



UNIVERSITI PUTRA MALAYSIA

**CLINICOPATHOLOGICAL CHARACTERISTICS OF
CANINE LYMPHOMA CASES SUBMITTED TO
UNIVERSITY VETERINARY HOSPITAL,
UNIVERSITI PUTRA MALAYSIA**

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SHAZIMA HANNY NATASHYA BINTI SHAHARULLIZAM

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ABSTRAK

Abstrak daripada kertas projek yang dikemukakan kepada Fakulti Perubatan Veterinar untuk memenuhi sebahagian daripada keperluan kursus VPD 4901 Projek.

**CIRI-CIRI PATOLOGI KLINIKAL KES LIMFOMA ANJING YANG
DIKEMUKAKAN KEPADA HOSPITAL VETERINAR UNIVERSITI,
UNIVERSITI PUTRA MALAYSIA**

Oleh

Shazima Hanny Natashya Shaharullizam

2021

Penyelia: Dr Azalea Hani Othman

Penyelia bersama: Prof. Dr Rasedee Abdullah

Kini, limfoma sering didiagnosis dalam anjing. Buat masa ini, maklumat mengenai ciri-ciri patologi klinikal dalam kes limfoma anjing masih terhad. Objektif kajian ini adalah untuk menentukan ciri-ciri patologi klinikal limfoma anjing yang dikemukakan kepada Hospital Veterinar Universiti (HVU), Universiti Putra Malaysia (UPM). Rekod pesakit limfoma anjing dari tahun 2016 hingga 2020 diperolehi daripada Makmal Hematologi dan Biokimia Klinikal, Unit Perkhidmatan Makmal Veterinar, UPM. Sebanyak seratus sebelas kes telah dikumpul dan disusun mengikut ciri-ciri penemuan morfologi limfoma dan hematologi dan biokimia klinikal. Daripada kes-kes ini, ciri-ciri yang paling

kerap adalah banyak badan limfoglandular (52.3%), lembaga mitosis (41.4%), sel-sel limfoid pleomorfik (28%), banyak sel-sel limfoid (24.3%) dan sel-sel limfoid bersaiz berbeza-beza (19%). Antara penemuan kerap hematologi dan biokimia dalam limfoma anjing adalah anemia (25.2%), hiperglobulinemia (16.2%), azotemia (12.6%) dan limfopenia (9%). Di antara kes anemia, 16.2% adalah responsif dan 9% adalah tidak responsif. Analisis air kencing menunjukkan anjing yang menghidap limfoma mengalami proteinuria (4.5%) dan haematuria (2.7%). Dengan itu, ciri-ciri patologi klinikal yang paling kerap dilihat dalam kes limfoma anjing yang dikemukakan kepada HVU adalah anemia.

Kata kunci: *anjing; limfoma; ciri-ciri sitologi; badan limfoglandular; anemia; proteinuria*

ABSTRACT

An abstract of the project paper presented to the Faculty of Veterinary Medicine in partial fulfilment of the course VPD 4901- Project.

CLINICOPATHOLOGICAL CHARACTERISTICS OF CANINE

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by

Shazima Hanny Natashya Shaharullizam

2021

Supervisor: Dr Azalea Hani Othman

Co-Supervisor: Prof. Dr Rasedee Abdullah

Lymphoma is now more often diagnosed in dogs. Currently, there is still limited information on the clinicopathological characteristics of canine lymphoma cases. The objectives of this study were to determine the clinicopathological features of canine lymphoma cases presented to the University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM). The records of canine lymphoma patients from the year 2016 to 2020 were obtained from the Haematology and Clinical Biochemistry Laboratory, Veterinary Laboratory Services Unit, UPM. One hundred and eleven cases were retrieved and compiled according to the morphological characteristics of lymphoma, and

haematological and clinical biochemical findings. Of these cases, the most common cytological features were numerous lymphoglandular bodies (52.3%), mitotic figures (41.4%), pleomorphic lymphoid cells (28%), an abundance of lymphoid cells (24.3%) and variable-sized lymphoid cells (19%). Among the common haematological and biochemistry findings in canine lymphoma were anaemia (25.2%), hyperglobulinaemia (16.2%), azotaemia (12.6%) and lymphopaenia (9%). Among cases with anaemia, 16.2% were responsive and 9% were non-responsive. The urinalysis revealed that lymphoma dogs had proteinuria (4.5%) and haematuria (2.7%). Thus, the most common clinicopathological feature of canine lymphoma cases presented to UVH was anaemia.

