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A Case of Nasal Diffuse Large B-Cell Lymphoma in a Cat

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Abstract : A 6-year-old spayed female Turkish Angora cat presented with sneezing, nasal discharge, and decreased appetite lasting for 21 days. Skull radiography revealed slightly increased density of soft tissue in the left nasal cavity. Computed tomography (CT) scan revealed an extensive mass with nasal septum destruction and moderate contrast enhancement in the left nasal cavity. After surgical biopsy, histopathological examination confirmed that the mass was an infiltrative round cell neoplasm, composed of sheets of large neoplastic cells. Immunohistochemical analysis revealed that most of the neoplastic cells were strongly positive for CD79a and weakly positive for PAX5. Additionally, numerous mature lymphocytes were found to be positive for CD3. This is the first reported case of nasal diffuse large B-cell lymphoma (DLBCL) in a Turkish Angora cat in Korea.

Key words **:** nasal tumor, diffuse large B-cell lymphoma (DLBCL), histopathology, immunohistochemistry (IHC), cat

Introduction

Lymphoma is the most common neoplasm in cats, accounting for almost 90% of all hematopoietic tumors (10,14). The most common locations for these tumors are the intestine and mediastinum, while the nasal cavity is an uncommon site (6). Nasal lymphoma is usually limited to the nasal cavity and systemic metastasis is rarely reported (4,11). Differences in the immunophenotypic features of feline nasal lymphoma have been studied and nasal T-cell lymphoma accounts for 29% of all cases (2,11). Biopsy is the standard diagnostic test for nasal lymphoma (9). Diffuse large B-cell lymphoma (DLBCL) is an aggressive lymphoma that affects B-lymphocytes (2). Treatment options are radiation or chemotherapy (COP or CHOP protocols) (13).

This report describes the immunophenotypical features and treatment response of nasal DLBCL in a cat with respiratory symptoms.

Case Report

A 6-year-old spayed female Turkish Angora cat weighing 3.7 kg presented with a history of sneezing, nasal discharge, and decreased appetite lasting for 21 days. The results from the complete blood cell count were within the normal laboratory reference ranges, except for white blood cells (22.2×10^9/L; reference range, $5.5\text{-}19.5 \times 10^9$/L). Serum biochemistry revealed slightly increased levels of electrolytes and hyperproteinemia (total protein, 9.2 g/dL; reference range, 5.7-7.8 g/dL). The result of the feline leukemia virus (FeLV)/feline immunodeficiency virus (FIV) test (SNAP combo FeLV/FIV kit; IDEXX Laboratories, Westbrook, ME) was negative.

Skull radiography revealed slightly increased density of the soft tissue in the left nasal cavity. A computed tomography (CT) scan showed significant changes in the overall nasal cavity, especially in left cavity. The well-marginated, extensive soft tissue mass from the external nare to the nasopharynx in left nasal cavity had destructive bony changes (nasal septum), moderate contrast enhancement, and internal calcified foci (Fig 1).

The cat was treated with amoxicillin-clavulanate potassium (62.5 mg, PO, BID; Amocla, Kuhnil Pharm, Chungnam, Korea), prednisolone (1 mg/kg, PO, BID; Solondo, Yuhanmedica, Chungbuk, Korea), theophylline (15 mg/kg, PO, SID; Uniphyl, Mundipharma Korea, Seoul, Korea), bromhexine (1 mg/kg, PO, SID; Bromhexine HCl, Sinil Pharm, Seoul, Korea), and famotidine (0.5 mg/kg, PO, BID; Famotidine, Nelson, Chungbuk, Korea) for 4 days. There was no improvement in the cat's clinical signs. Treatment options for nasal cavity tumors include radiation, surgery, and chemotherapy. For a definitive diagnosis and treatment plan, a cytological evaluation and histopathological confirmation was needed. Because the owner wanted surgical resection, partial rhinectomy and resection of the mass was performed. Cytological evaluation of the biopsy sample revealed a mixture of small and large lymphocytes. The large lymphocytes had broad basophilic cytoplasm and large nuclei. These cells also had anisokaryosis with multiple nuclei (Fig 2). The cat was tentatively diagnosed with nasal lymphoma.

