

Pattern of lymph node pathology in a private pathology laboratory

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Abstract

Lymph node excision biopsy is commonly carried out for the investigation of lymphadenopathy. The objective of this study is to elucidate the pattern of nodal pathology seen in a private pathology practice. A total of 137 nodal biopsies for primary investigation of nodal enlargement were retrieved from the files in a private diagnostic pathology laboratory in the year 1997. Lymph nodes excised for cancer staging were excluded from this study. The histology was reviewed based on H&E stained sections, and with additional histochemical and immunoperoxidase stains when deemed necessary. Cases of malignant lymphomas were sub-classified with the aid of further immunophenotyping using a panel of monoclonal and polyclonal lymphoid antibodies. One case was excluded from this study due to inadequate tissue for further assessment. There were 58 males and 78 females, giving a ratio of 1:1.3 in the remaining 136 cases. They consisted of 13 Malays (M), 108 Chinese (C), 14 Indians (I) and 1 other ethnic group (O). The ratio of M:C:I:O was 1: 8.3: 1.1: 0.1. The majority of the cases were in the age range of 20 to 50 years. The pathology consisted of 17 (12.5%) malignant lymphomas [6 Hodgkin's lymphoma, 11 non-Hodgkin's lymphoma], 35 (25.7%) metastatic carcinomas, 45 (33.1%) reactive hyperplasia, 19 (13.9%) tuberculosis, 11 (8.2%) Kikuchi's disease and 9 (6.6%) others (Castleman's disease 2, cat scratch disease 2, Kimura's disease 1, sarcoidosis 1, non-specific lymphadenitis 3). All categories of nodal disease showed approximately similar ratio of ethnic and gender distribution as above, except for Kikuchi's disease, for which 100% of the patients were female. The most common site of biopsy was from the head and neck region, particularly the cervical group of nodes. The most common nodal pathology seen in the private laboratory was reactive hyperplasia, followed by metastatic carcinoma. Malignant lymphoma constituted only 12.5% of the cases.

Key words: lymphadenitis, lymphadenopathy, lymphomas.

INTRODUCTION

In the last two decades there has been a remarkable increase in the numbers of private medical centres throughout Malaysia, particularly in the Klang Valley. Many of these centres are serviced by clinical specialists of various disciplines who can offer different aspects of specialised medical care. The need for laboratory medicine correspondingly increased following the demand for more detailed investigations to arrive at a diagnosis prior to treatment, or during the course of continuous assessment, in line with the practice of the specialised medical disciplines. Information on the spectrum of diseases diagnosed and managed by doctors is important for the planning and development of the health care system. There are some reports available on diseases encountered in the

government/public hospitals¹⁻⁷, however such information is not readily and directly accessible from the private health care centres. A private laboratory-based study may yield data which reflects on the pattern of diseases managed in private medical practice.

The objective of this study is to elucidate the pattern of pathology presenting in the lymph node from a private pathology laboratory, and directly compared it with the spectrum seen in a laboratory of a public hospital of comparable workload.

MATERIALS AND METHODS

A total of 137 lymph nodes excised for primary investigation of nodal enlargement were retrieved from the files of B.P.Clinical Lab Sdn Bhd, Ipoh in the year 1997. The tissues were received from

various private hospitals and surgical clinics. Lymph nodes excised for cancer staging were excluded from this study. The diagnostic material was sent to the collaborators in the Department of Pathology, University Hospital Kuala Lumpur for this study. The histopathology of Haematoxylin & Eosin (H&E) stained sections was reviewed by two of the collaborating authors (KSC and SCP). Additional histochemical and immunoperoxidase stains were performed when deemed necessary to arrive at a definitive diagnosis. Cases of malignant lymphomas were sub-classified with the aid of further immunophenotyping using a panel of monoclonal and polyclonal lymphoid antibodies.

Antibodies to B-cell, CD20 (L26, Dako, Denmark) and T-cell, CD3 (polyclonal CD3, Dako, Denmark) were routinely used for sub-typing in malignant lymphomas. Additional antibodies such as CD15 (Leu-M1, Becton Dickinson, USA) and CD30 (Ber-H2, Dako, Denmark) were used when the diagnosis of Hodgkin's lymphoma (HL) was made for the purpose of studying the phenotype expression. Antigen retrieval steps such as microwave pre-treatment or enzymatic digestion with trypsin, were carried out depending on the antibodies used. Three-step Labelled Streptavidin-Biotin system (LSAB[®]+ Kit, Dako, Denmark) was employed in the immunohistochemical staining technique.

