CASE REPORT
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CANINE CUTANEOUS EPITHELIOTROPIC LYMPHOMA: A CASE REPORT

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ABSTRACT

Cutaneous epitheliotropic lymphoma is a rare and aggressive neoplastic disease in dogs with poor prognosis even with various chemotherapeutic protocols. A ten-year-old mixed breed male neutered dog was presented with two cutaneous erythematous nodules which were removed surgically. Two months later the patient was presented with similar lesions all over the body which was confirmed as cutaneous epitheliotropic lymphoma with excisional biopsy, clinical signs and history. Chemotherapy protocol CHOP (vincristine, cyclophosphamide, doxorubicin and prednisolone) was initiated and the quality of life improved initially. But by fourth week of CHOP protocol patient's health deteriorated along with severe anaemia, leucopenia and thrombocytopenia, and the dog had to be humanely put to sleep upon request of the pet parent.

Keywords: Cutaneous epitheliotropic lymphoma, Dog, Chemotherapy.

INTRODUCTION

Lymphoma is the uncontrolled and pathological clonal expansion of lymphoid cells of either B-cell or T-cell immunophenotype. It can be classified as epitheliotropic or non-epitheliotropic. Canine epitheliotropic lymphoma is rare. The epitheliotropic form is classically of T-cell origin (also called mycosis fungoides) and the non-epitheliotropic form is typically of B-cell origin (Hoskins *et al.,* 2006). Usually, the involvement of primary and secondary lymphoid tissues, including the bone marrow, thymus, lymph nodes, and spleen are seen. In addition to these lymphoid-rich organs, the other areas of affection are extra nodal sites such as skin, intestinal tract, liver, eye, central nervous system and bone. The epitheliotropic form initially appears as pruritic inflammation of the skin progressing to nodules and plaques. The non-epitheliotropic form can have a wide variety of appearances, from a single lump to large areas of bruised, ulcerated, hairless skin (Hoskins *et al.,*

2006). The differential diagnosis for the epitheliotropic lymphoma is pemphigus vulgaris, bullous pemphigoid and lupus erythematosus (Bhang *et al.,* 2006).

The aetiology of canine malignant lymphoma is incompletely characterized and is likely to be multifactorial. Major contributing factors include infectious viruses or bacteria, environmental contamination with phenoxyacetic acid herbicides or other chemical exposures, chromosomal abnormalities and immune dysfunction; however cutaneous lymphoma is mostly associated with chronic inflammatory response of skin, proliferation of activated lymphocytes in response to the continuous exposure to the antigens can trigger neoplastic activity. (Fontaine *et al.*, 2009) Advanced genetic research has revealed that canine lymphoma can be molecularly distinguished and categorized into distinct groups that correlate with biological aggressiveness (Fan, 2023). Lymphoma is an aggressive tumor, the prognosis is generally poor with mean survival time reported from few months to two years (Chan *et al.,* 2018; Fontaine *et al.*, 2009). Various treatment protocols have been suggested including lomustine (CCNU), masitinib, polyethylene glycol (PEG)ylated L-asparaginase, PEGylated liposomal doxorubicin, retinoids, prednisolone, surgery and radiation (Chan *et al.,* 2018). The diverse treatment protocols and deficiency of standardised treatment reflect the volatile response to treatment and generally poor outcome of this disease (Aslan *et al.,* 2021).

CASE HISTORY AND OBSERVATION

Scooby, an approximately 10-year-old, male neutered mixed breed dog had been previously adopted from the streets and was presented to the clinic in November 2023 with a history of progressive dermatological lesions. Scooby's pet parent observed two raised nodules on his body, one on the ventrolateral aspect of neck and the other on right side of face caudal to the oral commissure (Fig.1). Due to the financial constrains the pet parents opted for empirical treatment options, Antibiotics and anti-inflammatory medication was initiated; however the animal's condition

Figure.1 Initial dermatological lesions when the patient was presented in November 2023

worsened progressively with an increase in the size of the nodules. The mass on the ventrolateral aspect of the neck became ulcerated and started to bleed due to itching. No haematological changes were observed. The masses were removed under general anaesthesia using Medetomidine sedation, Propofol- Ketamine induction and maintenance with Isoflurane. The surgical wound healed remarkably without any complications. The dog was presented again at the end of January 2024 with small nodules all over the body (Fig. 2). Erythematous, well circumscribed non-pruritic lesions ranging from 0.3 – 5 cm in diameter were observed throughout the body (Fig.3). Marked lymphocytosis was also observed in haematology. An excisional

Figure.2 Clinical presentation of the patient with small nodules all over the body in January 2024

