Original Article

Clinicopathological Profiles of Lymph Node Enlargement at Mayo Hospital, One Year Study

Samina Qamar, Shahid Mahmood, Ahmad Hameed and Sobia Ashraf

ABSTRACT

Objective: This study aimed at evaluating the causes of lymphadenopathy and demographic distribution of patient load at mayo hospital, Lahore.

Study Design: Descriptive / cross-sectional study.

Place and Duration of Study: This study was conducted at the Pathology Department King Edward Medical University/ Mayo Hospital, Lahore from January 2016 to December 2016.

Materials and Methods: All lymph node biopsies were reviewed at histopathology section of Pathology Department King Edward Medical University/ Mayo Hospital, Lahore. Demographic details of patients, site of lymph node enlargement and diagnoses of lymph node biopsy were recorded on proforma. SPSS 21 and descriptive statistics were used to obtain results of age, gender, site of lymphadenopathy, residential address and diagnoses were evaluated.

Results: Total of 308 cases were included in study. Most common cause was reactive hyperplasia 218(70.8%), 56 (18.2%) showed Tuberculosis, 14 (4.5%) exhibited metastatic carcinoma, 9 (2.9%) were labeled as Atypical lymphoprolifertaive disorder, 6 (1.9%) were of Non-Hodgkin lymphoma, 3 (1.0%) of Hodgkin lymphoma and 2 (0.6%) of abscess. 206(66.9%) patients were from Lahore, 43 (14.0%) from Sheikhupura, 19 (6.2%) from Narowal, 17 (5.5%) from Nankana, 11(3.6%) from Okara, 7(2.3%) from Mianwali and 5 (1.6%) belonged to Bahawalnagr.

Conclusion: Reactive lymph node enlargement is most common cause of lymphadenopathy in tertiary care setup. Tuberculosis is second most common cause, seen more in females. Mayo Hospital is catering a large number of patients from cities other than Lahore. It is suggested that tertiary care services should be strengthened in areas surrounding Lahore to lower patient burden and improve health facilities at Mayo Hospital. Government hospitals should be equipped with special tests like immunomarkers and molecular techniques to precisely diagnose lymphoid malignancies.

Key Words: Atypical Lymphoproliferative disorder, Demographic, Hodgkin Lymphoma, Lymphadenpathy, Non-Hodgkin Lymphoma, Tuberculosis.

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INTRODUCTION

Lymph nodes are organized centers of immune cells that filter antigens from extracellular fluid. Lymph is ultra-filtrate of blood that passes through lymph node to get screened for antigens.[1] Lymph nodes change their size and shape according to age, location and antecedent immunological consequences. If their number, size or consistency changes they are considered abnormal and result in lymphadenopathy[2].

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Lymphadenopathy of inflammatory type is called lymphadenitis. Common causes of lymphadenopathy range from common cold to autoimmune diseases to cancers[3]. Since lymph nodes are superficially located they are available for Fine needle aspirations and biopsy for histopathological evaluation that is considered gold standard for confirmation of pathology underlying node enlargement. Reactive enlargement of lymph nodes can also occur due to internal malignancy[4]. Since many infections can mimic malignancy and vice versa, lymphadenopathy requires careful screening[5]. Clinical history of fever, weight loss, isolated/ multiple node enlargements are important signs in evaluating patients presenting with lymphadenopathy.[6] According to World Health Organization (WHO) 8.6 million people are affected with tuberculosis (TB) worldwide[7]. Most of the reported cases are from Asia (58%) and Africa (27%), with highest incidence in India (2.4 million) and China (1.1 million). Pakistan is 5th amongst countries with highest burden of TB and 4th highest in drug resistant

Tuberculosis. 420,000 new cases occur annually in Pakistan. Still there is under-detection and under-notification of TB[8]. As no tertiary care hospital is equipped with facility of immunomarkers, lymph node biopsies that do not fulfill the criteria of completely benign or malignant features have to be labeled as atypical lymphoid disorder or atypical lympho-proliferative disorder (ALP)[9].