Based on the same selection criteria and methods as above, a total of 53 lymph node biopsies for primary investigation were also retrieved from the files in the Department of Pathology, University Hospital Kuala Lumpur (UHKL) for the purpose of comparison.

RESULTS

B.P. Clinical Lab, Ipoh

Out of the 137 cases from B.P. Clinical Lab, one case was excluded due to inadequate tissue for further assessment. The remaining 136 cases were from 58 male and 78 female patients, giving a male: female ratio of 1:1.3. There were 13 (9.6%) Malays (M), 108 (79.4%) Chinese (C), 14 (10.3%) Indians (I) and 1 (0.7%) other ethnic group (O). The M: C: I: O ratio was 1: 8.3: 1.1: 0.1. Fig. 1 shows the age distribution of these patients. The mean age of patients was 40.1 years. Only 18 cases (13.4%) were in the paediatric age group (aged 14 years and below).

The sites where lymph nodes were excised are as shown in Table 1. The head and neck region was the most common location, particularly the cervical group of lymph nodes (70/136, 51.5%). The most frequent lymph node pathology diagnosed was reactive hyperplasia, 45 (33.1%), followed by 35 (25.7%) metastatic carcinomas. The most common types of carcino-

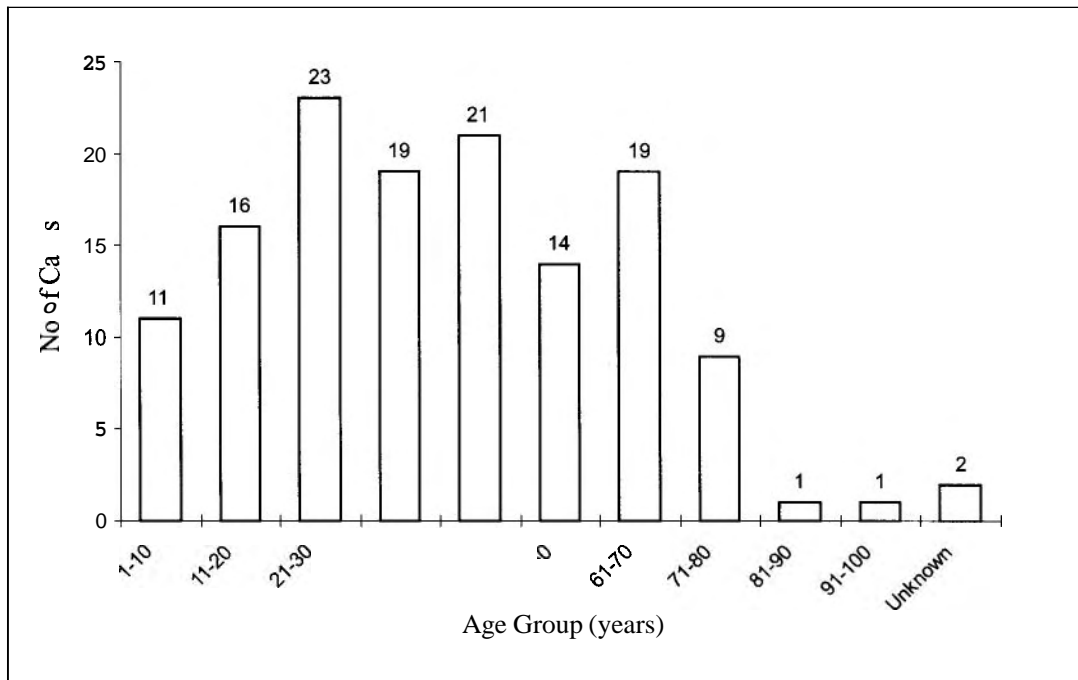


FIG. 1: Age distribution of patients with lymph nodes excised for primary investigation in B.P. Clinical Lab, Ipoh in the year 1997.

mas were undifferentiated carcinoma followed by adenocarcinoma (Table 2). There were 17 (12.5%) cases of malignant lymphomas. Six of these were Hodgkin's lymphoma (3 nodular sclerosing, 2 lymphocyte rich and 1 lymphocyte predominant) and 11 were non-Hodgkin's lymphoma (2 large- cell not otherwise specified, 2 B- cell large- cell type, 2 follicular lymphoma grade 1, 3 follicular lymphoma grade 2, 1 mantle cell lymphoma and 1 peripheral T-cell lymphoma-angioimmunoblastic lymphadenopathy, PTCL-AILD like). The common non-malignant lymphadenopathies encountered were tuberculous lymphadenitis 19 (14.0%) and Kikuchi's disease 11 (8.1%). The ratio of malignant: non-malignant lymphadenopathy was 1: 1.6.