Keywords: *canine; lymphoma; cytological features; lymphoglandular bodies; anaemia; proteinuria*

CHAPTER 1

1.0 INTRODUCTION

Lymphoma is one of the most diagnosed cancer in dogs (Ettinger, 2003). Lymphoma is a cancer that arises from the hematopoietic system and can affect any anatomical region where lymphocytes travel or are located. Lymphoma in dogs is characterised by enlarged, non-painful, generalised lymphadenopathy, and when tumor load is high, clinical indicators such as lethargy and weight loss become prominent (Fan, 2019).

Lymphoma affects dogs of all ages, but it is commonly seen in middle-aged dogs. There is no preference for one gender over another (Ettinger, 2003), although some studies found that lymphoma was more frequently observed in female dogs (Jagielski et al, 2002). According to Vail et al. (2001), Airedale terriers, Boxers, Beagles, Basset hounds, Bulldogs, Golden retrievers, Poodles, Rottweilers, Scottish terriers, and Saint Bernards are among breeds with high risk of being affected with lymphoma. Dachshunds and Pomeranians on the other hand are less vulnerable. These dogs are frequently asymptomatic, but with less than half of them may show anorexia, lethargy, fever, weight loss, vomiting, diarrhea, and melena. Hepatosplenomegaly and pulmonary infiltration may also occur in advanced stages of this disease (Vail et al, 2001).

Lymphoma encompasses a variety of cancer sub-types that emerges due to neoplastic transformation of B and T cells at various stages of development. While diagnosing lymphoma is reasonably simple using standard cytology, defining the

many sub-types and anticipating their biological behaviour remains difficult (Aresu, 2016).

Lymphoma in dogs can be accurately diagnosed through cytological examination. In most situations, pathologists can correctly diagnose lymphoma using cytology and immunocytochemistry, which is why it is widely used in scientific research (Kliczkowska-Klarowicz et al., 2021). Among 90% to 95% of canine lymphoma cases, peripheral lymph nodes are diffusely and homogeneously effaced. Therefore, fine-needle aspiration (FNA) frequently gives adequate specimen for cytopathologic interpretation. Fine-needle aspiration is the most popular first-line diagnostic method, and it can be done with or without restraining most canine patients (Bienzle and Vernau, 2011). However, cytological findings describing the morphology of canine lymphoma is still limited (Aresu, 2016). Furthermore, like other cancers, dogs that suffer from lymphoma also exhibit clinicopathological changes. Therefore, the purpose of the current study is to describe the cytological and clinicopathological findings including haematological, biochemical and urinalysis of canine lymphoma cases from the year 2016 to 2020 presented at the University Veterinary Hospital, University Putra Malaysia.

The objectives of this study are:

- To determine the clinicopathological features of canine lymphoma
- To develop a clinicopathological profile for canine lymphoma cases

CHAPTER 2

2.0 LITERATURE REVIEW

2.1 Types of Lymphoma

Lymphoma is the most frequently diagnosed hematopoietic cancer in dogs (Jagielski et al (2002). The majority of canine lymphomas are of B cell origin (60-80%) and 10-38% are of T cell origin (Calvalido et al., 2016). Lymphoma is generally classified according to anatomical structures which are multicentric, gastrointestinal, mediastinal, and cutaneous forms (Ettinger, 2003).

2.1.1 Multicentric

Multicentric lymphoma is the most common type of canine lymphoma that accounts nearly 80-85% of lymphoma cases in dogs (Barnette, 2021). In one study, it was found frequently in dogs aged 4 – 8 years old, more often in Rottweilers (Jagielski, 2002). The prognosis of dogs with multicentric lymphoma depends on the staging and sub-staging of the disease according to the World Health Organisation's classification, at the time of diagnosis (Table 1).

Table 1: World Health Organisation's clinical staging system for lymphoma in dogs

Stage	
I	Involvement of a single lymph node or lymphoid tissue in a single organ
II	Involvement of multiple lymph nodes in one side of the diaphragm
III	Generalised lymph node involvement
IV	Liver and/or spleen involvement (+/- stage I-III)
V	Manifestation in the blood and involvement of bone marrow and/or other organ systems (+/- stage I-IV)
Substage	
a	Without systemic signs
b	With systemic signs

Adapted from Calvalido (2016).

