



## UNUSUAL OCULAR HODGKIN'S-LIKE LYMPHOMA IN A DOG

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### Summary

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Hodgkin's disease is a malignant lymphoproliferative disease with various gross morphology. The present paper reports gross and microscopic features of Hodgkin's-like lymphoma in a dog. An eight years-old dog was presented to our hospital due to complete blindness associated with the presence of proliferative tissue on the globe surface. The tissue biopsy sample was soft and frigid with high bleeding tendency and was processed for histopathological evaluation. Sections of 5 µm in thickness were stained with haematoxylin-eosin and melan-A and S-100 by immunohistochemistry (IHC) for differential diagnosis with ocular melanoma. Histologically, regarding the negative Melan-A and S100 IHC findings, and particular histological features, a mixed cellularity type of Hodgkin's disease which included a large number of lymphocytes with different size and shape together with single necrosis was diagnosed. Additionally, Reed-Sternberg cells which had a deeply lobulated nucleus were demonstrated.

**Key words:** dog, histopathology, Hodgkin's disease, Reed-Sternberg cell

Hodgkin's disease is known a malignant lymphoproliferative disease of humans (Jox *et al.*, 1997). It was proposed that the disease is related with Epstein-Barr virus, although it occurs in virus-negative condition (Dolcett & Boiocchi, 1998). The pathological examination is necessary for diagnosis which is based on the detection of the Reed-Sternberg cell in tissue section of affected organ. In this regard, the cellular components and background appearance are important for characterisation of histological types of Hodgkin's disease (Valli, 2007). Accordingly, there

are four histological types including lymphocytic depletion (<5%), lymphocytic predominance (<5% of cases), mixed cellularity (<30%) and nodular sclerosis (>60%) (Valli *et al.*, 2017). In veterinary medicine, Hodgkin's-like lesions have been reported in the horse, pig, dog and skunk (Wells & Barker, 1983; Maeda *et al.*, 1993; Valli, 2007). Moreover, an unusual Hodgkin's-like lymphoma in cats presenting unique appearance, morphology and biology was identified (Valli *et al.*, 2017).

According to the authors' knowledge, there is little information on Hodgkin's disease and Hodgkin's-like disease in animals. The present paper describes the clinical and histopathological investigation of Hodgkin's-like lymphoma in a dog which involved both eyes.

#### Case presentation

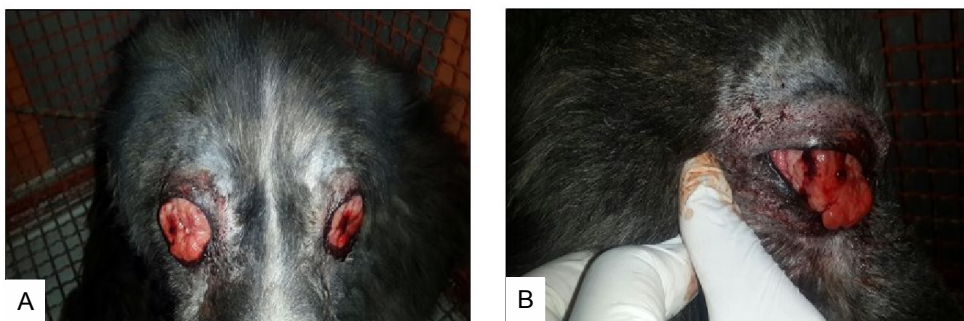
A male mixed breed eight years-old dog was presented to the hospital of the Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran due to the complete blindness and presence of a proliferative tissue on the both globe surfaces (Fig. 1). First, a complete examination was performed and the patient was found to have a normal body score and temperature, associated with good appetite. Then, it was referred to the surgery department for tissue biopsy. The biopsy of the eyes was taken under general anaesthesia using a cocktail of ketamine (5.5 mg/kg, Alfasan, The Netherlands) and diazepam (0.3 mg/kg, Caspian, Iran). The tissue biopsy sample was soft and frigid with high bleeding tendency. It was processed for histopathological evaluation by fixing in 10% neutral buffered formalin and processed routinely. Sections of 5 µm in thickness were stained with haematoxylin

and eosin (H&E) and examined by light microscopy.

