

# Role of FNAC in Chronic Childhood Lymphadenopathy with Suspected Tuberculosis

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## ABSTRACT

**Introduction:** Tuberculous lymphadenitis is one of the common cause of Paediatric lymphadenopathy in India. This study was aimed to assess the usefulness of Fine needle aspiration cytology of lymph nodes as a diagnostic tool in suspected Tuberculosis and to observe the cyto morphological changes for better understanding of immune response.

**Material and methods:** This was a cross sectional observational study conducted between the year 2016 to 2018 at Melmaruvathur tertiary care hospital. Children up to 14 years with suspected Tuberculosis symptoms and chronic lymphadenopathy irrespective of the sizes of nodes were subjected to Fine needle aspiration cytological study. Cyto smears morphology were observed and analysed.

**Results:** A total of 81 cases were studied and the predominant age group affected were between five to ten years (n=46; 56.8%). 42 patients were female (51.9%) and 39 were male (48.1%). Most of them had cervical nodes and 44% of nodes were less than 1 cm size. Out of 81 cases, 32 (39.5%) were diagnosed as nonspecific adenitis and 46 cases (56.8%) as granulomatous lymphadenitis. Among the size of the nodes, 57% of small nodes, 65% of medium sized nodes and 100% of large nodes showed granulomatous adenitis. Among sexes, female preponderance (63.1%) for granulomatous adenitis and male predominance (62.5%) for nonspecific adenitis were observed.

**Conclusion:** Fine needle aspiration cytological study of paediatric lymphadenopathy is a useful diagnostic indicator in suspected Tuberculosis even for small size nodes and can be recommended if clinically warranted.

**Keywords:** Paediatric Lymphadenopathy, Childhood TB, FNAC Node, Node Cytology, TB Node

## INTRODUCTION

Lymphadenopathy is one of the commonest clinical finding among paediatric patients having several aetiologies from inflammatory to malignant condition.<sup>1</sup> Sub-acute or chronic lymphadenopathy is a manifestation of a number of diseases such as tuberculosis, leprosy, mycoses, sarcoidosis, lymphoma and metastatic lymphadenopathy.<sup>2</sup> The size of nodes in the above cases are usually significant (>1cm) on clinical presentation. But in routine clinical practice, many patients presented to the paediatric outpatient department with suspected Tuberculosis symptoms such as underweight, failure to thrive, persistent cough and persistent /recurrent fever possess multiple small discrete/matted nodes. It is unnoticed by parents due to its small size but are identified by clinician. We know that the diagnosis of childhood Tuberculosis is a challenging one and in most

cases still it is based on clinical evidence alone. Though the recommended size of any swelling for doing Fine needle aspiration cytological procedure is at least 1cm, here we tried an attempt to do cytological study of chronic childhood lymphadenopathy with suspected tuberculosis irrespective of the size to assess its utility as a diagnostic tool in Tuberculosis and also to observe the cyto morphological changes for better understanding of immune mechanism behind the changes.

## MATERIAL AND METHODS

This was a cross sectional observational study conducted at Melmaruvathur tertiary health care hospital between the year 2016 to 2018. All children up to 14 years presented to Paediatric outpatient department with suspected tuberculosis symptoms such as persistent/recurrent cough, persistent/recurrent fever, malnutrition, weight loss, failure to thrive, history of contact with adult TB patients, chronic superficial lymphadenopathy irrespective of the size of the nodes were included in the study. Children having chronic lymphadenopathy with non-resolution of lymphadenopathy after a course of antibiotics as well as clinical abscess mimicking as acute bacterial abscess with incomplete resolution were also included in our study. All the children were subjected to fine needle aspiration cytological (FNAC) study of lymph nodes. Patients with small deep seated nodes near carotid vessels and uncooperative violent children were excluded from the study to avoid unnecessary procedural injury to the child. FNAC procedure was done after getting consent from the parent under aseptic precautions. All cyto smears were fixed in 70% alcohol and stained with Haematoxylin and Eosin. Slides were screened by single pathologist and morphological findings were observed and analysed.

