

Cytological Study of Cervical Lymphadenopathy in a Tertiary Care Institution from Kashmir Valley, India

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Abstract

Background: Cervical lymphadenopathy is a common clinical finding in all age-groups that ranges in etiology from inflammation to malignancy. Fine needle aspiration cytology (FNAC) is a standard first-line investigation in the evaluation of cervical lymphadenopathy.

Objective: The study aimed to analyze the clinical profile and causes of cervical lymphadenopathy in different age-groups and the diagnostic utility of FNAC in our setup.

Methods: This retrospective study included all the patients of cervical lymphadenopathy of more than 2-3 weeks duration, who underwent FNAC in our tertiary care institution in Kashmir valley, India during the two-year study period (January 2009-December 2011) in whom the aspirated material was adequate and satisfactory for evaluation.

Results: A total of 790 patients were selected. Upper deep cervical lymph nodes were involved most frequently (38.9%); reactive lymphadenitis (39.4%) followed by metastasis (38.2%) were the commonest causes, in general. In addition, reactive lymphadenitis was the most common cause of lymphadenopathy in all age groups less than 40 years and at all topographic sites of cervical lymph node. However, in more than 40 years age-groups and at supraclavicular region, metastasis was the commonest cause of enlargement. Squamous cell carcinoma (36.4%) followed by adenocarcinoma, (25.8%) were the most common metastatic tumors.

Conclusion: Enlargement of cervical lymph nodes, particularly in elderly patients involving supraclavicular nodes, should raise a suspicion of malignancy; and cervical lymphadenopathy can be effectively evaluated by FNAC without the need for surgical biopsy.

Keywords: Cervical; Fine needle aspiration cytology; Lymphadenopathy; Lymph node

Introduction

Cervical lymphadenopathy is a common clinical finding and may be a sign of an indolent inflammation, infection or a malignant disorder, depending upon many factors including the geographical conditions and socio-economical set up [1-3]. In our country, infective (tubercular) lymphadenopathy is quite common. However, still a large percentage of cervical lymphadenopathy in adults turns out to be malignant. Hence, it is necessary to evaluate a patient of unexplained cervical lymphadenopathy without any delay.

Although, histopathology is considered as gold standard criteria, lymph node sampling by FNAC has potential benefits over the other diagnostic modalities like simplicity, minimal trauma and complications, and easy availability of results, that have made it a frequently practiced investigation in the initial diagnosis and management of patients with cervical lymphadenopathy; in the diagnosis and follow up of primary lymph node malignancies; and in following patients with other malignancies and identifying metastasis or recurrence [3-5].

Since, Kashmir valley (a part of North India) differs from rest of the country in its geographical and socioeconomic conditions, this study was done to analyze the clinical profile of patients presented with cervical lymphadenopathy to our tertiary care institution and determine the causes in different age-groups along with the diagnostic accuracy of FNAC, in our set up.

Materials and Methods

This retrospective study was conducted over a period of two years (January 2009 to December 2011) on all patients (both in-patient and

out-patient) of cervical lymphadenopathy of more than 2-3 weeks duration presented to our tertiary care Institution. A total of 900 patients underwent FNAC of enlarged cervical lymph nodes during this study period. Among them, aspirated material was either inadequate or smears were unsatisfactory for evaluation in 85 cases and in 25 cases, after aspiration, apparently looking cervical nodal swellings were found to be non-lymphoid in nature like schwannoma, lipoma etc. Hence, these 110 cases were excluded from the study and the remaining 790 cases were studied, which included patients with solid malignancy (like breast, lung, thyroid, pancreas etc.). All the relevant clinical details like age, sex, site, duration, involvement of other nodes and cytological diagnosis of the selected patients were noted, their slides were reviewed and different cytological features studied.

