NOTE *Surgery*

Primary Intra-Axial B-Cell Lymphoma in a Cat

Yuya NAKAMOTO[1,3], Tsuyoshi OZAWA[1], Kazuyuki UCHIDA[2], Kengo OMORI[1], Kousuke HASE[1] and Munekazu NAKAICHI[3,4]*

[1]Ozawa Animal Hospital, 4, Niban-Uji, Uji city, Kyoto, 611–0021 , [2]Department of Veterinary Pathology, Graduated School of Agricultural and Life Sciences, The University of Tokyo, 1–1–1, Yayoi, Bunkyo-ku, Tokyo 113–8657, [3]The United Graduate School of Veterinary Science, Yamaguchi University, 1677–1 Yoshida, Yamaguchi 753–8515 and, [4]Department of Veterinary Radiology, Faculty of Agriculture, Yamaguchi University 1677–1 Yoshida, Yamaguchi 753–8515, Japan

(Received 18 July 2008/Accepted 27 September 2008)

ABSTRACT. A 3-year-old spayed, female, domestic shorthair cat presented in the recumbent position. Clinical examination revealed decreased consciousness and ataxia. Neurological findings suggested a lesion in the forebrain and brainstem, and magnetic resonance imaging (MRI) of the brain was performed. A nodular lesion approximately 1 cm in diameter in the left parietal lobe, overlying the temporal lobe, was observed on MRI scans. T2-weighted images revealed iso- to slightly low-intensity signals in the cerebral white matter. The lesion was detected as low-intensity signals by T1-weighted images and was emphasized by enhanced T1-weighted images. The cat died on the 3rd hospital day. By complete pathological examinations including immunohistochemical investigations, the cat was diagnosed as primary intra-axial B-cell lymphoma.

KEY WORDS: B-cell, feline, lymphoma, magnetic resonance imaging.

J. Vet. Med. Sci. 71(2): 207–210, 2009

Introduction of magnetic resonance imaging (MRI) into the clinical care of small animals has drastically improved the accuracy of imaging diagnosis, enabling better decisions for appropriate treatment or surgery. Currently, MRI is mainly applied to the central nervous system (CNS), including the intracranial region and spinal cord [7, 8, 12].

Primary CNS lymphomas in cats have been reported previously [1, 5, 7, 11, 13]. Most cases of the tumors are extradural within the spinal canal, and most affected cats are Feline leukemia virus (FeLV)-positive [1, 7, 13]. Lymphomas located primarily in the brain have rarely been reported in cats [5, 11]. This paper describes MRI and clinicopathological features of the CNS primary B-cell lymphoma in a cat.

A 3-year-old spayed, female, domestic shorthair cat (3.4 kg) presented in the recumbent position. According to the owner's information, the cat had fallen from a bed few days ago. Clinical examination revealed decreased consciousness and ataxia. Body temperature, heart rate, and respiratory rate were within normal limits. Neurological examination revealed proprioceptive deficits in all limbs. Palpebral, corneal, and papillary light reflexes, as well as olfaction were depressed, and menace response was absent. Neurological findings suggested a lesion in the forebrain and brainstem. The results of complete blood count (CBC) and blood chemistry profile were within normal ranges. FeLV and feline immunodeficiency virus (FIV) tests (SNAP FeLV/FIV Combo, IDEXX LABORATORIES, Tokyo, Japan) were negative.