MATERIALS AND METHODS

All lymph node biopsies received at Pathology department of King Edward Medical University (KEMU) were collected from January 2017 to December 2017. Patients presenting with lymphadenopathy were included in study after taking their informed consent. History regarding site of lymph node enlargement and residential address of patient (resident of area for past five years) was noted along with age and gender. Inadequate or insufficient tissue was excluded from study. All biopsies were received in formalin. Tissue was processed; slides were prepared and stained with Hematoxylin-Eosin stain. Slides were examined by two consultant pathologists and diagnosis was noted on the proforma. Patient's identity, age, gender, residence, site of lymph node biopsy, diagnosis was noted. All data was entered in SPSS 21 and descriptive statistics were used to obtain results of age, gender, site, residence and diagnosis. All variable were analyzed be descriptive statistics. Chi-Square test was used to see association between gender and diagnosis and frequency of various diagnoses among different areas of patient presentation.

Sampling Technique: Non-probability purposive sampling

Inclusion Criteria: All adequate lymph node biopsies were included.

Exclusion Criteria: Insufficient tissue or tissue that showed autolysis or crushing was excluded.

RESULTS

Our results showed that during year 2017, 308 cases of lymph node biopsy were received at pathology department, KEMU. Out of 308, 149 (48.4%) were males and 159 (51.6%) were females. Their ages ranged from 1 to 89 years and mean age was 25.1 ±16.89. Most common site of lymphadenopathy was cervical and then mesenteric both in males (31.8%, 8.4% respectively) and females (35.4%, 5.8%). After cervical and mesenteric, axillary (3.9%) and supraclavicular (1.6%) nodes were more commonly enlarged in females. Males presented more commonly with Inguinal (4.2%) and submandibular node (1.6%) enlargement when compared with females (Table I). Among male patients 108 (35.1%) were reactive, 1 (0.3%) showed abscess, 23 (7.5%) had TB, 4 (1.3%) showed ALP, 4 (1.3%) were of NHL, 2(0.6%) had HD, and 7 (2.3%) had metastatic carcinoma. In females 110 (35.7%) were reactive, 1(0.3%) had abscess, 33 (10.7%) had TB, 5 (1.6%) showed ALP, 2 (0.6%) had NHL, 1 (0.3%) had HD and 7 (2.3%) had metastatic disease. Regarding areas from where patients belonged 206 (66.9%) were from Lahore, 43(14%) from Sheikhupura, 19(6.2%) from Narowal, 17(5.5%) from Nankana, 11(3.6%) from Okara, 7(2.3%) from Mianwali, 5(1.6%) from Bahawalnagar. Most common site of lymphadenopathy was cervical lymph node enlargement 207 (67.2%), then mesenteric 44 (14.3%), inguinal 24 (7.8%), axillary 17 (5.5%), submandibular 9 (2.9%) and supraclavicular 7 (2.3%). The diagnosis of lymphadenopathy varied from reactive to malignancy as follows: 218 (70.8%) were reactive, 56 (18.2%) showed TB, 14 (4.5%) exhibited metastatic carcinoma, 9 (2.9%) were labeled as Atypical lymphoprolifertaive disorder, 6 (1.9%) were of Non-Hodgkin lymphoma, 3 (1.0%) of Hodgkin lymphoma and 2 (0.6%) of abscess. As we observed relationship of malignancy to site of lymph node enlargement, we concluded that out of 308 cases 276 (89.6%) were reactive, 9 (2.9%) remained undiagnosed as ALP and 23 (7.4%) showed malignancies. Most common site of metastatic malignancy presentation was cervical node (69.5%), then axillary (17.3%) then submandibular, inguinal and mesenteric (4.3% each). No malignancy was seen in supraclavicular lymph node. (Table II) Among the population of Lahore residents 146 (47.4%) were reactive, 40 (13 %) had tuberculosis, 9 (2.9%) had metastatic carcinoma, 5 (1.6%) were diagnosed as ALP, 3(1%) had NHL 2 (0.6%) had HD and only 1 (0.3%) had abscess. From Sheikhupura 26 (8.4%) patients had reactive nodes, 10 (3.2%) had tuberculosis, 2 (0.6%) had ALP, NHL and Metastasis each. Only 1(0.3%) case had abscess. Group from Narowal showed 12(3.9%) to be reactive, 3 (1%) each had TB and HD and 1 (0.3%) case of NHL.

Table No.I: Site of lymphadenopathy among males and females.