Results

A total of 790 cases of FNACs done from enlarged cervical lymph nodes, in whom the aspirated material was adequate and smears were satisfactory for evaluation, were studied. A male to female ratio of 1.5:1

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Received April 27, 2016; Accepted June 15, 2016; Published June 20, 2016.

Citation: Qadri SK, Hamdani NH, Besina S, Makhdoomi R, Rasool R, et al. (2016) Cytological Study of Cervical Lymphadenopathy in a Tertiary Care Institution from Kashmir Valley, India. J Cytol Histol 7: 418. doi:[10.4172/2157-7099.1000418](https://doi.org/10.4172/2157-7099.1000418)

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(age-range 4-87 years) was observed with males contributing to 473 cases (59.9%) and females 317 cases (40.1%). The size of lymph nodes ranged from 1-2 cm in 538 cases (68.1%) and more than 2 cm in the remaining 252 cases (31.9%).

On the basis of age, patients were divided into nine age-groups, viz., 0-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90 years. Topographically, palpable cervical lymph nodes were divided into eight groups, viz., upper, middle and lower deep cervical; supraclavicular; submandibular; preauricular; postauricular; and submental lymph nodes. Majority of cases of cervical lymphadenopathy involved upper deep cervical lymph node (n=308, 38.9%) followed by supraclavicular lymph nodes (n=254, 32.1%). In the first two age groups (0-10 and 11-20 years), commonest topographic sites involved were upper deep cervical lymph nodes (52.6% and 55.5%, respectively) followed by submandibular nodes (18% and 10.1%, respectively) with less frequent involvement of supraclavicular nodes (5.1% and 7%, respectively). In 21-30 and 31-40 years age groups, following upper deep cervical lymph node involvement (49.6% and 42.9%, respectively), supraclavicular lymph nodes were involved most frequently (14.5% and 26.8%, respectively). Compared to lower age groups, in all age groups above 40 years, there was predominant involvement of supraclavicular lymph nodes comprising 48.5%, 56%, 58.9%, 54.5% and 100% cases in 41-50 years, 51-60 years, 61-70 years, 71-80 years and 81-90 years age groups (Table 1).

In general, reactive lymphadenitis (n=311, 39.4%) was the most common cytological diagnosis followed by metastasis (n=302, 38.2%) and tuberculosis (n=91, 11.5%). In the first three age groups reactive lymphadenitis contributed to majority of cases (69% in 0-10 yrs; 68% in 11-20 yrs and 58% in 21-30 yrs) followed by tuberculosis (12.8% in 0-10 yrs; 13.3% in 11-20 yrs and 18% in 21-30 yrs). In 31-40 years age group, reactive lymphadenitis and metastasis contributed to equal number of cases (39.3% each) followed by tuberculosis (13.4%). However, in

all age-groups above 40 years, metastasis outnumbered the reactive lymphadenitis and contributed to 53.4%, 74.6%, 67.4%, 68.1% and 100% cases in 41-50, 51-60, 61-70, 71-80 and 81-90 years age-groups, respectively (Table 2).

Reactive lymphadenitis was observed to be the most common cytological diagnosis at all sites except for supraclavicular region, where metastasis was the commonest cause of enlargement (n=203, 80%). Lymphomas, both Hodgkin's lymphomas (HL) and non-Hodgkin's Lymphomas (NHL) constituted to only 6.8% cases of cervical lymphadenopathy, affecting most frequently upper deep cervical lymph nodes. Tuberculosis also involved upper deep cervical lymph nodes most commonly (48.3%) followed by submandibular lymph nodes (16.5%) while as acute suppurative lymphadenitis involved mainly submandibular lymph nodes (43.3%) (Table 3).

Squamous cell carcinoma (36.4%) followed by adenocarcinoma, (25.8%) and poorly differentiated carcinoma (13.6%) were the most common tumors to metastasize cervical lymph nodes (Figures 1-3).

