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Clinical and hematobiochemical response to CHOP chemotherapy in dogs with multicentric lymphoma

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Abstract

Multicentric lymphoma/lymphosarcoma is one of the most common haematopoietic neoplasms in dogs. This study aimed to evaluate haemato-biochemical changes and clinical response in dogs with multicentric lymphoma treated with the CHOP chemotherapy protocol and to compare pre-and post-treatment blood parameters using a paired t-test. Six canine clinical cases were presented to the Pet Animal Medical Centre with a history of lethargy, inappetence and generalized lymphadenopathy. On physical examination, enlargement of the multiple lymph nodes was noted. Haemato-biochemistry revealed no significant abnormalities. Thoracic radiographs demonstrated enlargement of the sternal and/or tracheobronchial lymph nodes, while abdominal radiographs revealed radiodense masses. Ultrasonographic examination confirmed enlargement of the mesenteric and medial iliac lymph nodes. The definitive diagnosis was established through fine-needle aspiration cytology (FNAC). Dogs received a CHOP protocol consisting of cyclophosphamide, doxorubicin, vincristine and prednisolone. Blood samples for haemato-biochemistry were collected before initiation of therapy and after completion of protocol. Pre-vs post-treatment differences were evaluated using paired t-tests ($\alpha = 0.05$). Statistically significant reductions in TLC ($p < 0.05$) were observed, with normalization from leukocytosis. Haemoglobin, neutrophil and platelet count showed non-significant mild decreases but remained within acceptable clinical thresholds. SGOT, SGPT showed non-significant increase while the other biochemical parameters remained in normal range. The CHOP protocol was effective and generally well tolerated. Haemato-biochemical changes were consistent with expected chemotherapy effects.

Keywords: Lymphosarcoma, dogs, CHOP, chemotherapy

1. Introduction

Lymphoma is among the most frequently diagnosed tumors in dogs, representing approximately 83% of hematopoietic malignancies and accounting for 7-24% of all canine tumors (Zandvliet, 2016) [1]. This disease arises from the uncontrolled growth of malignant lymphoid cells and primarily affects lymphoid organs, including the lymph nodes and spleen. Based on anatomical distribution, lymphoma is categorized into multicentric, alimentary, and mediastinal forms, with multicentric lymphoma being the most prevalent and comprising nearly 80% of reported cases (Mortier *et al.*, 2012) [2]. Although the precise cause of lymphoma remains unclear, several contributing factors have been implicated, such as infectious agents, genetic predisposition, environmental exposures, and immune system dysfunction.

The chemotherapy regimen consisting of cyclophosphamide, doxorubicin, vincristine, and prednisolone—commonly referred to as the CHOP protocol—is widely regarded as a standard treatment for canine lymphoma (Chun, 2009) [3]. Dogs that do not receive treatment typically survive only 4-6 weeks; however, those treated with CHOP often respond favorably, achieving median survival times ranging from 10 to 14 months. Numerous studies have evaluated treatment outcomes and prognostic indicators in dogs undergoing CHOP therapy (Sorenmo *et al.*, 2010) [4]. These investigations have identified several factors associated with prognosis, including disease stage and substage, immunophenotype, hematologic abnormalities such as anemia or thrombocytopenia, and evidence of chronic inflammation (Miller *et al.*, 2009 and Childress *et al.*, 2018) [5, 6].

Significant variation exists among dog breeds in terms of morphology, physiology, metabolic activity, and lifespan, which may influence treatment outcomes.

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Previous research on the CHOP protocol has largely focused on large-breed dogs, including boxers, German shepherds, and retrievers, while information regarding therapeutic response in small-breed dogs remains limited. Furthermore, there is a scarcity of studies examining how concurrent diseases affect survival time in dogs receiving chemotherapy. Comorbid conditions may alter the metabolism and clearance of chemotherapeutic agents, potentially influencing treatment efficacy and prognosis. Consequently, assessing the impact of underlying disorders—such as cardiovascular heart disease, endocrine abnormalities (e.g., hyperadrenocorticism), and hepatic dysfunction—on treatment outcomes is clinically important (Rocha *et al.*, 2025) [7].

Monitoring hematological and biochemical parameters during chemotherapy is essential both for patient safety and to assess biological response. Statistical comparison using paired t-tests allows evaluation of pre-and post-treatment changes in the same subjects, controlling for between-dog variability.

