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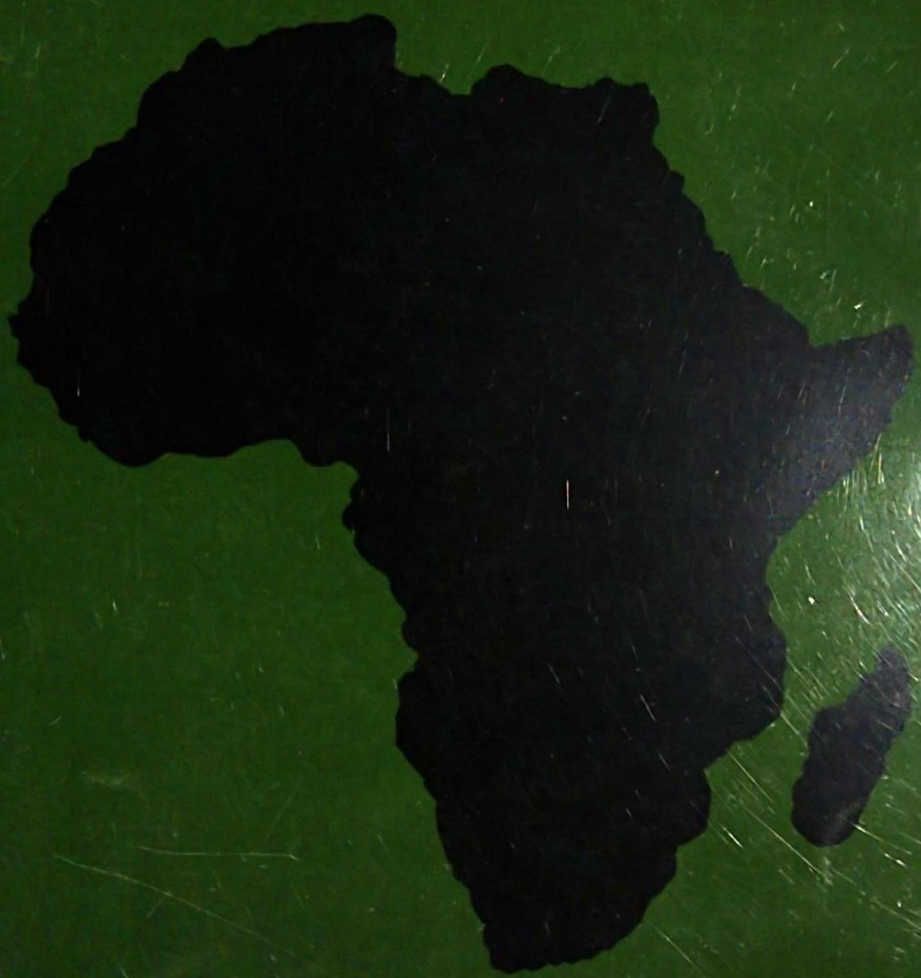

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Peripheral lymphadenopathy in Nigeria

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Summary

A review was carried out on the histopathological diagnosis of peripheral lymph node biopsies processed and reported within a period of 18 years (1979–1996) in the Department of Pathology of University of Ilorin Teaching Hospital, Ilorin, Nigeria. A total of 751 cases from 468 male and 283 female patients within the age range of 1 year to 80 years were reviewed. Non-neoplastic lesions made up 50.8% while neoplastic lesions constituted 49.2%. Tuberculosis was the commonest cause of peripheral lymphadenopathy (31.4%) followed by metastatic lesions (19.3%). As a group, the lymphomas constituted 28.2% and were made up of Hodgkin's disease 12.6%, non-Hodgkin's lymphoma including Burkitt's lymphoma 15.6% (with Burkitt's alone constituting 3.3%). Few other infectious diseases found included toxoplasmosis, histoplasmosis and onchocerciasis. Non-specific reactive and inflammatory changes (both acute and chronic) collectively formed 17.6%.The primary sites of lymph node metastases could not be determined in 36.6% of metastatic lesions while the breast was the origin in 13.8% and was the highest incidence of metastatis. The commonest lymph node group affected was the cervical (42.6%) followed by inguinal (24.1%).