The tissue samples were fixed in 10% neutral buffered formalin and sent to IDEXX Laboratories (Westbrook, ME, USA) for histopathological examination and immunophenotyping. CD3 (pan-T-lymphocyte), CD79a (B-cell antigen receptor complex), and PAX5 (B-cell specific activator protein) antibodies were used. Histological results revealed that

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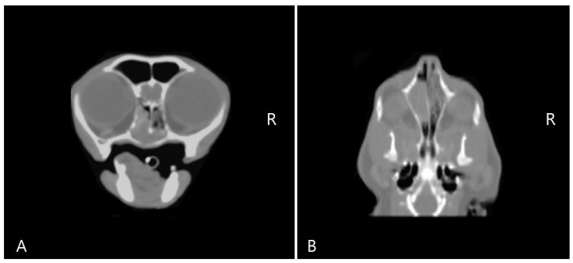

Fig 1. Computed tomography (CT) scan of a Turkish Angora cat with nasal lymphoma. (A) Axial and (B) reformatted CT images show a very extensive mass with nasal septum destruction and moderate contrast enhancement in the left nasal cavity.

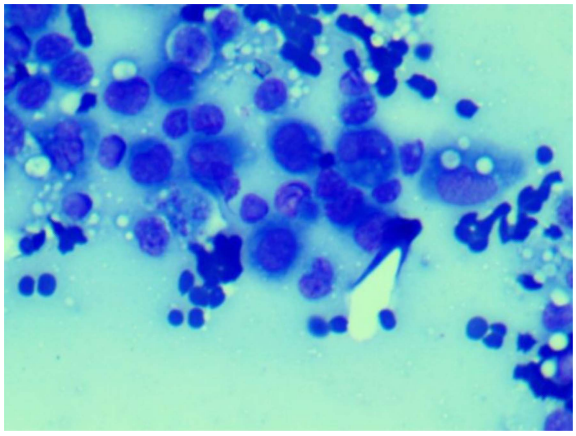

Fig 2. Impression cytology of nasal lymphoma. Lymphocytes exhibit mild anisocytosis, anisokaryosis, and mitotic activity. H&E, 400X.

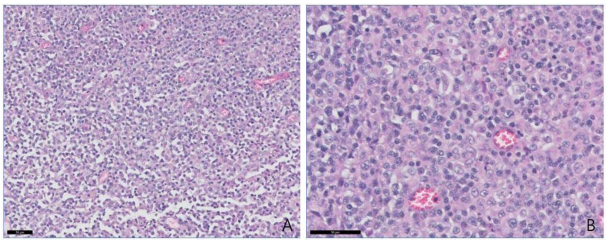

Fig 3. Histopathology of nasal lymphoma. (A) The cellularly dense neoplasm is composed of sheets of round cells. (B) Neoplastic cells have distinct cell borders and a small amount of eosinophilic cytoplasm. Scale bars, 50 μm.

the lamina propria was expanded and replaced by an unencapsulated, infiltrative, densely cellular neoplasm. The neoplasm was composed of densely aggregated sheets of round cells supported by preexisting stroma. The neoplastic cells were large with a small amount of eosinophilic cytoplasm and distinct cell borders. The nuclei were round with finely stippled chromatin and contained prominent nucleoli. Mild anisocytosis and anisokaryosis were seen. Scattered small lymphocytes were present in the neoplastic cell population (Fig 3). Immunohistochemical (IHC) analysis revealed that most of the neoplastic cells were strongly labeled with CD79a and weakly labeled with PAX5. Numerous non-neoplastic mature lymphocytes were labeled with CD3. The

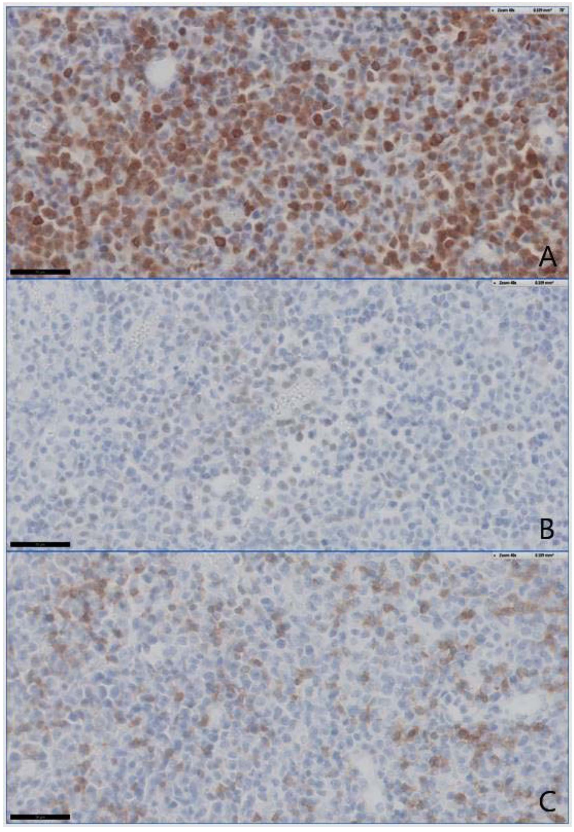

Fig 4. Immunohistochemistry (IHC) of nasal lymphoma. Large lymphocytes stained positively for both (A) CD79a (strong) and (B) PAX5 (weak). (C) Small lymphocytes stained positively for CD3. Scale bars, 50 μm.

definitive diagnosis was nasal DLBCL (Fig 4).

