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Fine Needle Aspiration Cytology (FNAC): An Easy and Effective Tool for the Evaluation of Cervical Lymph Node Masses

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Abstract

Background: Given that the clinical and radiological examinations of lateral cervical masses are not always sufficient for deciding on appropriate management, the cytological examination of the material obtained by fine-needle aspiration might be an efficient tool in the preoperative investigation of these lesions. *Aim*: To assess the usefulness of FNAC in the diagnosis of cervical lymph node masses and study the cytological features of common pathological conditions affecting the lymph nodes,in correlation with histopathological examination. *Materials and Methods*: A retrospective study of enlarged cervical lymph nodes is undertaken &evaluated between the period from 2013 to 2016 .Cervical lymph node biopsieswere received from 90 patients out of a total of 100cases of previous FNACs and were subjected to unbiased histopathological examination, after fixing in 10% formalin. *Results*: All 90 cases correlated well with the histopathological diagnosis.Two of the AFB positive cases were subsequently diagnosed to be HIV positive. Epitheloid cell granulomas were observed in all cases of tuberculosis with or without caseation and/or AFB. Two cases of granulomatous lymphadenitis did not show caseation,both cytologicallyand histologically, and were labelled negative for AFB,both on smear and culture. They were further followed up, and subsequently diagnosed as Sarcoidosis and toxoplasmosis respectively. Cytological diagnosis for Non –Hodgkins lymphoma was rendered as lymphoproliferative disease,suspicious for malignant lymphoma,which on histopathological examination confirmed the diagnosis of NON –Hodgkins lymphoma. *Conclusion*: Fine-needle aspiration cytology (FNAC) is an accurate, reliable, cost effective, minimally invasive, and pain free, first line diagnostic technique to investigate both superficially palpable&deep seated masses.

Keywords: FNAC; Cervical Lymphadenopathy; Metastatic Carcinoma; Infectious Granulomatous Lymphadenitis.

Introduction

The role of FNAC in the investigation of lymphadenopathy has previously been established by a number of studies. Overall, infective conditions (reactive and infective granulomatous) are responsible for the majority of lesions. M. tuberculosis is the most common cause of infective granulomatous lymphadenitis in India. FNAC with other ancillary tests (microbiological, immunohistochemical, radiological, biochemical and special staining techniques) is useful for obtaining a definitive diagnosis. The biopsy of the cervical lymph node has always been the gold standard, however, it is more resource intensive than FNAC, since the biopsy procedure requires anaesthesia, strict asepsis, operation theatre time, often leaving a scar. In contrast, FNAC of the cervical node is relatively simpler and offers quick reliable results. There is no evidence that the tumour spreads through the skin track created by the fine hypodermic needle puncture during the technique operation. Hence the purpose of the study is to assess the usefulness of FNAC in the diagnosis of cervical lymph node masses and to study the cytological features of common pathological conditions affecting the lymph nodes, viz. tuberculosis, lymphoma and metastatic malignancy. Also to evaluate the diagnostic accuracy between FNAC and open biopsy in cervical lymphadenopathies.

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Materials and Methods

A retrospective cohort study was carried out over a three year period at Kamineni diagnostic laboratory services, L.BNagar, Hyderabad, for FNAC of enlargedcervical lymph nodes during the period between Jan 2013 to Jan 2016. Out of 100 cytologically diagnosed cases, only 90 cases with histopathological correlation were available in this study,since the biopsy procedure in the remaining cases was not performed due to various logisticreasons. A detailed history, clinical examination and relevant investigations were documented for all the cases. FNAC of the enlarged cervical lymph nodes was carried out understrict aseptic precautions. Following the aspiration, several smears were prepared only after assessing the adequacy of the aspirated material. These smears were fixed both by air drying and 100% alcohol, followed by four different stain applications,that includes Giemsa, Ziehl Neelsen, Hematoxylin - Eosin, and Papanicolaou.