Site	Male	Female	Total
Cervical	98 (31.8%)	109(35.4%)	207(67.2%)
Subman-dibular	5(1.6%)	4(1.3%)	9(2.9%)
Supracla-vicular	2(0.6%)	5(1.6%)	7(2.3%)
Axillary	5(1.6%)	12(3.9%)	17(5.5%)
Inguinal	13(4.2%)	11(3.6%)	24(7.8%)
Mesenteric	26(8.4%	18(5.8%)	44(14.3%)
Total	149(48.4%)	159(51.6%)	308(100%)

From Nankana out 17 cases 14 (4.5%) showed reactive nodes and 3(1%) had tuberculosis. Cases from Okara showed reactive hyperplasia in 9 (2.9%), 1 (0.3%) labeled as ALP and 1(0.3%) had HD. 7 (2.3%) cases belonged to Mianwali and all showed reactive hyperplasia. Cases that belonged to Bahawalnagr

showed reactive hyperplasia in 4 (1.3%) and 1(0.3%) was diagnosed as ALP. (Table 3) As we evaluated frequency of reactive hyperplasia, TB and malignancy in various age groups. We concluded that children (under 18 years) and old patients (over 70 years) presented commonly with reactive nodes. Adults (19-69 y) showed more frequent involvement with tuberculosis and metastatic malignancy. (Table 4).

Table No.2: Frequency of causes of lymphadenopathy and their sites of presentation.

Site	Reactive	TB	ALP	NHL	HD	Abscess	Metastasis
Cervical	139 (45.1%)	44 (14.3%)	6 (1.9%)	5 (16%)	2 (0.6%)	2 (0.6%)	9 (2.9%)
Submandibular	7 (2.3%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.3%)
Suprclavicular	7 (2.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Axillary	8 (2.6%)	3 (1.0%)	2 (0.6%)	0 (0%)	1 (0.3%)	0 (0%)	3 (1.0%)
Inguinal	19 (6.2%)	3 (1.0%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	1 (0.3%)
Mesenteric	38 (12.3%)	5 (1.6%)	0 (0%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
Total	218 (70.8%)	56 (18.2%)	9 (2.9%)	6 (1.9%)	3 (1.0%)	2 (0.6%)	14 (4.5%)

Table No.3: Frequencies of diagnoses from various residential areas.

Diagnosis	Lahore	Sheikhpura	Narowal	Nankana	Okara	Others	Total
Reactive	146(47.4%)	26(8.4%)	12(3.9%)	14(4.5%)	9(2.9%)	11(3.6%)	218(70.8%)
Abscess	1(0.3%)	1(0.3%)	0(0%)	0(0%)	0(0%)	0(0%)	2(0.6%)
TB	40(13%)	10(3.2%)	3(1%)	3(1%)	0(0%)	0(0%)	56(18.2%)
ALP	5(1.6%)	2(0.6%)	0(0%)	0(0%)	1(0.3%)	1(0.3%)	9(2.9%)
NHL	3(1%)	2(0.6%)	1(0.3%)	0(0%)	0(0%)	0(0%)	6(1.9%)
HD	2(0.6%)	0(0%)	0(0%)	0(0%)	1(0%)	0(0%)	3(1%)
METS	9(2.9%)	2(0.6%)	3(1%)	0(0%)	0(0%)	0(0%)	14(4.5%)
Total	206(66.9%)	43(14.0%)	19(6.2%)	17(5.5%)	11(3.6%)	12(3.9%)	308(100%)

Table No.4: Frequency of diagnosis according to age groups.

Diagnosis		Age groups			Total
		Under 18	19-69	70 and above	
	Reactive	112(36.4%)	101(32.8%)	5(1.6%)	218(70.8%)
	Abscess	1(0.3%)	1(0.3%)	0	2(0.6%)
	TB	20(6.5%)	36(11.7%)	0	56(18.2%)
	ALP	4(1.3%)	5(1.6%)	0	9(2.9%)
	NHL	2(0.6%)	4(1.3%)	0	6(1.9%)
	HL	2(0.6%)	1(0.3%)	0	3(1.0%)
	Metastatic CA	0(0%)	14(4.5%)	0	14(4.5%)
Total		141(45.8%)	162(52.6%)	5(1.6%)	308(100%)

DISCUSSION

In our study, age range of lymphadenopathy of 308 cases was 1-89 years with mean of 25.1±16.89. Similar study conducted on 185 patients in Turkey showed an average age of 41.01 ± 20.62 years[10]. This is much higher than our age range. However age range matched with ours and was 1-86 years. Their patient population comprised of 47% females and 53% males. Our group had 51.6% females and 48.4% males. So in our group females predominated.