## RESULTS

A total of 81 cases were studied and the distribution among age group affected were 25 cases (30.9%) within 5 years of age, 46 cases (56.8%) between 5-10 years of age and 10 cases (12.3%) were between 11-14 years of age. The distribution among sexes were 42 patients female (51.9%) and 39 cases male (48.1%) (Table-1). Most of the children were presented

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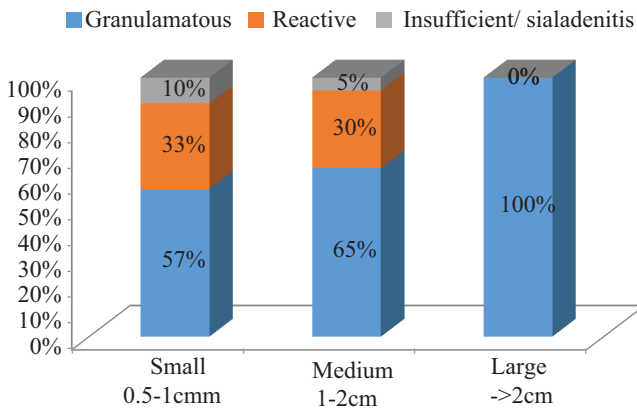


Figure-1:

with cervical lymphadenopathy and predominantly posterior upper cervical group of nodes were involved. Size of the nodes were categorised into small (0.5-1cm), medium (1-2cm), large(>2cm) and its distribution were 44%, 41.5% and 14.5% respectively. Among 81 cases, cyto diagnosis of Chronic nonspecific lymphadenitis was made for 32 cases (39.5%), 46 cases (56.8%) were diagnosed as Granulomatous adenitis, one case (1.2%) as chronic sialadenitis and two (2.5%) as insufficient cellularity for definitive diagnosis. Age wise distribution of granulomatous adenitis showed 52.2% among 5-10 years of age and 37% among less than 5 years of age, 10.9% between 11-14 years of age. Age wise distribution of chronic nonspecific adenitis showed 65.6%

Count		Sex				Total	
		Male		Female			
Age_group	<5 Years	12	14.8%	13	16.0%	25	30.9%
	5-10 Years	23	28.4%	23	28.4%	46	56.8%
	11-14 Years	4	4.9%	6	7.4%	10	12.3%
	Total	39	48.1%	42	51.9%	81	100.0%

Table-1: Age and sex wise distribution

Age_group	FNAC_report_									
	Insufficient cellularity		Chronic nonspecific adenitis		Granulomatous adenitis		Others			
	Count	Table N%	Count	Table N%	Count	Table N%	Count	Table N%		
<5 Years	1	1.2%	7(21.8%)	8.6%	17 (37%)	21.0%	0	0.0%	25	30.9%
5-10 Years	1	1.2%	21(65.6%)	25.9%	24(52.2%)	29.6%	0	0.0%	46	56.8%
11-14 Years	0	0.0%	4(12.5)	4.9%	5(10.9%)	6.2%	1	1.2%	10	12.3%
Total	2	2.5%	32(100%)	39.5%	46(100%)	56.8%	1	1.2%	81	100.0%

Table-2: Age wise distribution of Cyto diagnosis of lymphadenopathy

Sex	FNAC_Report_									
	Insufficient cellularity		Chronic nonspecific adenitis		Granulomatous adenitis		Others			
	Count	Table N%	Count	Table N%	Count	Table N%	Count	Table N%		
Male	2	100%	20	62.5%	17	36.9%	0	0.0%	39	48.1%
Female	0	-	12	37.5%	29	63.1%	1	100%	42	51.9%
Total	2	100%	32	100%	46	100%	1	100%	81	100%

