

Case report: ocular presentation of lymphoma

Roisin O’Mahony MVB MRCVS Cert AVP(SAM) ESVPS GPCERT (SAM), Animal Care Hospital, Douglas, Cork, outlines the clinical signs, investigations and diagnosis of ocular lymphoma in dogs

Lymphoma is the second most common neoplasm in the dog, comprising 7-24% of neoplasia cases (Richards, 2015). Frequent presentations of disease are haemaopoetic, for example, multicentric and splenic forms. However, Krohne (1994) reported a 37% rate of ocular involvement in canine lymphoma, which is now most commonly associated with multicentric lymphoma (Cuoto, 2003). This case report describes an ocular manifestation of lymphoma in a Labrador retriever causing uveitis.

Massa (2002) found bilateral uveitis was significantly associated with systemic illness and approximately 25% of cases of uveitis were diagnosed with underlying neoplasia, most commonly lymphoma. This case underlines the importance of conducting a full clinical examination for all ophthalmological presentations while also highlighting the limited options for restoration of vision in these cases.

HISTORY AND CLINICAL SIGNS

A seven-year-old neutered male Labrador presented with a 12-hour history of epiphora and ocular irritation. There had been building works in the home. On presentation, there was blepharospasm, photophobia, perilimbal hyperaemia and aqueous flare, vision was intact. Clinical examination was otherwise unremarkable. Bilateral uveitis was diagnosed. Symptomatic treatment was commenced with oral carprofen 2mg/kg bid (carprieve 50mg tablets, Norbrook), chloramphenicol eye drops qid (chloramphenicol 0.5%, Mercury Pharma) and atropine eye drops bid (minims

atropine drops, Bausch & Lomb).

Four days later, the patient presented with blindness of acute onset. Upon further questioning, the owner also reported two-day history of inappetance, soft stools and mild lethargy. There was no history of trauma. Annual vaccinations had been given three months previously. Worming and flea treatment was up to date. There was no history of foreign travel.

On examination, the dog was bright, alert and responsive. Body condition score (BCS) was high at 8/10. Heart rate was normal at 86bpm with synchronous femoral pulses. Respiration rate was normal at 20 breaths per minute. Mucous membranes were pink and moist with a brisk capillary refill time. Abdominal palpation was normal. Superficial lymph nodes were all increased in size. Body temperature was marginally elevated at 39°C. Neurological exam was unremarkable excluding ophthalmic findings. Ophthalmological examination is summarised in Table 1.

Ophthalmological exam	<p>Bumping into objects in consult room Absent visual tracking Dazzle normal Menace negative Direct and consensual pupillary light reflex (PLR) normal Perilimbal hyperaemia Conjunctival hyperaemia Hyphaema in anterior chamber preventing further examination of posterior chamber Schirmer tear test normal Fluorescein test negative Intraocular pressure not measured</p>
------------------------------	--

Table 1: Ophthalmological exam.

DIFFERENTIAL DIAGNOSIS

<ul style="list-style-type: none"> • Reflex uveitis • Infectious: bacterial (eg. leptospirosis, bacteraemia) parasitic (toxoplasma, neospora, toxocara)viral (adenovirus, distemper) • Immune-mediated • Idiopathic • Metabolic causes • Diabetes • Hyperlipidaemia • Drug-induced • Lens-induced uveitis • Neoplasia • Coagulopathy • Blood dyscrasias • Trauma • Hypertension 	<p>Hyphaema is presumed to be a sequel of uveitis. Idiopathic uveitis is not normally associated with systemic signs. Blood sampling and further ophthalmic exam required.</p>
---	--

Table 2: Differential list for hyphaema.



Figure 1: Uveitis with perilimbal and conjunctival hyperaemia, hyphaema, corneal oedema and aqueous flare. Photo: Natasha Mitchell.

Conjunctivitis Superficial keratitis Uveitis (causes as in Table 2) Glaucoma	No evidence of keratitis. Measurement of intraocular pressure required.
---	---

Table 3: Differential list for perilimbal hyperaemia and conjunctival hyperaemia.