Cervical lymph node biopsies were received from 90 patients and the biopsy specimens were subjected to histopathological evaluation (HPE) after fixing in 10% formalin. The latter results were correlated with that of the cytological reports to evaluate the efficacy of the procedure.

All the 90 cases from FNAC procedure showed 100% HPE correlation, and were accordingly categorized as 28 cases of tuberculous lymphadenitis, 41 of reactive changes, 12 of lymph nodemetastasis, 7 of lymphomasand 2 of granulomatous lymphadenitis after thorough evaluation.The diagnosis of reactive hyperplasia of lymph node was rendered by observing a polymorphous lymphoid population of cells, macrophages with tingible bodies & absence of Reed Sternberg cells. Granulomatous lesions were recognized cytologically by the presence of aggregates of epithelioid cells, with or without multinucleated Langhans type of giant cells. An amorphous necrotic background suggestive of caseation necrosis led to the diagnosis of tuberculosis. The cases with a high index of suspicion for Tuberculosis were further studied with Ziehl-Neelsen stain to detect acid fast bacilli (AFB). The eventual diagnosis of granulomatous inflammation on cytology was confirmed either by biopsy or by other complimentary investigations, such as TB Quatiferon, Gene expert studies or PCR methodologies.

The diagnosis of lymphoma was considered by observing sheets of monotonous lymphoid cell population displaying significantnuclear atypia, necrosis, rare granulomatous type reaction and variable number of mitoses. Metastatic carcinoma was diagnosed cytologically by presence of dual cell population composed of malignant epithelial cells admixed with predominant lymphoid cell population.

We could achieve 100% sensitivity and 99.7% specificity for tubercular lymphadenopathy,99% for reactive lymphadenopathy and for metastatic/ primary lymphoid malignancy it was 99.5% and 100% respectively, after correlating with the HPE findings. One case each from Sarcoidosis and Toxoplasmosis was encountered during the study period,which depicts the rarity of these two lesions.

Immunohistochemistry was performed later on the tissue biopsiesin four cases of lymphoma and two cases of adenocarcinoma for an additional confirmation.

In cases where unsuspected metastasis was given, the primary site of malignancy was searched for and subsequently biopsied. The cytological diagnosis was correlated with lymph node or primary tumor biopsy.

Inclusion Criteria

All cases of cervical lymph node masses where FNAC was done and those cases undergoing subsequent biopsy .

Exclusion Criteria

All cases of cervical lymph node masses, wth inadequate aspirate were excluded from the study. If the material was a hemorrhagic, such smears were also excluded.

Results

This study analyzed 100 cases of cervical lymphadenopathy. The age of patients ranged from >one year to up to 81 years in which 68% were males and 32% were females [Table 1]. The maximum incidence of cervical lymphadenopathy was observed in the age group of 18 to 60 years. Reactive lymphadenitis [Figure 1] was found to be the most common pathologic lesion in our study, accounting for 45% of cases followed by Tuberculous lymphadenitis [Figure 2] constituting 31% of cases, 7.0%cases of Lymphoma [Figure 3] and 17% cases of metastatic malignancies [Figure 4 and 5]. In these 100 cases, epithelioid cell granulomas with either caseation necrosis orveryrarely AFB were seen, thereby confirming the diagnosis of tubercular lymphadenitis. These patients with tuberculous lymphadenitis were

mainly in the third decade of life. The Ziehl Neelsen stain for AFB was positive in 05% out of the total of 100 cases showing epithelioid cell granulomas. AFB were cultured in 06%out of the 28 diagnosed cases of tuberculous lymphadenitis. Two of the AFB positive cases were subsequently diagnosed to be HIV positive. Epitheloid cell granulomas were observed in all cases of tuberculosis with or without caseation and/or AFB. Two cases of granulomatous lymphadenitis did not show caseation, both cytologicallyand on HPE analysis, and were found to be negative for AFB on smear and culture. They were further investigated, followed up, and finallydiagnosed as Sarcoidosis and toxoplasmosis respectively.