In 288 cases of cervical lymphadenitis, excision biopsy of cervical nodes was done in addition to FNAC for histopathological confirmation. Among 78 cases of them, which were diagnosed as benign on cytology, 75 cases (96%) were confirmed to be benign (true negatives) on histopathology while, rest of the cases (n=3, 3.8%) were proved to be malignant (false negatives). Out of 210 cases, diagnosed cytologically as malignant, 205 cases (97.6%) were confirmed to be malignant on histology (true positives) and rest of 5 cases, (2.4%) were found to be benign (false positives) (Table 4).

Discussion

Cervical lymphadenopathy often presents a diagnostic challenge to the medical professional as it may be the manifestation of a primary

Age (in yrs)	Upper Cervical	Mid-Cervical	Lower Cervical	Supra-clavicular	Sub-mandibular	Pre-auricular	Post-auricular	Sub-mental
0-10 (n=78)	41	7	6	4	14	1	5	-
11-20 (n=128)	71	15	7	9	13	4	7	2
21-30 (n=117)	58	16	7	17	11	1	4	3
31-40 (n=112)	48	15	5	30	8	1	3	2
41-50 (n=103)	29	11	1	50	5	1	5	1
51-60 (n=134)	32	11	2	75	7	2	3	2
61-70 (n=95)	21	9	1	56	5	2	1	-
71-80 (n=22)	8	1	1	12	-	-	-	-
81-90 (n=1)	-	-	-	1	-	-	-	-
Total (n=790)	308	85	30	254	63	12	28	10

Table 1: Age and topographical distribution of 790 patients.

Age (in yrs)	Reactive	AL	Tuberculosis	HL	NHL	Metastasis	LCH
0-10 (n=78)	54	7	10	2	1	3	1
11-20 (n=128)	87	7	17	6	7	4	-
21-30 (n=117)	68	8	21	2	1	16	1
31-40 (n=112)	44	3	15	3	3	44	-
41-50 (n=103)	26	3	12	2	5	55	-
51-60 (n=134)	17	1	12	-	4	100	-
61-70 (n=95)	12	1	4	-	14	64	-
71-80 (n=22)	3	-	-	1	3	15	-
81-90 (n=1)	-	-	-	-	-	1	-
Total (n=790)	311	30	91	16	38	302	2

HL: Hodgkin's Lymphoma; NHL: Non-Hodgkin's Lymphoma; LCH: Langerhan cell histiocytosis; AL: Acute Lymphadenitis

Table2: Cytological Diagnosis in different age-groups of patients of cervical lymphadenopathy.

Site	Reactive	AL	Tuberculosis	HL	NHL	Metastasis	LCH
Upper cervical (n=308)	174	7	44	7	20	56	-
Mid-Cervical (n=85)	36	1	14	4	7	23	-
Lower cervical (n=30)	22	-	1	-	1	6	-
Supraclavicular (n=254)	24	5	13	3	5	203	1
Submandibular (n=63)	22	13	15	2	3	8	-
Preauricular (n=12)	7	1	1	-	1	2	-
Postauricular (n=28)	18	3	2	-	1	3	1
Submental (n=10)	8	-	1	-	-	1	-
Total (n=790)	311	30	91	16	38	302	2

HL: Hodgkin's Lymphoma; NHL: Non-Hodgkin's Lymphoma; LCH: Langerhan cell histiocytosis; AL: Acute Lymphadenitis

Table 3: Cytological diagnosis in different groups of cervical lymph nodes.

FNAC Diagnosis	No. of cases	Histopathological Diagnosis				Sensitivity (%)	Specificity (%)	Accuracy (%)
		Reactive	Tuber-culosis	Lymphoma	Mets: Metastasis			
Reactive	41	38	1	2	-	90.5	98.8	97.6
Tuberculosis	37	1	35	1	-	92.1	99.2	98.3
Lymphoma	98	3	2	93	-	94.9	97.4	96.5
Metastasis	112	-	-	2	110	100	98.9	99.3
Total	288	42	38	98	110			
Overall						98.5	93.7	97.2

Mets: Metastasis

Table 4: Correlation of FNAC and Histopathology.