Keywords: *Peripheral lymphadenopathy, tuberculosis, metastatic cancer, lymphoma, non-specific reactive lymphadenitis.*

Résumé

Une revue a été faite sur le diagnostic histopathologique du lymphe périphérique de biopbie procédéc et reporte durant une période de 18 ous (1979 – 1996) ou département de pathologie du cnetre hospitalier universistaire d' Ilorin, Ilorin, Nigeria. Un total de 751 cas parmi 468 hommes et 283 femmes malades agés de 1 á 80 ous ont été revue les lésion non-néoplastiques formaient 50,8% alors que les lésions néoplastiques constitvaient 49,2%. La tuberculose était la cause commune de la lymphadenopatie périphérique (31,4%) suixie des lésions métastatiques (19,3%).néoplastiques constitvaient 49,2%. La tuberculose était la cause commune de la lymphadenopatie périphérique (31,4%) suixie des lésions associé á hodgkin avec les lymphomas de Burkitt (15,6%) (Avec Burkit métastatiques (19,3%). Comme un group, les lymphomas constituaient 28,2% et. faisaient part de la maladie de hodgkin (12,6%), les lymphomas non associe a lHodgkin avec les lymphomas de Burkitt (15,6%) (Avec Burkit seulement constituant 3,3%). Trés peu de maladeies infectienses trouvées sont: la toxoplasmos, l'histoplasmose et l'onchocercose. Les changements réaitif non-spécifique et inflammatoire (tons deux sévére et chronique) formaient collectivement 17,6%. Les sites primaires du lymphe inflammatoire (tons deux sévére et chronique) formaient collectivement 17,6%. Les sites primaires du lymphe métastase ne pouraient pas être déterminés dans 36,6% des cas de lésion métastaique, alors que le sein était á l'origine dans 13,8% des cas et était le taux le plus élevé de métastate. The group commum de node lymphatique le plus affecté était le con (42,6%) suivi de l'inguinale (24,1%).

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Introduction

Peripheral lymph node enlargement is commonly encountered in clinical practice in the tropics and biopsy of such nodes are important not for diagnostic purpose alone but for clinical staging as well as predicting prognosis in malignant diseases.

This study is a retrospective review of cases of peripheral lymph node biopsies seen in the Department of Pathology of University of Ilorin Teaching Hospital, Ilorin, Nigeria within a period of 18 years (1979–1996). Similar studies have been carried out in other parts of Nigeria [1-6] and Africa [7]. Some of these studies have come up with clear-cut patterns of lymph node diseases, whether inflammatory or neoplastic, in the localities where they were done with far-reaching benefits both therapeutically and epidemiologically. We considered it necessary to embark on this study to elucidate the pattern of lymph node diseases in our own centre.

Materials and methods

The data for this study was obtained from records in the Department of Pathology of the University of Ilorin Teaching Hospital, Ilorin, Nigeria. All the cases of peripheral lymph node biopsies processed and diagnosed in the department from January 1979 to December 1996 (18 years) were extracted from the histopathology register and duplicate copies of reports. Previous haematoxylin and eosin (H & E) slides were reviewed while special stains such as Ziehl-Neelsen (ZN), periodic acid Schiff (PAS), reticulin and methyl green pyronin (MGP) were employed where appropriate for the diagnosis of specific diseases

Results

Seven hundred and fifty one (751) cases of peripheral lymph node biopsies were studied. There were 468 (62.3%) cases in males and 283(37.7%) cases in females giving a male, female ratio of 1.7:1 in patients between the ages of 1 to 80 years (Table 1). The highest incidence of lymph node enlargement occurred in those below 20 years of age. They constitued 31,4% and were followed by those between 40 – 59 years wgho accounted for 23,0% of cases.