Cytological diagnosis for Non-Hodgkins lymphoma was rendered as lymphoproliferative disease, suspicious for malignant lymphoma, which on histopathological examination confirmed the diagnosis of NON-Hodgkins lymphoma.

Table 1: Age and gender wise distribution of cytological lesions

Age Group in Years	Males	Females	Total
<1-20	10	7	17
21-40	23	20	43
41-60	12	10	22
61-80	7	6	13
Upto 81	4	1	5

Table 2: Cytological diagnosis of aspirated cervical lymph nodes

Cytological Diagnosis	Number of Cases	Percentage
Tubercular lymphadenitis	28	31%
Reactive lymphadenitis	41	45%
Granulomatous lymphadenitis	2	3%
Lymphoma	7	7.9%
Metastasis	12	13%

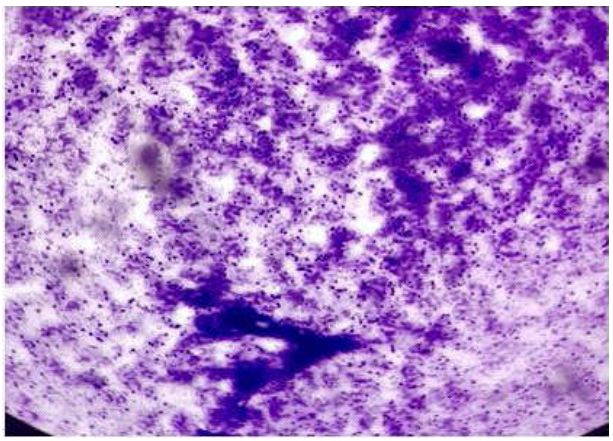

Fig. 1: Benign/Reactive Lymphadenitis

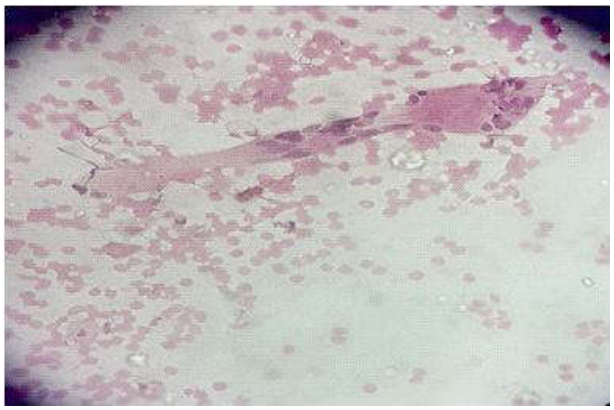

Fig. 2: Infective Agents

Photomicrograph of smear of reactive lymphadenitis, showing a pleomorphic population of benign lymphoid cells, admixed with few tingible body macrophages (Giemsa stain ×40).

Photomicrograph of smear of granulomatous T.B lmphadenitis with epithelioid cell clusters scattered against a multinucleated Langhans type of giant cell. (Hematoxylin and Eosin stain, ×40).

Photomicrograph of smear of malignant lymphoma constituted by monotonous group of scattered lymphoid cellpopulation scattered against hemorrhagic background (Giemsa stain 40×).

