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ORIGINAL ARTICLE

Fine Needle Aspiration Cytology (FNAC) As a Diagnostic Tool in Paediatric Lymphadenopathy

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ABSTRACT

Introduction: Lymphadenopathy is one of the commonest clinical presentations among paediatric patients, having several aetiologies and can pose as a diagnostic dilemma to a paediatrician. Therefore, it is necessary to arrive at a definitive diagnosis in order to administer proper treatment. The objective of this study was to evaluate the diagnostic role of fine needle aspiration cytology in lymphadenopathy in the paediatric age group.

Material and Methods: This study was carried out in patients up to 14 years of age, who had palpable lymph node masses. The duration of this study was 3 years. A total number of 270 cases were included in the study for cytological examination. Histopathological examination was performed in 90 patients. Both dry and wet fixed smears were prepared in all cases and were stained by MGG and Papanicolaou stains.

Results: Overall, inflammatory lymphadenopathy comprised 88.5% of the total lesions of the lymph nodes; it included 56% cases of reactive hyperplasia, 28.1% cases of granulomatous lymphadenitis and 4.4% cases of acute nonspecific lymphadenitis. Malignant lesions were seen in 11.5% patients. Overall, the diagnostic accuracy of the cytological examination was 98.89% and the overall sensitivity and specificity were 91.3% and 99.1%, respectively.

Conclusions: Fine needle aspiration cytology is a reliable, easy and economical technique in the diagnosis of paediatric lymphadenopathy.

Key Words: Fine needle aspiration cytology, FNAC, paediatric, children, lymphadenopathy.

Key Messages

- FNAC is a very simple and expeditious procedure which can be carried out with ease in children.
- FNAC is fairly accurate in the diagnosis of lymphadenopathy
- It reduces the necessity to perform excision biopsy in many cases, thus saving children from surgical complications.

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Introduction

Lymphadenopathy is one of the commonest clinical presentations among paediatric patients attending the outdoor department. It has several aetiologies ranging from an inflammatory process to a malignant condition, thus posing diagnostic dilemma to a paediatrician. Therefore, it is necessary to arrive at a definitive diagnosis in order to administer proper treatment. FNAC is a very simple and expeditious procedure which can be carried out with ease in children [1]. The objective of this study was to evaluate the diagnostic role of fine needle aspiration cytology in lymphadenopathy in the paediatric age group. It has been shown in several studies like ours, that FNA is fairly accurate in the diagnosis of lymphadenopathy [2],[3]. In the last few years, FNAC has emerged as a reliable diagnostic procedure in the paediatric age group, thus obviating the need for excision biopsy [4],[5].

Material and Methods

The study was carried out in patients up to 14 years of age, who had palpable lymph node masses. Lymphadenopathy was considered to be significant if the cervical group was >1.0cm and the inguinal group was >1.5cm. The patients were selected from the OPD and the wards. The duration of the study was three years. In all these patients, a thorough work out was done, which included taking detailed clinical history and general, local and systemic examination, along with routine and special investigations which included X-ray chest (PA view), bone marrow aspiration, ultrasound and CT scan (if indicated). Two hundred and eighty eight patients were subjected to FNAC; however, in 18 cases (6.25%), the material was inadequate for cytological examination and they were excluded from the study. Only 270 cases were available for the study. Histopathological examination was performed in 90 patients. Both dry and wet fixed smears were prepared in all cases and were stained by MGG and Papanicolaou stains. Ziehl-Neelsen's stain was used wherever indicated.

Results

In this study, 153 patients were males and 117 patients were females. The male and female ratio was 1.30:1.

The maximum number of cases were in the age group of 7-14 years (156 cases, 57.8%), followed by 84 (31.2%) and 30 cases (11%) in the range of 2-6 and 0-1 years, respectively.

The sites of distribution of the enlarged lymph nodes were divided into generalised and localised. Generalised lymphadenopathy was defined as the enlargement of more than two non-contiguous node regions [6]. In the present study, localised lymphadenopathy was seen in 243 cases (90%) and the generalised category was seen in 27 cases (10 %). The maximum number of cases had cervical lymphadenopathy (79%), followed by involvement of the axillary (11%) and the inguinal (10%) nodes. Out of the cervical group of nodes, the upper anterior and the upper posterior deep cervical nodes were involved in a majority of cases (68.0%). The size of the nodes was measured in all the cases. The largest node which was seen had a maximum diameter of 5.5 cm. .

