

## Observations on ocular changes in multicentric lymphoma of dogs

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### Abstract

The study was conducted to record ocular lesions in multicentric lymphoma in dogs. Three dogs with acute onset of blindness associated with multicentric lymphoma were selected. Complete physical and ocular examination as well as blood work was performed. Hyphema, uveitis, glaucoma with deficit menace were seen in the affected dogs. Systemic lymphoma was confirmed with fine needle aspiration cytology from multiple lymph nodes. Lymphoblast cells from the conjunctiva of an affected dog were seen in ocular cytology suggesting lymphoma of conjunctiva. All the dogs were treated with doxorubicin and prednisolone. A rapid and favorable response was seen in overall condition of patients as well as vision restoration within four days of treatment.

**Keywords:** Lymphoma, Ocular, Uveitis, Dogs.

Lymphoma is responsible for 7 to 24 percent of all canine neoplasia and 83 percent of all canine hematological malignancies (Harvey 1990). Lymphoma primarily affects dogs in their middle to late years of life (AW 1965, Parodi *et al.*, 1968). The cause of canine lymphoma is unknown, however it is likely complex. Dogs can be affected with various forms of lymphoma viz. multicentric, mediastinal, alimentary, cutaneous and extra nodal. The multicentric form of lymphoma develops in 80 % of dogs with lymphoma, which is defined by the presence of superficial lymphadenopathy (Madewell 1986). The most prevalent symptom of abdominal involvement is hepato-splenomegaly, which is usually linked with a more advanced stage of multicentric disease. Ocular lymphoma is characterized by infiltration and thickening of the iris, uveitis, hyphema, hypopyon, posterior synechia and glaucoma (Swanson 1990). Eye can be involved either in extra nodal or in multicentric form. Anterior uveitis was most often seen in stage V. In about one-third to one-half of dogs with lymphoma, an eye examination with fundus examination may indicate abnormalities such as uveitis, retinal hemorrhages, and ocular infiltration (Krohne *et al.*, 1987, Massa *et al.*, 2002). In most situations, fine-needle aspirate cytology can be used to diagnose lymphoma. Thoracic radiographs show abnormalities in 60 to 75 percent of dogs with multicentric lymphoma; one-third have signs of pulmonary infiltrates, and two-thirds have thoracic lymphadenopathy (sternal and tracheobronchial lymph nodes). Most dogs with lymphoma die within 4 to 6 weeks if they are not treated

(Keller *et al.*, 1993). It is really rewarding to treat dogs with lymphoma because a substantial percentage of them respond completely. The aim of this study was to put on record various ocular changes in multicentric lymphoma in dogs.

### Materials and Methods

Three dogs presented for acute onset of blindness associated with multicentric lymphoma were selected for this study. The diagnosis of multicentric lymphoma was confirmed by fine needle aspiration cytology from pre-scapular and popliteal lymph nodes in each of the dog. Physical examination was performed as described by Birchard and Sherding (2006). Visual examination of eye was undertaken as per Gelatt *et al.* (2013). Direct ophthalmoscopy (Welch allyn®) was done to examine corneal and conjunctival lesions, iris deformities or fundic changes. The eyes were also subjected to indirect ophthalmoscopy (20 diopter lens and fin-hoff trans-illuminator) for larger view of fundus. Intraocular pressure was measured with iCare tonovet tonometer. Ocular ultrasonography was performed with 12 MHz linear probe. Blood samples were collected from dogs for complete blood count, serum creatinine, blood glucose and liver function tests (ALT, ALKP, total bilirubin). Samples for ocular conjunctival cytology were collected from two dogs with a sterile cotton swab and smears were stained with Leishman's stain. Stained smears were examined microscopically for cellular profile and cell morphology. Chest and abdominal radiography was performed. All the dogs were treated on the same day

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of the presentation with doxorubicin @ 30mg/m<sup>2</sup> and prednisolone @1mg/m<sup>2</sup>.