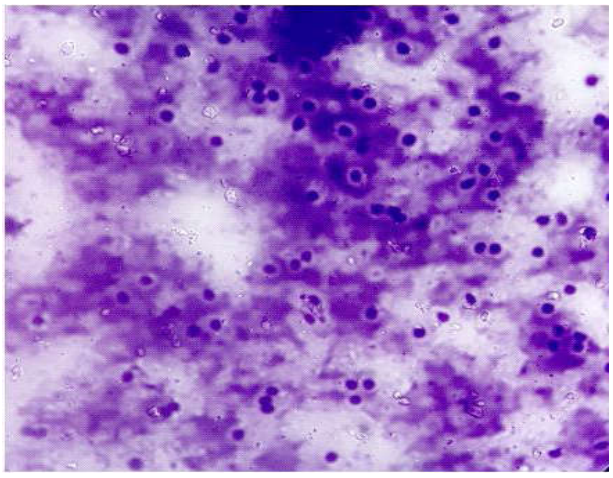

Fig. 3: Smear of malignant lymphoma

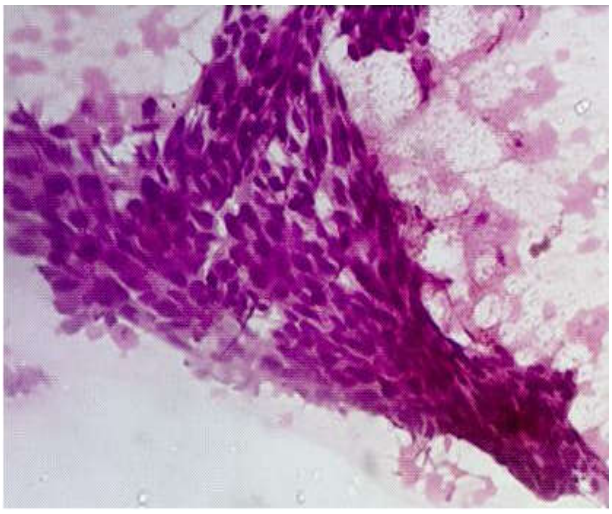

Fig. 4: Smear of metastatic squamous cell carcinoma

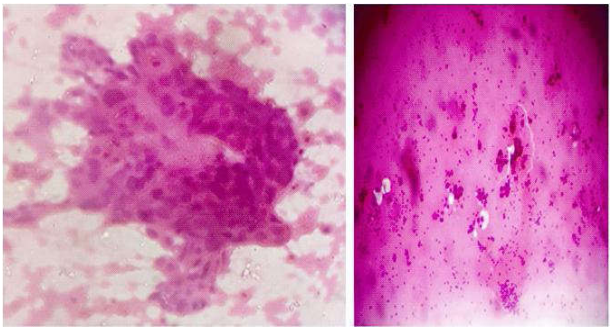

Fig. 5: Smear of metastatic gastric adenocarcinoma

Photomicrograph of smear of metastatic squamous cell carcinoma, showing tumour cells with pleomorphic nucleus anddeeply eosinophilic cytoplasm (Hematoxylin and Eosin stain, ×40).

Photomicrograph of smear of metastatic gastric adenocarcinoma , showing tumour cells arranged in acinar pattern against reactive lymphoid cell background (Hematoxylin and Eosin stain, ×40 & 10x).

Discussion

Papanicolaou (1883-1962) – the father of exfoliative cytology introduced needle aspiration in 1841. Erichson (1853) adopted this method of using an exploring needle to withdraw cells from tumours for cytological diagnosis. In 1904 Greig and Gray [2,3]. isolated trypanosomes by aspirating lymph nodes in patients with sleeping sickness. It was, however, only after Papanicoloau's basic discovery in 1928 of the usefulness of exfoliated cells in the diagnosis of carcinoma, that the cytological diagnosis of tumour became popular. Modified ultrafast Papanicolaou stain is useful for rapid diagnosis by FNAC [1].

Fine needle aspiration of cervical lymph nodes has been practiced since a long time. Since the mid- 1960's, it has been increasingly used and a high degree of accuracy has been achieved as it is construed as simple and rapid. Cervical lymphadenopathy is one of the commonest presenting symptoms of all age groups. The etiology can vary from general inflammatory reactive lesions to a malignant condition.The diagnosis offered on FNAC has been shown to correlate very well with histopathological diagnosis after biopsy [2,3]. Enlarged cervical lymph nodes are easily accessible, depending on the palpable sizes for FNAC and therefore, this procedure is of great importance in the diagnosis of these disorders. It plays a significant role in developing countries like India, as it is relatively an inexpensive procedure, with practically no significant complications [4,5,6]. The reactive lymph nodes formed the major group among the commonly encountered lesions seen in upto 41 patients. The aspirate showed various stages of maturing lymphocytes, as seen in a reactive lymphoid follicle. In this group, six patients showed features of viral infection with prominence of immunoblasts and plasma cells,the background of lymphocytes was however polymorphous. The peripheral blood smear in these six cases showed antigenically stimulated lymphocytes. In a follow up of these cases over a period of 6 months, the clinical and peripheral blood findings totally regressed and therefore the patients were informed that their condition did not warrant any further treatment.

