RESEARCH ARTICLE

Profile of Lymphadenopathy in Kashmir Valley: a Cytological Study

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Abstract

Lymphadenopathy is one of the commonest and significant manifestations of local as well as systemic ailments, especially malignancies. Fine needle aspiration cytology (FNAC) helps in diagnosing the disease itself, in general, but more importantly ruling out malignancy, in particular. Hence it saves much of the cost and use of resources incurred with excision biopsy of such lymph nodes. This prompted us to study the cytologic patterns of lymphadenopathy in our setting and the diagnostic utility of FNAC in the evaluation of lymphadenopathy. In this retrospective observational study, 1,579 patients (953 males and 626 females) with lymphadenopathy who were subjected to FNAC over a period of three years (January 2009 to December 2011) were studied. The cervical region was involved in most of the cases (76%) followed by the axillary region (17.5%). Metastatic malignancy (38.2%) was the commonest cause of lymphadenopathy followed by reactive lymphoid hyperplasia (36.9%), tuberculosis (9.1%) and lymphomas (8.6%). Squamous cell carcinoma (32.2%) followed by adenocarcinoma (21.9%) were the most frequent metastatic tumors. FNAC is a useful diagnostic tool in the management of patients presenting with lymphadenopathy and should be considered before more invasive and costly procedures are performed, particularly in developing countries.

Keywords: Lymphadenopathy - FNAC - Kashmir valley - diagnostic utility

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Introduction

Lymph nodes are the easily accessible components of lymphoid tissue that not only clean and filter lymph but also produce lymphocytes and antibodies. The human body has approximately 600 lymph nodes, some of which (submandibular, axillary or inguinal lymph nodes) may normally be palpable in healthy people. Lymphadenopathy refers to nodes that are abnormal in size, consistency or number (Darnal et al., 2005). It is one of the commonest and significant clinical presentations of patients, attending the outdoor clinics in most hospitals. The aetiology varies from an inflammatory process to a malignant condition (Hafez et al., 2011). For assessment of lymphadenopathy, different modalities are used which include FNAC, automatic core needle biopsy, flow cytometry, radiologically guided core needle biopsy and open biopsy. FNAC is an easy, safe, reliable, rapid and inexpensive method for diagnosing enlarged lymph nodes with a high degree of accuracy (Ahmad et al., 2009). Because of early availability of results, the aspiration cytology is now considered as a valuable diagnostic aid and it provides ease in following patients with known malignancy and ready identification of metastasis or recurrence (Khan et al., 2011).

Materials and Methods

This study was carried out in the department of Pathology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar from January 2009 to December 2011 (3 years). A total of 1902 patients presenting clinically with localised or generalised lymphadenopathy, who underwent FNAC (with or without image guidance) during that period were studied retrospectively. Cases with haematological malignancy were excluded. Relevant clinical details like age, sex, site and size of lymph nodes and cytological diagnosis were retrieved from the records maintained in the department of Pathology and Medical Records department. The slides of all the cases were reviewed and different cytomorphological features studied. Among 1902 cases, 323 cases were excluded from the study (247 cases: FNAC was inconclusive either due to inadequate aspirated material or poor quality smears; 76 cases: swellings other than lymph nodes had got aspirated). Hence, the remaining 1,579 cases of lymphadenopathy were selected for study. These cases were divided into three groups: 1. Benign (Reactive lymphoid hyperplasia, Acute non-specific lymphadenitis and Tuberculous lymphadenitis), 2. Malignant (Lymphomas and Metastatic tumors); and 3. Miscellaneous group (showing features that did not

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conform to those of any of the earlier mentioned groups)

Results

A total of 7519 FNACs from different swellings were performed during the 3-year study period. Among them 1579 cases of FNAC (21%), done from enlarged lymph nodes, in whom the aspirated material was adequate and smears were satisfactory for evaluation, were studied.