Magnetic resonance imaging (MRI) of the brain was performed at 0.3 tesla (Hitachi Airis II, Hitachi Medical Systems, Tokyo, Japan). Sequences included a fast spin echo (FSE) T2 and a spin echo (SE) T1 on the sagittal, transverse, and dorsal planes, as well as a fluid attenuated inversion recovery (FLAIR) with cerebrospinal fluid (CSF) suppression on the transverse plane. Following intravenous injection of meglumine gadopentate (Magnevist, Bayer Health Care, Osaka, Japan) at 93.8 mg/kg, T1-weighted (Gd-T1W) images were obtained. A nodular lesion approximately 1 cm in diameter in the left parietal lobe, overlying the temporal lobe, was observed on MRI scans. T 2-weighted (T2W) images (Fig. 1A) and FLAIR (Fig. 1B) detected iso- to slightly low-intensity signals in the white matter; T1-weighted (T1W) images (Fig. 1C) revealed low-intensity signals; Gd-T1W images (Fig. 1D) detected intense enhancement. A markedly high-signal area on T2W and FLAIR images surrounded the nodular lesion. Left transtentorial and tonsillar herniations were observed (Fig. 2). Cerebrospinal fluid was not obtained because of the tonsillar herniation.

The findings suggested the presence of a glial tumor compared with the previous report [12]. Immediate intracranial decompression was required because of decreased consciousness and tonsillar herniation. To reduce intracranial pressure, medical treatment including mannitol (Mannitol, Kowa, Tokyo, Japan; drip infusion at 2 g/kg for 30 min), furosemide (Lasix, Sanofi Aventis, Tokyo, Japan; 0.7 mg/kg IV), and prednisolone (Predonine, Shionogi, Osaka, Japan; 1 mg/kg SC BID) were administered. At the same time, ranitidine hydrochloride (Zantac, Daiichi Sankyo, Tokyo, Japan; 2 mg/kg IV BID) and cefalexin (Rasenazolin, Nichi-iko, Toyama, Japan; 22 mg/kg IV BID) were administered. Following medical treatment, the cat regained the ability to stand up and the level of consciousness slightly

* CORRESPONDENCE TO: NAKAICHI, M., Department of Veterinary Radiology, Faculty of Agriculture, Yamaguchi University 1677–1 Yoshida, Yamaguchi 753–8515, Japan.
e-mail: nakaichi@yamaguchi-u.ac.jp

