
LOMUSTINE CHEMOTHERAPY OF CUTANEOUS EPITHELIOTROPIC LYMPHOMA IN A BEAGLE DOG

Anjana Thankachan.^{*1}, Nithin C. J.², Anju S.³ and Harish Chandrasekharan⁴

¹ Veterinary Surgeon, ² Veterinary Surgeon, Veterinary Hospital, Attingal, Thiruvananthapuram, ³ Animal Birth Control Surgeon, Thiruvananthapuram Municipal Corporation, ⁴ Veterinary Surgeon, Clinical Veterinary Lab, District Veterinary Centre, Thiruvananthapuram

*Corresponding author: anjanathankachan2015@gmail.com

ABSTRACT

A beagle dog aged 1.5 years was presented with the history of multiple nodules on left ear pinnae, which were non-responsive to corticosteroid and antibiotic therapy. Enlarged pre scapular lymph node was noted on physical examination and characteristic lymphocytosis was identified on complete blood count. Histopathology revealed lymphoma of subcutaneous epithelial tissue with predominant T cells. Based on history, physical examination and laboratory findings, the case was diagnosed as Cutaneous Epitheliotropic Lymphoma, generally known as Mycosis Fungoides. Treatment with Lomustine capsules- 40mg at the dose rate of 65mg/m² once in every three weeks, with six total doses, resulted in an uneventful recovery, with no recurrence of the condition till 6 months.

Keywords: Beagle dog, epitheliotropic lymphoma, histopathology

INTRODUCTION

Canine cutaneous epitheliotropic T-cell lymphoma is a rare neoplastic condition characterized by infiltration of neoplastic T lymphocytes, which expresses CD3+ and CD8+ as common cell surface markers (Fontaine *et al.*, 2010). Malignant lymphoma account for 7 to 24 % of all canine neoplasm, while incidence of Canine epitheliotropic T-cell lymphomas is only 3 to 8% of all canine lymphomas. Although aetiology remains unclear, some researchers suggest chronic inflammation as the possible predisposing factor.

According to The Revised European-American Classification of Lymphoid Neoplasm (REAL), canine cutaneous epitheliotropic T-cell lymphoma is sub-classified as pagetoid reticulosis (PR: neoplastic lymphocyte confined to epidermis and adnexa), mycosis fungoides (MF: neoplastic lymphocytes infiltrating

epidermis, adnexa and dermis) and sézary syndrome (MF in combination with leukaemia) (Fontaine *et al.*, 2009). The present study deals with case of Mycosis fungoides in a female beagle dog aged 1.5 years, which was treated successfully by chemotherapy. To the author's knowledge this is the first reported case of clinical improvement using lomustine chemotherapy in India.

CASE HISTORY AND OBSERVATION

A female beagle dog aged 1.5 years was presented with the history of multiple nodules on left ear pinnae along with severe pruritus, its size increased in a period of 3 months and it was not responding to corticosteroids and antibiotic therapy. Physical examination revealed enlarged prescapular lymph nodes on both sides. All vital parameters were within the normal range. On dermatological examination, multiple, firm, single to

confluent erythematous cutaneous nodules of approximately 2mm to 4mm diameter were noticed on the lateral aspect of the left ear pinnae (Fig1). Complete blood count revealed marked lymphocytosis (Table1). Ultrasonography of the internal organs didn't show any architectural abnormality. Chest radiograph didn't show any signs of metastasis. The fine needle aspiration cytology was done and the smear examined under oil immersion objective of a microscope revealed, discrete round cells with moderate to scant basophilic cytoplasm, dense and moderately large nucleus with occasional indentation (Fig 3). Histopathology examination revealed hyperplastic epidermis uniformly infiltrated by medium to intermediate sized lymphoid cell. The infiltration cells are pleomorphic with abundant cytoplasm, dense and moderately large nucleus with occasional indentation and folding (horse shoe shaped) and variable (1-2) number of nucleoli (Fig 4). Histopathological lesions confirmed the