The diagnosis of 270 cases of lymphadenopathy based on cytological examination alone is shown in [Table/Fig 1]. However, **Cytohistological correlation** could be done in 90 cases only, as shown in [Table/Fig 2].The cytological criteria which were adopted for classification were as follows:

(Table/Fig 1) Diagnosis of 270 cases of lymphadenopathy based on cytological examination

Disease	Total No.	Percentage (%)
* INFLAMMATORY	239	88.5
Reactive hyperplasia	151	56.0
Acute suppurative	12	4.4
Tuberculosis	76	28.1
* MALIGNANT	31	11.5
Non-Hodgkin lymphoma	21	7.8
Hodgkin lymphoma	06	2.2
Leukaemic infiltrate	04	1.5
Metastatic tumor	Nil	Nil
Total	90	100.0

(Table/Fig 2) Cytohistological correlation of the 90 cases

Disease	No. of cases diagnosed on cytology	No. of cases confirmed by histology	False positive
* INFLAMMATORY	80	78	02
- Reactive hyperplasia	49	48	01
- Acute suppurative	05	05	-
- Tuberculosis	26	25	01
* MALIGNANT	10	09	01
- Non-Hodgkin lymphoma	06	05	01
- Hodgkin lymphoma	02	02	-
- Leukaemic infiltrate	02	02	-
Total	90	87	03

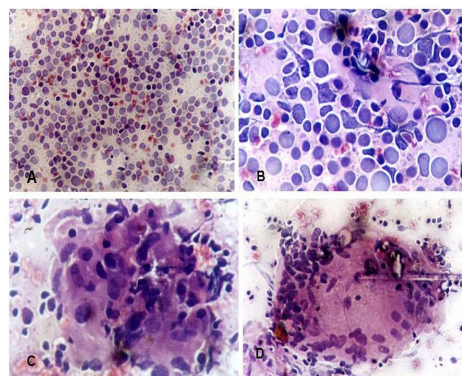
Inflammatory Lesions

Two hundred and thirty nine nodes were diagnosed as inflammatory by FNAC. They were further grouped into three sub-categories.

Reactive Hyperplasia

The cytospreads of these cases showed a mixed population of lymphoid cells. The cytological pattern of distribution of the cells depended on whether the follicular or intrafollicular tissue was aspirated. Thus, smears from a node containing cells of the active germinal centre had many centrocytes and centroblasts, while mature lymphocytes, plasma cells and immunoblasts were relatively sparse [Table/Fig 3] (Figure 3A) Smears which had cells of the interfollicular tissue were predominantly mature lymphocytes, plasma cells and immunoblasts. They were probably from cases of lymphadenopathy following viral infection. These cases were grouped as non-specific hyperplasia.

Besides these cells, smears of reactive hyperplasia showed numerous macrophages. In some of them, the cytoplasm contained intracytoplasmic nuclear debris (tingible body macrophage). The background of these smears also showed cytoplasmic fragments, known as lymphoglandular bodies [Table/Fig 3]. (Figure 3B)



(Table/Fig 3) (A): Aspiration smear showing polymorphic population of lymphoid cells in a case of reactive lymphadenitis (MGG, 100x)

(Table/Fig 3) (B): Aspiration smear showing polymorphic population of lymphoid cells in a case of reactive lymphadenitis (MGG, 400x)

(Table/Fig 3) (C): Aspiration smear showing cluster of epithelioid cells in a case of granulomatous lymphadenitis (MGG, 400x)

(Table/Fig 3) (D): Aspiration smear showing Langerhans' Giant Cell in a case of granulomatous lymphadenitis (MGG, 100x)

Out of the 49 cases diagnosed by cytology, 48 were confirmed by histopathology and one case turned out to be non Hodgkin's lymphoma instead of reactive hyperplasia