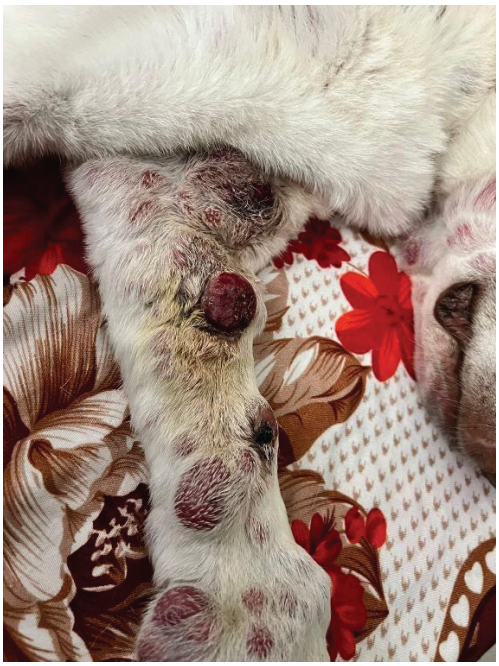

Figure.3 Erythematous, well circumscribed non-pruritic lesions ranging from 0.3 – 5 cm in diameter.

biopsy was done on the lesion present in the dorsal neck. Tissue specimen is fixed in 10% Neutral Buffered Formalin for 8-24 hours from the time the specimen is collected and processed overnight. Then embedded and cut using microtome. Tissue section was stained with H&E stain. Microscopically the mass was unencapsulated, partially ulcerated and composed of densely packed neoplastic lymphocytes. (Fig. 4) These lymphocytes were elevating the overlying epidermis, replacing the entire dermal structures, and infiltrating the subcutis (Fig.5). The lymphocytes were characterized by round cells with distinct cell borders, scant to moderate eosinophilic cytoplasm, and irregularly

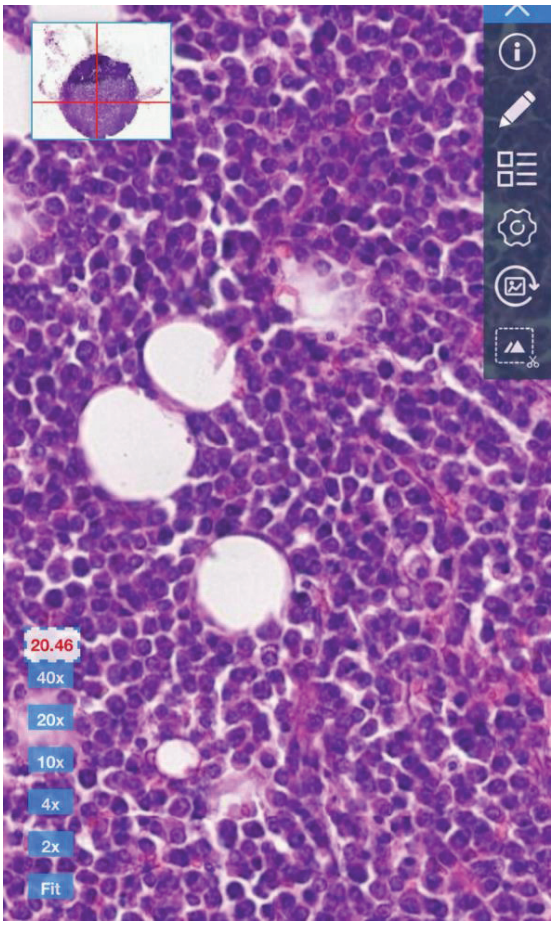

Figure.4 Centre of the mass with packed neoplastic lymphocytes with scant to moderate eosinophilic cytoplasm (H&E Staining)

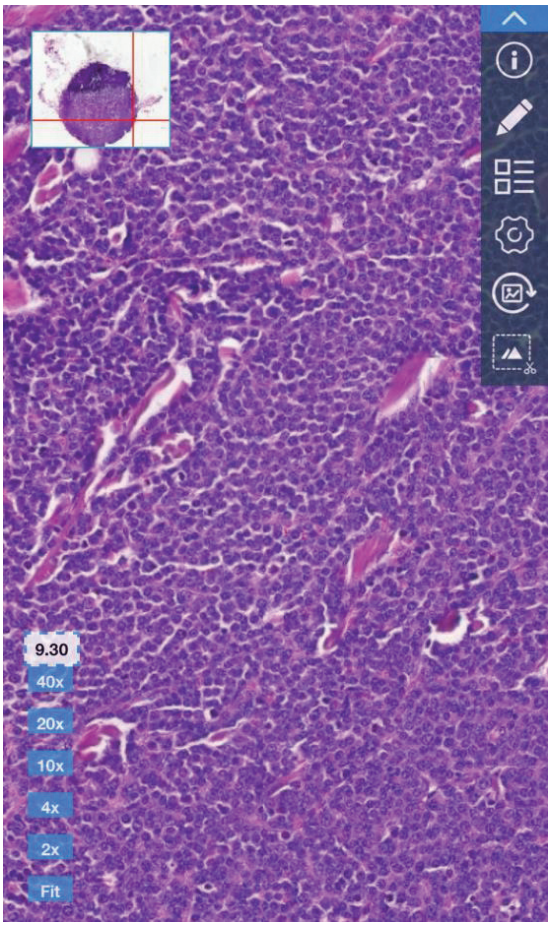

Figure.5 Neoplastic lymphocytes are elevating the overlying epidermis, replacing the entire dermal structures, and infiltrating the subcutis (H&E Staining)

round to indented nuclei with fine lacy chromatin and one or two nucleoli. Mitotic figures ranged from 4 - 5 per high power field. The neoplastic cells involved the cut margins. The patient history, gross and histopathological findings were consistent with Cutaneous Epitheliotropic lymphoma. Chest and abdominal radiography and abdominal ultrasonography were done to detect any metastasis. No radiographic or ultrasonographic changes were observed.