Of late Tuberculosis once thought to be a treatable entity, shows dramatic resurgence in the number of cases due to complacency and growing number of drug resistant strains. In our study, FNAC of the cervical nodes, invariably revealed epitheloid cell granulomas. Most of the patients with tuberculosis showed caseous material (28/100patients). The AFB were detected in 05/28 patients. The frequency of AFB positivity in FNAC smears in various studies ranges from 10% to 70% [10,11,12,21]. Overall, only two cases remained labelled as granulomatous lymphadenitis, and both cases were negative for M. tuberculosis on smear and culture. These cases were subsequently diagnosed as Sarcoidosis and toxoplasmosis, respectively. Some authors believe in regions where tuberculosis is very common that, morphologic findings of granulomatous inflammation are consistent with tuberculosis. Culture for AFB and Gene expert was advised in all such cases. Nevertheless, it is wise to mention that several weeks are needed to obtain the result,which may delay the initiation of treatment. In our study, 20/28 cases of tubercular lymphadenitis were positive for AFB culture. Patients with a concurrent HIV infection revealed a heavy load

of AFB, which is a well-documented feature in the literature [11,12].

FNAC maybe the only tool for initial diagnosis and further management of patients in some cases of metastatic malignancy.Malignancy from a variety of different cancers can spread to the lymph nodes to produce cervical lymph node swelling. Lymphoma is cancer that actually begins in the lymph node. Painless swelling of the cervical lymph node may be one of the few outward signs of lymphoma early on.

Hodgkin's and non-Hodgkin's lymphoma, are the two main categories of lymphoma. Generalized lymph node swelling refers to swollen nodes that arise in distinct areas of the body, sometimes all over the place, not seeming to follow a recognizable pattern. According to Mohseni and colleagues [22], haphazard type of lymph node swelling is usually seen in non-Hodgkin's lymphoma. Hodgkin lymphoma is distinguished by the localized involvement of the lymph node following a predictable, organized procession from one lymph node area to the next.

HL is rare in children younger than 10 years old. Most children with HL have painless lymph node swelling, and involvement of cervical lymph nodes is common. When children have NHL, clinical involvement in the head and neck is seen in only 5 to 10 percent, and most often it involves symptomatic cervical lymphadenopathy.

When lymph node involvement is limited to the neck, Hodgkin's disease, non-Hodgkin's lymphoma, and squamous cell carcinoma of the head and neck and metastatic carcinomas are common malignancies in the neck region [22].

The cervical group is the most common group of lymph nodes to be involved by squamous cell carcinoma metastasis and the primary is most often from the oral cavity/pharynx, esophagusandlarynx. These metastatic incidences from head andneck regionis highest in India, probably due to the excessiveusage of multiple tobacco products.Among the soft tissue tumors, rhabdomyosarcoma and extra skeletal Ewing's sarcoma/primitive neuroectodermal tumor are known to metastasize to lymph nodes, the other rare tumors being malignant granular cell tumor, epithelioid hemangioendothelioma, mediastinal ganglioneuroblastoma, angiosarcoma, and epithelioid sarcoma [16]. Specialized investigations such as the combination of lymphosyntigraphy and ultrasonography-guided FNAC's of sentinel lymph nodes in the head and neck area have been found to be good in picking up metastases in clinically undetectable cervical lymph nodes. In our study, the maximum number of cases were observed in the age group between 20-40 yearsandelderly people, as also observed by Chandanwale et al [7]. There was a slight male preponderance in our cases. Similar observations have been made by Gadre et al [8], and others. Some authors have reported a slight female preponderance.