## Results and Discussion

The history and physical examination findings are presented in Table 1. There was history of dysphagia and labored breathing in two dogs. All the animals were active on general inspection. Fever was recorded in two and generalized lymphadenopathy in all the dogs. Physical examination and abdominal radiography showed hepatomegaly and splenomegaly in all the dogs. Hemato-biochemical profile of all the cases is presented in Table 2. Hemogram showed leukocytosis with mature neutrophilia in all the dogs. There was marked lymphocytosis in one dog without any morphological abnormality.

### Ocular examination

The findings on ocular examination are given in Table 3. All the dogs were blind on presentation. There was bilateral mydriasis in all dogs, hyphema in two and hypopyon in one dog. Pupillary light reflex was sluggish in one dog and was absent in other two. Menace was absent

in all the eyes. Intra ocular pressure was high in all the dogs. Ocular ultrasonography showed retinal detachment in left eye of a dog. Multiple small growths were visible on iris of the left eye and the pupil was irregular in the German shepherd dog. Fundus examination performed in two dogs was of normal appearance. Ocular conjunctival cytology showed presence of lymphoblasts in both the eyes of one dog suggestive of lymphoma in conjunctiva.

On re-examination on fourth day after the first dose, the appetite was restored, dysphagia and dyspnea were reversed. Lymph nodes also regressed to normal size in all the dogs. Vision was restored in all the dogs bilaterally by fourth day except in one eye which was showing retinal detachment. All the other signs of eye ball (hyphema, hypopyon) disappeared. The pre and post treatment photographs of eyes are presented in figures (Fig.1-3). However granulomatous growths in one eye persisted. Intraocular pressure also declined to normal range in all the dogs.

Ocular lymphoma had been documented as the most frequent secondary ocular malignancy in dogs and

**Table 1. History and Physical examination of dogs with multicentric lymphoma.**

Breed	History	Temperament	Temperature(°F)	Superficial lymphnodes
Non-descript	-Blindness -Intermittent vomiting	Active	103.6	Enlarged
Labrador	-Blindness -Inappetance from 1 week -Intermittent vomiting -Dysphagia -Labored breathing -Change in barking sound	Active	102.8	Enlarged
German shepherd	-Blindness -Dysphagia -Labored breathing	Active	104.6	Enlarged

**Table 2. Hemato-biochemical profile of dogs with multicentric lymphoma**

Breed	Hb (gm/dl)	Platelets (×10 <sup>3</sup> per mm <sup>3</sup> )	TLC (cu mm)	Absolute Neutrophil count (per cu mm)	Absolute Lymphocyte count (per cu mm)	Absolute Eosinophil count (per cu mm)	Serum Creatinine (mg/dl)	Serum glucose (gm/dl)
Non-descript	14.7	1.05	21100	17724	2532	844	0.8	78
Labrador retriever	13	1.83	24440	15152	8309	0	1.3	638
German shepherd	10.6	1.79	21280	19152	2128	0	1.3	75

**Table 3. Ocular examination in dogs with multicentric lymphoma**

Breed	PLR	Menace	Ocular examination	IOP (mmHg)	USG
Non-descript	Absent	Absent	Granulomatous iritis, Hyphema, Aqueous flare	36	Left eye Retinal detachment
Labrador retriever	Sluggish	Absent	Hypopyon, Aqueous flare	38	NAD
German shepherd	Absent	Absent	Hyphema, Aqueous flare	35	NAD

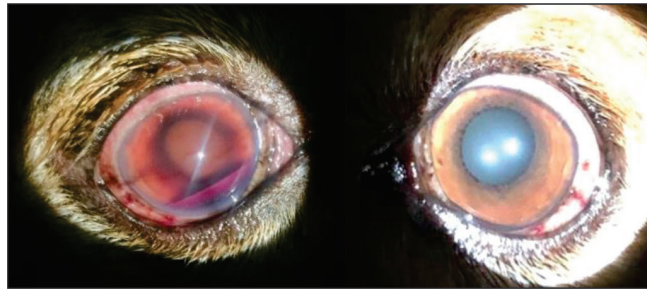


Fig. 1. Hyphema and peripheral corneal edema in non-descript dog (L). Same dog after four days of chemotherapy (R)



Fig. 2. Hyphema and irregular iris in German shepherd dog (L). Same dog after 4 days of chemotherapy. Persistence of granulomatous growth on iris (R).