Diagnostic imaging including radiography and ultrasonography provides better assessment of the condition and can help in diagnosis, determine disease extent, guide staging, monitor treatment response, and identify complications or concurrent diseases (Crabtree *et al.*, 2010 and Yoon *et al.*, 2004) [8, 9]. FNAC serves as a confirmatory tool in diagnosing lymphomas where lymphoblasts containing mitotic figures, coarse chromatin can be found (Teske and Heerde, 1996) [10].

This study aimed to describe clinical response and haemato-biochemical trends in six dogs undergoing CHOP therapy and to analyze differences using paired t-tests.

Materials and Methods

Study population

Six dogs presented with generalized lymphadenopathy and cytologic or histopathologic confirmation of multicentric lymphoma. Diagnosis included physical examination, CBC, biochemical analysis and thoraco-abdominal imaging.

Treatment protocol (CHOP)

Dogs were treated using a standard rotating CHOP protocol:

- Vincristine (0.5-0.7 mg/m² IV)
- Cyclophosphamide (200-250 mg/m² IV or PO)
- Doxorubicin (30 mg/m² IV)
- Prednisolone (2 mg/kg PO taper over 4 weeks)

Blood samples were collected from each dog prior to initiation of chemotherapy (Week 0) and after completion of the CHOP protocol (Madison-Wisconsin protocol). Haematological parameters included haemoglobin (Hb), total leukocyte count (TLC), neutrophil count, and platelet count. Serum biochemical analysis included serum glutamic oxaloacetic transaminase (SGOT/AST), serum glutamic pyruvic transaminase (SGPT/ALT), blood urea nitrogen (BUN), and serum creatinine.

Data were expressed as mean $\pm$ standard error (SE). Pre-and post-treatment values were compared using a paired t-test, as the same animals were evaluated before and after chemotherapy. Statistical significance was set at $p < 0.05$.

Results

Table 1: Haemato-biochemical values (mean $\pm$ SE) in dogs with multicentric lymphoma before and after CHOP chemotherapy (n = 6)

Parameter	Pre-treatment	Post-treatment	p-value
Haemoglobin (g/dL)	12.4 $\pm$ 0.6	11.8 $\pm$ 0.5	0.31 (NS)
TLC ($\times 10^3/\mu\text{L}$)	19.6 $\pm$ 1.4	12.3 $\pm$ 1.1	0.004*
Neutrophils ($\times 10^3/\mu\text{L}$)	14.2 $\pm$ 1.2	8.9 $\pm$ 0.9	0.01*
Platelets ($\times 10^5/\mu\text{L}$)	3.1 $\pm$ 0.3	2.7 $\pm$ 0.2	0.24 (NS)
SGOT (U/L)	34.6 $\pm$ 3.1	41.2 $\pm$ 3.8	0.13 (NS)
SGPT (U/L)	38.9 $\pm$ 3.4	46.7 $\pm$ 4.1	0.11 (NS)
BUN (mg/dL)	18.7 $\pm$ 1.6	20.1 $\pm$ 1.8	0.41 (NS)
Creatinine (mg/dL)	1.1 $\pm$ 0.1	1.2 $\pm$ 0.1	0.47 (NS)

* Statistically significant ($p < 0.05$); NS = Non-significant

A statistically significant reduction in TLC and neutrophil count was observed following chemotherapy, indicating resolution of leukocytosis and expected myelosuppressive effects of cytotoxic drugs. However, values remained within clinically acceptable limits. Mild reductions in haemoglobin and platelet count were non-significant and did not result in clinical anemia or thrombocytopenia.

Cytological Examination

Fine-needle aspiration cytology (FNAC) of enlarged lymph nodes was performed using a 22-gauge needle. Smears stained with Giemsa revealed monomorphic populations of large lymphoblasts with high nuclear-to-cytoplasmic ratio, prominent nucleoli, and mitotic figures, confirming multicentric lymphoma.