TREATMENT AND DISCUSSIONS

Epitheliotropic lymphoma is an uncommon neoplasm in canine patients, also dogs are rarely cured of lymphoma. Our goal with treatment was to extend a good quality of life for the patient for as long as possible. Because lymphoma is a systemic disease, chemotherapy was the treatment of choice. While there is currently no cure for lymphoma in dogs,

there are a number of drugs which have been evaluated in dogs with lymphoma that have been shown to improve both survival time and quality of life. T- cell epitheliotropic lymphoma is the most common form of cutaneous lymphoma, and causes the infiltration of neoplastic lymphocytes in the epidermis and adjacent structures (Calazans *et al.,* 2016). Pruritus is a common clinical condition in animals with mycosis fungoides, particularly in those with the erythrodermic form of the disease (Rodigheri *et al.*, 2007; Miller *et al.*, 2013). In this clinical case, the patient had experienced pruritis initially which led to bleeding from the lesions; later it resolved. Other dermatological clinical changes were similar to those described in literature.

Epitheliotropic lymphomas do not have any predilection based on sex or race and typically impact dogs aged nine years and older. Boxer, Cocker Spaniel, German Shepherd, English Bulldog, Golden Retriever, Scottish Terrier, Briard, English Springer Spaniel, Beagle, and English Cocker Spaniel breeds are frequently affected by these lymphomas (Fontaine *et al.,* 2009). Vail *et al.* (2013) explained that cutaneous lymphoma can have either a primary origin in the skin or a secondary origin, in which is accompanies the lymphoma found elsewhere in the body. In the present case, the primary origin was in the skin. Chemotherapy is the treatment of choice for epitheliotropic cutaneous lymphoma, particularly in cases with multifocal distribution. Protocol preferences vary with the stage of the disease, patient clinical and laboratory conditions and degree of toxicity (Cardoso *et al.,* 2006). Commonly used chemotherapy protocols include lomustine, L-CHOP (vincristine, cyclophosphamide, doxorubicin, L-asparaginase, and prednisolone), CHOP, COP (cyclophosphamide, vincristine, and prednisone), LAP (lomustine, L-asparaginase, and prednisolone), LOPP (lomustine, vincristine, procarbazine, prednisolone), chlorambucil, and prednisolone (Azuma *et al*.,2022; Silva *et al.,* 2020). However, the use of therapeutic regimes highlighted in literature does not promise long-term survival, but these treatments do increase the quality of life of patients (Laprais and Olivry, 2017). Protocols based on COP present a less aggressive approach, while the CHOP and L-CHOP protocols are classified as more aggressive chemotherapies and are commonly used for the treatment of lymphomas (Aslan *et al.,* 2021). The use of lomustine for the treatment of high-grade lymphomas has shown good results with acceptable levels of toxicity (Silva *et al.,* 2020). The use of L-asparaginase has shown a better response to lymphoma treatment when implemented in the therapeutic

protocol (Moore, 2016).In another study by Costa *et al.,* 2023 treatment based on the CHOP chemotherapy protocol was successful with initial remission and subsequent relapse. Then chemotherapy protocol was changed to lomustine and prednisolone; however, the patient did not respond, and later died.

Chemotherapy was performed with the CHOP regimen. Cyclophosphamide (250mg/m^2 PO), doxorubicin (30mg/m^2 slow IV), vincristine (0.5 -0.7mg/m^2 IV), Furosemide (1mg/kg PO q12h for 2 days - along with Cyclophosphamide) and prednisolone (in a tapering dose starting with 2mg/kg PO). Maropitant (1mg/kg IV) was given alongside doxorubicin. Haematology was performed prior to each treatment. Four chemotherapy sessions were completed with an interval of one week in between. There was improvement in patient's condition initially, but by fourth week the dog's health condition got worsened as evidenced by severe anaemia, leucopenia and thrombocytopenia. The animal was euthanised as per the request of the pet parent.

CONCLUSION

A ten-year-old mixed breed male neutered dog was presented with two cutaneous erythematous nodules which were removed surgically. Two months later the patient was presented with similar lesions all over the body which was confirmed as cutaneous epitheliotropic lymphoma with histopathology, clinical signs and history. Chemotherapy protocol CHOP (vincristine, cyclophosphamide, doxorubicin and prednisolone) was initiated and the quality of life of the animal initially improved. However, by the fourth week of CHOP protocol, the patient's health deteriorated as evidenced by severe anaemia, leucopenia and thrombocytopenia following which the animal was euthanised as per the request of the pet parent.

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