

## Intraocular Lymphoma in a Dog

Heung-Myong Woo

Division of Ophthalmology, Department of Surgical Science, School of Veterinary Medicine,  
University of Wisconsin, Madison, WI, USA

**Abstract :** Lymphoma is one of the most common malignant neoplasms of the dog. Little has been published on intraocular lymphoma in dogs. This report presents a 8-year-old neutered male mixed dog with a previous history of inflammatory debris on the anterior and posterior lens capsules, vitreal hemorrhage, generalized peri-pherical lymphadenopathy and a palpable mid-abdominal mass. History, clinical signs, radiography, cytology, histopathology and chemotherapeutic response confirmed multicentric lymphoma with secondary ocular inflammation. Intraocular lymphoma, the most common secondary neoplasm of the canine eye, may be the present-ing evidence of systemic disease. This report describes a dog that presented with ocular manifestations of multicentric lymphoma.

**Key words :** intraocular lymphoma, neoplasm, eye, dog

### Introduction

Lymphoma is one of the most common malignant neoplasms of the dog<sup>12,15</sup>. Lymphomas, characterized by neoplastic proliferation of lymphoid cells, may originate in lymph nodes, lymphoid tissue or bone marrow and infiltrate other tissues<sup>8</sup>. Lymphomas can be classified by anatomic and histologic criteria. Multicentric, cranial mediastinal, gastrointestinal, and cutaneous forms are commonly described based upon anatomic location<sup>15,19</sup>. Extralymphatic forms involving the central nervous system and eye are less common<sup>5,15</sup>. Histologically, lymphoma has been categorized by numerous morphologic, cytologic and immunologic schemes<sup>11,12,15,20</sup>.

Lymphoma usually affects middle to older aged dogs (avg. 6-7 yr)<sup>15</sup>. Multicentric lymphoma characterized by generalized lymphadenopathy is the most common presentation and occurs in the majority of cases (80%)<sup>15</sup>. Hepatosplenomegaly and mediastinal lymphadenopathy occur in 30% and 20% of multicentric cases respectively<sup>15</sup>. Respiratory, alimentary, hemopoietic, cutaneous, central nervous system and ocular complications may occur<sup>8</sup>. In addition, lymphoma may be associated with paraneoplastic syndromes to include anemia, hypercalcemia, gammopathies, cachexia and hypoglycemia<sup>8,15</sup>.

### Case Report

#### Patient

Canine, Mix, Neutered Male, 8 years of age.

The dog presented following a two-day history of poor vision. Recently the owner noted weight loss and lethargy.

### Clinical finding and differential diagnosis

#### Initial clinical finding

Ophthalmic examination revealed bilateral blepharospasm and pupillary constriction in ambient light. Direct pupillary light reflex (PLR) was absent in the right eye but present consensual to the left eye. Direct PLR was slowed in the left eye but absent consensual to the right eye. Menace response and dazzle reflex was present bilaterally. Biomicroscopy revealed conjunctiva congestion, ciliary flush, extensive aqueous flare and multifocal keratic precipitate deposition on the posterior corneas. The iris was dull and swollen, with a fixed right pupil. Sodium fluorescein stain (Fluori-J-Strip, Ayerst Laboratories, Inc., New York, NY) was not retained in either eye. Intraocular pressures (IOP) by applanation tonometry (Mackay Marg Applanation Tonometer, Model 12, Biotronics, Inc., Redding, CA) were 16 mmHg OU. Topical tropicamide (Mydracyl, 0.5%, Alcon Laboratories, Inc., Forth Worth, TX) resulted in slow and incomplete pupil dilation. Inflammatory debris was noted on the anterior and posterior lens capsules (Fig 1). The vitreous body exhibited extensive haze bilaterally with the presence of vitreal hemorrhage infcronasally in the right eye. Direct and indirect ophthalmoscopy revealed a fundic reflex although the retina could not be visualized due to vitreous changes.

On general physical examination the dog was depressed, lethargic and febrile (103.4 F). Remarkable findings were pale mucous membranes, generalized peripheral lymphadenopathy and a palpable mid-abdominal mass.

#### Differential diagnosis

Pyrexia, generalized peripheral lymphadenopathy and the presence of an abdominal mass suggested ocular abnormalities secondary to systemic disease. Diagnostic considerations included neoplasia (lymphoma, myeloma, sarcoma, carcinoma), immune-mediated diseases, systemic infection (bacterial - septicemia, Brucellosis; fungal - systemic mycoses; rickett-

<sup>1</sup>Corresponding author.