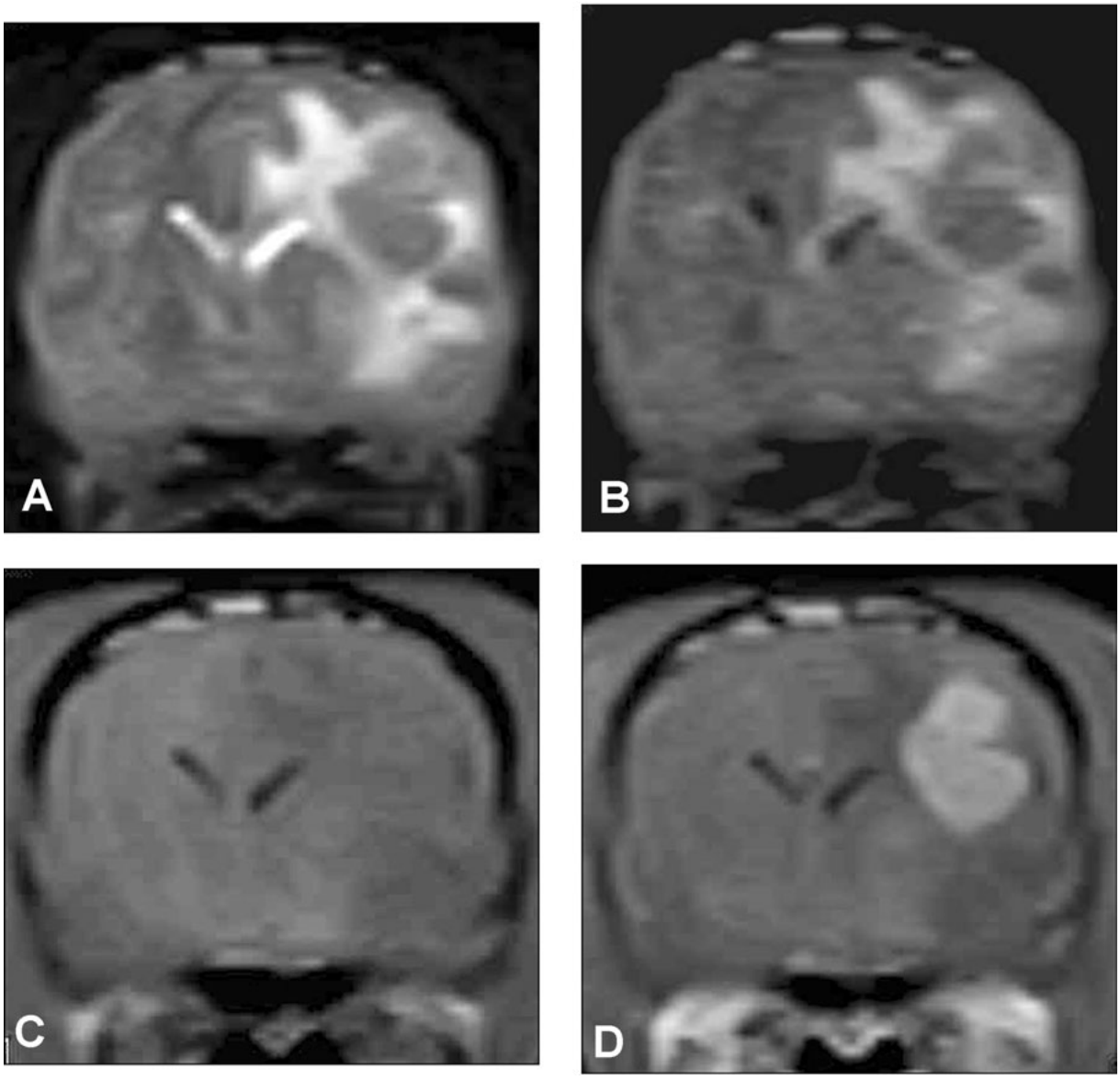

Fig. 1. (A) T2W images on the transverse plane. T2W images detecting iso- to slightly low-intensity signals compared to those of the brain parenchyma. The nodular lesion is surrounded by markedly high signal regions. (B) FLAIR on the transverse plane. FLAIR images detecting iso- to slightly low-intensity signals, and the nodular lesion is surrounded by markedly high-intensity signal regions. (C) T1W images on the transverse plane. T1W images detecting low-intensity signals. (D) Gd-T1W images (after an intravenous administration of meglumine gadopentate) on the transverse plane. Intense enhancement is demonstrated.

improved; however, the clinical condition still fluctuated presenting the improvement and worsening of symptoms. The cat died on the 3rd hospital day. Complete necropsy was performed after obtaining owner's permission.

At necropsy, gross lesion was not evident in the brain; however, the left cerebral hemisphere showed mild to moderate swelling. By cross-section of the brain, there was a heterogeneous, fragile lesion in the left temporal lobe corresponding to the findings of MRI images (Fig. 3). Cytological examinations using the stamp smear of the lesions revealed the proliferation of atypical round cells, presumably neoplastic lymphocytes. Significant gross lesion was not observed in the spinal cords and other visceral organs.

Histopathological examination revealed the neoplastic lesions in the left cerebral temporal lobe. The neoplastic foci composed of infiltrative proliferation of small- to intermediate-sized, markedly atypical round cells. The tumor cells had enriched cytoplasm and round to oval atypical round to oval nuclei with obvious nucleoli. Tumor cells were diffusely infiltrated the cerebral white matter. The neoplastic round cells also aggregated and proliferated in the perivascular spaces. Similar perivascular accumulates

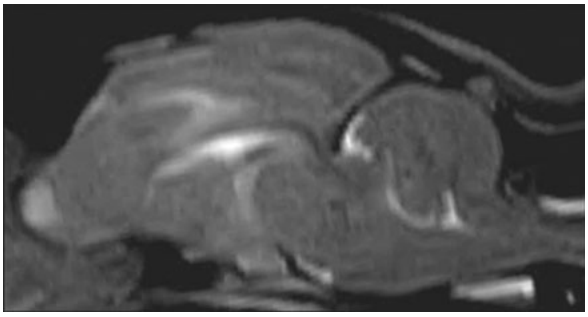

Fig. 2. T2W image on the midsagittal plane. Parencephalocele is observed.