2.1.2 Gastrointestinal

Gastrointestinal lymphoma is less prevalent in dogs although are more commonly seen in males (Priester and McKay, 1980). A study showed that the most common changes in the intestinal tract were altered wall thickening (Sagome et al., 2018). Dogs that have gastrointestinal lymphoma usually have signs of vomiting, anorexia, diarrhea weight loss, icterus and tenesmus (Couto et al. 1989).

2.1.3 Mediastinal

Mediastinal lymphoma encompasses approximately 20-35% of all canine lymphomas and is commonly associated with T cell phenotype with signs of hypercalcaemia (Moore et al, 2018). Clinical signs seen in dogs with mediastinal lymphoma include lethargy, anorexia, polyuria/polydipsia, coughing, dyspnea or tachypnea and vomiting (Stilwell, 2018).

2.1.4 Cutaneous

Canine cutaneous lymphoma can be presented in variety of lesions that include ulcer, nodules, plaques, reddish patches, or area of alopecia or scaling. Dogs may show signs of itching, and progression of cutaneous lymphoma may lead to inflammation and the lesion may ooze fluid (Downing, 2021).

2.2 Risk Factors

2.2.1 Breed

Canine lymphoma can affect any breeds from middle-sized to large. Large breeds are more genetically susceptible to lymphoma (Zandvliet, 2016). According to Mortier et al. (2012), the most prevalent dog breed diagnosed with lymphoma is Labrador retriever followed by mixed breed. Comazzi et al. (2018) mentioned that the most common breed to be affected with lymphoma are Labrador retriever, Boxer, German shepherd, Golden retriever, Rottweiler, Dobermann and Beagle. Boxers mostly appeared with cutaneous lymphomas and pleomorphic mixed T lymphomas (Pastor et al., 2009).

2.2.2 Age

Lymphoma affects dogs of all ages (ranging from 6 months to 15 years old), but it is commonly seen in middle-aged dogs, with a median age of 5 to 9 years (Ettinger, 2003). According to Sanchez et al. (2019), the mean age of dogs diagnosed with lymphoma are 7.5 years with most dogs being over the age of five.

2.3 Diagnosing Canine Lymphoma

Fine needle aspirate cytology is a frequently used method in veterinary medicine for diagnosing lymphoma because it is accurate and reliable (Fisher et al., 1995; Sapierzyński et al., 2016). Furthermore, most dog owners prefer FNA because it is a safe and non-harmful method of sample collection (Sapierzyński et al., 2016).

The cytological analysis of circulating lymphocytes or lymphoid tissue, or the histological study of lymphoid tissue, are used to detect canine lymphocytic cancers. The diagnosis is frequently simple, however there are some occasions that can be challenging. Some of the examples are difficulty in distinguishing early stages of lymphoma from lymphoid hyperplasia; body cavity fluids that contain numerous of small, mature-looking lymphocytes; cases with chronic or mild lymphocytosis; biopsy samples that do not entirely represent the lesion; and the detection of a small number of lymphocytes with atypical features in FNA samples (Burnett et al., 2003).

2.4 Common Clinicopathological Findings

2.4.1 Haematology and biochemistry

It is common to find lymphoma dogs to have slight anaemia (Madewell, 1986; Teske, 1994). This is more regularly seen in multicentric form of the disease, which leads to infiltration of multiple organs (Kayar et al, 2018). Normocytic normochromic anaemia is the most common feature in canine lymphoma (Miller et al., 2009; Thangapandiyan et al., 2017; Sánchez et al., 2019). Most dogs may have

mild to moderate non-responsive anaemia, however haemorrhagic or hemolytic anaemia can occur as seen in gastrointestinal lymphoma or a secondary immune-mediated, respectively (Zandvliet, 2016). Thrombocytopenia is also often observed (Neuwald et al., 2014). It was described that anemia and thrombocytopenia are associated with bone marrow infiltration, immune-mediated destruction, splenic infiltration and also chronic disease (Mortier et al., 2012). Hyperglobulinaemia is also found in dogs affected with lymphoma which was suggested to be associated with prolonged survival (Rout et al., 2021).

