [7]. However, in our case, metastatic liposarcoma in liver did not respond to doxorubicin. Capecitabine is currently approved by the Food and Drug Administration (USA) for single-agent therapy in human patients with metastatic colorectal, and breast cancers, and combination regimens have also shown benefits in human patients with prostate, pancreatic, renal cell, and ovarian cancers [11]. We chose capecitabine to treat the dog because following absorption through the intestine it is converted to 5-fluorouracil by a ubiquitous enzyme with high concentrations in the liver, and tumor tissues [6]. The dosage was 1255 mg/m^2 twice daily given orally in human [9]; and this dosage was served as reference in our treatment. Capecitabine was developed as a prodrug of fruorouracil, with the goal of improving tolerability and intratumor drug concentrations through tumor-specific conversion to the active drug. Fluorouracil, an antimetabolite, is a commonly used chemotherapeutic agent, showing effects to a variety of solid tumors including those of the head and neck, breast, prostate, pancreas, liver, and genitourinary and gastrointestinal tracts [8].

Factors that were not found to be significantly associated with survival time included tumor size, status of the margins, tumor location, and histologic type [1]. Surgery is still the first choice for liposarcomas treatment and wide excision is preferred to marginal excision [1]. In our case, surgical wide excision of primary liposarcoma and followed by two single-agent chemotherapy regimen for the metastatic lesions was introduced. We also performed wide excision to prevent recurrence. However, the chemotherpy regimen in this case did not attenuate the metastatic liposarcoma.

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