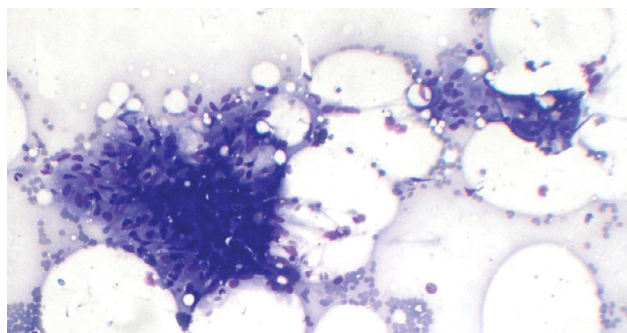


Figure 1: Epithelioid cell granuloma (Giemsa 40x).

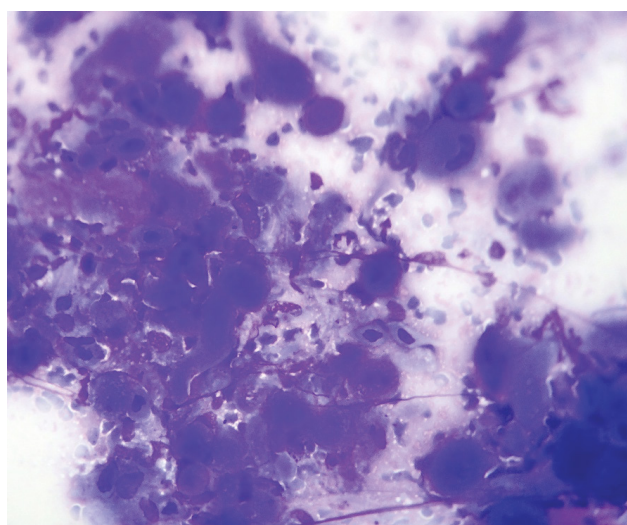


Figure 2: Squamous cell carcinoma metastasis to lymph node (Giemsa 40x).

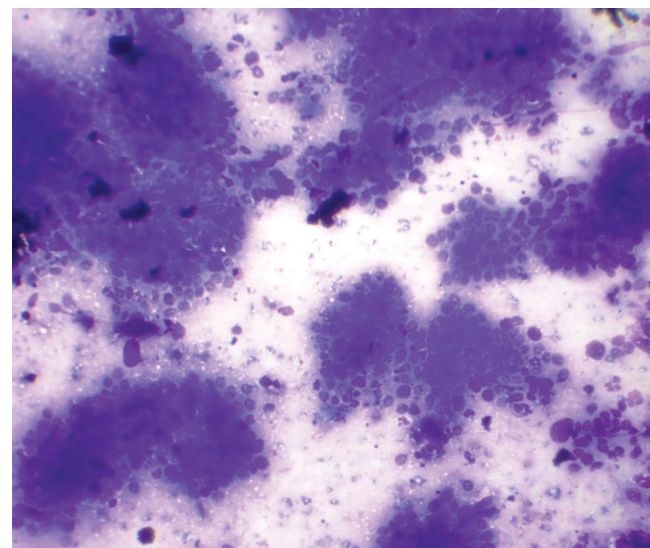


Figure 3: Adenocarcinoma metastasis to lymph node (Giemsa 10x).

or secondary malignancy or just a response to a trivial infection or inflammatory process, and therefore, requires thorough evaluation. FNAC is a simple, safe, rapid, accurate, minimally invasive and relatively pain free procedure which is of particular relevance in cervical lymphadenopathy because of easy accessibility of target sites and thus excellent patient compliance [2,6]. Since this technique lends itself to out-patient diagnosis, it is eminently suited for use in peripheral medical centers and places where facilities for histopathology are not available [7].

