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Original Research Article

Clinicopathological profile of significant cervical lymphadenopathy in children

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ABSTRACT

Background: In children enlarged cervical lymph nodes is one of the common presentations and requires evaluation. The aetiology of cervical lymphadenopathy can be either due to benign self-limiting conditions (viral or bacterial infection) or due to some serious systemic diseases like tuberculosis or malignancy. This study intends to analyse wide etiological presentations of cervical lymphadenopathy in children with cytopathological correlation by fine needle aspiration cytology (FNAC) for timely diagnosis and if required to refer early for further management.
Methods: This is a hospital based prospective observational study conducted at department of Paediatrics at IGICH, Bengaluru among children between 1 month-18 years of age with significant cervical lymphadenopathy.
Results: Total of 100 cases of significant cervical lymphadenopathy were included in the study. Most common age group involved was between 4-8 years with male preponderance (M:F=1.5:1). Fever and swelling in the neck were the most common presenting complaints. After investigation, reactive lymphadenitis (55%) was the most common aetiology among which tonsillitis (38%) and otitis media (11%) were most common. Second most common aetiology was tuberculosis (30%). Five (5%) patients had malignancy. Sensitivity of FNAC in detecting tuberculosis (TB) lymphadenitis was found to be 90.9% in this study.
Conclusions: Cervical lymphadenopathy is one of the common clinical conditions which paediatricians face in daily practice that requires detailed evaluation for accurate diagnosis and treatment. Reactive lymphadenitis and tubercular lymphadenitis remain the most common aetiologies. Presently FNAC has emerged as important tool in the initial diagnosis and management of patients with lymphadenopathy.

Keywords: Cervical lymphadenopathy, FNAC, Reactive lymphadenitis, Tuberculosis

INTRODUCTION

Lymphadenopathy is defined as an abnormality in the character or the size of lymph nodes.[1] Enlargement of 2 or more non-contiguous lymph node regions is known as generalized lymphadenopathy.[2] Enlargement of lymph nodes within contiguous anatomic regions is known as regional lymphadenopathy.[1] Cervical lymphadenopathy is considered as significant when it measures more than 1cm in its longest diameter.[3] Incidence of cervical lymphadenopathy in children is 38-45%.[4]

In about 80-90% of the cases, lymph nodes in the cervical region are palpable.[1] Palpable supraclavicular nodes are considered always abnormal.[5] Total number of lymph nodes in the body is around 800 out of which around 300 are cited in the neck.[6] So cervical lymphadenopathy is a common clinical condition encountered by the clinicians. As enlargement of lymph nodes more than 1 cm indicates a clinical manifestation of regional or systemic disease, it serves as an excellent clue to the underlying disease.[3] There are wide range of causes for lymphadenopathy. A thorough knowledge about the pattern of lymphatic drainage also helps in determining the aetiology.

Common causes for cervical lymphadenopathy in children are due to reactive hyperplasia secondary to infectious aetiology like viral and bacterial infection. However, in India TB is major health problem, so extrapulmonary TB in form of cervical lymphadenopathy should also be kept in mind while evaluating causes for cervical lymphadenopathy. Other causes include benign hyperplasia, malignancies, autoimmune diseases, drug reaction, histiocytosis and storage diseases.

Till the recent past, lymph node biopsy was the investigation of choice for cases with cervical lymphadenopathy. Presently FNAC has emerged as an important tool in the initial diagnosis and management of patients with lymphadenopathy. It is simple, rapid, reliable, safe, cost-effective technique, ensues minimal trauma to the patients with good diagnostic accuracy.[5]

In paediatric age group, sensitivity and specificity of FNAC is found to be 94 and 100% respectively as compared to gold standard of excision lymph node biopsy.[7] FNAC can be used for cytology, AFB stain, CBNAAT as well as culture depending on the aetiology suspected. FNAC serves not only as a mode to offer tissue diagnosis but also helps as a preliminary screening procedure for conditions like lymphoma, tuberculosis and metastases.[8] It remains the prime mode for differentiating between benign and malignant lesions of cervical nodes.[9] This study intends to analyse wide etiological presentations (TB, reactive lymphadenitis, malignancy etc) of cervical lymphadenopathy in children with cytopathological correlation by FNAC. Hence a thorough knowledge about clinico-demographic assessment of cervical lymphadenopathy for cytopathological diagnosis will help the clinicians to diagnose the child and if required to refer early for further management.[10]