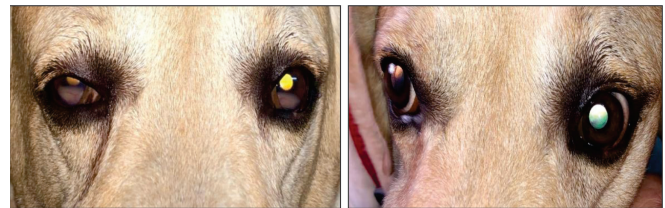


Fig. 3. Hypopyon in a Labrador retriever dog (L). Same dog after 4 days of chemotherapy (R).

cats (Vascellari *et al.*, 2005). The frequency of occurrence of ocular lesions had been observed to be 37 percent in lymphoma affected dogs (Krohne *et al.*, 1987). Neoplastic lymphocytes spread from affected lymph nodes or other sites to eyes and orbits.

All the three dogs in the study were presented in stage V (b) as based on the presence of generalized lymphadenopathy, hepatic and splenic involvement, blindness and low thrombocyte count based on criteria provided by World Health Organization Clinical Staging System for Lymphosarcoma in Domestic Animals. Presence of normal Hb concentration and normal to high total leukocyte count appeared to suggest that thrombocyte production might be affected prior to the effect on erythropoiesis and granulopoiesis. This observation was supported by the findings of Madewell (1986) where thrombocytopenia was observed in 58

percent cases. Absence of leukopenia in the study was partially explained by the observation of Teske (1994) who recorded leukopenia in only 19 percent of the lymphoma affected dogs. In contrast, leukocytosis due to mature neutrophilia without any evidence of left shift was observed in all the cases and was attributed to release of endogenous corticosteroids in response to disease stress. Teske (1994) also reported leukocytosis in 32 percent cases of lymphoma. Lymphocytosis observed in one of three dogs in the study. Previously also, lymphocytosis had been observed in 20 percent of dogs diagnosed for lymphoma (Teske 1994).

Blindness appearing in stage 5 lymphoma corroborated the observations of Withrow (2007), Lakooraj *et al.*, (2018) and Mahony *et al.*, (2015). The blindness in the study was associated with appearance of glaucoma and uveitis in all the three and also unilateral

retinal detachment in one dog. Retinal detachment, hypopyon, glaucoma, and hyphema observed in this study were similar to the observations by Swanson (1990). Glaucoma was present in all the dogs in the study as seen by Lanza *et al.*, (2017) in 85 percent of dogs with ocular lymphoma. Other case studies by Lakooraj *et al.*, (2018) and Mahony *et al.*, (2015) observed blindness with the signs of uveitis. A retrospective study by Lanza *et al.*, (2017) recorded glaucoma in 85 percent and uveitis in 65 percent of lymphoma affected dogs.

Rapid and favorable response to chemotherapy was the important finding of the study. The results of the study showed that chemotherapy with doxorubicin was effective in reversing vision loss within 3-4 days. However it is worth mentioning that loss of vision in these cases was of only 2-3 days of duration. In contrast, Mahony *et al.*, (2015) failed to treat lymphoma induced blindness in a week with oral prednisolone. It is hard to find any well controlled study on the effect of chemotherapy on lymphoma associated blindness in dogs. The available therapeutic studies had reported only the treatment of lymphoma, in general, with doxorubicin (Valerius *et al.*, 1997). The response rate in these studies varied from 50-75 percent. It was concluded that acute blindness of lymphoma origin can be effectively reversed by doxorubicin for at least six months.

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Received : 25.01.2022

Accepted : 28.05.2022