Hypercalcaemia is often observed in lymphoma dogs (Vail et al, 2010; Zandvliet, 2016; Kayar et al., 2018). This could be an organ failure due to tumor infiltration. Liver enzymes such as alkaline phosphatase may also elevate following corticosteroid stimulation, either through endogenous production or exogenous administration (Vail et al., 2010; Bryan, 2016; Kayar et al., 2018). Together with lactate dehydrogenase, both serum enzymes were described as biomarkers for lymphoma (Bryan, 2016). Dogs may also have azotemia, which can be due to tissue infiltration (Vail et al., 2010) or a pre-renal condition that is dehydration (Vail et al., 2010; Kayar et al., 2018).

2.4.2 Urinalysis

Dogs with lymphoma are more likely to have proteinuria than healthy dogs. Dogs with lymphoma often have proteinuria, but it is usually not severe. Proteinuria is independent of stage or sub-stages of lymphoma (Di Bella et al., 2013). In human studies, structural glomerular diseases have been linked to lymphoma (Pedersen and Johansen, 2005; Mallouk et al., 2006).

2.4.3 Cytology

Lymphoma is easily diagnosed cytologically if the tumor is widespread and has replaced the entire lymph node with a uniform population of large neoplastic lymphocytes. Several malignant characteristics are more frequently associated with lymphoma. Lymphoglandular bodies is a hallmark cytological feature of lymphoma, and is described as small, round, homogeneous, basophilic structures found around and between cells (Bukhard and Bienzle, 2013).

CHAPTER 3

3.0 METHODOLOGY

3.1 Data retrieval

The records of canine lymphoma patients from the year 2016 to 2020 were obtained from the Haematology and Clinical Biochemistry Laboratory, Veterinary Laboratory Services Unit, UPM. Patients' information including age, sex, breed, neuter status, tentative diagnosis, site of sample, haematology, biochemistry, cytology, and urinalysis data were recorded. Among the records, lymphoma cases were searched using keywords 'lymphoma' and 'suspected lymphoma' from the cytology tentative diagnostic comments made by the clinical pathologist on duty. The laboratory reference number of cytology record was then used to search for haematology and biochemistry and urinalysis records. Cases diagnosed as suspected lymphoma were also included. As a result, a total of 111 cases were found diagnosed with canine lymphoma.

3.2 Statistical analysis

Cytology, haematology, biochemistry, and urinalysis data were recorded in Excel WPS office and subjected to descriptive analysis.

CHAPTER 4

4.0 RESULTS

4.1 Age

Among the 111 cases of canine lymphoma, the common age dogs affected were from 1 to 8 years (51.4%) and >8 years (44.1%). Five cases had no information of age stated (Table 2).

Table 2: Age distribution of canine lymphoma cases.

Age	Number (%)
1-8 years	57 (51.4)
>8 years	49 (44.1)
Unknown (no information)	5 (4.5)

All percentages were calculated per 111 of canine lymphoma cases

4.2 Sex

Among the lymphoma cases, intact male dogs were the most commonly affected with lymphoma followed by spayed female (Table 3). Four cases were recorded as unknown because sex was not stated in the report.

Table 3: Sex distribution of canine lymphoma cases.

Sex	Number (%)
Intact male	49 (44.1)
Intact female	19 (17.1)
Castrated male	13 (11.3)
Spayed female	26 (23.5)
Unknown (no information)	4 (3.6)

All percentages were calculated per 111 of canine lymphoma cases

4.3 Breed

The most common breeds that were affected with lymphoma were local, followed by Shih Tzu, Rottweiler, Golden Retriever and mix (Table 4). Twenty-three were recorded as others which represent as one dog per breed that includes Boxer, Corgi, Jack Russell, Bull Terrier X, Cocker Spaniel, Poodle and Toy Poodle.

Table 4: Breed distribution of canine lymphoma cases.

Breed	Number (%)
Local	17 (15.3)
Shih Tzu	14 (12.6)
Rottweiler	11 (10.0)
Golden Retriever	9 (8.1)
Mixed	7 (6.3)
Beagle	5 (4.5)
Labrador	5 (4.5)
German Shepherd Dog	4 (3.6)
Dobermann	3 (2.7)
Pug	3 (2.7)
Terrier	3 (2.7)
Schnauzer	3 (2.7)
Miniature Schnauzer	2 (1.8)
African Mastiff	2 (1.8)
Others	23 (20.7)

All percentages were calculated per 111 of canine lymphoma cases.

4.4 Specimen

Table 5 describes the method of collection and specimen used for diagnosing canine lymphoma cases. The most common collection methods used were impression smear, FNA and fluid collection. For the impression smear cases, the most common sites of collection were prescapular combined with popliteal lymph nodes. The unknown category refers to site that were not stated in the cytological report.