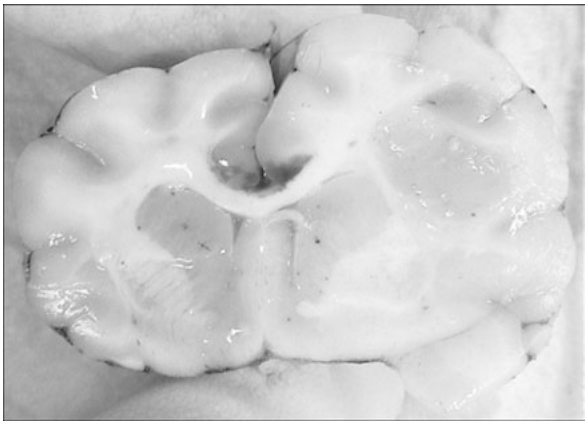

Fig. 3. Transverse section at the level of the caudate nuclei of brain. A heterogeneous, fragile lesion, compared to the surrounding brain parenchyma, is present in the left temporal lobe.

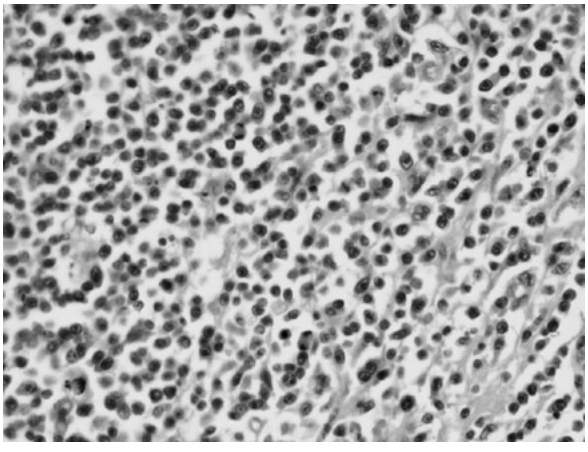

Fig. 4. Histologic section of the brain parenchymal mass. Small- to middle-sized atypical round cells with rich cytoplasm and round-to-oval atypical nuclei containing apparent nucleoli proliferate, forming a solid lesion and infiltrating brain parenchyma. Tumor cells are unicellular and mainly infiltrate into the cerebral white matter and simultaneously aggregate and proliferate in the perivascular spaces. (HE staining, × 200).

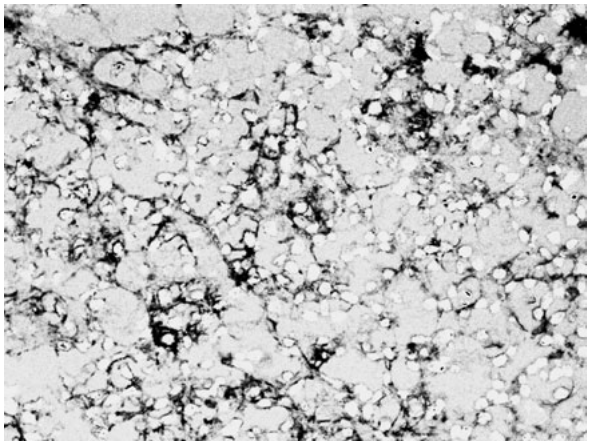

Fig. 5. Immunohistochemical staining of brain tissue with BLA-36. The majority of cells are stained for cytoplasmic BLA-36, indicating their B-lymphocyte origin.

and infiltrative lesions were also found multifocally in the cortex (Fig. 4). Mild perivascular aggregates of the tumor cells were also recognized in several cerebral regions other than temporal lobe, while no significant histological lesions were observed in the spinal cords. In the spleen and other systemic lymph nodes including the superficial cervical, mandibular, axillary, popliteal, inguinal, and mesenteric lymph nodes, the follicles and lymphatic sinus structures were effaced, and a few typical round cells found in the brain were scatted. No atypical round cells were observed in the kidney, liver, lung, and heart.