METHODS

Source of data

This is a hospital based prospective observational study conducted over a period of one and a half year from January 2018 to May 2019 among children between 1 month to 18 years with significant cervical lymphadenopathy, attending outpatient department of paediatrics at Indira Gandhi Institute of Child Health Bengaluru. The study included all the children between 1 to 18 years with significant cervical lymphadenopathy of more than 1cm attending outpatient department (OPD) after taking informed written consent. Patients not willing to give written informed consent, lymphadenopathy of <1 cm, children <1 and >18 years, patients with cervical abscess with sinuses and cases previously investigated and on treatment were excluded from study.

Methodology

The total number of cases studied were 100. Informed consent has been taken from the parents of the children included in the study. The demographic details, history, examination and laboratory data was recorded in a predesigned proforma. Necessary laboratory investigations done which included complete blood count, peripheral smear, ESR was done by standard haematological techniques. Chest x-ray and Mantoux was done in all patients. The FNAC procedure was performed in all 100 cases by a pathologist, using a10 cc disposable syringes with 18 G needles. Smears were stained accordingly using Giemsa, Papanicolaou, Ziehl Neilsen and H and E stains. CBNAAT, AFB staining and serological tests done whenever required. The final diagnosis of cervical lymphadenopathy is made after clinical details and investigations.

Statistical analysis

Since it is an observational study results will be presented in absolute number and percentage. Data were entered into SPSS software version 16 and analysed using R software version 3.6.1. All categorical information was presented as frequency and percentage. All continuous measurements were summarized using Mean (SD). Chi square test and ‘t’ test was used to compare the difference between categorical data and one way ANOVA to compare means of laboratory values in different causes of CLA. The level of significance was set at $p \leq 0.05$.

RESULTS

The following results were obtained from the study.

History and examination

In this present study, the majority of the patients with cervical lymphadenopathy were in the age group 4 to 8 years (45%), followed by 1 month to 4 years (20%), 8 to 12 years (19%) and 12 to 18 years (16%) (Table 1). Cervical lymphadenopathy was more commonly observed in male children (60%) as compared to female children (40%) with the ratio of 1.5:1 (Table 2).

The most common presenting complaints observed in the study were, fever and swelling in the neck, which were 89% and 87% respectively followed by cough (29%), weight loss (17%) and throat pain (15%), ear pain (11%) (Figure 1).

Examination revealed that the majority of lymph nodes were between 2-4 cm in size (58%), firm consistency (85%), nontender (82%) and mobile (75%). Level II (upper deep cervical/ upper jugulodigastric) group (49%) and level V (posterior triangle) group (45%) were predominantly seen to be affected in the study; more than one lymph node level involvement was seen in 33% of children.

Right side (48%) lymph node involvement was most commonly seen than left side (33%). Bilateral involvement was seen in 19% of cases. Matted lymph

nodes were present in 15% of the cases. Hard consistency lymph nodes were found in 5% of cases, all of them were diagnosed to have malignancy.

On general physical examination, nineteen (19%) patients had tonsillopharyngitis, two (2%) patients had follicular tonsillitis, eleven (11%) patients were diagnosed to have otitis media, among these patients 4 children had ear discharge. Two (2%) patients had scalp infection in the form of impetigo. One patient had a pleomorphic maculopapular rash all over body, diagnosed to have varicella. Hepatosplenomegaly was seen in 16% of the cases.

Investigations

In this study, investigations showed that anaemia was present in 67% of cases with mean Hb of 10.3±1.7 which was predominantly normocytic and normochromic. It correlates with the present national incidence of anaemia in the paediatric population. An elevated ESR value was observed in 66% of children among which, children with malignancy had mean ESR value of 64 and children with TB had mean ESR of 48.

The Mantoux test was done in 94 cases. Twenty-three (24.4%) cases were Mantoux positive and seventy-one (75.5%) cases were Mantoux negative.

Chest X-ray was done in all patients; showed abnormal findings in 26% of the cases, remaining were normal.

FNAC findings

In this present study, FNAC was done in all 100 cases, which showed 55% cases of reactive lymphadenitis contributing to the majority of cases followed by tubercular lymphadenitis which was 27%.