Table 5: Method and site of specimen collected for diagnosing canine lymphoma cases.

Specimen	Frequency (n)	%	Site	Frequency (n)	%
Impression smear	85	76.6	Prescapular and popliteal	10	9.0
			Popliteal	2	1.8
			Submandibular	2	1.8
			Inguinal & popliteal	1	0.9
			Unknown	70	63.1
Fine needle aspirate	20	18.0	Prescapular & Popliteal	3	2.7
			Submandibular & Popliteal	1	0.9
			Submandibular & inguinal	1	0.9
			Submandibular & popliteal	1	0.9
			Submandibular & prescapular	1	0.9
			Liver	1	0.9
			Eye & Tail	1	0.9
			Unknown	11	9.9
Fluid	6	5.4	Lymph node fluid	1	0.9
			Abdominal fluid	1	0.9
			Pericardial effusion	1	0.9
			Popliteal fluid	1	0.9
			Unknown	2	1.8

All percentages were calculated per 111 of canine lymphoma cases.

4.5 Cytology

The cytological features that were described were presence of lymphoglandular bodies, mitotic figures, pleomorphism, and size of the lymphoma cells, as presented in Table 6. Numerous lymphoglandular bodies was the most common cytological finding, followed by presence of mitotic figures, high number of pleomorphic cells and anisocytosis. Only two cases were found to be of small cell lymphoma, while seven cases were large cells. Cytological images showing morphological features of canine lymphoma are as presented in Appendices.

Table 6: Cytological findings of canine lymphoma cases.

Cytology features	Frequency (n)	Percentage according to number of cases (%)	Category	Frequency (n)	Percentage according to cytological features (%)
lymphoglandular bodies	76	68.5	Few	9	8.1
			Some	9	8.1
			Numerous	58	52.3
Mitotic figures	46	41.4			
Pleomorphic lymphoid cells	42	37.8	Low	1	09
			Moderate	10	9.0
			High	31	28
Size	32	28.8	Small	2	1.8
			Medium	3	2.7
			Large	7	6.3
			Various	20	19

All percentages were calculated per 111 of canine lymphoma cases.

4.6 Haematology and biochemistry

Among the 111 lymphoma cases, 35 of them were requested for haematology and biochemistry analysis (Table 7). It was found that anaemia was the most common feature in lymphoma cases, which were mostly responsive. Hyperglobulinaemia was also a common finding, although majority were only slightly elevated from the reference range. Biochemical results showed that azotaemia of blood urea concentration between 7 to 20 mmol/L, which categorised as slightly azotaemic, was common among lymphoma cases. Lymphopaenia was also a feature found in ten of the lymphoma cases.

Table 7: haematology and biochemistry finding of canine lymphoma cases

Haematology and biochemistry	Frequency (n)	Percentage according to number of cases (%)	Category	Frequency (n)	Percentage of cases according to haematology and biochemistry category (%)
Anaemia	28	25.2	Responsive	18	16.2
			Non-responsive	10	9.0
Hyperglobulinaemia	18	16.2	Slight (40-55 g/L)	9	8.1
			High (56-70 g/L)	6	5.4
			Marked (>70 g/L)	3	2.7
Urea	14	12.6	Slight (7.2-20 mmol/L)	9	8.1
			High (>20 mol/L)	5	4.5
Lymphopaenia	10	9.0			

All percentages were calculated per 111 of canine lymphoma cases.

4.7 Urinalysis

Among the lymphoma cases, five cases had urinalysis requested. Proteinuria and turbid urine were the most common findings followed by presence of bacteria and haematuria as presented in Table 8.

Table 8: Common urinalysis features in canine lymphoma cases.

Urinalysis	Frequency (n)	Percentage according to number of cases (%)	Category	Frequency (n)	Percentage of cases according to haematology and biochemistry category (%)
Proteinuria	5	4.5	Slight (1-2+)	3	2.7
			High (3-4+)	2	1.8
Turbidity	5	4.5			
Bacteria	4	3.6			
Haematuria	3	2.7			

All percentages were calculated per 111 of canine lymphoma cases.

CHAPTER 5

5.0 DISCUSSION

In the present study, it was found that dogs aged 1-8 years are commonly affected with lymphoma followed by those aged more than 8 years. This finding is supported by other studies in which lymphoma is commonly seen in middle-aged dogs, with a median age of 5 to 9 years (Ettinger, 2003; Dobbins, 2019). This shows that young dogs are more susceptible than older dogs to develop lymphoma.