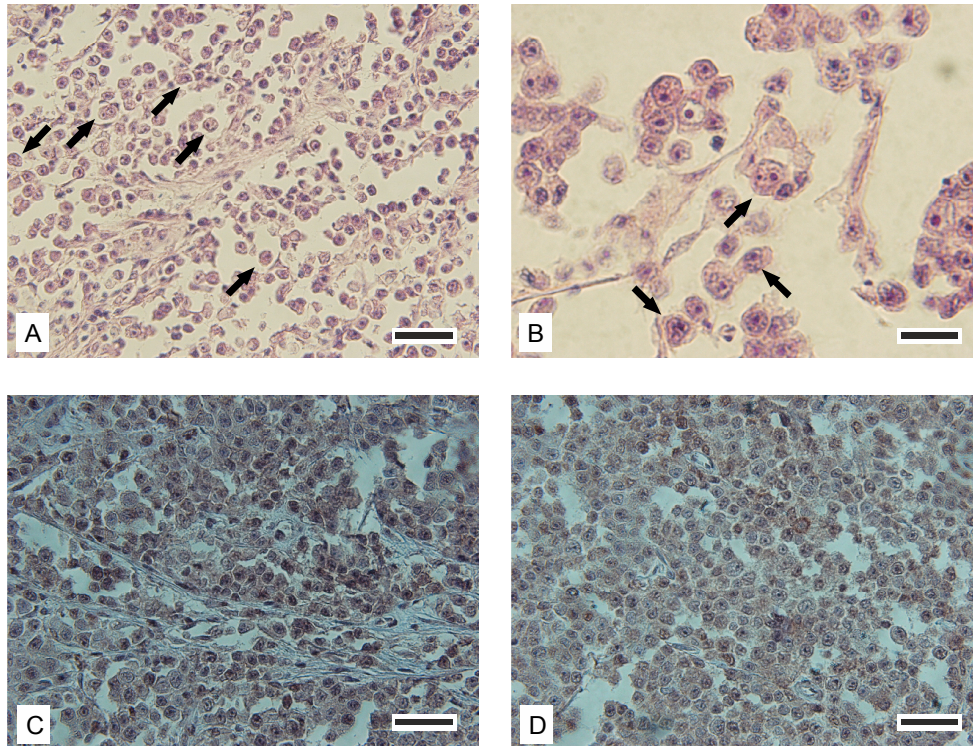
At first, ocular malignant melanoma was suspected and for confirmation, immunohistochemistry (IHC) was performed for Melan-A and S100. The sections were stained using a streptavidin-biotin peroxidase complex method (Avalone *et al.*, 2007). For negative controls specific antibodies were replaced an isotype-matched irrelevant monoclonal antibody or the primary antibody was omitted. Sections were finally stained with DNA fluorochrome Hoechst 33342 (Sigma, St Louis, MO) (0.25 mg/mL, 3 minutes), washed in phosphate-buffered saline and a coverslip was applied with aqueous mounting media (Dako, Glostrup, Denmark).

Importantly, the animal died within 10 days.

Histologically, mixed cellularity type of Hodgkin's disease was diagnosed with particular histological features including a large number of lymphocytes of different size and shape together with single foci of necrosis. Additionally, there were Reed-Sternberg cells which had deeply lobulated nuclei. Often the nuclei of Reed-Sternberg cells that appeared binucleate were mirror images of each other (Fig. 2A and 2B). The cytoplasm of the Reed-



**Fig. 1.** A complete blindness and presence of a proliferative tissue on both eye globe surfaces in a dog with Hodgkin's-like lymphoma.



