Lymphoplasmacytic lymphoma (LPL) has been described in both veterinary and human medicine. LPL is defined as a small B-cell lymphoma with plasmacytic differentiation [2, 10, 12, 13]. It is composed predominantly of lymphocytes, but plasmacytoid or typical plasma cells are an essential component [2, 10, 12, 13]. The differential diagnosis between LPL and lymphomas, especially other small cell lymphomas and plasmacytoma, is not always clear [1]. In veterinary medicine, LPL is defined by the World Health Organization (WHO) and has been described in other studies [2, 12, 13]. It occurs in several domestic species, such as dogs, cats, cattle, and horses [2, 12, 13]. However, there have been very few case reports of LPL except those reported in the horse [3] and the pig [4]. We report here a case of cutaneous LPL with systemic involvement in a cat.

A 10-year-old, castrated male domestic shorthair cat was presented with a 2-month history of a growing mass on the distal part of the left hind limb. A slightly raised, subcutaneous mass approximately 3 cm in diameter was found over the left metatarsus (Fig. 1). There were no visible clinical signs such as enlargement of popliteal and inguinal lymph nodes. The mass showed no significant abnormalities (packed cell volume (PCV) 37%; white blood cell (WBC) 9,400/μl; segmented neutrophils 6,768/μl; and lymphocytes 2,068/μl). The mass was surgically resected, and was processed for histological examination. The tumor appeared invasive and was not completely removed. Three months later, the mass recurred at the same site. The tumor was resected again but appeared to have invaded between the metatarsal bones. Shortly after the second operation, the tumor recurred and no further treatment was provided.

Seven months after the second surgery, the tumor became ulcerative and involved the metatarsal bones. At that point, other clinical signs, such as enlargement of superficial lymph nodes, were not observed. As a result of the invasive growth, the left hind limb was amputated. Two months after amputation, the cat showed clinical signs such as vomiting, anorexia, weight loss, and nonregenerative anemia (PCV 27%; WBC 14,400/μl; segmented neutrophils 11,232/μl; and lymphocytes 864/μl). Three months after amputation, the cat died due to gastric rupture.

A complete postmortem examination was performed at the Veterinary Teaching Hospital of Hokkaido University. A rupture, 2 cm in diameter, was found in the pylorus. The part of the stomach was thickened to approximately 1 cm. Numerous pale white, fairly well demarcated masses, 0.8–1.5 mm in diameter, were observed in various organs, including the liver, kidneys, heart, abdominal wall and diaphragm. Mediastinal, gastric and pancreatic lymph nodes were moderately enlarged; however, superficial lymph nodes appeared normal in size. The liver, spleen, kidneys, heart, lung, abdominal wall, diaphragm and bone marrow from the humerus were fixed in 10% neutral formalin, routinely processed, embedded in paraffin, sectioned at 4 μm, and stained with hematoxylin and eosin (HE).

In the primary cutaneous lesion, there was an invasive mass in the deep dermis extending to the subcutaneous layer. It was clearly separated from the epidermis and superficial dermis. The tumor consisted of three types of lymphoid cells (Figs. 2, 3). The first type was composed of round cells with scant basophilic cytoplasm and round nuclei without nucleoli resembling a small lymphocyte. The second type was of medium-sized round cells that...
appeared like well-differentiated plasma cells with an abundant, densely stained, eccentrically located cytoplasm and stippled nucleoli. The third type exhibited a various degrees of differentiation of lymphocytes including plasma cells (plasmacytoid transformed lymphocytes). The latter cell type had a small to moderate amount of densely stained, slightly eccentrically located cytoplasm and stippled nucleoli or occasionally a few prominent nucleoli larger than those of the other cell types. The main component of this tumor was plasmacytoid transformed lymphocytes. Plasma cells and small lymphocytes were scattered among and admixed with them. Multinucleated giant cells, mostly

Fig. 1. A slightly raised, mass is observed over the metatarsal region of the left hind limb.
Fig. 2. The tumor consists of sheets of round cells with abundant deposition of eosinophilic material (amyloid). HE. Bar: 100 μm.
Fig. 3. Tumor cells are divided into 3 types; small lymphocytes, plasma cells and plasmacytoid-transformed lymphocytes. HE. Bar: 10 μm.
Fig. 4. Some small round tumor cells (small lymphocytes) are scattered among other cells and are positive for CD20. Hematoxylin counterstain. Bar: 50 μm.
Fig. 5. Well-differentiated plasma cells and transformed cells are diffusely positive for λ-lg light chains. Hematoxylin counterstain. Bar: 50 μm.
Fig. 6. Well-differentiated plasma cells and transformed cells are diffusely positive for MUM1/IRF-4. Hematoxylin counterstain. Bar: 10 μm.
binucleated, were occasionally observed. Tumor cells were observed in the stomach, liver, kidneys, heart, abdominal wall, diaphragm, bone marrow as well as mediastinal and pancreatic lymph nodes. The stomach wall was completely replaced by neoplastic cells. In the cutaneous and stomach lesions, as well as mediastinal and pancreatic lymph nodes, varying amounts of eosinophilic materials were observed between tumor cells. These materials were positively stained with Congo red, with and without 5% potassium permanganate pretreatment and exhibited a green birefringence under polarized light, being comparable to the characters of amyloid.

