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Pathology of Peripheral Lymph Node Biopsies in Kano, Northern Nigeria

[1]O. Ochicha, [2]S.T. Edino, [1]A. Z. Mohammed, [1]A. B. Umar and [1]A. T. Atanda

Departments of [1]Pathology and [2]Surgery, Bayero University and Aminu Kano Teaching Hospital, Kano, Nigeria
Reprint requests to: Dr. O. Ochicha, Pathology Department, Aminu Kano Teaching Hospital, P. M. B. 3452 Kano, Nigeria. E-mail: ochicha@googlemail.com

Abstract
Background: Lymphadenopathy is a common clinical problem here in Kano, Northern Nigeria but there has been no formal study. We therefore undertook this review to evaluate the pattern in our locality.
Method: This is a seven-year (1998-2004) retrospective review of all histologically diagnosed lymph node biopsies received at Aminu Kano Teaching Hospital, Kano.
Results: Cervical, axillary and inguinal nodes were the most frequently biopsied accounting for 46%, 23% and 13%, while tuberculosis, lymphomas and metastases were the most commonly diagnosed lesions comprising 30%, 24% and 19% respectively. In general, benign lesions were more common constituting 57% of nodal biopsies. Lymphadenopathy was observed to be most prevalent in the first three decades.
Conclusion: Our findings were broadly similar to most other Nigerian studies and slightly at variance with other African countries but significantly different from the Western World. The limitations of lymph node histopathology in the absence of modern molecular diagnostic techniques are highlighted.

Key words: Lymphadenopathy, tuberculosis, lymph node metastases, reactive hyperplasia

Résumé
Introduction: La lymphadenopathie est un probléme clinique courant ici à Kano, Nord du Nigeria, cependant il n'ya encore eu aucune étude formelle sur ce sujet. C'est pour cette raison que nous avons décidé d'entreprendre cette étude pour evaluer la distribution dans notre localité.
Méthodes: Voici une etude retrospective faite en sept ans (1998-2004) de tous les diagnostique histologique des ganglions lymphatiques reçus á Aminu Kano Teaching Hospital Kano.
Resultats: Les echantillons des ganglions cervicaux, axillaires et inguinaux etaient les plus fréquents, avec une frequence de 46%, 23% et 13% respectivement. Par ailleurs la tuberculose, les lymphomes et les metastases etaient les lesions les plus diagnostiquées avec les pourcentages de 30%, 24% et 19% respectivement.
En general, les lesions benignes etaient les plus observées avec un pourcentage de 53%. La lymphadenopathie etait plus frequente pendant les trois premiere decenies.
Conclusion: Nos resultats etaient identiques à ceux obtenus au cours des études faites dans les autres localités du Nigeria juste avec les petites differences. Ceci s'applique aussi dans le autres pays Africains, mais il ya une trés grande difference avec les pays Occidentaux. En l'absence des techniques de diagnostique moleculaire morderne, les limitations de l'histopathologie des ganglions lymphatiques ont été mentionées.

Mots clés: Lymphadenopathie, tuberculosis, metastases, les ganglion lymphatiques, hyperplasie reactive

Introduction

Lymphadenopathy is a common clinical problem, and biopsies are usually undertaken to determine the cause of nodal enlargement, which may be neoplastic or non-neoplastic. The neoplastic disorders are mainly lympho-haematogenous malignancies and metastases while the non-neoplastic causes are more varied – infections, drug reactions (including certain vaccines), lipid storage disorders and a wide variety of miscellaneous non-neoplastic lymphoproliferative disorders such as Castleman and Rosai Dorfman diseases.[1]

Published reports from within and outside Nigeria document a preponderance of non-neoplastic lesions with non-specific reactive hyperplasia predominating in the developed world, and tuberculosis the leading cause in Africa particularly with the current

HIV/AIDS pandemic. [2-9] HIV not only directly causes lymphadenopathy but is also an indirect cause via several AIDS-defining illnesses. [10]

Clinically, lymphadenopathy may be peripheral or visceral. Peripheral lymphadenopathies are easily detected by routine physical examination and are often biopsied as they are easily accessible for lymphadenectomy, which is a minor surgical procedure. Visceral lymphadenopathy on the other hand, requires laparatomy or sophisticated imaging techniques for detection.

Among the peripheral nodes, those in the upper part of the body (cervical, supraclavicular, axillary) are preferentially biopsied than lower limb nodes (popliteal, inguinal or femoral) as the former are more likely to yield definitive diagnosis whereas the latter are often characterized by non-specific reactive or chronic inflammatory and fibrotic changes. [1, 3]

Materials and Methods

This is a retrospective study of histologically diagnosed lymph node biopsies at the histopathology laboratory of Aminu Kano Teaching hospital, Kano, Nigeria from 1998 – 2004. This is the referral centre offering histopathology services to Kano and neighbouring states of Jigawa, Kastina and Bauchi.