E-mail : woo@surgery.wisc.edu



**Fig 1.** Initial appearance right eye. Anterior capsular inflammatory deposits evident.

sial - Ehrlichiosis; protozoal - Toxoplasmosis; viral - Distemper), coagulopathies, and vasculitis<sup>2,10</sup>. Trauma, toxicity and hypertension were possible but considered less likely<sup>2,10</sup>.

#### *Laboratory Results*

The CBC revealed leukocytosis (absolute lymphocytosis), and thrombocytopenia. Atypical, immature lymphocytes were noted in the peripheral blood smear. A serum chemistry profile was unremarkable.

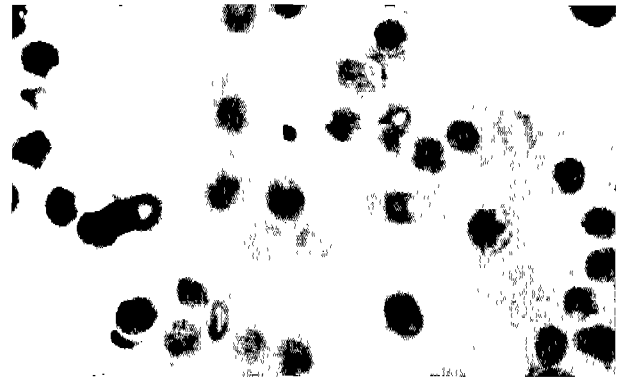
Thoracic radiography revealed prominence and widening of the cranial mediastinum, hilar lymphadenopathy and normal lung fields. Hepatosplenomegaly was noted by abdominal radiography (unshown).

Multiple fine needle aspirations of peripheral lymph nodes were accomplished. Cytologic examination of modified Wright stained impression smears revealed a cell population consisting of erythrocytes and abundant lymphoid cells. Lymphoid cells were large and exhibited variable nuclear/cytoplasmic ratios, multiple nucleoli, and angular borders characteristic of neoplasia (Fig 2).

Following local anesthesia (Anthocaine Injection 2%, Anthomy Products Co., Arcadia, CA) the right mandibular and right prescapular lymph nodes were biopsied (Bard Biopsy Instrument, 14G, C.R. Bard, Inc., Covington, GA). Monotonous sheets of neoplastic lymphocytes, with scant cytoplasm, prominent nucleoli, and occasional mitotic figures were noted on histopathologic examination. Bone marrow biopsy, and diagnostic vitreal aspiration were recommended for clinical staging but declined.

#### *Initial treatments*

Triamcinolone (Kenalog-10, E.R. Squibb and Sons, Inc., Princeton, NJ) 5 mg OU subconjunctively was administered for ocular anti-inflammation and chemotherapeutic affects.



**Fig 2.** Cytology of lymph node aspirate. Cell population consisting of RBCs and lymphoid cells characterized by variable N/C ratio, multiple nucleoli and angular cell borders.

Antibiotic dexamethasone acetate suspension (AkTrol Ophthalmic Suspension, Akorn Inc., Abita Springs, LA) QUID OU was utilized topically for similar affects. Atropine (Atropine Solution, 1%, ProVet, Loves Park, IL) BID OU was initiated for mydriasis and cycloplegia to reduce the potential for pupil seclusion due to posterior synchia and to reduce ciliary spasm respectively. Tetracycline (Tetracycline capsules, 500 mg, 250 mg, United Research Laboratories, Inc., Philadelphia, PA) 24 mg/kg TID PO  $\times$  14 days was administered for bacterial prophylaxis considering pyrexia and compromised immune status.

Chemotherapeutic strategies were discussed with the owner. Prednisone (Prednisone, 20 mg tablets, Mutual Pharmaceutical Co., Inc., Philadelphia, PA) 0.9 mg/kg BID PO  $\times$  7 days, then tapered and cyclophosphamide (Cytosan tablets, 50 mg, Bristol-Myers Squibb Co., Evansville, IN) 50 mg/M<sup>2</sup> Q 48 hours PO were selected for efficacy and minimization of expense. Chemotherapeutic agents and ocular corticosteroids are noted for their benefit in control of the ocular consequences of lymphoma<sup>10</sup>.