The canine lymphoma cases presented in VLSU-UPM were mostly among local breed dogs followed by Shih Tzu. In another study, Boxers are frequently described as being commonly affected with lymphoma (Van Rooyen et al., 2018) while in Europe, Labrador retrievers were most predisposed (Comazzi et al., 2018). In Malaysia, local breed may be over represented in University Veterinary Hospital, hence leading to high frequency of lymphoma.

In the present study, it was found that intact male dogs were commonly presented with lymphoma followed by spayed female. Sex is not a risk factor for dogs in developing lymphoma (Dorn and Schneider, 1970). However, similar for menopausal women, spayed bitches have higher risk in developing lymphoma. This sex effect has been a constant finding for the past few decades for both humans and dogs (Villamil et. Al 2009).

The most common diagnostic method in sampling the lymphoma lesions was impression smear followed by fine needle aspiration. Fine needle aspiration is said to be the accurate method for diagnosing and sub-typing canine lymphoma (Caniatti et

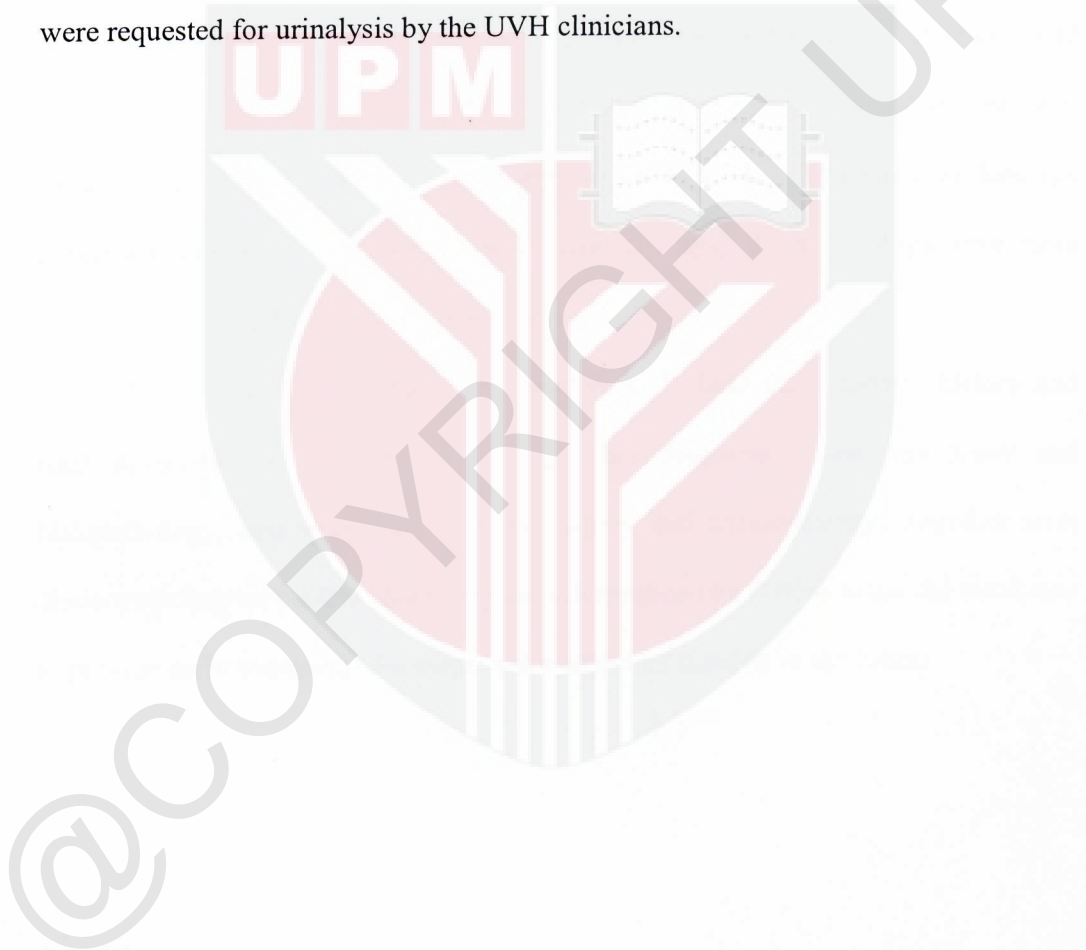
al., 1996). However, impression smear seems to be a popular collecting method among clinicians at UVH.