Age and Gender

The age of the patients ranged from two months to 87 years. Overall (and in males, 18.6%), maximum number of cases (284, 18%) were seen in 6th decade followed by 4th (265, 16.8%) and 5th (252, 15.9%) decade. However, in females, maximum cases occurred in 4th decade (23.5%). In general, a male-to-female ratio of 1.5:1 was observed, with males contributing 953 cases (60.3%) and females 626 cases (39.6%). However, in 3rd and 4th decade, females outnumbered the males with a male-to female ratio of 1:1.14 and 1:1.25 respectively.

Site

Cervical region was found to be the most common site of lymphadenopathy (1,201 cases, 76%) followed by axillary region (248 cases, 15.7%). Retroperitoneal lymphadenopathy was present in 19 cases and 2 cases had epigastric lymphadenopathy, which were aspirated under image guidance (both CT and USG) (Table 1).

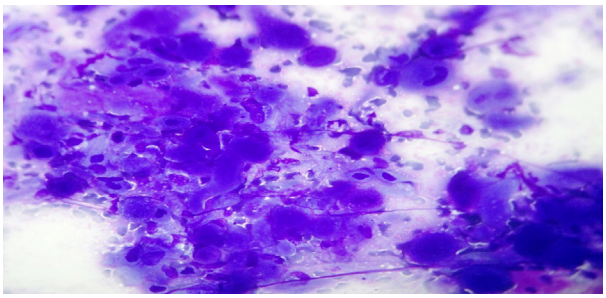

Figure 1. Metastatic Keratinizing Squamous Cell Carcinoma, MGG x40.

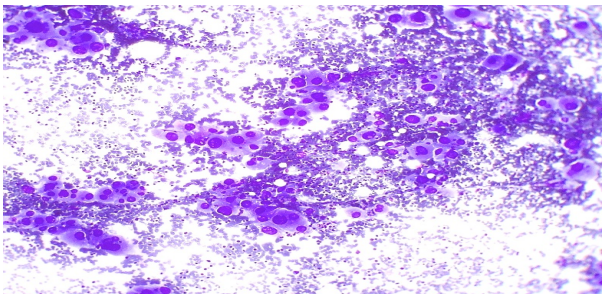

Figure 2. Metastatic Infiltrating Ductal Carcinoma, MGG x10.

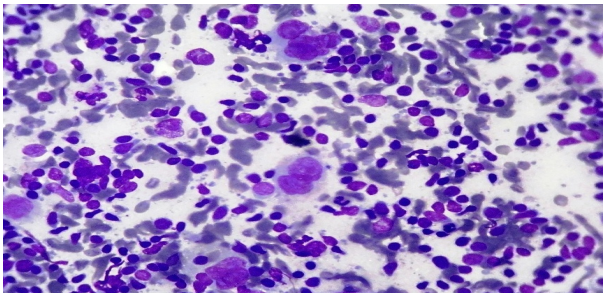

Figure 3. Hodgkin's Lymphoma with Abundant RS Cells, MGG x40.

Size

The size of the lymph nodes ranged from 1-2 cm in 1,007 cases (63.8 %) and >2 cm in remaining 572 cases (36.2 %).

Diagnosis

The cytological features were observed to be benign in 798 cases (50.5%), and malignant in 738 cases (46.7%). Rest of the 43 cases (2.72%) were categorised as miscellaneous. In these cases, atypical cells were seen and the possibility of either a lymphoma or a viral infection was considered. Overall, metastatic malignancy, (603 cases, 38.2%) was the single most common cause of lymphadenopathy. The next common causes were reactive lymphoid hyperplasia, (583 cases, 36.9%) and tuberculous lymphadenopathy, (143 cases, 9.1%).