There were more females than males in all types of lymph node pathology, except for metastatic carcinoma which was encountered more in males (Table 1). All cases of Kikuchi's disease were female.

Non-malignant lymphadenopathy occurred more frequently in the younger adults and the paediatric group. Malignant lymphadenopathy i.e. malignant lymphomas and metastatic carcinomas occurred more commonly in the older age groups. The mean age at presentation for metastatic carcinomas and malignant lymphomas were 57.4 and 59 years respectively.

University Hospital, Kuala Lumpur (UHKL)

In the UHKL series, there were 23 male and 30 female patients, giving a male: female ratio of 1: 1.3. There were 11 (20.8%) Malays (M), 30 (56.6%) Chinese (C), 11 (20.8%) Indians (I) and one (1.9%) Eurasian (O). The M: C: I: O ratio was 1: 2.8: 1: 0.1 (Table 2). The age of these patients ranged from one year to 77 years old, with the mean age of 33 years. Eleven (20.8%) cases were from the paediatric age group. Fig. 2 shows that there is a higher percentage of paediatric cases being encountered in UHKL when compared to the private laboratory.

The most common site of biopsies was from the head and neck region, especially the cervical group of nodes (27/53, 50.9%). The most frequently seen lymph node pathology was malignant lymphoma [19 cases (35.8%)]. 3 of these were Hodgkin's lymphoma (HL), there being one each of nodular sclerosing, lymphocyte-depleted and lymphocyte-predominant sub-type. 16 were non-Hodgkin's lymphoma (NHL). The latter group consisted of 2 T-cell type, 12 B-cell large- cell type, 1 follicular lymphoma and 1 anaplastic large cell lymphoma of non-B, non-T type. The ratio of HD: NHL was 1: 5.3. Other common lymphadenopathies seen were 18 (34.0%) reactive hyperplasia and 7 (13.2%) metastatic carcinomas.

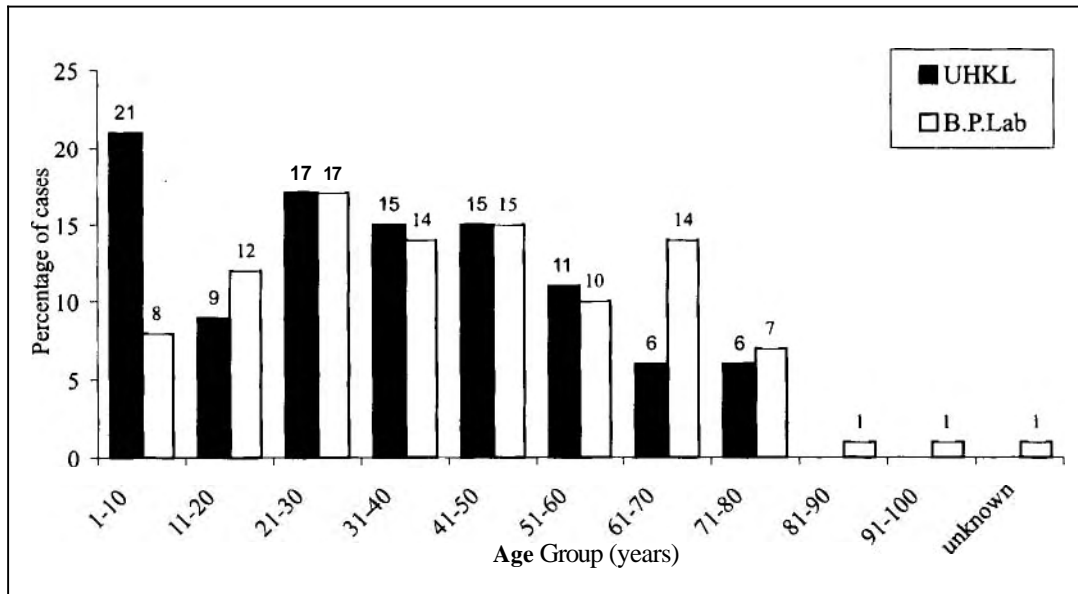


FIG. 2: Comparison of lymph node pathology by age group in UHKL and B.P. Clinical Lab, Ipoh in the year 1997.