Granulomatous Lymphadenitis

Out of the 76 cases which were diagnosed as granulomatous lymphadenitis, 51 cases showed epithelioid granuloma with caseous material and 25 cases had epithelioid granuloma without caseous material. Epithelioid cells with the characteristic curved elongated nuclei with indistinct cytoplasm were usually seen in clusters [Table/Fig 3] (Figure 3C). Occasionally, (five cases) Langerhans' multinucleated giant cells were seen [Table/Fig 3] (Figure 3D). Caseous material was eosinophilic and granular and lacked recognizable cell remnants. Some cases presented with secondary infection and in them, a course of antibiotics was advised and repeat FNAC was done. In those cases in which only caseous material was seen, repeat FNAC was

advised to search for a granuloma. In all these cases, cytological smears were stained with Ziehl Neelsen's stain for Acid Fast Bacilli (AFB) and only 7% cases proved to be positive. Though granulomatous response is seen in a wide variety of infectious agents and non infectious processes (both benign and malignant), as tuberculosis is so common in our country, every clinically relevant case of granulomatous lymphadenitis should be considered as tuberculous lymphadenitis, unless proved otherwise [7]. We had correlated all our cases of granulomatous lymphadenitis with the clinical presentation, Montoux test, AFB, culture, PCR and their response to Anti Tubercular Agents.

Out of 26 cases which were diagnosed by cytology, 25 were confirmed by histopathology. One case where the diagnosis of tuberculosis was made on the basis of epithelioid cells, turned out to be Hodgkin's lymphoma by histopathology.

Acute Suppurative

The cytosmears showed degenerated and viable inflammatory cells, predominantly polymorphs. Repeat aspiration was advised after a course of antibiotic therapy.

Malignant Lesions

Non-Hodgkin's Lymphoma

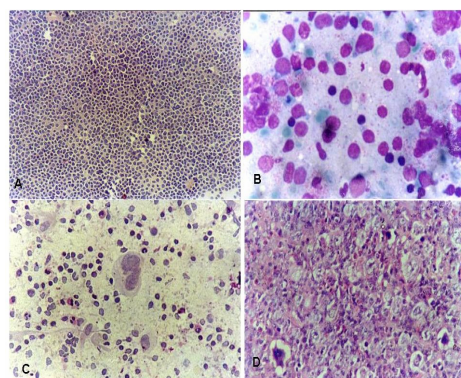
Monotonous population i.e. single cell type predominating the smear, was the most important basis for the diagnosis of non-Hodgkin's lymphoma in cytological smears [Table/Fig 4] (Figure 4A and 4B) In this study, five cases were diagnosed correctly by FNAC. One case diagnosed by us as reactive hyperplasia turned out to be non-Hodgkin's lymphoma. Conversely, one case which we diagnosed as non-Hodgkin's lymphoma was reactive hyperplasia.

Hodgkin's Lymphoma

The presence of Reed Sternberg cells was essential to diagnose Hodgkin's lymphoma. In all our cases, Reed Sternberg cells were seen in the cytosmears [Table/Fig 4] (Figure 4C) Numerous atypical large mononuclear cells with

prominent nucleoli were also seen. Besides these cells, variable numbers of plasma cells, lymphocytes, eosinophils and reactive cells were seen in the background.

In the present study, two cases were diagnosed as Hodgkin's lymphoma by FNAC and both were confirmed by histology [Table/Fig 4] (Figure 4D) One case which was misdiagnosed as tuberculosis by FNAC was actually Hodgkin's lymphoma.



(Table/Fig 4) (A) : Aspiration smear from Non Hodgkin's lymphoma, showing monomorphic population of lymphoid cells (Pap, 100x)

(Table/Fig 4) (B) : Aspiration smear from Non Hodgkin's lymphoma, showing monomorphic population of lymphoid cells (MGG, 400x)

(Table/Fig 4) (C): Aspiration smear Hodgkin's lymphoma, showing single Reed Stenberg cell (Pap, 400x)

[Table/Fig 4] (D): Paraffin section of lymph node. Hodgkin's lymphoma, nodular sclerosis, showing lacunar cells (H&E, 100x)

Leukaemic Infiltrate

Four cases of acute lymphoblastic leukaemia which were diagnosed by GBP and bone marrow examination presented with lymphadenopathy; however, only two cases were confirmed by histopathology. Cytosmears of all these cases showed lymphoblasts which were similar to those which were found by GBP and bone marrow examination and were diagnosed as leukaemic infiltrates.

In the present study, we found the overall diagnostic accuracy of the cytosmears to be 98.89% and the overall sensitivity and the specificity to be 91.3% and 99.1%, respectively.

Discussion

This study was carried out primarily to evaluate the role of FNAC as a diagnostic tool, with its advantages and limitations, in paediatric lymphadenopathy. In the present study, cytological examination was done on 270 patients, but histopathological examination of the lymph nodes could be done only in 90 patients.