In males, the most common cause of lymphadenopathy was found to be metastasis, (349 cases, 36.6%) followed by reactive lymphoid hyperplasia, (335 cases, 35.1%) and lymphomas, 100 cases (10.5%). Whereas, in females, following metastatic tumors, (254 cases, 40.6%) and reactive lymphoid hyperplasia, (248 cases, 39.6%), tuberculous lymphadenopathy, (64 cases, 6.72%) was the single most common cause of lymphadenopathy (Table 2). Both Hodgkin's lymphomas and non-Hodgkin's lymphomas were found to be almost three times more common in males than females. A male-to-female ratio of 3:1 and 2.8:1 was observed in Hodgkin's lymphoma and non-Hodgkin's lymphoma respectively.

In paediatric age group (<18 years age), reactive lymphoid hyperplasia, (59.7%) followed by tuberculosis

Table 1. Distribution of 1579 Cases of Lymphadenopathy by Site and Sex.

	Total	Males	Females
Cervical	1201	739	462
Axillary	248	131	117
Inguinal	95	61	34
Retroperitoneal	19	13	6
Epigastric	2	1	1
Femoral	1	1	
Epitrochlear	1	1	
Multiple site	12	6	6
Total	1579	953	626

Table 2. Diagnostic Patterns of Lymphadenopathy on FNAC

Cytological Diagnosis	Total Cases	%	Males	Females
Reactive Hyperplasia	583	36.9	335	248
Acute Lymphadenitis	72	4.5	50	22
Tuberculous Lymphadenopathy	143	9.1	79	64
Lymphoma	135	8.5	100	35
HL	32	2.0	24	8
NHL	103	6.5	76	27
Metastatic Malignancy	603	38.2	349	254
Miscellaneous	43	2.7	35	8

Table 3. Cyto- and Histopathological Correlation in 367 Cases of Lymphadenopathy.

Cytological Diagnosis		Histopathological Diagnosis				Sensitivity	Specificity
		Reactive Hyperplasia	Tuberculous Lymphadenopathy	Lymphoma	Metastatic Malignancy		
Reactive Hyperplasia	56	43	2	8	3	86.0	72.9
Tuberculous Lymphadenopathy	45	-	41	4	-	91.1	98.7
Lymphoma	123	7	2	114	-	89.0	96.2
Metastatic Malignancy	143	-	-	2	141	97.9	99.1
Total cases	367	50	45	128	144	-	-
Overall	-	-	-	-	-	94.5	90.5

(14%) were the most frequent causes of lymphadenopathy. Whereas in adults, (>18 years age), metastatic tumors followed by reactive lymphoid hyperplasia contributed for most of the cases of lymphadenopathy.

Among the metastatic tumors, squamous cell carcinoma (32.2%), followed by Adenocarcinoma (21.9%) and poorly differentiating carcinoma (14.6%) were the most common metastatic tumors. In females, following squamous cell carcinoma (25.6%), infiltrating ductal carcinoma (23.2%) was the next most common metastatic tumor.

Sensitivity and specificity

In 367 cases of lymphadenopathy, the results obtained on FNAC were compared with the histopathological diagnosis of the corresponding excised lymph node. Among the 101 cytologically benign cases, 86 cases were proved to be histopathologically benign, true negative and rest of the 15 cases were diagnosed histopathologically as malignant, false negative. Among the 266 cytologically malignant cases, 257 cases were proved to be malignant histopathologically, true positive, and rest of the 9 cases were diagnosed as benign histopathologically, false positives. Thus, a sensitivity of 94.5%, specificity of 90.5%, positive predictive value of 96.6%, negative predictive value of 85.2% and accuracy of 92.4% was observed (Table 3).

Discussion

Lymphadenopathy is a clinical manifestation of regional or systemic disease which serves as an excellent clue to the underlying disease (Bhuyan et al., 2008). It can arise either from benign or malignant causes depending upon the geographical condition and socioeconomic set up (Ahmad et al., 2009). FNAC of lymph node has become an integral part of the initial diagnosis and management of patients with lymphadenopathy due to early availability of results, simplicity, and, minimal trauma with less complication. FNAC has also been advocated as a useful method in comparison to more expensive surgical excision biopsies in developing countries with limited financial and health care resources (Hafez et al., 2011).