In our study, the youngest patient with cervical lymphadenopathy was a 4 month old infant and the oldest one was 87 years old. Similar figures were noted in other studies [4,8-10]. A male preponderance was noted in the current study with a male to female ratio of 1.5:1 which

correlates with other studies [9,11]. However, a female predominance was seen in other studies [2,12].

In an Egyptian FNAC study on cervical lymphadenopathy, the commonest site of involvement was the upper deep cervical lymph nodes (37.6%) followed by supraclavicular lymph nodes (28%); 0-20 years age-group involved the upper deep cervical lymph nodes much more frequently (88.9%) than supraclavicular lymph nodes (11.1%) while the later were predominantly involved after 41 years of age [5]. Similar results were obtained in our study also where the upper deep cervical lymph nodes (38.9%) followed by supraclavicular lymph nodes 32.1% contributed to majority of cases; and 0-20 years age-group involved the upper deep cervical lymph nodes (54.4%) while the supraclavicular lymph nodes were preferentially involved after 40 years of age. Results of another FNAC study on pediatric cervical lymphadenopathy also correlated well with our study [10].

Many studies from Bangladesh, [6,13] Nepal [9,14] and India [8] reported reactive lymphadenitis followed by tuberculosis and metastasis as the most common causes of cervical lymphadenopathy. In our study also, reactive lymphadenitis (39.4%) was the most common cytological diagnosis, however, metastasis (38.2%) was found to be much more common than tuberculosis (11.5%). Other studies from Pakistan, [3,15] Nepal [7] and India [16] reported tubercular lymphadenitis as the most common cause of cervical lymphadenopathy. In contrast, metastasis was the most common cytological diagnosis in some other studies [17,18].

The etiological factors of lymphadenopathy in adults are likely to be different from that in children. While metastatic cancer is documented widely as a major cause of lymphadenopathy in adults, a contrasting rarity of metastatic cancer has been consistently reported in children. Moreover, reactive hyperplasia to minor stimuli has been reported as a significant cause of lymphadenopathy in children with a yet developing immune system [19]. This correlated well with our study where reactive lymphadenitis (68.4%) followed by tuberculosis (13.1%) and acute suppurative lymphadenitis (6.7%) were the most common causes of cervical lymphadenopathy in children while metastasis contributed to majority of cases in adults (more than 40 years of age). Consistent results were reported by many other studies [1,10,20].

In our study, reactive lymphadenitis was the most common cytological diagnosis at all topographical sites of cervical lymph nodes except for supraclavicular region, where metastasis was the dominant diagnosis (80% cases). Similar findings were reported by other researchers [21].

Squamous cell carcinoma followed by adenocarcinoma were found to be the most common tumors to metastasize to cervical lymph node in many studies [5,9,16,21] similar to our study. However, adenocarcinoma was found to be the most common metastatic tumor followed by squamous cell carcinoma in some other study [22].

Overall, a sensitivity of 98.5%, specificity of 93.7%, positive predictive value of 97.6%, negative predictive value of 96% and accuracy of 97% were observed in our study. The results were comparable with that of other studies. [2,4,8-10,18,23]

Conclusion

In the present study, cervical lymphadenopathy was found to be more common in males than females; and in adults than children. In patients less than 40 years of age, upper deep cervical lymph nodes were

involved more frequently and lymphadenopathy occurred mostly in response to inflammatory and infectious disorders. Whereas, more than 40 years old patients involved supraclavicular nodes most commonly with metastasis being the commonest reason of their enlargement. Thus, an increasing trend towards involvement of supraclavicular lymph nodes with malignancy was observed with increasing age. Although FNAC cannot replace histopathology, because of the easy accessibility of cervical lymph nodes and simplicity of the procedure, it is possible to establish a rapid and accurate diagnosis with FNAC in majority of patients of cervical lymphadenopathy with maximum patient compliance, minimal trauma and complications.

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