In 5% of cases FNAC was suggestive of malignancy. Infectious mononucleosis and suppurative lymphadenitis were 2% each. One (1%) case of hemophagocytic lymphohistiocytosis was identified which was secondary to Rickettsial fever. Eight (8%) cases had inconclusive FNAC results (Figure 2).

Findings related to TB lymphadenitis

Among the total number of 30 cases, Tuberculosis was diagnosed by FNAC in twenty-seven (90%) cases, remaining 3 cases were diagnosed based on clinical history and other laboratory findings like Mantoux, ESR, Chest X-ray.

Association between FNAC s/o TB lymphadenitis v/s ESR, Mantoux positive, abnormal chest X-ray and AFB positivity were compared which was significant statistically ($p<0.005$).

Raised ESR value was found in 90% of children with tuberculosis with a mean ESR value of 48. The mean ESR in cases with FNAC s/o TB lymphadenitis was 48.6 (±26.8SD) and mean ESR in group with FNAC not s/o TB lymphadenitis was 30.1 (±22.8SD) and this difference in mean ESR value was found to be statistically significant ($p\leq0.001$).

Mantoux was positive in 19 (70.4%) children out of 27 children with FNAC s/o TB lymphadenitis. This association between Mantoux and FNAC diagnosis was statistically significant ($p<0.001$).

AFB was positive in 13 (48.1%) of children with FNAC s/o TB lymphadenitis. This association between AFB positivity and FNAC diagnosis was statistically significant ($p<0.001$).

Chest X-ray was abnormal in 12 (55.6%) children with FNAC s/o TB lymphadenitis. This association between abnormal chest X-ray and FNAC diagnosis was statistically significant ($p<0.001$).

In this study, total cases of tubercular lymphadenitis where 30, among which Mantoux was positive in 21 (70%) patients, X-ray was suggestive of TB in 14 (53.8%) patients, AFB was positive in 13 (43.3%) patients, 27 (90%) patients had raised ESR value (Figure 3). The sensitivity of FNAC to detect TB lymphadenitis in this study was found to be 90.9% and specificity was 100%.

Aetiology

In our study various aetiologies were identified as a cause for cervical lymphadenitis. Fifty-five (55%) of cases who had reactive lymphadenitis showed most common aetiology to be tonsillitis (38%), followed by otitis media (11%) and impetigo.

Thirty (30%) children with cervical lymphadenitis had tuberculosis. Five (5%) patients had malignancy. Aetiology was not identified in 25% of cases.

FNAC was suggestive of malignancy and infectious mononucleosis in 5% and 2% of cases respectively among the study population. Two cases were suppurative lymphadenitis and one case was hemophagocytic lymphohistiocytosis (HLH). Eight (8%) cases had inconclusive FNAC results, out of which 5 had blood mixed lymphoid cells and 3 had inadequate material hence it was difficult to interpret. No complications of FNAC noted in the present study.

In the present study, five (5%) cases were diagnosed to have malignancy of which two (2%) cases were Hodgkin's lymphoma, two (2%) cases were Acute lymphoblastic leukaemia and one (1%) case was nasopharyngeal carcinoma.

Among fifty-five (55%) cases of reactive lymphadenitis nineteen (34.5%) children had tonsillopharyngitis, eleven (20%) children had otitis media, two (3.6%) children had scalp infection, dental infection, retropharyngeal abscess each. One (1.8%) child had varicella. Three children who had reactive hyperplasia in FNAC, were diagnosed to have tuberculosis and treated with ATT. Among 2 children with FNAC suggestive of suppurative lymphadenitis had follicular tonsillitis. In the remaining 15 children aetiology of reactive lymphadenitis could not be identified.

Table 3 depicts various clinicopathological findings of cervical lymphadenopathy in relation to its aetiology. Table 4 and Figure 4 depicts etiological distribution of cervical lymphadenopathy in detail.