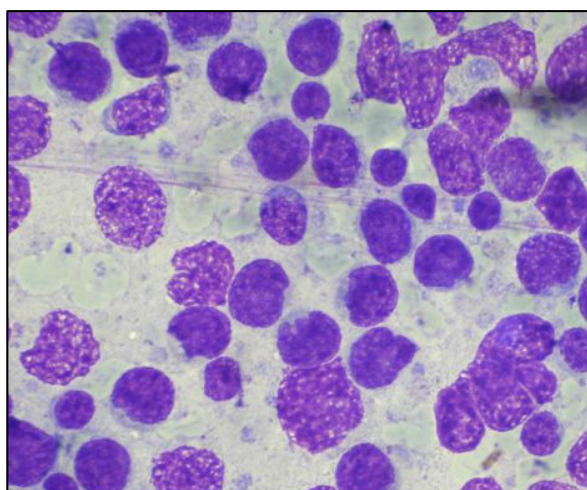


Fig 1: FNAC of lymph nodes showing lymphoblasts with coarse chromatin material

Imaging Studies

Thoracic radiographs demonstrated enlargement of sternal and/or tracheobronchial lymph nodes. Abdominal radiographs revealed radiodense masses exerting pressure on adjacent visceral organs. Ultrasonography confirmed enlargement of mesenteric and medial iliac lymph nodes.

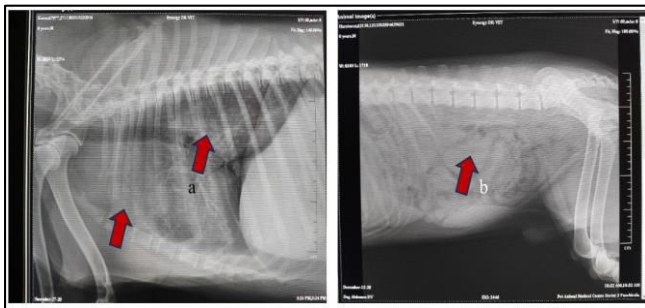


Fig 2: Thoracic (a) and abdominal (b) radiographs of dogs with multicentric lymphoma

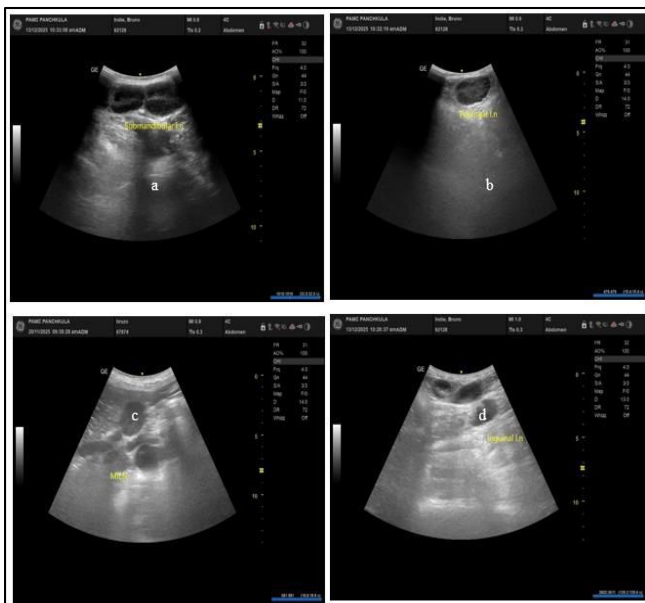


Fig 3: Abdominal ultrasonographic images of dogs with multicentric lymphoma in: a) Submandibular lymph node; b) Popliteal lymph node; c) Medial iliac lymph node; d) Inguinal lymph node

Discussion

The findings support the effectiveness of the CHOP protocol in inducing remission in dogs with multicentric lymphoma while producing predictable and manageable hematologic changes (Garrett *et al.*, 2002; Vail *et al.*, 2013) [11, 12].

Non-significant elevations in liver enzymes may be attributed to drug metabolism (Withrow *et al.*, 2019 and Fleischer *et al.*, 2008) [13, 14], particularly doxorubicin and cyclophosphamide (Olson *et al.*, 1990) [15], but did not necessitate treatment discontinuation. The maintenance of normal renal parameters suggests good overall tolerability of the protocol.

FNAC proved to be a rapid, minimally invasive, and reliable diagnostic tool, consistent with earlier studies emphasizing its utility in routine lymphoma diagnosis (Raskin & Meyer, 2016 and Zandvliet, 2016) [1, 16].

Conclusion

CHOP chemotherapy remains a practical and effective treatment for canine multicentric lymphoma. Paired t-test

comparisons demonstrated clinically meaningful reductions in leukocyte and neutrophil counts, consistent with therapeutic response and expected myelosuppression. Monitoring CBC values remains essential to ensure safety and guide dosing adjustments.

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