Table-3: Sex wise distribution of Cyto diagnosis of lymphadenopathy

Age_group		Granulomatous adenitis – Sub categorization					Total
		1	2	3	4	5	
<5 Years	Count	10	4	3	0	0	17
	%	50.0%	28.6%	42.9%	.0%	.0%	37.0%
5-10 Years	Count	9	10	2	0	3	24
	%	45%	71.4%	28.6%	.0%	75.0%	52.2%
11-14 Years	Count	1	0	2	1	1	5
	%	5%	.0%	28.6%	100.0%	25.0%	10.9%
Total	Count	20	14	7	1	4	46
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

1. Reactive adenitis with early granulomatous changes
2. Granulomatous adenitis,
3. Granulomatous adenitis with caseation,
4. Cold abscess with extensive caseation and degenerated epithelioid granulomas
5. Epithelioid granuloma with superadded neutrophilic suppurative changes.

Table-4: Morphological spectrum of Granulomatous adenitis among age group

among 5-10 years of age and 21.8% among less than 5 years of age, 12.5% between 11-14 years of age. (Table-2). Among sexes, female preponderance was noted for granulomatous adenitis (63.1%) and nonspecific reactive adenitis was commonly seen in male children (62.5%).(Table-3).Among the size of the nodes 57% of small nodes, 65% of medium sized nodes and 100% of large nodes showed granulomatous changes.(Figure-1)

All granulomatous lymphadenitis was sub categorised into 5 types based on morphology into

1. Reactive adenitis with early granulomatous changes showing polymorphous lymphoid cells and the presence of transforming epithelioid cells.
2. Granulomatous adenitis with classic mature epithelioid cells aggregates
3. Granulomatous adenitis with caseation necrosis
4. Cold abscess with extensive caseation and degenerated ghost like epithelioid cell aggregates
5. Epithelioid cell aggregates with superadded neutrophilic suppurative changes.

Out of 46 cases of granulomatous adenitis, 20 cases had fallen into the category of reactive adenitis with early granulomatous changes, 14 cases into granulomatous adenitis, seven cases into granulomatous adenitis with caseation necrosis, one case presented as cold abscess with caseation necrosis and four cases showed epithelioid aggregates with neutrophilic suppurative necrosis features (Table-4). Langhans giant cells were not appreciated in our study materials.

## DISCUSSION

Childhood cervical lymphadenopathy is most commonly caused by reactive inflammatory response to viral upper respiratory infection or streptococcal pharyngitis.<sup>2</sup> But persistent chronic lymphadenopathy and increasing prevalence of extra pulmonary tuberculosis (EPTB) evoke the need of diagnostic evaluation of the lymphadenopathy. Fine needle aspiration cytology is a simple, safe and minimally invasive procedure that help in the diagnosis of causes of lymphadenopathy.<sup>3</sup> Many studies were done to assess the role of FNAC in the diagnosis of lymphadenopathy. The sensitivity and accuracy of FNAC diagnosis was also proved by many studies.<sup>4,5</sup> But cytological studies of clinically insignificant small sized nodes were not reported so far which we tried for children with suspected tuberculosis symptoms. Though FNAC is an easy procedure, we experienced difficulties in doing the procedure in children especially under 5 years of age and for too small nodes. The difficulties faced were in positioning the child and fixing the node to get representative sample as well as to minimize the deep tissue injury by violent movement of the child. Moreover, upper posterior cervical nodes were commonly involved that pose additional risk of injuring major vessels during the procedure by movement of child.