There were seven patients of lymphoma and twelve cases of malignant metastases. The aspirate in lymphoma cases was highly cellular and showed predominantly monotonous population of round cells with scanty cytoplasm which were larger than small lymphocytes. All the seven patients of lymphoma were confirmed through lymph node biopsy. Five cases were follicular lymphoma andtwo were of Hodgkins disease (mixed cellularity). The classical Reed-Sternberg cells were unequivocally identified both on cytologyand biopsy. The overall incidence of malignancy in this study was 20.9%. Studies published in literature reveal the incidence of malignancies in lymph nodes varying from 5.8% to 25.03%. A well processed FNAC sample helps us to diagnose lymphomas; however, proper evaluation of lymphomas is best done on a lymph node biopsy [14]. In our study, all cases of lymphomas diagnosed by FNAC were subjected to lymph node biopsy for a detailed evaluation before they were managed by the onco-physician [15,17]. The sensitivity of FNAC for metastatic lesions to lymph nodes has varied from 97.9% to 100%, whereas the specificity has been found to be upto 100%.

For the lymphomas the sensitivity has been found to be 80% and specificity 100%.A full history, radiological investigations and immunohisto-chemistry in difficult cases may help to arrive at a definitive diagnosis.

The presence of granulomata in an aspirate may also indicate the presence of a neoplastic process. Granulomata may be encountered in both Hodgkin's disease and non-Hodgkin's lymphoma, particularly T-cell lymphoma. Hodgkin's lymphoma is characterised by the classic Reed-Sternberg cells in a background of sarcoid-like granulomata, reactive lymphoid cells and occasional eosinophils. Granulomatous inflammation found in lymph nodes draining carcinomas is a recognised phenomenon [18]. Such phenomenon are reported in pulmonary small cell carcinoma, malignant melanoma, papillary thyroid carcinoma, gastric carcinomaand rhabdomyosarcoma [19]. Previous reports have been described in metastatic nasopharyngeal carcinoma, seminoma and malignant melanoma. This has been suggested to be either a response to necrotic material or an immunological T-cell mediated hypersensitivity reaction to cell surface antigens. However, the precise mechanism is largely speculative as the exact tumour

or host factors that enable such a response remains unknown. These can be indistinguishable from granulomatous inflammation from other non neoplastic causes, if the cell yield is low. A series by Khurana *et al* highlighted the difficulties encountered in making a definitive diagnosis of malignant neoplasm that mimics, or occurs, in association with granulomata [20].

Nodal metastases from gastric cardia tumours (6%) were more common than from the body (2%) or antrum (3%). Neck node metastases are uncommon in stomach cancer at presentation, are usually associated with extensive intra-abdominal metastatic spread, and adversely influence tumour staging in only a small minority of patients [23]. We encountered three cases of metastatic gastric adenocarcinoma in our study accounting to 25% of all metastatic cases.

Lastly, the typical FNAC features of toxoplasmosis include the presence of follicular hyperplasia with secondary germinal centres rich in macrophages, presence of groups of epithelioid cells and presence of monocytoid histiocytes have been previously described. A combination of FNA features with positive serological testing and history of animal contact, as in the two patients here, gives the diagnosis of toxoplasmosis [21] and thus avoids unnecessary surgical excision.

Conclusion

Our experience suggests that FNAC combined with clinical correlation is useful as a first line investigation. The high specificity of the technique helps to single out those that need further investigation or biopsy. The improved diagnostic ability of FNAC in the diagnosis of cervical lymph node lesions is probably due to a combination of factors such as the increased use of the technique, better and easier availability of reference material of similar studies, and increased experience of the trained observers over the years. The evaluation of FNA in patients should be interpreted by experienced cytopathologists in the context of clinical, radiological, and laboratory finding and if any of these findings is suspicious, further investigation is justified.

Source of Support

Nil

Conflict of Interest

None declared.

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