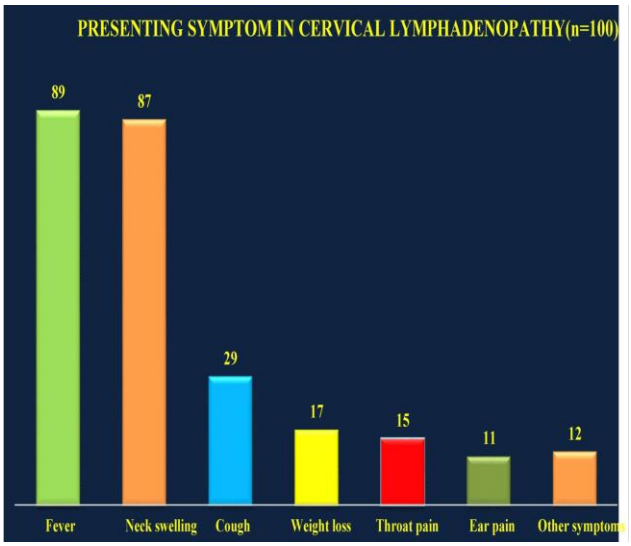

Figure 1: Presenting complaints in cervical lymphadenopathy.

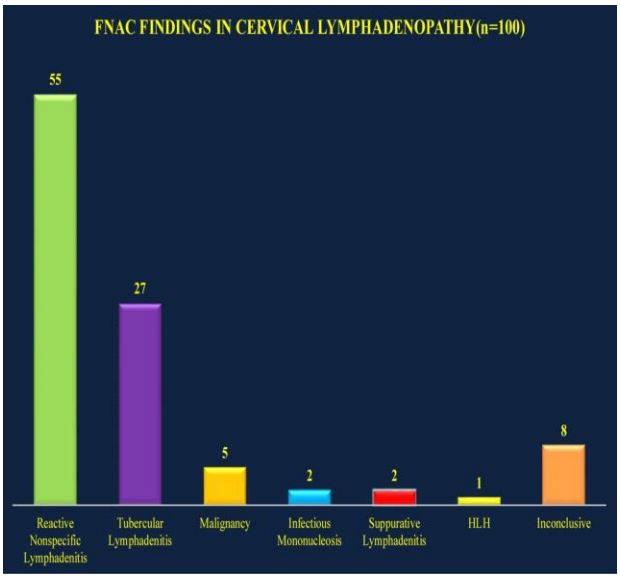

Figure 2: FNAC findings in cervical lymphadenopathy.

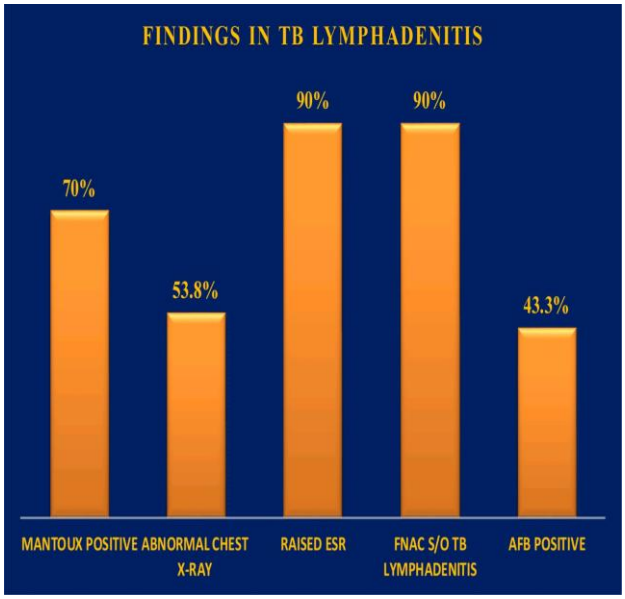

Figure 3: Findings in TB lymphadenitis.

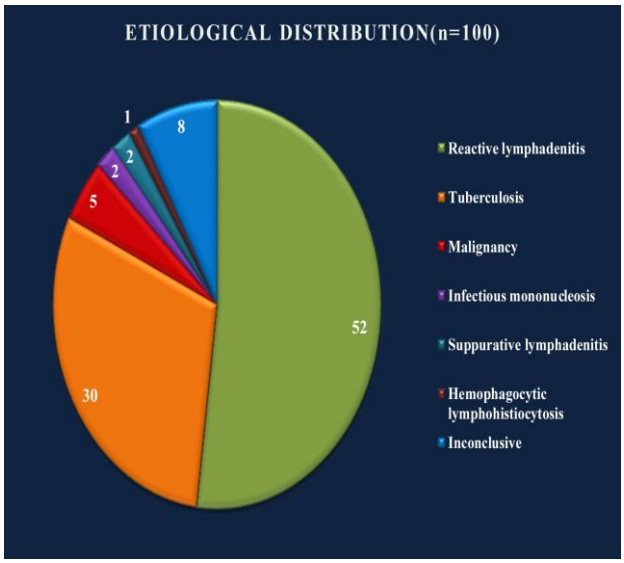

Figure 4: Etiological distribution of cervical lymphadenopathy.