Tuberculosis was the commonest disease constituting 31.4% of cases. Few other infectious disesases such as onchocerciasis, histoplasmosis and toxoplasmosis were seen. About 10.5% were cases of reactive hyperplasia

Table 1: Distribution of lymph node diseases by age and sex

Diagnosis	0-19	20-39	40-59	60-79	≥ 80	Age unspecified	M:F	Total	%
Tuberculosis	118	57	31	13		17	115:121	236	31.4
Metastasis	5	24	58	49	1	8	84:61	145	19.3
Hodgkin's Lymphoma	20	32	28	9		6	65:30	95	12.6
Non-Hodgkin's Lymphoma	8	13	25	30	1	15	67:25	92	12.3
Non-specific Reactive changes	40	11	13	11		4	54:25	79	10.5
Chronicnon-specific lymphadenitis	12	10	11	8	1	4	41:5	46	6.1
Burkitt's Lymphoma	22	3					16:9	25	3.3
Leukaemic infiltrate	2	5	5	1			12:1	13	1.7
Toxoplasmosis	6	1	1				7:1	8	1.1
Acute pyogenic inflammation	2	2	1	1	1		3:4	7	1.0
Histoplasmosis	1	1		1			2:1	3	0.4
Onchocerciasis		2					2:-	2	0.3
Total	236	161	173	123	4	54	468:283	751	100.0
%	31.4	21.5	23.0	16.4	0.5	7.2	62.3:37.7	100	

while chronic non-specific and acute pyogenic inflammatory conditions made up 6.1% and 1% of cases, respectively.

All other cases were malignant diseases either primary or metastatic. Altogether, malignant lymph node diseases made up 49.2% of all the lesions seen. Metastatic lymph node diseases constituted 19.3%, Hodgkin's lymphoma 12.6%, non-Hodgkin's lymphoma including Burkitt's lymphoma 15.6% (Burkitt's alone, Fig. 1, constituted 3.3%) while leukaemic infiltrate made up 1.7%.

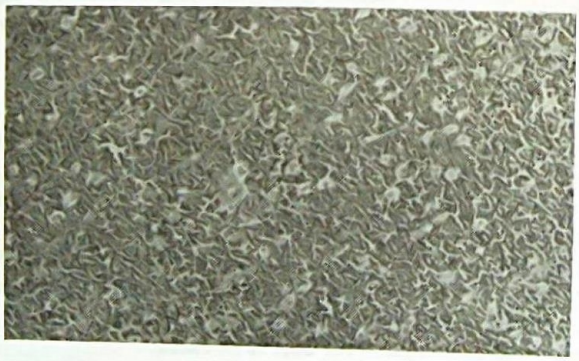

Fig. 1: Burkitt's lymphoma section shows "starry-sky" appearance (H & E x 160

The subclasses of the 95 cases of Hodgkin's disease seen were lymphocyte predominance 36, mixed cellularity 24, nodular sclerosis 21 and lymphocyte depleted 14.

The origin of metastatic tumours (Table 2) could not be determined in 36.6% of cases while 13.8% were from the breast. Next was squamous cell carcinoma (from the skin) which accounted for 11.8% and malignant melanoma (from the foot) which constituted 8.3%. The stomach and nasopharynx accounted for 6.2% and 4.1%, respectively. As it is to be expected, metastates were more to the lymph node groups draining the diseased organs before spreading to more distant sites. This was evident in breast carcinoma where 17 of the 20 cases metastasized to the axillary while 2 metastasized to the supraclavicular lymph nodes. The cervical lymph nodes had the highest incidence of metastasis accounting for 42.8% (Table 2). This was followed by the inguinal and axillary lymph nodes, which made up 24.8% and 22.1%, respectively.

Overall, the anatomical distribution of lymph node diseases from various sites is shown in Table 3. The cervical lymph nodes had the highest involvement of 42.6%. The inguinal and axillary lymph nodes accounted for 24.1% and 19.9%, respectively. About 4.5% of the diseases involved more than one group of lymph nodes and 44% of lesions belonging to this group (i.e., multiple sites) were cases of non-Hodgkin's lymphoma.