Histology slides of all cases were reviewed and clinical data (age, sex, site) obtained from histology request forms and register. All slides were made from paraffin embedded blocks, then routinely stained with haematoxylin and eosin. Special stains like Ziehl-Neelson were employed where necessary. Immunohistochemistry, cytogenetics and molecular diagnostic techniques like lymphocyte receptor gene rearrangements were not employed as these are not available in our laboratory. Consequently, our classification of non-Hodgkin lymphomas was based on the working formulation. [11]

Results

Three hundred and fifty six peripheral node biopsies were received during the period under review, accounting for 5% of all surgical biopsy specimens. Two hundred and three of these were from males and 153 from females (M: F = 1.3: 1).

Table 1 presents the histological diagnoses and age distribution of lymph node biopsies in Kano. Lymphadenopathies mostly occurred in the first three decades of life, with a gradual decline in prevalence after the 3rd decade.

Benign lesions were more common comprising 57% (249 cases), and tuberculosis (TB) was by far the most frequent cause accounting for 29.5% (105 cases) of peripheral lymphadenopathy in this series. TB was most prevalent in children and young adults with 80% of cases in the first three decades of life. Reactive hyperplasia (mostly follicular and paracortical) were the second commonest non-neoplastic lesion occurring in 19% of nodal biopsies in Kano.

Malignancies comprised 43% of enlarged peripheral lymph nodes, with lymphomas predominating accounting for 24%, making them collectively the second most prevalent cause of lymphadenopathy in this series. Among the lymphomas, non-Hodgkin lymphomas (NHLs) were more common accounting for 14% of lymphadenopathies, with intermediate and high-grade types predominant comprising 38% and 33% of NHL respectively (Table 2). Hodgkin's disease (HD) constituted 10% of lymphadenopathies with mixed cellularity as the commonest form comprising 39% (Table 3).

Metastases constituted the remaining malignancies representing 19% of palpably enlarged peripheral nodes. Breast cancer involvement of axillary nodes was the most frequent (38%) cause of lymph node metastases, followed by involvement of cervical nodes by carcinomas of the nasopharynx, thyroid & salivary glands. Eight lymph node biopsies were characterized by non-caseous granulomas, three of which had necrotic foci with neutrophils suggestive of lymphogranuloma venereum or cat-scratch disease. The remaining five were mostly granulomas without caseation or other specific features. Other lesions included Kaposi sarcoma, chronic inflammatory fibrosis, acute lymphadenitis and nodes without significant pathology.

Cervical, axillary and inguinal were the most frequently biopsied comprising 46%, 23% and 13% respectively Table 2).

Table 1: Histological diagnosis and age in 356 patients with lymph node biopsies

Histological diagnosis	Age (years)							Total (%)
	≤10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 60	>60	
Tuberculosis	27	29	28	16	2	3	-	105 (29.5)
Reactive hyperpalsia	21	14	10	10	7	3	3	68 (19.1)
Metastases	-	-	9	14	26	11	8	68 (19.1)
Non-Hodgkin lymphoma	12	8	6	6	7	6	3	48 (13.5)
Hodgkin's lymphoma	6	8	9	2	5	6	-	36 (10.1)
Non-caseous granulomas	1	3	3	-	1	1	-	8 (2.2)
Others	5	3	4	4	5	2	1	23 (6.7)
Total	72	64	68	51	53	32	15	356 (100)

Table 2: Site of lymph node biopsies in 356 patients

Diagnosis	Cervical	Axillary	Inguinal	Others	Total (%)
Tuberculosis	61	22	3	19	105 (29.5)
Metastases	20	26	12	10	68 (19.1)
Reactive hyperplasia	21	11	16	20	68 (19.1)
Non-Hodgkin lymphoma	27	11	3	7	48 (13.5)
Hodgkin lymphoma	25	7	2	2	36 (10.1)
Non-caseous granulomas	3	2	2	1	8 (2.2)
Others	7	4	7	6	23 (6.7)
Total (%)	163 (46)	83 (23)	45 (13)	65 (18)	356 (100)

Table 3: Nodal lymphomas in 84 patients

Histological type	No. (%)
Non-Hodgkin's	
Low grade	14 (29)
Intermediate grade	18 (38)
High grade	16 (33)
Total	48 (100)
Hodgkin's	
Lymphocyte predominant	4 (11)
Lymphocyte rich	5 (14)
Nodular sclerosing	11 (30)
Mixed cellularity	14 (39)
Lymphocyte depleted	2 (6)
Total	36

Discussion

As in virtually all other lymph node studies within and outside Nigeria, [2 - 9] cervical nodes were by far the most frequently biopsied constituting 46% of nodal biopsies in this review. This was followed by axillary and inguinal biopsies, which comprised 23% and 13% respectively. The preponderance of cervical lymphadenopathy is a reflection of the fact that these nodes drain the upper aero-digestive tract through which most foreign antigens enter the body via inhalation or ingestion. Benign lesions were more preponderant comprising 57% of peripheral node enlargement, which is also consistent with all other studies. [2-9]