Overall, inflammatory lymphadenopathy comprised 88.5% of the total lesions of the lymph nodes; it included 56% cases of reactive hyperplasia, 28.1% cases of tubercular lymphadenitis and 4.4% cases of acute nonspecific lymphadenitis. Malignant lesions were seen in 11.5% of the patients. These findings are in agreement of those reported by Locham *et al*, who diagnosed reactive hyperplasia in 68% cases, tubercular lymphadenopathy in 29% cases and malignancy in 3% cases [8]. Tripathi *et al* found reactive hyperplasia in 64% cases and tuberculosis and neoplasia in 4% of the patients [9]. Sankaran *et al* also observed lymphoid hyperplasia as the most common condition in benign lesions, followed by tuberculosis [10]. Jain *et al* reported 1.8% malignant cases in their study [11]. The present finding of 11.5% is much higher than those reported by the above workers; this could probably be because of relatively more referral of the suspected cases of lymphoma to our centre.

The maximum number of cases (79%) in the present study involved the cervical group of lymph nodes. This could be attributed to the predominant population reporting to our centre being from the low socio-economic group. As they have a high incidence of oropharyngeal, dental and scalp infections which results in enlargement of the cervical lymph nodes, draining the above regions and manifesting with reactive lymphadenitis.

Hemalatha *et al* and Sen *et al* showed a higher incidence of tuberculosis in the cervical group of lymph nodes, followed by the axillary group [12],[13]. Kumar *et al* stated that the cervical group of lymph nodes were mainly involved in the cases of tuberculosis in children, whereas the cervical and the axillary types were both involved in adults [14]. The present findings are in agreement with the above studies.

In the present study, it was noticed that a maximum number of cases; 243 out of 270 (90.0%) presented with localized lymph node enlargement as compared to 10% which presented with generalised lymphadenopathy. These observations are similar to the findings of Gupta *et al* [15]. On further break-up in their work, they found that the maximum number of their cases of lymphoma presented with generalized lymphadenopathy. Similarly, in our study, we also found that 17 out of 31 (55%) cases of lymphoma presented with generalized lymphadenopathy.

The overall sensitivity and specificity reported by Prasad *et al* were 89.2% and 100%, respectively, which matched with our findings [16].

As far as the diagnosis of tubercular lymphadenitis was concerned, the diagnostic accuracy of the cytosmears in the present study was 98.89%, which was similar to that reported by Singh *et al* and Patra *et al* [17],[18]. The specificity of 98.4% in this study matched with that of Sankaran *et al*.

The sensitivity of the cytosmears in the cases of Hodgkin's disease in this study was 66.6%. Sankaran *et al* reported the sensitivity in his work as 30%, which is lower as compared to this study. The specificity of 100% in the present study is at par with that of Sankaran *et al* i.e. 98.6%.

In cases of non-Hodgkin's lymphoma, the diagnostic accuracy in the present study was 97.78%, which was slightly higher than that reported by Gupta *et al*. The sensitivity of 97.95% in the cases of non-Hodgkin's lymphoma in the present study is higher as

compared to 80.3% which was observed by Sankaran *et al*, whereas the observed specificity of 98.80% in cases of non-Hodgkin's lymphoma is in agreement with the findings of Sankaran *et al* i.e. 95.4%. Jain *et al* reported a diagnostic accuracy of 100% in malignant lymphadenopathy in children.

Overall, the diagnostic accuracy of the cytospreads was 98.89% and the overall sensitivity and specificity were 91.3% and 99.1%, respectively. These findings are in agreement with the findings of Godvin *et al* and Frable *et al*. [19], [20]

Thus, fine needle aspiration cytology is a reliable, easy and economical technique with a high diagnostic accuracy; but it is not 100% accurate. Many lymph node diseases may require the confirmation of cytodiagnosis by histopathological examination.

With the increasing costs of medical facilities, any technique which speeds up the process of diagnosis, limits the physical and the psychological trauma to the patient and saves the expenditure of hospitalization, is of tremendous value. FNAC also helps the surgeon to select, guide and modify treatment planning in patients who require surgery. It reduces the necessity to perform excision biopsy in many cases, thus saving children from surgical complications. Thus, FNAC can be recommended as a first line of investigation in the diagnosis of lymphadenopathy in the paediatric age group.

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