The common collection site were mostly prescapular together with popliteal lymph nodes. Mandibular and popliteal lymph nodes are said to be easiest to locate in dogs and the latter is easiest to be sampled when peripheral lymphadenopathy is present (Wright and Oblak, 2016).

Common cytological feature in the current study were lymphoglandular bodies and mitotic figures. Lymphoglandular bodies are cytoplasmic fragments that is a typical distinction of lymphomas from other malignant tumours (Bavle, 2014). Stern et al. (2001) described that lymphoglandular bodies are highly associated with B-cell malignancies in myeloid leukemias and lymphomas. Mitotic figures are typical criteria of malignancy especially if bizarre and haphazardly arranged (Selting, 2014).

Anaemia and hyperglobulinaemia are the most frequent haematological finding in lymphoma patients. Unlike studies by Zandvliet (2016) and Thangapandiyar et al. (2017), majority of the anaemic cases in the present study were responsive anaemia. Hyperglobulinemia is also a common feature of canine lymphoma (Ashok, 2016; Rout, 2021).

Some of the lymphoma dogs in the present study had proteinuria. In humans, structural glomerular disease can be a result of lymphoma (Mallouk et al, 2016). Canine lymphoma patients are more at risk to develop proteinuria compared with healthy dogs, although it tends to be mild and the clinical impact is probably low (Di Bella et al., 2012). However, urinalysis result for lymphoma patients in VLSU-UPM was not of significance, because among the 111 cases of canine lymphoma, only five were requested for urinalysis by the UVH clinicians.



CHAPTER 6

6.0 CONCLUSION AND RECOMMENDATIONS

This study had allowed us to determine the clinicopathological characteristic of canine lymphoma in dogs presented to UVH-UPM, based on cytological diagnosis and haematology and biochemistry findings. Presence of lymphoglandular bodies and mitotic figures were the most frequent finding in canine lymphoma. It was also found that dogs with lymphoma commonly have anaemia and hyperglobulinaemia. The most common breed affected with canine lymphoma was local although this breed may be overrepresented at UVH. The most prevalent age group was between 1 to 8 years. Intact male and spayed female dogs were more likely to be affected with canine lymphoma.

It is recommended that future studies to include the complete history and final diagnosis by the clinicians using other diagnostic tools like x-ray and histopathology, and treatments such as surgery and chemotherapy. Together with clinicopathological profile, this complete information can further assist the clinicians to provide early treatments for suspected lymphoma patients in the future.