Table 1: Age wise distribution of cervical lymphadenopathy, (n=100).

Age (in years)	N	Percentage (%)
1 month-4	20	20
≥4 -8	45	45
≥8 -12	19	19
≥12-18	16	16

Table 2: Gender wise distribution, (n=100).

Gender	N	Percentage (%)
Male	60	60.0
Female	40	40.0

Table 3: Clinicopathological findings in relation to etiology.

Findings	RL, (n=52)	TB, (n=30)	Malignancy, (n=5)	Others, (n=13)	Total, (n=100)
Fever	48	26	5	10	89
Neck swelling	44	25	5	13	87
Cough	13	14	1	1	29
Weight loss	7	5	4	1	17
TB contact	5	8	1	1	15
Right side LN	21	22	0	5	48
Left side LN	23	6	1	3	33
Bilateral	8	2	4	5	19
Soft	7	1	0	2	10
Firm	45	29	0	11	85
Hard	0	0	5	0	5
Tender LN	6	6	0	6	18
Mobile	45	21	0	9	75
Fixed	7	9	5	4	25
Matted	4	7	0	4	15
Hepatosplenomegay	5	3	4	4	16
Neutrophilia	36	14	1	7	58
Lymphocytosis	7	10	4	1	22
Anemia	30	25	5	7	67
Raised ESR	28	27	4	7	66
Mantoux positive	2	21	0	0	23
Abnormal CXR	11	14	1	0	26
Mean Hb	10.7	10.1	8	10	-
Mean ESR	26.2	48	64.4	29.7	-

Table 4: Etiological distribution of cervical lymphadenopathy, (n=100).

FNAC etiology	Clinical etiology	N	Total
Reactive lymphadenitis	Unidentified etiology	15	55
	Tonsillopharyngitis	19	
	Otitis media	11	
	Impetigo/scalp infection	2	
	Retropharyngeal abscess	2	
	Dental infection	2	
	Varicella	1	
	Tuberculosis	3	
Tubercular lymphadenitis	Tuberculosis	27	27
Malignancy	Hodgkins	2	5
	Acute lymphoblastic leukamia	2	
	Nasopharyngeal carcinoma	1	
Infectious mononucleosis	Infectious mononucleosis	2	2
Supparative lymphadenitis	Follicular tonsillitis	2	2
Hemophagocytic lymphohistiocytosis	Rickettsial fever	1	1
FNAC inconclusive	Unidentified etiology	8	8

DISCUSSION

In this study, an attempt was made to study the aetiology of children with cervical lymphadenopathy after correlating it with history, clinical findings, and relevant laboratory diagnosis by doing FNAC.

It was found that the majority of the patients with significant cervical lymphadenopathy were in the age group of 4-8 years (45%), followed by 1month to 4 years (20%), 8 to 12 years (19%) and 12 to 18 years (16%). This finding was consistent with Kumar et al and Somaiah et al where the most common age group involved was between 4-8 years in 43% and 40.7% of children respectively.[1,5] Maximum number of cases in this age group can be attributed to normal peak lymphatic growth between 4 to 8 years of age.

Cervical lymphadenopathy was more commonly found in male children (60%) than female children (40%) with male to female ratio of 1.5:1. In comparison, Jalal et al found similar results in their study with male to female ratio of 1.5:1. Somaiah et al observed greater incidence of male children, with male to female ratio of 2.5:1. Moore et al found male preponderance, with male to female ratio of 3:2.[5,11,12]

The most common presenting complaints in children with cervical lymphadenopathy were fever (89%) and swelling in the neck (87%). Similar results were observed by Kumar et al in which neck swelling and fever were present in 90% and 89.5% respectively.[1] Somaiah et al found neck swelling and fever in 90% of children each.[5]

In this study cough was present in 29% of cases of which 46.7% children had tuberculosis. Among the total number of cases of cervical lymphadenopathy 15% children had a history of contact with tuberculosis. Jalal et al found 16% of children with TB contact and Somaiah et al found TB contact in 10% of children.[5,11]

The study showed predominant involvement of level II group (upper deep cervical/ upper jugulodigastric) of lymph nodes (49%) followed by level V group (posterior triangle) (45%), least common involvement was seen in submental group (4%). Balkishan et al and Maheshwari et al observed similar result in their study where level II (upper jugulodigastric) group was most commonly involved (45%, 50%) followed by level V (posterior triangle) (17%, 25%).[9,15] Sachin et al found most common group involved was jugulodigastric (43%).[13] More than one lymph node level involvement was seen in 33% of children.