Cervical lymph node enlargement was most frequently due to tuberculosis that is also the commonest cause of all lymphadenopathy in this series accounting for 29.5%. This is comparable to other Nigerian centres - 26% in Ibadan, [12] 31.4% in Ilorin, [5] 33% in Jos [6] and 33% in Maiduguri [7] but much lower than 47.8% in Ethiopia [8] and 52% in Zambia. [9] The higher rates of tuberculous lymphadenitis in some African countries like Zambia is due to their higher HIV infection rates, tuberculosis being an AIDS-defining illness. [9, 10] In the last two decades, HIV/AIDS has also been responsible for the resurgence of tuberculosis in the Western world. [13] Prior to the HIV pandemic, tuberculosis was declining due to improved living standards. [13] Most (80%) of our tuberculous lymphadenitis were diagnosed within the first three decades of life, which is consistent with the fact that primary TB, the commonest type in childhood and adolescence chiefly involves lymph nodes. [14,15]

Collectively, lymphomas were the commonest malignancies and second most prevalent cause of palpably enlarged peripheral nodes accounting for 23.6%, which is similar to 23.8% in Ife, [15] 28.2% in Ilorin [5] and 28.8% in Jos [6] but higher than 19.1% in Maiduguri. [7] Among the lymphomas, non-Hodgkin lymphomas (NHL) were more common comprising 13.5% of histologically diagnosed lymphadenopathies while Hodgkin's disease constituted just 10%. With the exception of Maiduguri, [7] most other Nigerian studies also document a preponderance of NHL over Hodgkin's. [5, 18-20] In the western world non-Hodgkin lymphoma (NHL) is reported to be three to four times more common than Hodgkin's and the incidence is rising while that of Hodgkin's is falling. [23-25] The much higher proportion of NHL in the Western world than here in Africa, may be partly explained by racial and genetic factors as comparative studies in the United States document higher incidence among Whites than Blacks particularly for low grade follicular lymphomas.[23-25] Intermediate and low grade lymphomas accounted for over 80% of NHL in the United States, [23, 25] whereas high and intermediate grades were predominant in this review comprising 72%. Mixed cellularity was the commonest form of Hodgkin's in this series as in most other reports [18-20] from Nigeria.

Metastases comprised the remaining nodal malignancies constituting 19.1% of peripheral lymphadenopathies in Kano. Again, this is similar to reports from other parts of Nigeria [5,7,14] but significantly higher than in Zimbabwe and Ethiopia. [8, 15] In the United States metastases comprised 29% of peripheral nodal enlargement, second only to reactive hyperplasia. [2] Breast cancer involvement of axillary node was the commonest form of nodal metastases comprising 38% in this series. This reflected the growing scourge of breast malignancy, which globally is now the commonest female cancer. [21]

Reactive hyperplasia constituted nearly one-fifth (19.1%) of enlarged peripheral nodes in this study, which is comparable to 22% in Maiduguri [7] and 26% in Ethiopia [8] but lower than 29% in Ife [16] and 33% in Zimbabwe. [14]

In the United States, non-specific reactive hyperplasia is the premier cause of lymphadenopathy

comprising nearly half of all cases. [2, 4] The relative absence of tuberculosis and earlier diagnosis of malignancies before the onset of nodal metastases may explain the prominence of reactive hyperplasia in the Western world.

Several cases of granulomas lacking caseation or other specific features were seen in this review. It is possible that some of these were early tuberculosis before the development of caseous necrosis, although they were negative for acid-fast bacilli (AFB). Histological demonstration of AFB by Ziehl-Neelsen stain in tuberculosis is notorious for its poor sensitivity. [13] A study in Singapore demonstrated AFB in only 13.4%[26] of tuberculosis, while in Ibadan AFB was demonstrated in just over one quarter (27%) of cases. [12] This underscores the need for more sensitive techniques like fluorescence auramine staining, immunofluorescence and nucleic acid hybridization, which are presently unavailable in our laboratory. Sarcoidosis is also a differential diagnosis for these non-caseous granulomas but is uncommon in Africa although some reports indicate the contrary. [27] Unfortunately the absence of confirmatory Kveim test in our centre makes it impossible to confirm or refute these claims. Granulomatous lesions of unknown significance (GLUS), a newly designated entity is a differential for these non-caseous granulomas. [28]

This study was carried out using routine histochemical stains (haematoxylin and eosin and a few special stains). These are inadequate for a modern histopathology laboratory in a referral tertiary health institution, particularly as histo-diagnostic errors occur more frequently in lymph node biopsies than in other organs or tissues. [29] Immunohistochemistry and cytogenetics will go a long way to improve the diagnostic accuracy of lymphoproliferative disorders and infectious diseases like tuberculosis. Proper histological classification of lymphoproliferative disorders requires molecular diagnostic techniques like immunohistochemistry and cytogenetics. It is important that these facilities are provided in Nigerian tertiary hospitals.

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