A standard 6-month multi-agent chemotherapy protocol was initiated after partial resection of the tumor. Briefly, the chemotherapy was composed of vincristine (0.7 mg/m^2, IV; Vincristine sulfate, Hospira Korea, Seoul, Korea), L- asparaginase (400 U/kg, SC; Erwinase, Blnh, Gyeonggi, Korea), and daily prednisone (2 mg/kg, PO, SID) for the first week, cyclophosphamide (250 mg/m^2, PO; Alkyloxan, JW Pharm, Seoul, Korea) and daily prednisone (2 mg/kg, PO, SID) for the second week, and vincristine (0.7 mg/m^2, IV) and daily prednisone (1 mg/kg, PO, SID) for the third week. The cat's clinical signs were markedly improved after surgical removal of the tumor and combined chemotherapy. However, clinical signs, including sneezing and nasal discharge recurred 33 days after the treatment. The cat was euthanized 37 days after the surgery because of the poor response to treatment.

Discussion

Nasal lymphomas are relatively rare, representing less than 1% of all feline tumors (8,14). The mean age at time of diagnosis for cats with nasal lymphoma is 9 years (13). The most common clinical signs in affected cats are nasal discharge (84%), sneezing (68%), decreased appetite (60%), increased upper respiratory noise (60%), increased respiratory effort (34%), and coughing (22%) (9). This report described nasal

lymphoma in a 6-year-old Turkish Angora cat with a history of sneezing, nasal discharge, and decreased appetite. Nasal lymphoma should be considered in the differential diagnosis of cats presenting with chronic respiratory symptoms.

Cats with nasal neoplasia are more likely to have CT evidence of a contrast-enhanced mass with soft tissue opacity, destruction of turbinates and bone surrounding the nasal cavity, and septal deviation (9,12). Biopsy impression smears match histological findings in 89% of cases (9). This case showed a correlation between the results of the cytological and histological examination. Impression cytology was a sensitive and practical diagnostic tool in this case. Impression should be considered as a diagnostic tool for cats with nasal tumors.

Immunophenotypic analysis is an integral component of human lymphoma classification and immunophenotypic data is used in REAL/WHO classification schemes (5). A previous study found that, 67% (12/18) of feline nasal lymphomas are DLBCL (2). Two of the 12 DLBCLs had numerous small T lymphocytes. Our patient presented with a diffuse large neoplastic cell population that stained strongly for CD79a and weakly for PAX5. Numerous CD3-positive T-cells were scattered throughout the lesion.

The immunohistochemical detection of CD79a and PAX5 is regarded as a valuable tool for confirmed B-cell differentiation (15). A previous report demonstrated that CD79a is a better B-cell marker than PAX5 in feline non-Hodgkin lymphomas (CD79a, 87%; PAX5, 82.6%) (3). This case study showed strongly positive immunoreactivity for CD79a and weakly positive reactivity for PAX5. Two out of the 23 B-cell lymphomas (8.7%) were positive for PAX5 and negative for CD79a (3). The expression of the PAX5 gene is high during early development and low during maturation (1,7). We conclude that examining the expression of both CD79a and PAX5 are important for the diagnosis of B-cell lymphoma.

Radiation therapy, surgery, and chemotherapy are used as single or multi-modality treatments for localized lymphoma (12). Treatment outcomes for cats with nasal lymphoma treated with chemotherapy are variable, with a median survival time of 749 days in cats achieving complete remission and 54 days in cats achieving partial remission (13). In our case study, the cat was treated with multi-modality therapy, using surgery along with chemotherapy. The cat showed poor prognosis despite partial rhinectomy, resection of the mass, and combined chemotherapy (CHOP protocol). Early diagnosis and treatment are important to improve outcomes.

Conclusions

In conclusion, we have documented the diagnostic features and prognosis of nasal DLBCL in the cat. This is the first reported case of nasal DLBCL in a Turkish Angora cat in Korea.

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