Paraffin-embedded sections of the primary cutaneous mass were used for immunohistochemical examination. Immunohistochemical staining was performed using a polyclonal rabbit anti-human CD20 antibody (Thermo Scientific, Fremont, CA), a multiple myeloma 1/interferon regulatory factor 4 (MUM1/IRF-4) antibody (Dako Cytomation, Carpinteria, CA), a λ-Ig light chains antibody (Dako Cytomation), a polyclonal rabbit anti-human CD3 antibody (Dako Cytomation), and a polyclonal rabbit amyloid AA antibody (Kyowa Medix, Tokyo, Japan). Sections of normal feline lymph node were used to verify the availability of antibodies used. CD20-positive lymphocytes were limited to the follicles and medulla of the B-cell zone. λ-Ig light chains and MUM1/IRF-4-positive cells suggesting plasma cells were mostly in the medulla and sinus.

In the current case, scattered small round tumor cells (small lymphocytes), especially those with relatively small, darkly stained nuclei and scant cytoplasm, were positive for CD20 throughout the sections (Fig. 4). These cells were negative for λ-Ig light chains and MUM1/IRF-4. Both well-differentiated plasma cells and plasmacytoid transformed lymphocytes were positive for λ-Ig light chains (Fig. 5) and MUM1/IRF-4 (Fig. 6) in their cytoplasm. These neoplastic cells were negative for CD20. No CD3-positive neoplastic cells were found. The eosinophilic materials resembling amyloid did not react with the amyloid AA antibody.

The three types of tumor cells, small lymphocytes, plasma cells, and plasmacytoid transformed lymphocytes, were positive for CD20, λ-Ig light chains and MUM1/IRF-4. The tumor cells exhibited various degrees of differentiation from lymphocytes to plasma cells.

LPL is defined as a small B-cell lymphoma that shows maturation to plasma cells without the defining features of other types of lymphoma [10]. Histopathologically, LPL is characterized by plasmacytic differentiation and is composed of small lymphocytes with various differentiated lymphocytes (plasmacytoid transformed lymphocytes) [10]. In animals, the WHO classification describes LPL as a relatively common tumor of domestic animals [2, 12, 13]. In the typical immunohistochemical staining of LPL, most neoplastic cells express surface immunoglobulin (Ig) and plasmacytic cells express cytoplasmic Ig. B-cell-associated antigens (CD19, CD20, CD22, CD79a) are also typically expressed [10].

The histological appearance of feline extramedullary plasmacytomas (EMP) has been previously reported [6]. The tumors were composed mostly of differentiated plasmacytic tumor cells with abundant cytoplasm and could be diagnosed on the basis of immunohistochemical λ-Ig light chains expression [6]. Whereas LPL is an admixture of various differentiated lymphocytes, EMps could be derived from a clonal plasma cell proliferation.

Recognition of LPL is crucial because the overall prognosis may be worse than that for the other types of small B-cell lymphomas and EMP [1]. Despite of the anaplastic and malignant histological features, plasmacytomas progress very slowly and rarely metastasize to the regional lymph nodes. In contrast, LPL might be more progressive in biological behavior with the possibility of systemic involvement. In the case reported here, total survival time was 16 months without chemotherapy. The prognosis was considered to be worse than that for EMP, and the tumor cells ultimately become disseminated systemically.

Amyloidosis is a heterogeneous condition in which extracellular deposition of characteristic fibrillar material is indicated by staining with Congo red. Amyloid deposits in canine and feline EMP have been demonstrated by several authors [6, 7, 9]. Such deposits are considered to be one of the characteristic features of EMP. In veterinary medicine, there has been no report of amyloid deposition in lymphoma. However, amyloid has been occasionally noted in human LPL and is considered one of the characteristic features of B-cell lymphoma, including LPL [1, 5, 10]. In cats, LPL can be readily given the differential diagnosis from EMP by the abundant amyloid deposition in the interstitium.

REFERENCES