#### *Progress results*

Successive re-examinations occurred over seven weeks (12, 16, 25, 37, 47, 51 days). Significant visual improvement with resolved blepharospasm was noted 12 days following presentation. Biomicroscopy revealed widely dilated pupils, and significantly decreased conjunctiva hyperemia, ciliary flush, and aqueous flare (Fig 3, 4). Vitreal haze was reduced and the inferonasal hemorrhage in the right eye had organized. Direct and indirect ophthalmoscopy was permitted and mild hyperemia of the optic papilla with congestion of retinal venules was noted bilaterally. IPO was 2 mmHg on OD, 16mmHg OS. On general physical examination pyrexia had resolved and lymphadenopathy and organomegaly were decreased. A repeat CBC showed leukocytosis (neutrophilia with left shift, resolved lymphocytosis), normocytic, normochromic anemia, and normal thrombocyte count. Oph-



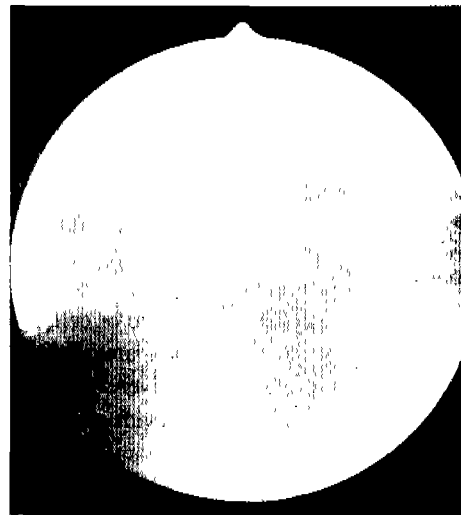
**Fig 3.** Appearance of right eye 12 days following presentation. Aqueous flare is decreased and a large inflammatory deposit is present on the anterior lens capsule. Hemorrhage is noted in the nasal posterior compartment.



**Fig 4.** Appearance of left eye 12 days following presentation. Pupil is dilated and aqueous flare is decreased.

thalmic and systemic medications were continued unchanged. The patient's primary care veterinarian to minimize expense was currently managing the chemotherapeutic protocol initiated originally.

Re-examination 25 days following presentation revealed several flame and dot shaped hemorrhages adjacent to the optic papilla in the right eye (Fig 5). Aqueous flare and vitreal haze was mild bilaterally with no other significant changes. IOP was 14 mmHg OD, 18 mmHg OS. Antibiotic dexamethasone suspension QID OU, atropine Q 24 hours OU, and prednisone 0.9 mg/kg Q 24 hours PO were maintained. Progressive anemia, rapidly decreasing WBC and thrombocyte count prompted discontinuation of cyclophosphamide 20 days following initiation. L-asparaginase (Elspar,



**Fig 5.** Several peripapillary areas of flame and dot shaped hemorrhages in the right eye. Vitreous haze is evident.

10,000 I.U./Vial, Merck Sharp and Dohme, West Point, PA) 10,000 units/M<sup>2</sup> quickly IM was initiated by the primary care veterinarian.

Re-examination 37 days following presentation revealed increased inferonasal vitreal hemorrhage in the right eye. A diffuse, white retinal infiltrate was present nasally in the left eye with inferior vitreal hemorrhage. The retina was edematous and the optic papilla swollen bilaterally. IOP was 8 mmHg OD, 14 mmHg OS. Lymph nodes and spleen were unchanged. Normocytic, normochromic anemia continued. A biochemical and coagulation profile (PT, PTT) were unremarkable. Antibiotic dexamethasone suspension TID OU, atropine Q 48 hours OU, prednisone 0.9 mg/kg Q 24 hours PO and L-asparaginase 10,000 units/M<sup>2</sup> IM were continued.

Re-examination at 51 days revealed multifocal dot hemorrhages of the left superior retina. The remaining ophthalmic examination was unchanged IOP was 16 mmHg OD, and 12 mmHg OS. Relapse was evident with peripheral lymph nodes (prescapular, L popliteal) and spleen enlarged from recent examinations. Chemotherapeutic rescue was suggested but the owner due to expenses declined further treatment. Antibiotic dexamethasone suspension BID OU and prednisone 0.9 mg/kg Q 48 hours PO was continued.

#### Clinical diagnosis and conformation

History, clinical signs, radiography, cytology, histopathology and chemotherapeutic response confirmed multicentric lymphoma with secondary ocular inflammation. Neoplastic infiltration of the eyes was suspected.