To elucidate the nature of neoplastic round cells, immunohistochemical examinations were performed using Envision Polymer reagent (Dako-Japan, Kyoto, Japan) with autoclave pretreatment. As primary antibodies, rabbit serum against human CD 3 (T cell marker [5], Dako-Japan) and mouse monoclonal antibodies against human HLA-DR (histiocyte-monocytes marker, Dako-Japan) and human B-lymphocyte antigen-36 (BLA-36, B cell marker [11], Dako-Japan) were used. The majority of the neoplastic round cells were intensely positive for BLA-36 (Fig. 5). There were few CD3- and HLA-DR positive cells in the neoplastic foci of the brain. Based on these pathological features, the present case was diagnosed as primary intra-axial B-cell lymphoma.

Malignant lymphoma is the second most common spontaneous tumor of the CNS in cats. In cats and dogs, the CNS involvement in lymphomas usually occurs as part of a multicentric process [13]. In cats, primary CNS lymphomas are rare and usually involve the spinal cord [1, 8, 13]. Lymphomas in the brain, involving the third ventricle, olfactory bulb, leptomeninges, thalamus, hypothalamus, and cerebrum, have been reported in cats [5, 9]. Most reported cases of intracranial lymphomas in humans have derived from B-cells [4]. In cats, B- and T-cell lymphomas in the brain parenchyma, 1 case each [7, 9], have been reported. The precise incidence of primary brain B-cell lymphoma in felines is unclear, as in humans.

There have been a limited number of reports on the MRI findings of parenchymal lymphomas of the brain in cats. In a report evaluating 46 cases of feline intracranial tumors [12], 6 were intracranial lymphomas. In 5 of these 6 cases, MRI confirmed the neoplastic lesions. The lesions were located in the supratentorial region in 4 of the 5 patients and in the brain parenchyma in 2 of the 4 patients. High-intensity signals were detected on T2W images in the 4 patients, and iso-intensity signals were detected in 1 of the 5 patients. Iso- to low-intensity signals were detected on T1W images in all the patients whose lesions were enhanced by contrast medium. However, the enhancement was heterogeneous in 3 of the 5 patients. Widespread cerebral edema was observed in all the patients, but cerebral herniation was not present in any patient. In the same report, 4 were glial tumors [12]. All cases were intra-axial and were described as round or lobulated. The tumors were high-intensity signals on T2W images and low-intensity signals were detected. Intensity of contrast enhancement was variable, but all patients had ring enhancement.

In the present cat, the tumor showed an irregular shape on MRI scans, iso- to slightly low-intensity signals in the white matter were detected on T2W images, and transtentorial herniation and tonsillar herniation were noted. These findings are different from those in the abovementioned report. The MRI findings in the present cat and those of previous reports suggest variations in the characteristics of intracranial lymphomas in cats.

In humans, neoplastic lymphocytes with severe morphological atypia infiltrate into the brain parenchyma that surrounds a primary mass, hampering its complete surgical removal. Nowadays, good outcomes are obtained by the combination of radiotherapy and chemotherapy [2]. High-dose methotrexate was administered to patients with particularly good outcomes, followed by whole brain irradiation (30 Gy) [6]. In veterinary medicine, no therapeutic approach has been established for intracranial primary lymphomas; however, a combination of radiotherapy and chemotherapy should be considered owing to the systemic nature of the tumors.

In cats, serologic studies have established a strong correlation between FIV or FeLV infection and lymphoproliferative malignancies [1, 3, 10], although some cats with leukemias/lymphomas are consistently negative for circulating FIV or FeLV [3, 10], as in the present cat.

In conclusion, the paper demonstrated the MRI and pathological features of feline intra-axial B-cell lymphoma. The MRI findings of the tumor obtained were slightly different from those of previous cases, presumably due to the heterogeneity of lymphomas. To know the detailed biological natures of CNS primary lymphomas in cats, further case studies with information of MRI and cell typing of the lymphomas, will be needed.