Most common site of lymph node enlargement was cervical node and was reactive (45.1%). This is in accordance with findings of Mohseni S, who also found this enlargement was frequently due to reactive changes[11]. Iqbal et al showed that 70.45% of cervical lymphadenopathy was due to TB and only 13.63% was due to reactive changes[12]. Upadhyay N reported a rare case of cervical lymphadenopathy as only presentation of NHL[13]. Therefore cervical lymph node should be screened with caution as it can be either benign or malignant. Tracy JC observed metastatic malignancy in all supraclavicular nodes[14]. This is in contrast with our findings as we did not observe metastasis in supraclavicular nodes, rather they were all reactive. (Table 2) We found out that metastasis was most common in cervical (2.9%) and then axillary nodes (1.0%).

Sibanda EN reviewed all lymph node biopsy reports collected at Histopathology unit in Harare, Zimbabwe. The commonest diseases in 2194 lymph node specimens submitted were: (a) non specific hyperplasia (33%); (b) tuberculous lymphadenitis (26.7%); (c) metastases (12.4%); (d) Kaposi's sarcoma (9%); (e)

lymphomas (7%).[4] In our study out of total 308 cases, 218 (70.8%) were reactive, 56 (18.2%) showed TB, 14 (4.5%) exhibited metastatic carcinoma, 9 (2.9%) were labeled as Atypical lymphoprolifertaive disorder, 6 (1.9%) were of Non-Hodgkin lymphoma, 3 (1.0%) of Hodgkin lymphoma and 2 (0.6%) of abscess Similarly Vali et al reported reactive nodes in 54.2% of patients and malignant in 11.4% of patient population.[15]

Saini stated that infection was predominantly diagnosed in younger patients, sarcoidosis in the middle aged, and tumor in older patients ($p<0.001$)[16]. We concluded that young and old patients had reactive nodes while malignancy was seen in middle age group. (Table 3)

Toraks reviewed data of 69 tuberculous patients in Rabat in 2016. He observed female (70%) and a young age predominance of patients (31.4 year +/-13.1)[17]. We also observed female predominance (10.7%) in tuberculous infection as compared to males (7.5%). As Qadeer E et al reported increasing prevalence of tuberculosis with age and 1.8 times higher among older men than women. Their data also suggested under-detection and/or -notification of TB, especially among young men and elderly.[8] Many studies like Begum A, Fazal et al reported tuberculosis in females and commonly in cervical nodes.[18,19] In children, abdominal tuberculosis is more prevalent.[20] In contrast to that our patients under 18 showed reactive hyperplasia to be commoner than tuberculosis. (Table 4)

According to AA armadas, the prevalence of malignancy n a primary care set up, associated with unexplained lymphadenopathy was as low as 1.1%. However, in referral centers, the prevalence of malignancy was found to be 40%–60%. NHL is considered as the fourth common worldwide malignancy in males with a frequency of 6.1%.[21] Our results showed frequency of NHL to be 1.9% and HD was 1.0%. NHL was common in both males (1.3%) and females when compared with HD (0.6%, 0.3%).

As we analyzed areas from where patients belonged, we concluded that 66.9% of patients were from Lahore. Most common cause of lymphadenopathy was reactive hyperplasia and tuberculosis was second most common cause. Similar findings were seen in Sheikhpura, Nankana and Narowal patients. Patients who belonged to Okara, Mianwali and Bahwalnagr showed reactive hyperplasia and malignancy. Tuberculosis was not seen in them. Reactive Hyperplasia can be diagnosed with the help of simple test like Fine needle aspiration. For this ailment patients had to travel a long way to Lahore to get diagnosed. If this simple test is available there, expense of travel and stay can be avoided which will help patient population. We could not find any local study to compare with these findings.

CONCLUSION

Reactive lymph node enlargement is most common cause of lymphadenopathy in tertiary care setup. Tuberculosis is second most common cause, seen more in females. Mayo Hospital is catering a large number of patients from cities other than Lahore. It is suggested that tertiary care services should be strengthened in areas surrounding Lahore to lower patient burden and improve health facilities at Mayo Hospital. Government hospitals should be equipped with special tests like immune-markers and molecular techniques to precisely diagnose lymphoid malignancies.

Author's Contribution:

Concept & Design of Study:	Samina Qamar
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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