Intraocular cause	Trauma Uveitis Glaucoma Hyphaema Retinal detachment Sudden acquired-retinal degeneration Cataracts Lens luxation Optic neuritis	There is mild pupillary dilation in incidental light. This, together with hyphaema and the absence of other neurological deficits, suggests intraocular blindness. Unable to visualise posterior chamber.
Extraocular cause	Trauma Intracranial lesion-neoplasia Granulomatous meningoencephalitis (GME) Toxoplasma Optic-chiasm lesion	

Table 4: Differential list for blindness.

Lymphoma Other haematopoietic neoplasia Reactive – infectious, immune-mediated	Marked generalised nodal enlargement. No history of foreign travel. Fine needle aspiration of lymph nodes is warranted.
--	---

Table 5: Differential list for superficial lymphadenopathy.

Pyrexia, lethargy, soft stools and inappetence are non-specific systemic signs likely associated with underlying disease. Blood, urine and lymph-node sampling are required, along with full ophthalmological examination including tonometry and ultrasound.

DIAGNOSTIC INVESTIGATION

A jugular blood sample was collected for haematology and biochemistry. Results showed mild haemoconcentration and leukocytosis with lymphocytosis and monocytosis. There was also mild thrombocytopaenia. There was both increased alanine aminotransferase (ALT) and resting bile acids on biochemistry.

Haemoconcentration can occur secondary to splenic hyperfunction in dogs with lymphoma (Cuoto, 2003). Here, it may have been secondary to mild dehydration, due to diarrhoea. No leukaemic cells were seen on the blood smear. Lymphocytosis and monocytosis can also result from the local or systemic production of bioactive factors by the tumour cells. Thrombocytopaenia may indicate bone marrow suppression. High-resting bile acids and increased ALT may have been secondary to the infiltration of the liver by neoplastic cells or a paraneoplastic syndrome. Urinalysis was normal.

Fine-needle aspirates taken from pre-scapular, popliteal and sub-mandibular lymph nodes (see Appendix 1). Results were consistent with an intermediate to large-cell lymphoma. Referral to a specialist ophthalmologist for examination and ultrasound of eyes revealed the following:

- Negative menace, normal dazzle and normal direct and consensual PLR;
- Conjunctival hyperaemia;
- Hyphaema more marked dorsally;
- Significant aqueous flare;
- Low intra-ocular pressures (6mmHg); and
- Ocular ultrasound showed no posterior chamber disease.

DIAGNOSIS

Intermediate/large cell lymphoma – stage 5b (see Appendix 2 for World Health Organization staging guidelines).

TREATMENT

Full therapeutic options were discussed. Owners elected against multi-drug chemotherapy. Treatment with carprofen and atropine ceased. Patient was discharged with prednisolone acetate eye drops (1-2 drops qid [Pred forte 1%, Allergan]) and 2mg/kg bid of oral prednisolone (Prednidale 25mg tablets, Veterinary Essentials) while a decision was taken.

OUTCOME

The dog was euthanised a week later. There had been no restoration of vision.

DISCUSSION

Krohne (1994) reported 37% rate of ocular involvement in canine lymphoma. Uveitis can occur due to neoplastic cells inducing an inflammatory response from the uveal tract. Intraocular tumours can also mimic uveitis-causing ‘uveitis masquerade syndrome’ (Crispin, 2002). Presumed solitary ocular lymphomas are known to occur in dogs with enucleation, in these cases often curative (Matthew, 2018). Ultrasound did not reveal presence of intraocular tumours and this patient had systemic involvement.

At initial presentation, diagnostic tests were declined by owners due to mild clinical signs. Uveitis in dogs is documented to have an idiopathic cause in 60% of cases (Massa, 2002; Wiggins 2013; and Miller, 2008). Massa (2002) found bilateral uveitis was significantly associated with systemic illness and approximately 25% of cases of uveitis were diagnosed with underlying neoplasia, most commonly lymphoma. In future, the importance of diagnostic work-up will be stressed in these cases.

Papillary light reflex requires fewer functioning optic-nerve fibres than the menace response. It is not rare to find blind animals with a reasonable papillary light reflex (Montiana-Ferreira, 2002). Intact-dazzle reflex also suggests a functional retina and optic nerve (Turner, 2008). Ultrasound examination of the eye including the posterior chamber provided valuable prognostic information. Exudation and cellular infiltration from the choroid may cause retinal detachment (Miller, 2008).