In this study, unilateral involvement of lymph nodes was most common (81%) compared to bilateral involvement (19%). Similar results were observed by Gorle et al (80.3%, 19.7%), Rao et al (76%, 24%) and Shaik et al (71%,29%).[16-18] Cervical lymphadenopathy was most commonly seen on the right side (48%) followed by left side (33%). This finding was consistent with Shaik et al where right side was most commonly involved (38.5%) than left side (32.5%).[18] Prasad et al found right side involvement in 50% and left side in 32.8%.[17]

In this study, 30 cases of tuberculosis were identified, among which level V group involvement was seen in 17 (56.6%), followed by level II (46.6%). Shaik et al found level V group of lymph node involvement as most common in tuberculosis.[18] Rao et al found 53.3% of cases with level V followed by 30.6% in level II.[17] Gorle et al observed similar results where 31.3% had level V followed by 21.5% level II.[16]

In this study, majority of the patients had firm consistency lymph nodes (85%). Hard consistency was found in 5% of cases, all of them were diagnosed to have malignancy. Jalal et al found similar results with 96.2% of children with firm consistency.[11] Reddy et al observed 95% of children to have firm consistency lymph nodes.[7]

In this study, lymph nodes were tender in 18% of cases and the majority of patients had non tender lymphadenopathy (82%). Similar result was seen by Jalal et al where lymph nodes were tender in 16.2% and nontender in 83.8%.[11] Reddy et al found 80% of lymph node to be nontender.[7]

The study showed mobile lymph nodes in 75% of cases and fixed lymph nodes in 25% of cases. In reactive hyperplasia 86% cases had mobile, in tuberculosis 70% cases had mobile lymph nodes. All 5 malignancy cases had fixed lymph nodes. Similar findings were seen by Jalal et al and Somaiah et al where lymph nodes were mobile in 87.5% and 83.8% respectively.[5,11]

In this study, 85% of the lymph nodes were discrete and 15% of the lymph nodes were matted. Somaiah et al found 16.2% of matted lymph nodes in their study.[5]

Systemic examination revealed hepatosplenomegaly in 16% of cases. This finding was consistent with Reddy et al who observed organomegaly in 15% of cases.[7] Among the total of 5 malignancies identified in our study, four (80%) had hepatosplenomegaly. Two infectious mononucleosis cases were identified in this study, both of them had hepatosplenomegaly.

In this study, 67% of children had anaemia with mean Hb of 10.3±1.7. It correlates with the present national incidence of anaemia in paediatric population. This finding was consistent with Somaiah et al where 53.8% of children had anaemia.[5] Similar results were observed by Appaasaheb et al and Reddy et al who observed anaemia in 51.4% and 45% respectively.[7,14]

In this study, 66% of children had an elevated ESR value. Similar findings were observed by Reddy et al where ESR was raised in 62% of cases. Raised ESR value was found in 90% of children with tuberculosis.[7]

In this study, FNAC as a primary diagnostic tool was done in all cases of cervical lymphadenopathy. FNAC finding was most commonly suggestive of reactive lymphadenitis (55%) followed by tubercular lymphadenitis (27%). Similar results were observed by most of the researchers like Kumar et al (74.4%, 15%), Somaiah et al (74.3%, 23.8%), Reddy et al (54%, 31%), Moore et al (47.8%, 25%), Appaasaheb et al (72.8%, 22.8%) and respectively.[1,5,7,12,14]

FNAC was suggestive of malignancy and infectious mononucleosis in 5% and 2% of cases respectively among the study population. Two cases were suppurative lymphadenitis and one case was hemophagocytic lymphohistiocytosis (HLH). Eight (8%) cases had inconclusive FNAC results, out of which 5 had blood mixed lymphoid cells and 3 had inadequate material

hence it was difficult to interpret. No complications of FNAC noted in the present study.