**Fig. 2.** **A:** Hodgkin's disease of a mixed cellularity type with a large number of lymphocytes with different size and shape and a small amount of connective tissue. Scattered huge binucleated cells or a deeply lobulated nucleus with abundant cytoplasm (Reed-Sternberg cells; arrows). Often, Reed-Sternberg cells' nuclei that appeared binucleate were mirror images of each other (H&E; scale bar=30  $\mu$ m). **B:** Higher magnification of 2A (H&E; scale bar=10  $\mu$ m). **C:** Negative reaction for Melan-A (IHC; scale bar=30  $\mu$ m). **D:** Negative reaction for S-100 (IHC; scale bar=30  $\mu$ m).

Sternberg cell was frequently shrunken away from the surrounding dense background of lymphocytes or fibrous tissue. The popcorn or multilobulated variant of the Reed-Sternberg cell was rare. Besides, the negative Melan-A and S100 IHC findings in (Fig. 2C and 2D), confirmed Hodgkin's lymphoma as a definitive diagnosis.

In the present case, Reed-Sternberg cells were histopathologically diagnosed like in human Hodgkin lymphoma. However, it is believed that some lesions suspected to be Hodgkin's-like neoplasms in the dog, horse, pig and skunk have proven

to be atypical mast cell tumours or granulomatous inflammatory lesions (Wells & Barker, 1983; Maeda *et al.*, 1993; Valli, 2007). In this connection, in dogs reported with Hodgkin's-like disease, there was a widespread lymph node involvement (unlike humans) and lesions in the liver, spleen, lung, and occasionally skin (Maeda *et al.*, 1993). It seems that the affected dog in the present study died due to the extensive distant metastasis. Unfortunately it was not necropsied after death.

It was demonstrated an unusual lymphoma in cats that exhibits a unique mor-

phology and biology resembles human Hodgkin lymphoma (Valli *et al.*, 2017). In affected animals, there are commonly enlarged-unilaterally encapsulated mobile cervical node with discoid shape. Histologically, a large B-cell lymphoma with a background of sclerosis with small and medium T-cells was found. Particularly, presence of scattered huge binucleated cells with abundant cytoplasm suggesting similarity to Reed-Sternberg cells of human Hodgkin lymphoma was reported (Valli, 2007). A previous study in dogs (Balint & Manolescu, 2010) classified four morphological characteristics for Hodgkin's lymphoma on the basis of cellular components: 1) Hodgkin's paraganuloma- predominant in inflammatory cells; 2) Hodgkin's granuloma – all cells are very well cast; 3) Lymphocytic depletion – high fibrosis and cell loss; 4) Hodgkin's sarcoma – giant Hodgkin cell and Reed-Sternberg-Paltauf cell. Accordingly, we almost observed the fourth classification in this study.

In contrast to other malignancies, where the majority of the cells including the tumour appear to be malignant, Reed-Sternberg cells were usually few in number and surrounded by a large number of reactive, yet benign, inflammatory cells (Balint & Manolescu, 2010). Similarly, we found the same feature in the tissue section of the present case.

In the present case, on the basis of gross appearance, we first suspected ocular melanoma. Malignant ocular melanoma comprises about 20% of intraocular melanocytic tumours in dogs which tends to be less darkly pigmented and locally aggressive. Occasionally these tumours arise diffusely in the anterior uvea, and very rarely, in the choroid. High bleeding tendency was observed after gentle palpation of the lesion in the present case,

which has not been reported for melanoma. Even among malignant intraocular melanomas in dogs, systemic metastasis to the extent of changing the quality of life of dogs have rarely been reported. A melanocytic melanoma can be confused with anaplastic carcinoma, fibrosarcoma or lymphoma, and differentiation is best made by IHC melan-A and S100 staining (Dubielzig, 2017). For this reason, melan-A and S100 was used for definitive diagnosis of the present case.

Altogether, it seems that the incidence of Hodgkin lymphoma in animals is not very low. However, little is known about Hodgkin lymphoma in veterinary medicine and further extensive studies on a large population of affected animals is still needed.

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