Table 2: Primary origins of metastatic tumours

Origin	Cervical	Inguinal	Axillary	Supra-Clavicular	Sub-mandibular	M:F	Total	%
Undetermined	27	8	14	4		30:23	53	36.6
Breast	1		17	2		-:20	20	13.8
Skin(Squamous cell carcinoma)	8	8		1		11:6	17	11.8
Foot(Malignant Melanoma)		12				10:2	12	8.3
Stomach	7			2		7:2	9	6.2
Naso-pharynx	5				1	4:2	6	4.1
Lung	4			2		4:2	6	4.1
Thyroid	3			2		3:2	5	3.4
Colon	1	4				4:1	5	3.4
Prostate	3	1	1			5:-	5	3.4
Liver	2	1		1		3:1	4	2.8
Kidney	1	1				2:-	2	1.4
Urinary Bladder		1				1:-	1	0.7
Total	62	36	32	14	1	84:61	145	100.0
%	42.8	24.8	22.1	9.6	0.7	57.9:42.1	100	

Discussion

The findings in this study clearly show that the spectrum of infectious diseases usually encountered in the tropics does not feature prominently as a cause of superficial lymph node enlargement. Tuberculosis was the singular disease that caused the highest incidence of peripheral lymphadenopathy. It accounted for 31.4%. This is similar to the findings of Obafunwa *et al.* [1] at Jos where tuberculosis was also the leading cause of peripheral lymphadenopathy although it occurred in 48% of cases, a figure that is higher than ours. In Ibadan, Attah [2,3] and Thomas *et al.* [4] reported non-specific (reactive) change as the leading cause of peripheral lymph node enlargement. Over 50% of the cases of tuberculosis in our study involved the cervical lymph node, a finding that agrees with many previous studies [1,4-6]. This may not be unexpected since the primary organs infected are the lungs with drainage through the hilar nodes to the mediastinum and the neck. About 50% of the cases of tuberculosis occurred in people below 20 years, a finding similar to that of Thomas *et al.* [4] in Ibadan. These indicate that the neck lymph node is the most frequent site for extra-pulmonary tuberculosis and that cervical node tuberculosis is most common in children and adolescents.

A very important finding in this study is the preponderance of tuberculous lymphadenitis in females which some other researchers have also reported [7]. This is of public health importance in the tropics where mothers' breast-feed their babies and this may account for the high incidence of the disease in children. Possible reasons adduced for the female preponderance include an inherent low resistance against the disease in females [7] and early exposure of female African children to the tubercle bacilli in the course of sweeping, hawking or assisting their mothers to trade in crowded markets with poor environmental sanitation scattered all over the continent. Other specific inflammatory conditions accounted for only 1.8% and as stated earlier, this is rather unexpected in an environment where infectious diseases are rampant. Similar low figures have however been reported in other reviews [1,5,6].

Non-specific reactive changes, chronic non-specific lymphadenitis and acute pyogenic infections accounted for 10.5%, 6.1% and 1%, respectively. As such they collectively formed 17.6% and placed third after tuberculosis and metastatic lesions. The third place of this group of lesions in our study is similar to that found by Obafunwa *et al.* [1] at Jos although non-Hodgkin's lymphoma was second after tuberculosis in the latter study. Our experience differs from that of Attah [2], Thomas *et al.*[4] and Kasili *et al.* [7]. In Ibadan, Attah [2] reported that non-specific (reactive) change was highest (33%) followed by tuberculosis (30%). At the same centre 16 years later, Thomas *et al.* [4] reported that non-specific reactive changes constituted 37%. In Kenya, Kasili *et al.* [7] reported the leading cause to be tuberculosis (44.5%) followed by non specific (reactive) change (24.9%). These variations in incidence of the non-specific reactive changes might not be unconnected with the habits, culture and practices in the various locales. Tattooing, barefoot walking, scarification/

Table 3: Anatomical distribution of lymph node diseases from various biopsy sites