The predominant age group affected in our study were between 5-10 years (56.8%) as the study by Bhatia whereas Minime et al study showed the predominant age group were under 5 years of age (45.8%).<sup>6,7</sup> Similar to the study by

Paliwal et al, Cyto diagnosis of granulomatous lymphadenitis was more (56.8%) in our study whereas reactive hyperplasia was the common findings in some studies.<sup>8,9,10</sup> Similar to the study by sunali gupta, our study also showed sex predilection of female predominance for granulomatous adenitis (63.1%) and reactive adenitis (62.5%) for male children.<sup>11</sup> No malignancies were observed in our study whereas some studies showed malignant diagnosis in childhood lymphadenopathy.<sup>12,13</sup>

We categorised the morphological spectrum of changes in granulomatous adenitis into 5 types that indicated the evolutionary immune response to the persistent infection. Early phase of immune response showed predominant reactive polymorphous population of lymphoid cells with transforming epithelioid cells that tend to form aggregates followed by mature epithelioid cell aggregates without caseation. It indicated that the initial nonspecific inflammatory response to any infection followed by specification based on mediators produced by antigen presenting cells and transformation to T<sub>H</sub>1 cells. Third phase of caseating granuloma indicated the beginning of killing and destructive immune response which in turn followed by cold abscess characterised by extensive caseation necrosis with degenerated ghost epithelioid cell granuloma. Highest AFB positivity in necrotic nodes than granulomatous nodes proved in some studies also supported this destructive immune response attempt by epithelioid cells.<sup>14</sup> This evolutionary immune responses and morphological changes also correlated well with the size of the nodes. Most of the small less than 1 cm sized nodes showed first category of reactive hyperplasia with transforming epithelioid cells and all large sized nodes showed granulomatous adenitis.

The fifth entity of epithelioid cell granulomatous changes along with neutrophilic infiltration and liquefactive suppurative necrosis arouse the suspicion of either superadded bacterial infection or the emerging atypical mycobacterial infection. Literature stated that the granulomatous morphology is overshadowed and masked by neutrophils in atypical mycobacterial infection. Studies also proved that AFB positivity was high in nodes with necrosis and polymorphs.<sup>8</sup> The presence of neutrophils signifies its role in immune protection against Atypical mycobacterial infection which also was proved in some studies by demonstrating Phagocytised AFB especially Mycobacterium avium complex (MAC) within neutrophils.<sup>15</sup> Usually the Immune Mechanism behind Mycobacterial granulomatous inflammation is delayed hypersensitivity response by T<sub>H</sub>1 cells transformation which is further mediated by interferon gamma. But the presence of many neutrophils along with epithelioid cells and presence of AFB indicated the possibility of Atypical Mycobacterial infection. It probably triggers the immune mechanism of delayed hypersensitivity response by T<sub>H</sub>17 cells transformation which secretes IL-17, IL-22 that might be responsible for this neutrophilic recruitment.

In summary, the authors concluded that FNAC is a useful diagnostic tool for children with suspected tuberculosis. Chronic persistent lymphadenopathy of even smaller sized

nodes showed significant evolutionary morphological changes of granulomatous lymphadenitis. So FNAC is indicated even for smaller less than 1 cm sized nodes if there is clinical suspicion and confusion in arriving at a definitive diagnosis. However, the possibilities of procedural difficulties and chances of getting accidental procedural injury to deeper tissues in an uncooperative child should be borne in mind for selecting this FNAC procedure as a diagnostic tool for smaller nodes.

Our study had limitations that we did not do microbiological (Ziehl Neelsen staining) and histopathological confirmation of granulomatous adenitis since the size of many nodes were small and insufficient material obtained.

Since the gold standard confirmatory tool for tuberculosis is microbiological demonstration of AFB by Ziehl Neelsen staining, it can be incorporated as an adjunct study along with cyto morphological study by FNAC to improve the diagnostic accuracy.

## CONCLUSION

Fine needle aspiration cytological study is a useful diagnostic indicator especially for paediatric lymphadenopathy. Though the size of the node is small and clinically insignificant, it showed significant morphological changes that helped the clinician to arrive at a diagnosis. So cyto smear study of lymphadenopathy can be recommended if clinically warranted irrespective of the size of the nodes.

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