Table 1: The haematological findings

Parameters	Day 0	Day 180	Normal range
WBC ($10^3/\mu\text{L}$)	8.67	4.27	5-14.1
Lymphocytes (%)	51.9	22	8-21
Neutrophil (%)	66	59	58-85
Monocytes (%)	3.4	2.5	2-10
RBC ($10^6/\mu\text{L}$)	6.7	5.1	4.95-7.87
Hemoglobin (g/dl)	13.2	8.9	11.9-18.9
Platelet ($10^3/\mu\text{L}$)	354	321	211-621



Fig 1: Day 0- Multiple, firm, single to confluent cutaneous nodules on left ear pinnae



Fig 2 : Day 150- complete recovery after lomustine oral therapy

lymphoma of subcutaneous epithelial tissue with predominance of T-cells(Mycosis fungoides).

TREATMENT AND DISCUSSION

Chemotherapy was initiated with lomustine (lomustine 40mg, GLS pharma) at the rate of $65\text{mg}/\text{m}^2$ (body surface area in square metre = $0.101 \times \sqrt[3]{W^2} \sqrt[3]{W^2}$ in dog, where W is weight in kg, which is 12 kg

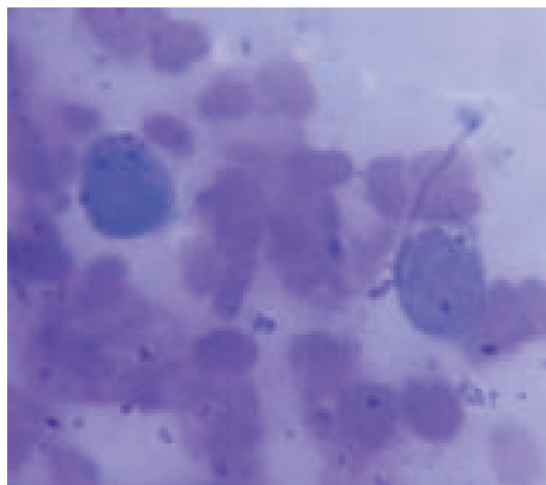


Fig 3: Discrete round cells, moderate to scant basophilic cytoplasm, dense and moderately large nucleus (Giemsa X1000)

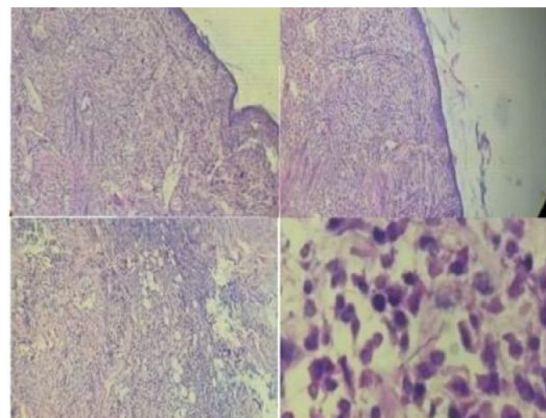


Fig 4 : Day 0- Epidermis is hyperplastic and uniformly infiltrated by medium to intermediate sized lymphoid cells(Biopsy, H&E)

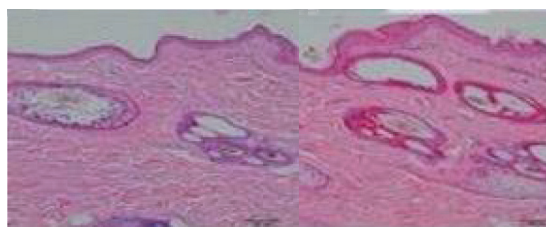


Fig 5: Day 150- Decreased infiltration of lymphoid cells with normal tissue architecture (Biopsy, H&E)

in the present case), PO, once every three weeks as per Risbon *et al.*, (1995). A total

of six doses of lomustine (34 mg total dose at each cycle) were administered without any dosage adjustments. Chemotherapy was well tolerated by the dog; animal was completely recovered after 5 months of lomustine oral therapy (Fig 2).

Complete blood count after recovery revealed anaemia with marked leukopenia (Table 1). Biopsy after 5 months identified reduced infiltration of lymphoid cells with normal tissue architecture. No recurrence of the condition noticed till 6 months.