In the present study, five (5%) cases were diagnosed to have malignancy of which two (2%) were Hodgkin's lymphoma, two (2%) were Acute lymphoblastic leukaemia and one (1%) case was nasopharyngeal carcinoma. Sensitivity of FNAC in diagnosing malignancy was found to be 100%. These cases were referred to higher centre for further management.

In the present study, Hodgkin's lymphoma was seen in 2% of cases, this was similar with Reddy et al and Jalal et al who found 3% and 5% cases of Hodgkin's lymphoma in their study respectively.[7]

In the study, 2 cases of infectious mononucleosis were diagnosed, both were positive for Paul Bunnell test. Reddy et al identified 1 case of infectious mononucleosis with Paul Bunnell test positivity in their study.[7]

Mantoux test was done in 94 cases. Twenty-three (24.4%) patients were Mantoux positive and seventy-one (75.5%) patients were Mantoux negative. Among the Mantoux positive cases twenty-one (91.3%) cases were diagnosed as tubercular lymphadenitis. Similar results were seen by Somaiah et al were 24.8% of children were Mantoux positive and all of them were diagnosed to have Tuberculosis.[5] Reddy et al observed 26% of children with Mantoux positive.[7]

Chest X-ray showed abnormal findings in 26 patients (26%) of which 14 (53.8%) were diagnosed as tubercular lymphadenitis. Somaiah et al found abnormal chest x-ray finding in 30.6% of cases.[5]

In this present study, a total of 30 cases of tubercular lymphadenitis was diagnosed, in which FNAC was suggestive of Tubercular lymphadenitis in 27 (90%) cases. Sensitivity of FNAC in diagnosing Tubercular lymphadenitis was found to be 90.9%. Mantoux was positive in 21 (70%) patients of tuberculosis. 14 (53.8%) cases had chest X-ray findings suggestive of TB. AFB was positive in 13 (43.3%) patients.

In the present study, association between FNAC findings suggestive of Tuberculosis versus ESR, Mantoux, Abnormal chest X-ray and AFB positivity were compared which were statistically significant ($p<0.001$). In this study sensitivity of FNAC was found to be 90.9% and 100% in identifying tuberculosis and malignancy respectively.

After history, examination findings, laboratory results and cytopathological findings specific aetiologies could be identified in 77% of cases. Aetiology could not be identified in 23% of cases. In the study done by Somaiah et al and Sachin et al, aetiology could not be identified in 16.2% and 15% of cases respectively.[5,13] However, in a study done by Jalal et al aetiology could not be identified in 37.5% of cases.[11]

Limitations

Cervical lymphadenopathy has a wide variety of aetiologies, infectious/non-infectious, which are not picked up in the first line of investigations. Etiological work up requires detailed evaluation like viral PCR/culture which are difficult to be done. Our study had a smaller sample size with selection bias due to referred cases. Hence a multicentred study with larger sample size is required to know the exact incidence of different aetiologies of cervical lymphadenopathy in children.

CONCLUSION

Cervical lymphadenopathy is one of the common clinical conditions which paediatricians face in day-to-day practice that requires detailed evaluation for accurate diagnosis and treatment. Clinical evaluation followed by FNAC is the most reliable diagnostic tool which is easy to perform, cost effective, accurate and speedy results can be obtained. Till the recent past, lymph node biopsy was the investigation of choice for cases with cervical lymphadenopathy. Presently FNAC has emerged as an important tool in the initial diagnosis and management of patients with lymphadenopathy. So, it should be done always before the consideration of any open procedure. Although reasonably accurate diagnosis can be made clinically, cytopathological examinations are mandatory to establish and confirm the diagnosis. The findings of the present study may act as first-hand knowledge regarding age-sex distribution of lymph node diseases, their mode of presentation and predilection for different lymph node groups. It will help the caregiver doctors to think in a systematic way for detection/referral of the respective cases early and thereby avoiding the diagnostic delay in cases like tuberculosis or malignancy of lymph nodes.

Recommendations

Etiological profile of cervical lymphadenopathy varies from region to region in developing countries like India wherein Tubercular lymphadenitis continues to be the major reason. So, this study is very helpful to know about the various aetiology and to create awareness among the community.

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