The lesion arising in lymph nodes can be found in patients ranging from early to advanced age. In our study, the youngest patient with lymphadenopathy was a two month male infant and the oldest one was 87 years old, with a mean age of 52 years. Similar figures were noted in one study (Steel et al., 1995) and other study on paediatric lymphadenopathy (Dhingra et al., 2010). Others (Ahmad et al., 2005; Hirachand et al., 2009) also had comparable figures in their studies.

In our study, a male preponderance was noted with a male-to-female ratio of 1.5:1 which correlated with others (Patra et al., 1983; Hirachand et al., 2009). In contrast, other studies (Nidhi et al., 2011; Ageep et al., 2012), found a slight female predominance with a male to female ratio of 1:1.2.

Cervical region was the most frequent site of lymphadenopathy in our study (76%). Many others (Pandit et al., 1987; Ahmad et al., 2005; Nidhi et al., 2011) also found cervical region to be the most common site of involvement.

In one study, (Hafez et al., 2011), the size of the lymph nodes was found to be <2 cm in 87.5% of the benign cases and >2 cm in 78.9% of the malignant cases. In our study, the size of the lymph node was <2 cm in 63.8% of all cases which included about 82% of benign cases.

Collectively, benign disorders (50.5%) were more common than malignant disorders (46.7%) in the present study. This correlates well with other studies from India and other developing countries. In one study, (Ahmad et al., 2005) from India, benign causes contributed to 86.4% of lymphadenopathies. Studies from other developing countries like Pakistan (Khan et al., 2011; Fatima et al., 2011) also reported 92% and 73.2% benign lymphadenopathies. In one study from Nepal, benign lesions were reported in 81.5% cases of lymphadenopathy compared to only 18.5% of malignant lesions.

Metastatic malignancy was reported to be the most common cause of lymphadenopathy, 53.8% in a study (Steel et al., 1995) and 80.4% in other study (Alam et al., 2010). Similar results were also seen in another study from India (Izhar et al., 2007) where 65.7% cases of lymphadenopathy were found to be suspicious or positive for malignancy. An Iranian study (Rakhshan et al., 2009) reported metastatic malignancy, 17.9% cases, as the second most common cause following reactive lymphadenopathy, 59.6% cases. In the current study, metastatic malignancy was the single most common cause of lymphadenopathy, 38.2% (603 cases) followed by reactive lymphoid hyperplasia 36.9% (583 cases), probably due to the fact that majority of our patients were older adults.

Reactive lymphadenopathy, 53.6%, followed by tuberculous lymphadenopathy, 32.8% was the most common cause of lymphadenopathy in one Indian study (Ahmad et al., 2005). A study from Dhaka (Kafi et al.,

2012) reported non-specific lymphadenitis (50%) followed by tuberculosis (28.3%) and metastasis (10.8%) as the most common causes of lymphadenopathy. Studies from Nepal (Hirachand et al., 2009; Shakya et al., 2009) also reported most of the lymphadenopathies, 41.5% and 50.4%, to be reactive followed by 28% and 22.4% tuberculous lymphadenopathies. However, most of the studies from Pakistan reported tuberculous lymphadenopathy as the most common pathology. One study (Khan et al., 2011) reported 52% and others as 66.9% and 52.7% (Shahid et al., 2010; Fatima et al., 2011) tuberculosis. Some other Indian studies (Khajuria et al., 2006; Nidhi et al., 2011), also found tuberculosis as the most common cause, 52.3% and 55%, of lymphadenopathy. A study from Sudan (Ageep et al., 2012) reported that the commonest cause of lymphadenopathy in their set up was tuberculosis (39.5%) followed by metastatic disease (24.7%). In contrast, one Pakistani study (Javaid et al., 2006) found metastatic lymphadenopathy, 42.8% more common cause than tuberculous lymphadenitis, 26.2%.