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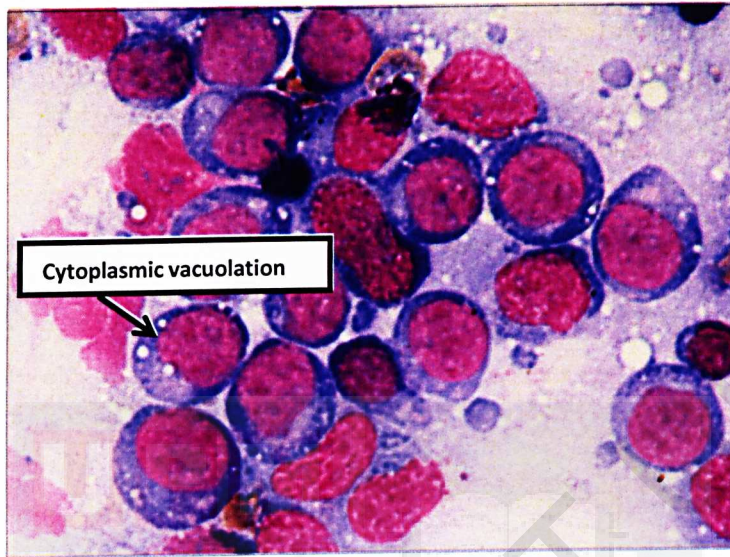
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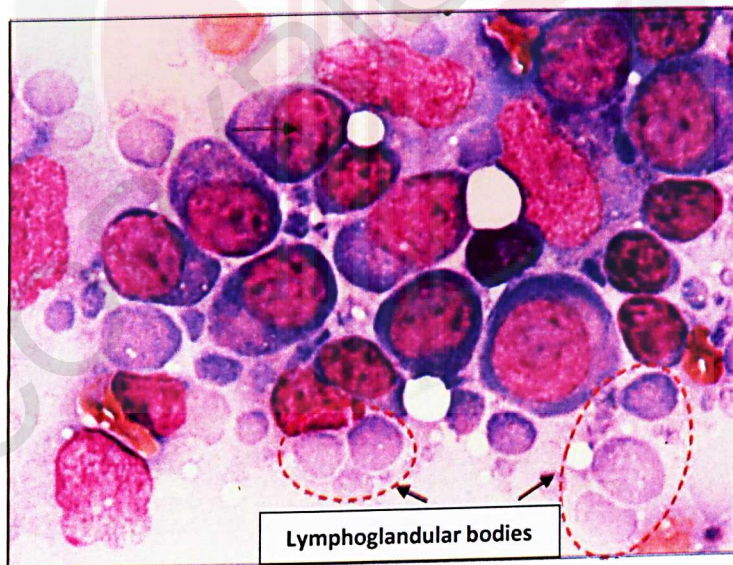
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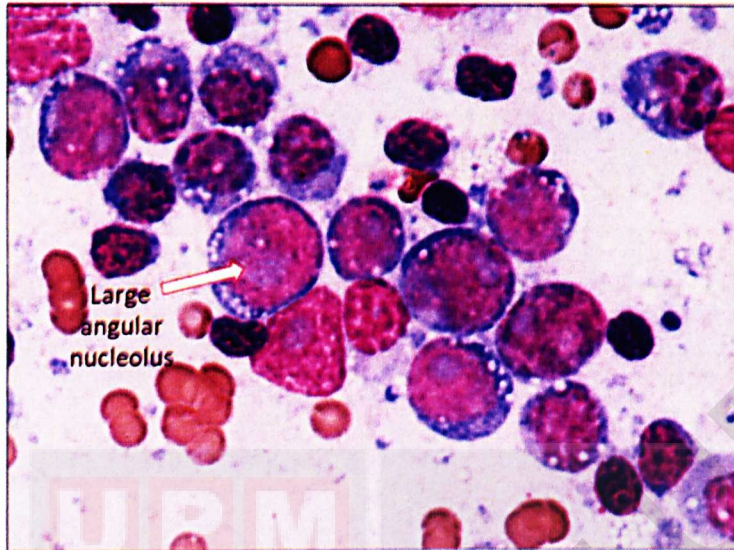
APPENDICES



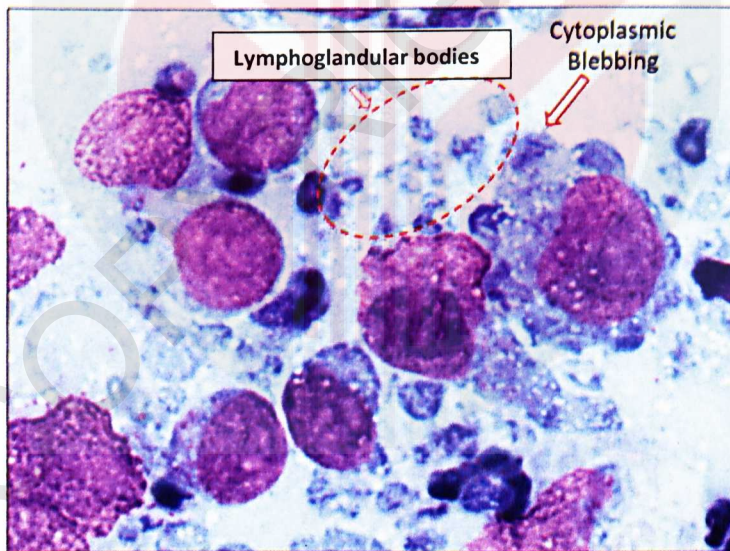
APPENDIX 1. Variable sizes of lymphoid cells in lymphoma with cytoplasmic vacuolation. (Magnification $\times 1000$)



APPENDIX 2. Presence of lymphoglandular bodies in lymphoma. (Magnification $\times 1000$)



APPENDIX 3. Lymphoma showing pleomorphic lymphoid cells with large angular prominent nucleoli. (Magnification $\times 1000$)



APPENEDIX 4. Lymphoma showing lymphoglandular bodies and lymphoid cells with cytoplasmic blebbing. (Magnification $\times 1000$)