#### Discussion

Intraocular lymphoma, the most common secondary neoplasm of the canine eye, may be the presenting evidence of

systemic disease<sup>1,6,7,13</sup>. Ocular involvement is the result of direct neoplastic invasion or altered metabolism and function. The clinical signs of intraocular lymphoma are diverse and usually bilateral<sup>17</sup>. Conjunctivitis of varying severity is frequently noted<sup>7</sup>. Corneal involvement, a unique feature of canine lymphoma, may occur following direct infiltration of the cornea by neoplastic cells. Keratitis, edema, vascularity, keratic precipitates and intrastromal hemorrhage may be exhibited<sup>17</sup>. The most common ocular tissue involved is the anterior uvea<sup>6,11,13</sup>. Anterior chamber flare or cell, hypopyon, hyphema, mitosis and ciliary injection are reported<sup>6,7</sup>. The posterior uvea tends to be less extensively involved. Alteration of tapetal coloration may be evidence of choroidal infiltration. Intraocular hemorrhage, manifest as hyphema, intravitreal hemorrhage or retinal hemorrhage is typical. Hemopoietic disorders or tissue destruction may produce hemorrhage. Preretinal or subretinal hemorrhage, vascular congestion and tortuosity, papilledema, and detachment are characteristic of retinal involvement<sup>17</sup>. Glaucoma may occur subsequent to neoplastic infiltration of the anterior chamber angle, obstruction by inflammatory or cellular debris or synechia<sup>13,17</sup>. Orbital involvement, more common in man<sup>9</sup>, is a rare finding in the dog.

Systemic lymphoma may be diagnosed by clinicopathologic findings, radiography, lymph node aspiration/biopsy and bone marrow evaluation<sup>8,15,19</sup>. Ocular lymphoma may be confirmed by cytologic evaluation of aqueous and vitreous humor when systemic evidence is not corroborative<sup>4,13,18</sup>. Dogs with peripheral lymphocytosis are more likely to demonstrate neoplastic lymphoid cells on diagnostic ocular aspiration<sup>16</sup>. Lymphocytic, lymphoblastic or histiocytic cell types are described. Erythrocytes, neutrophils and proteinaceous material may be seen concurrently<sup>13</sup>. Vitreous cell, when visualized by ophthalmic examination, may be characteristically large and clumped<sup>16</sup>.

Chemotherapy is the treatment of choice for canine lymphoma. Prednisone, vincristine, cyclophosphamide, L-asparaginase and doxorubicin are among the most effective chemotherapeutic agents for lymphoma<sup>15</sup>. Scheduled utilization of multiple drugs with different mechanisms of cytotoxicity increase cell death, maximize success, and allow recovery of the host immune system and bone marrow<sup>3</sup>. Resistance to chemotherapeutic agents is common and mediated by inherent cellular ability or mutational mechanism<sup>3</sup>. Successful systemic chemotherapy and topical corticosteroids may decrease ocular neoplastic infiltration and inflammation<sup>10</sup>. Irradiation is used for primary or secondary intraocular lymphoma in man<sup>4</sup>, although infrequently considered in animals. Surgery, either enucleation or exenteration, may be a practical alternative following poor response to therapy.

The prognosis for canine lymphoma may depend upon the clinical stage of disease, location, histologic classification,

and concurrent paraneoplastic to syndromes<sup>15</sup>. Dogs with multicentric lymphoma and concurrent ocular disease may have a more guarded prognosis than those without ocular involvement<sup>14</sup>. Clinical staging, a controversial indicator of prognosis may correlate less significantly with survival or remission times in the dog than previously thought<sup>12</sup>. Histologic classification of lymphomas is being revised by advances in immunohistochemical and cell surface marker analysis, which may have more profound prognostic significance than previous methods of clinical staging<sup>9,12</sup>.

This report describes a dog that presented with ocular manifestations of multicentric lymphoma.