Squamous cell carcinoma (32.2%) followed by adenocarcinoma (22%) were the most common metastatic tumors in our study. Similar figures were also seen in a study (Mitra et al., 2011). Other studies (Khajuria et al., 2006; Izhar et al., 2007; Hirachand et al., 2009; Wilkinson et al., 2012) also found squamous cell carcinoma as the most common metatatic malignancy.

In our study, reactive lymphadenopathy, 59.7% followed by tuberculosis, 14% were responsible for most of the cases of lymphadenopathy in children (<18 years age). Similar findings were reported in a study (Dhingra et al., 2010) where reactive lymphadenopathy (56%) was the most common cause followed by granulomatous lymphadenitis (28.1%). Chronic non-specific lymphadenitis (46%) followed by granulomatous lymphadenitis (21%) was the commonest causes of lymphadenopathy in children in a study (Darnal et al., 2005). A study from Jordan (Rimawi et al., 2011) also found reactive hyperplasia (54%) as the most common cause of lymphadenitis in children.

Lymphomas constituted only 8.55% of lymphadenopathies in our study. Others (Fatima et al., 2011; Hirachand et al., 2011) also reported similar figures, 5.2% and 6.1%. In contrast, a study from Egypt (Hafez et al., 2011), found that cases suspicion of NHL (32.5%) contributed to most of the cases of lymphadenopathy followed by metastatic tumors (19.7%).

Overall, the sensitivity of 94.5%, specificity of 90.5%, positive predictive value of 96.6%, negative predictive value of 85.2% and accuracy of 92.4% was achieved in our study. Other study (Hafez et al., 2011) reported the same as 90.9%, 67.2%, 82.6%, 81.3% and 82.2% respectively. One more study (Advani et al., 2008) had an overall sensitivity of 87.5%, specificity of 90% and accuracy of 91.4% respectively.

In malignant conditions of lymph nodes, FNAC enjoys a high sensitivity and specificity, the average being 95% (Engzell et al., 1972). The sensitivity and specificity of FNAC in metastatic tumors was reported to be 100% by many studies (Ahmad et al., 2005; Hirachand et al., 2009). One more study (Javaid et al., 2006) also reported the accuracy of 100% in diagnosing metastatic lymphadenopathy. In one study (Prasad et al., 1996), the sensitivity rates of FNAC in tuberculosis, metastatic tumors, Hodgkin's disease and non-Hodgkin's lymphoma were found to be 83.3%, 97%, 30% and 80.3% respectively, the specificity being 94.3%, 98.9%, 98.6%, and 95.4% respectively. A different study (Malakar et al., 1991) found the sensitivity and specificity of 100% with regards to lymphomas while that for secondaries were 94.7% and 100% respectively. In the current study, the sensitivity and specificity of FNAC in lymphomas were found to be 89% and 96.2% while that for metastatic lymphadenopathy were 97.9% and 99.1% respectively. Others (Ahmad et al., 2005) also reported similar sensitivity and specificity of FNAC in lymphomas, 89.6% and 97.6% respectively. With regards to tubercular lymphadenopathy, the sensitivity and specificity of 79.1% and 94% respectively were seen in one study (Malakar et al., 1991). In our study, the same were observed to be 91.1% and 98.7% respectively. A high sensitivity, specificity and accuracy of 97%, 97.5% and 97.4% respectively was reported in a study (Ahmad et al., 2005).

To conclude, metastasis contributes to most of the lymphadenopathies in our set up, which is particularly more common in older adults, and FNAC can be regarded as the first line approach to such palpable lymph nodes. Besides its simplicity and requirement of little equipments, FNAC has many advantages which makes it suitable for use on outpatient basis, in peripheral hospitals and dispensaries, thus reducing the incidence of surgery and, therefore, bed occupancy. However, it is not a substitute for conventional surgical pathology but is complimentary to it. FNAC is a part of the diagnostic processes in combination with clinical, radiological and other laboratory data.

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