TABLE 1: Distribution of lymph node pathology by ethnic group, gender, mean age and site of biopsy in B.P. Clinical Lab, Ipoh

Diagnosis	Ethnic			Gender		Age Mean Age years	Site			
	Malay No. (%)	Chinese No. (%)	Indian No. (%)	Other No. (%)	Male No. (%)		Female No. (%)	Head & Neck	Deep nodes*	Axillary/ Inguinal
Metastatic Carcinoma	3 (2.2)	31 (22.8)	-	1 (0.7)	18 (13.2)	17 (12.5)	30	1	4	-
Lymphomas	2 (1.5)	12 (8.8)	3 (2.2)	-	8 (5.9)	9 (6.6)	13	-	1	3
Reactive Hyperplasia	3 (2.2)	37 (27.2)	5 (3.7)	-	19 (14.0)	26 (19.1)	36	2	3	4
Tuberculous Lymphadenitis	3 (2.2)	15 (11.0)	1 (0.7)	-	9 (6.6)	10 (7.4)	18	-	-	1
Kikuchi's Disease	2 (1.5)	7 (5.2)	2 (1.5)	-	-	11 (8.1)	10	-	-	1
Miscellaneous	-	6 (4.4)	3 (2.2)	-	4 (2.9)	5 (3.7)	5	1	2	1
TOTAL	13 (9.6)	108 (79.4)	14 (10.3)	1 (0.7)	58 (42.6)	78 (57.4)	112	4	10	10

* Biopsy from mesenteric, iliac, peripancreatic and hilar nodes.

DISCUSSION

Lymph node biopsies constituted 1.6% (136/8483) of all surgical pathology material received by B.P. Clinical Lab in the year 1997 (Table 2), whereas it constituted only 0.5% (53/9968) of the material received by the UHKL laboratory.

One possible reason for this difference is that lymph node excision, especially of superficial nodes is a relatively easy procedure. It can be performed without the need of extensive supportive facilities, such as in small surgical clinics. Furthermore, government hospitals

TABLE 2: Comparison of lymph node pathology in the University Hospital Kuala Lumpur and BP Clinical Lab, Ipoh

	University Hospital	B.P. Clinical Lab, Ipoh
Total Biopsy in year 1997	9968	8483
No of cases under study	53 (0.5%)	136 (1.6%)
Gender:		
Male	23 (43.4%)	58 (42.6%)
Female	30 (56.6%)	78 (57.4%)
Ethnic Groups:		
Malay	11 (20.8%)	13 (9.6%)
Chinese	30 (56.6%)	108 (79.4%)
Indian	11 (20.8%)	14 (10.3%)
Others	1 (1.9%)	1 (0.7%)
<u>Malignant Lymphadenopathy</u>	26 (49.0%)	52 (38.2%)
Metastatic Carcinoma	7 (13.2%)	35 (25.7%)
Adenocarcinoma	1	9
Nasopharyngeal (NPC)	-	8
Papillary	3	1
Squamous cells	1	4
Small cells/ oat cells	-	3
Undifferentiated	-	10
Unspecified	2	-
Malignant Lymphoma	19 (35.8%)	17 (12.5%)
Hodgkin's Lymphoma	3	6
Non-Hodgkin's Lymphoma	16	11
<u>Other Lymphadenopathy</u>		
Reactive Hyperplasia	18 (34.0%)	45 (33.1%)
<u>Lymphadenitis</u>	9 (17.0%)	39 (28.7%)
Tuberculous lymphadenitis	3 (5.7%)	19 (14.0%)
Kikuchi's Disease	-	11 (8.1%)
Miscellaneous	6 (11.3%)	9 (6.6%)
No Pathology	5	-
Non-specific lymphadenitis	1	3
Castleman's Disease	-	2
Cat-scratch disease	-	2
Kimura's Disease	-	1
Sarcoidosis	-	1

normally perform more major complicated and massive operations and thus 'dilute down' the numbers of lymph node biopsies. The facility for fine needle aspiration cytology provided in UHKL is another possible reason for the reduction of lymph node excision for primary investigation.

The male: female ratio was similar in both private and government pathology laboratory. Ethnic Chinese was noted to be the predominant ethnic group presented with primary nodal pathology in UHKL and also the private medical facilities, being 56.6% and 79.4% respectively. 89.7% of the B.P. Clinical Lab cases in this series (data not shown) were received from the district of Kinta. This higher proportion of ethnic Chinese cases possibly reflects the ethnic pattern in the utilisation of the private medical service since the State Population Report 1991⁸ showed that ethnic Chinese only constituted 52.2% of the population in the district of Kinta, followed by Malays 32.7%, Indians 14.3% and others 0.8%.