Lymphocytosis occurs in 20% of dogs presenting with lymphoma (Vail, 2003). It is usually mild (Cuoto, 2003) and reports are varied on prognostic significance (Vail, 2013). The pathogenesis of the thrombocytopenia associated with

APPENDIX 1: FINE-NEEDLE ASPIRATE CYTOLOGY

DESCRIPTION: PRESCAPULAR LYMPH NODE

The sample is non-diagnostic as lymphoid cells are not evident.

POPLITEAL AND MANDIBLAR LYMPH NODES APPEAR SIMILAR

The samples are highly cellular, are of excellent quality and are composed of lymphoid cells mixed with large numbers of disrupted cells, cytoplasmic fragments (lymphoglandular bodies) and low numbers of red blood cells (RBCs) seen against a stippled basophilic background. Intermediate to large lymphoid cells predominate and are mixed with rare macrophages containing cellular debris and rare small lymphocytes. The intermediate to large lymphoid cells are 2-3.5x the diameter of an RBC, round and have scant to moderate amounts of moderately to deeply basophilic cytoplasm. The nuclei are round, eccentric and have finely stippled chromatin and contain one to four, distinct, round nucleoli that vary in size. Low numbers of mitotic figures are present. Neutrophils are present in numbers consistent with peripheral blood contamination. No organisms are seen.

INTERPRETATION

Consistent with lymphoma, intermediate to large-cell lymphoma.

COMMENTS

Biopsy with histopathologic evaluation, flow cytometry or polymerase chain reaction (PCR) for clonality (PARR, 70-90% sensitive - 10-30% false-negative rate) or could be performed to confirm the cytologic impression and potential type of lymphoma.

APPENDIX 2: WHO STAGING SYSTEM FOR LYMPHOMA.

Stage	Clinical features
1	Solitary lymph-node involvement
2	>1 lymph node involved but on one side of diaphragm only
3	Generalised lymph-node involvement
4	As stage 3 but also hepatomegaly/splenomegaly
5	As above with bone marrowextra-nodal involvement (central nervous system [CNS], ocular, etc)

Substage a - asymptomatic; substage b - symptomatic.

Author notes

neoplasia may include increased platelet consumption, decreased platelet production, immune-mediated destruction, and sequestration of platelets, or a combination of the above (Grindem, 1994). Reported incidence of thrombocytopaenia varies, but bleeding diathesis are rarely found due to the mild nature of the thrombocytopaenia (Vail, 2003). Hyphaema arose through changes to blood-aqueous barrier caused by uveitis.

Fine-needle aspirates were taken from a selection of superficial lymph nodes, including the submandibular nodes. Submandibular lymph nodes can often yield poor diagnostic samples due to their high level of reactivity. Aspirates of lymph nodes confirmed intermediate/large-cell lymphoma. Aqueous humour examination can also be of value in diagnosis of ocular neoplasia (Wiggins, 2013). Lymphoma was WHO stage 5b. There is moderate association between WHO staging and prognosis, with higher-grade lymphomas associated with worse outcome (Vail, 2003; Zandvliet, 2013; and Marconata, 2011). Sub-stage is strongly associated with prognosis. (Vail, 2003, Cuoto, 2003). It is also suggested that lymphoma cases with ocular involvement have a poor prognosis (Miller, 2008). Dogs that undergo chemotherapy have the potential to recover lost vision (Miller, 2008).

Initial treatment was symptomatic. Atropine was used both as an analgesic and to prevent formation of synechia leading to glaucoma or iris bombe. Topical antibiotics could potentially interfere with further diagnostic work-up. Systemic carprofen was administered as an analgesic. Non-steroidal anti-inflammatory drugs (NSAIDs) are not as potent as corticosteroids in the treatment of immune-mediated uveitis (Miller, 2008). Carprofen treatment ceased when hyphaema developed due to potential effects on clotting (Miller, 2008; and Gould 2002). Multidrug chemotherapy protocols result in remission rates of 70-90% and a disease-free period of nine to 11 months (Vail, 2013). Clients elected against chemotherapy. Topical steroids are recommended for treatment of hyphaema (Turner, 2008). Treatment with immunosuppressive doses of steroids may induce remission for approximately two months (Ogilvie, 2004).

REFERENCES ON REQUEST

A version of this case report was submitted as part of the Cert AVP (SAM) modules. Thanks to Natasha Mitchell MVB DVOphthalm MRCVS for ophthalmological examination for this case and for the images supplied.