REFERENCES

1. Callanan, J. J., Jones, B. A., Irvine, J., Willett, B. J., McCandlish, I. A. and Jarrett, O. 1996. Histologic classification and immunophenotype of lymphosarcomas in cats with naturally and experimentally acquired feline immunodeficiency virus infections. *Vet. Pathol.* **33**: 264–272.
2. DeAngelis, L. M., Seiferheld, W., Schold, S. C., Fisher, B. and Schultz, C. J.2002. Combination chemotherapy and radiotherapy for primary central nervous system lymphoma: Radiation Therapy Oncology Group Study 93–10. *J. Clin. Oncol.* **24**: 4643–4648.
3. Endo, Y., Cho, K. W., Nishigaki, K., Momoi, Y., Nishimura, Y., Mizuno, T., Goto, Y., Watari, T., Tsujimoto, H. and Hasegawa, A. 1997. Molecular characteristics of lymphomas in cats naturally infected with feline immunodeficiency virus. *Vet. Immunol. Immunopathol.* **57**: 153–167.
4. Ferracini, R., Pileri, S., Bergmann, M., Sabattini, E., Rigobello, L., Gambacorta, M., Galli, C., Manetto, V., Frank, G. and Godano, U. 1993. Non-Hodgkin lymphomas of the central nervous system. Clinico-pathologic and immunohistochemical study of 147 cases. *Pathol. Res. Pract.* **189**: 249–260.
5. Fondevila, D., Vilafranca, M. and Pumarola, M. 1998. Primary central nervous system T-cell lymphoma in a cat. *Vet. Pathol.* **35**: 550–553.
6. Hiraga, S., Arita, N., Ohnishi, T., Kohmura, E., Yamamoto, K., Oku, Y., Taki, T., Sato, M., Aozasa, K. and Yoshimine, T. 1999. Rapid infusion of high-dose methotrexate resulting in enhanced penetration into cerebrospinal fluid and intensified tumor response in primary central nervous system lymphomas. *J. Neurosurg.* **91**: 221–230.
7. Kippenes, H., Gavin, P. R., Bagley, R. S., Silver, G. M., Tucker, R. L. and Sande, R. D. 1999. Magnetic resonance imaging features of tumors of the spine and spinal cord in dogs. *Vet. Radiol. Ultrasound.* **40**: 627–633.
8. Koestner, A. and Higgins, R. J. 2002. Tumors of the Nervous System. pp. 697–738. *In*: TUMORS in Domestic Animals, 4th ed. (Meuten, D. J. ed.), Iowa State Press, Iowa.
9. Morrison, J. A. and Fales-Williams, A. 2006. Hypernatremia associated with intracranial B-cell lymphoma in a cat. *Vet. Clin. Pathol.* **35**: 362–365.
10. Shelton, G. H., Grant, C. K., Cotter, S. M., Gardener, M. B., Hardy, W. D. Jr. and DiCiacomo, R. F. 1990. Feline immunodeficiency virus and feline leukemia virus infections and their relationships to lymphoid malignancies in cats: a retrospective study (1968–1988). *J. Acquir. Immune Defic. Syndr.* **3**: 623–630.
11. Steele, K. E., Saunders, G. K. and Coleman, G. D. 1997. T-cell-rich B-cell lymphoma in a cat. *Vet. Pathol.* **34**: 47–49.
12. Troxel, M. T., Vite, C. H., Massicotte, C. A., McLear, R. C., Van Winkle, T. J., Glass, E. N., Tiches, D. and Dayrell-Hart, B. 2004. Magnetic resonance imaging features of feline intracranial neoplasia: retrospective analysis of 46 cats. *J. Vet. Intern. Med.* **18**: 176–189.
13. Zaki, F. A. and Hurvitz, A. I. 1999. Spontaneous neoplasms of the central nervous system of the cat. *J. Small. Anim. Pract.* **40**: 411–416.