## References

1. Aquino SM, Hamor R, Valli VE, Kitchell BE, Tunev SS, Bailey KL, Ehrhart EJ. Progression of an orbital T-cell rich B-cell lymphoma to a B-cell lymphoma in a dog. *Vet Pathol* 2000; 37: 465-9.
2. Boldy KL, Clerc B. Ocular Manifestations of Systemic Disease. Chap. 17. In: *Textbook of Veterinary Internal Medicine*. Third ed. W.B. Saunders, Philadelphia, 1989; 75-84.
3. Chaber BA. Clinical Strategies for Cancer Treatment: The Role of Drugs. Chap.1. In: *Cancer Chemotherapy: Principles and Practice*. J.B. Lippincott, Philadelphia, 1-15.
4. Char DH. *Clinical Ocular Oncology*. Churchill Livingstone, New York, 1989.
5. Couto CG, Cullen J, Pedroia V, Turrel JM. Central nervous system lymphosarcoma in the dog. *JAVMA* 1984; 184: 809-813.
6. Cullen CL, Caswell JL, Grahn BH. Intravascular lymphoma presenting as bilateral panophthalmitis and retinal detachment in a dog. *J Am Anim Hosp Assoc* 2000; 36: 337-42.
7. Donaldson D, Day MJ. Epitheliotropic lymphoma (mycosis fungoides) presenting as blepharconjunctivitis in an Irish setter. *J Small Anim Pract* 2000; 41: 317-20.
8. Feldman BF, Zinkl JG. Diseases of the Lymph Nodes and Spleen. Chap.79. In: *Textbook of Veterinary Internal Medicine*. Second ed. Vol. II W.B. Saunders Co., Philadelphia, 1983; 2045-2076.
9. Garner A, Klintworth GK. Tumors of the Orbit, Optic Nerve, and Lacrimal Sac. Chap. 26. In: *Pathobiology of Ocular Disease: A Dynamic Approach*. (Part A) Marcel Dekker, Inc., New York, 1982.
10. Gelatt KN. *Veterinary Ophthalmology*. Second ed. Lee and Febiger, Philadelphia, 1991.
11. Green WR. Uveal Tract. In: *Ophthalmic Pathology: An Atlas and Textbook*. Third ed. Vol. III W. B. Saunders Co., Philadelphia, 1981; 1352-2024.
12. Greenlee PG, Filippa DA, Quimby FW, Patnaik AK. Lymphomas in dogs: A morphologic, immunologic, and clinical study. *Cancer* 1990; 66: 480-490.
13. Gwin RM, Gelatt KN, Williams LW. Ophthalmic neoplasms in the dog. *J Am Anim Hosp Assoc* 1982; 18: 853-866.
14. Krohne SG. *Tran Am Coll Vet Ophthalmol*, 1987; 18: 68, 1-13.
15. MacEwen EG, Young KM. Hematopoietic Tumors. In: *Clinical Veterinary Oncology*. J.B. Lippincott Col, Philadel-

- phia, 1989; 380-393.
16. Nussenblatt RB, Palestine AG. UVEITIS Fundamentals and Clinical Practice. Year Book Medical Publishers Inc., Chicago, 1989.
  17. Saunders LZ, Barron CN. Intraocular tumors in animals. Brit Vet J 1964; 120: 2535.
  18. Schachat AP. Intraocular Lymphoid Tumors. Chap. 54. In: Retina. Vol. One. C.V. Mosby Co, St. Louis, 1989; 775-791.
  19. Theilen GH, Madewell BR. Leukemia-Sarcoma Disease Complex. Chap.13. In: Veterinary Cancer Medicine. Lee and Febiger, Philadelphia, 1979; 204-288.
  20. Weller RE, Holmberg CA, Theilen GH, Madewell BR. Histologic classification as a prognostic criterion for canine lymphosarcoma. Vet Res 1980; 41: 1310-1314.

## 개의 Intraocular Lymphoma

우 흥 명

위스콘신 대학교 수의과대학 수의외과, 안과학교실

**요 약** : 림프종은 임상에서 많이 발생하는 개의 악성 종양이지만, 눈 안에서의 발생은 그 예가 드물다. 본 연구는, 수정체낭의 혼탁, 초자체 출혈, 전신적인 임파선증 및 복부중앙의 응괴가 관찰되는 8년령 잡종견에서 병력, 임상증상, 방사선 검사, 세포 및 조직병리학 검사, 화학요법에 의한 반응을 통하여 속발성 안내 염증을 동반하는 전신적인 다발성 lymphoma를 확진하는 방법을 알아보았다. 개의 눈 안에서 관찰되는 속발성 lymphoma는 전신적인 lymphoma를 예견하는 중요한 임상조건이 될 수 있으므로 수의 임상에 응용이 가능하리라 판단된다.