Canine cutaneous epitheliotropic lymphoma is a rare disease that generally occurs in old dogs at an average age of 9 years. (Fontaine *et al.*, 2009). However, patient in the present case report was only 1.5-year-old. No true breed predisposition was cited by literatures. Cutaneous lymphoma has been reported in Beagle dog by Moore *et al.*, (1994) as in the present case. Clinical presentation is markedly variable, characterized by exfoliative erythroderma, multiple patches, plaques, skin nodules and tumours, which initially localize to the skin and mucous membrane and eventually metastasize to lymph node and beyond. (Moore and Olivry, 1994; Fontaine *et al.*, 2009). Coexistence of different skin lesions has also been reported in studies. The present case has nodular form, with severe pruritus in accordance and Fontaine *et al.*, (2009). Merkel cell

carcinoma and cutaneous histiocytoma are the differential diagnosis at the nodular stage. Although enlarged lymph node suggested systemic involvement, which was not pointed out in further studies. Cytological studies revealed discrete round cells however neoplastic lymphocyte could not be differentiated from the study. Histopathologically, tropism of neoplastic cells for epidermis along with dermis and subcutaneous epithelial tissue observed. These findings were concurrence with Moore and Olivry *et al.*, (1994); Dettwiler *et al.*, observations on histological lesions in classical mycosis fungoides.

Studies conducted by Risbon *et al.*, (1994) and William *et al.*, (2006) reported that treatment of mycosis fungoides with lomustine chemotherapy was effective 83% and 78% of their respective study population. In dog the recommended dosage is 60-70 mg/m² once every 3 weeks. (Fontaine *et al.*, 2009). The median number of treatments received for a response was 4 by Risbon *et al.*, However, in the present case, 6 doses of chemotherapy received for complete remission. Neutropenia, thrombocytopenia, anaemia, myelosuppression and increased liver enzyme activities were some of the reported toxicities caused by lomustine chemotherapy, which justifies the marked leukopenia and anaemia after chemotherapy in the present case.

SUMMARY

A female beagle dog aged 1.5 years with history of multiple nodules with pruritus on left ear pinnae was diagnosed with cutaneous epitheliotropic lymphoma, also known as Mycosis fungoides based on history, clinical signs, cytology and histopathological examination. The animal was treated with lomustine capsule 40mg at the rate of 65mg/m² once in every three weeks, with six total doses, resulted in uneventful recovery and no recurrence of condition till six months.

ACKNOWLEDGEMENT

The authors are thankful to the Director, Animal Husbandry Department, Kerala and the District Animal Husbandry Officer, Thiruvananthapuram, Kerala for providing facilities for the study.

REFERENCES

- Moore, P.F., Olivry, T. and Diane N. (1994). Canine cutaneous epitheliotropic lymphoma (mycosis fungoides) is a proliferative disorder of CD8+ T Cells. *Am. J. Patho.* 144(2): 421-429.
- Moore, P.F., Olivry, T. (1994). Cutaneous lymphomas in companion animals. *Clin. Dermatol.* 12(4):499-505.
- Fontaine, J., Bovens, C., Bettenay and Muller, R.S. (2009). Canine cutaneous epitheliotropic T-cell lymphoma: a review. *Vet. Comp. Oncol.* 7(1):1-14
- Fontaine, J., Heimann, M., and Day, M. J. (2010). Canine cutaneous epitheliotropic T-cell lymphoma: a review of 30 cases. *Vet. Dermatol.* 21(3): 267-275.
- Risbon, R. E., De Lorimier, L.P., Skorupski, K., Burgess, K. E., Bergman, P. J., Carreras and Clifford, C. A. (2006). Response of canine cutaneous epitheliotropic lymphoma to lomustine (CCNU): a retrospective study of 46 cases (1999-2004). *J. Vet. Intern. Med.*, 20(6), 1389-1397.
- Williams, E.L., Kenneth, M.R., Helen, T. P., Susan, E. L., Kirsten, E., Morrison, C., Hansen, K., and Jeffrey, L. J. (2006). CCNU in the treatment of canine epitheliotropic lymphoma. *J. Vet Intern. Med.* 20:136-143