Diagnosis	Cervical	Inguinal	Axillary	Supra-Clavicular	Multiple sites	Sub mandibular	Total	%
Tuberculosis	126	33	48	14	3	12	236	31.4
Metastases	62	36	32	14		1	145	19.3
Hodgkin's lymphoma	45	19	20	5	5	1	95	12.6
Non-Hodgkin's lymphoma	28	25	13	6	15	5	92	12.3
Non-specific reactive changes	28	27	20	1	2	1	79	10.5
Chronic non-specific lymphadenitis	10	27	4		4	1	46	6.1
Burkitt's lymphoma	8	6	4	1	4	2	25	3.3
Leukaemic infiltrate	2	3	7	1			13	1.7
Toxoplasmosis	7			1			8	1.1
Acute pyogenic inflammation	2	3	1			1	7	1.0
Histoplasmosis	2				1		3	0.4
Onchocerciasis		2					2	0.3
Total	320	181	149	43	34	24	751	100.0
%	42.6	24.1	19.9	5.7	4.5	3.2	100	

tribal marking, etc., are common practices in different parts of Africa and these will no doubt produce reactive changes in the lymph nodes draining the affected areas. It is pertinent to note that close to 60% of the cases of chronic non-specific lymphadenitis involved the inguinal lymph nodes. This is not surprising, as barefoot walking is a common practice in our environment. Such habits lead to repeated trauma and infections of the foot with consequent chronic inflammation and fibrosis of the inguinal lymph nodes. These are presumed to distort pathological appearances and make diagnosis of specific diseases difficult.

The 49.2% of malignant diseases (28.2% of lymphoma and 21% metastatic) agree with the 48.3% reported by Oluwole *et al.* [5] in a similar study in Ile-Ife, Nigeria. The lymphomas were made up of Hodgkin's 12.6%, non-Hodgkin's 12.3% and Burkitt's 3.3%. Burkitt's lymphoma was separated from other non-Hodgkin's lymphomas because of its peculiar occurrence in our environment in children and adolescents. About 88% of patients with Burkitt's lymphoma were below 20 years and this is the usual pattern in endemic areas such as ours [8]. It used to be said that Burkitt's lymphoma arising in the lymph node was not common and none was recorded in the review by Attah in Ibadan [2]. In Ile-Ife, Oluwole *et al.* [6] found nine cases while Obafunwa *et al.* [1] reported two cases at Jos. We found 25 cases representing 3.3% in the present study. It therefore appears that the incidence of Burkitt's lymphoma in the peripheral lymph nodes is probably not as rare as it is thought to be.

After the age of 40 years, the incidence of malignant diseases generally increased in contrast to inflammatory diseases which decreased and this agrees with the findings in Ibadan by Thomas *et al.* [4]. An exception however was Hodgkin's disease, which had a peak in children and young adults. A correlation had been postulated between the state of economic development of a nation and the incidence of childhood Hodgkin's disease [9]. This may in part explain why the disease is commoner in children and young adults in our environment. Non-Hodgkin's lymphoma gradually rises from early adult life and middle age to reach a peak in the elderly. It is more than twice common in males compared to females and these patterns are similar to the findings of Oluboyede *et al.* [10] in Ibadan.

The 21% metastatic diseases (19.3% carcinomas and 1.7% leukaemic infiltrate) were lower than the 24.49% reported by Oluwole *et al.* [6] in Ile-Ife but higher than the 16.8% recorded by Kasili *et al.* [7] in Kenya. About 36.6% of metastatic tumours in our study were of undetermined origin and agree in terms of proportion with the 34.72% reported in Ile-Ife [6]. Both studies revealed that the most common location of lymph node metastasis of undetermined primary site was the neck, a finding that had been reported in other reviews [11,12]. Furthermore the two studies reported the breast as the commonest primary site and all the cases occurred in females. Over 80% in each study metastasized to the axillary lymph node. This was so because most cases

came when the diseases were far advanced with clinically palpable axillary lymph nodes and the breast and axillary lymph nodes were usually biopsied simultaneously. Metastatic squamous cell carcinoma of the skin and malignant melanoma of the foot placed second and third, respectively, in our study while metastatic malignant melanoma placed second after breast in the study by Oluwole *et al.* [6]. It is possible that the superficial nature of these tumours was helpful in clinical evaluation of the probable cause of lymphadenopathy moreso that patients in our environment report late in hospital when such metastasis is the rule than the exception.

There were 13(1.7 %) cases of leukaemic infiltrate. The histological appearances were those of non-specific reactive lymphadenitis with pleomorphic leukaemic cells within the sinusoids. The peripheral blood pictures were indispensable corroborative features in such diagnosis.

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