The spectrum of lymph node pathology encountered in both private and government laboratories did not differ significantly. Reactive hyperplasia was commonly diagnosed in both the laboratories. However, malignant lymphomas were more commonly reported in UHKL (35.8%) when compared to B.P. Clinical Lab, Ipoh (12.5%). The nodal HL: NHL ratio was 1: 1.8 in the private laboratory and 1:5.3 in UHKL. However, in another larger study of 232 cases of combined nodal and extranodal malignant lymphomas from UHKL from 1987 to 1992 showed a HL: NHL ratio of 1: 9.² The data of General Hospital Kuala Lumpur based on the study of 33 cases of nodal lymphomas from year 1983 to 1987 showed a ratio of 1:4.3.³ Hence, the apparent higher prevalence of Hodgkin's lymphoma seen in the private laboratory was probably the result of relatively small numbers of cases studied in one year.

There were more metastatic carcinomas and tuberculous lymphadenitis encountered in the private laboratory when compared to UHKL. 31/35 (88.6%) of the metastatic carcinomas seen in the private laboratory was observed in Chinese. Six out of eight cases of metastatic nasopharyngeal carcinoma (NPC) was noted in Chinese males, which reconfirms the experience recorded by others.^{4-6,9}

We noted that tuberculous lymphadenitis was commonly encountered in cervical lymph node excisions. The majority of patients were in their

third decade of life. This finding was similar to another published report.¹ Recent studies showed the association of tuberculosis and HIV infection,^{10,11} emphasising the need of further investigation to elucidate the disease trend in the country.

Kikuchi's disease was diagnosed only in females in this study. This concurs with other reports^{12,13} that showed the disease to be more prevalent in the female gender.

CONCLUSION

The spectrum of lymph node pathology in the private medical service did not differ much from UHKL. However, the proportion of disease groups differed. The most common nodal pathologies seen in the private laboratory was reactive hyperplasia followed by metastatic carcinoma. Lymphomas constituted only 12.5% of the cases. Head and neck nodes, particularly the cervical lymph nodes, were the most commonly excised.

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REFERENCES

1. Bosco J, Cheriah R, Lin HP, Pang T. A survey of Lymphoid malignancy at UHKL, Malaysia. Pathogenesis of Lymphoma and Leukaemia, 1984: 61-5.
2. Peh SC. Symposium 6: The pattern of malignant lymphoma. 2nd National Conference of Haematology, 1997: 66-7.
3. Mancer K. The spectrum of lymphoma in Malaysia: a histopathological study utilising immunophenotyping. Malays J Pathol 1990; 12: 77-88.
4. Chong SM. Malignant Neoplasm at the University Kebangsaan Malaysia, 1980-1984. Malays J Pathol 1986; 8: 41-8.
5. Thanaletchumy N. A review of malignancy at the Pathology Department, General Hospital, Kuala Lumpur. Malays J Pathol 1988; 10: 51-60.
6. Lim KG. A review of diseases in Malaysia: Cancers. Petaling Jaya: Pelanduk Publication, 1993: 80-119.
7. Jayalakshmi P, Malik AK. Histopathology of lymph node tuberculosis-University Hospital experience.

- Malays J Pathol 1994; 16 : 43-7.
8. State Population Report-Perak: Population and Housing Census of Malaysia 1991. **Kuala Lumpur**: Department of Statistic Malaysia, 1995: 6-10.
 9. Chua CL. The value of cervical lymph node **biopsy**-a surgical audit. Aust N Z J Surg 1986; 56: 335-9.
 10. Bekedam HJ, Boeree M, Kamenya A et al. Tuberculous lymphadenitis, a diagnostic problem in areas of high prevalence of HIV and **tuberculosis**. Trans R Soc Trop Med Hyg 1997; 91: 294-7.
 11. Cavert W. Preventing and treating major opportunistic infections in AIDS. What is new and what is still true. Postgrad Med 1997; 102: 125-40.
 12. **Aqel N**, Henry K, **Woodrow D**. **Skin** involvement in Kikuchi's disease. Virchows-Arch 1997; 430: 349-52.
 13. Ma DD, **Hollis RR**, Delbridge L. Histiocytic necrotising **lymphadenitis** (Kikuchi's Disease). Aust N Z J Med 1986 Oct; 16: 711-3.