Use of FNAC in Cervical Lymphadenopathy

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A prospective study is presented in which role of FNAC in cervical lymphadenopathy was assessed. This study was carried out in Surgical Unit-I, Allama Iqbal Medical College/Jinnah Hospital, Lahore from 1.1.1997 to 31.12.1997 worked over one year. Initially one hundred and seventy eight patients were aspirated but the smears of twenty six patients (14.6%) were not suitable for cellular interpretation. So ultimately one hundred and fifty two cases were included. The aims of the study were to find out the sensitivity and accuracy of FNAC and to correlate the results of FNAC with histopathology findings.
Key Words:. FNAC, cervical lymphadenopathy, histopathology

Superficial lymphadenopathy is a sign of inflammation, metastatic malignant tumour or lymphoma. FNAC of superficial lymph nodes is convenient for patient and physician, useful for outpatients, relatively painless and provides good correlation between cytological morphology and histopathology[1]. It is the investigation of choice as preoperative FNAC does not predispose to either early or late complications. In contrast, the use of open biopsy before definitive surgery is associated with two to three fold increase in the rate of wound infection/breakdown and fifty percent increase in the rate of chronic lymphoedema[2]. The concept proposed by martin and stressed more recently by McComb and Fletcher, that biopsy of regional disease is contraindicated unless unavoidable., places FNAC in the forefront which is not only an accurate, safe and complication free but also a cost effective diagnostic tool.

Tuberculous lymphadenopathy is the most common form of extra pulmonary tuberculosis in regions where mycobacterial infection is highly prevalent like in Pakistan. The conventional diagnostic measure of excisional biopsy is potentially hazardous as it may spread the tuberculous disease and give rise to sinus formation. For the above reason FNAC is increasingly used as the sole method to reach a pathological diagnosis of tuberculous lymphadenopathy as it is quick and have a low false positive rates. The diagnosis of lymphoma based solely on the cytological findings is often difficult, particularly in low grade lymphomas, notably the small cell and mixed cell subgroups[3]. Some of the early reports concerning the use of FNA cytology for the diagnosis of malignant lymphoma documented poor accuracy rate whereas other demonstrated acceptable accuracy rate. Although its rate has remained controversial, recent experience has indicated that FNA cytology is important in the management of patients with lymphoma[4]. If a diagnosis of lymphoma can confidently be made with subclassification of the tumour into histological subgroupings, appropriate therapeutic regimens may be chosen based upon the needles aspiration specimen., in general there is a good correlation between the subclassification of lymphoma by FNA cytology and that obtained by histological examination. The cases that are difficult to subclassify by FNA cytology are also difficult to subclassify by examination of biopsy specimens. As far as the Hodgkin's disease is concerned, the first case was diagnosed of FNAC by Guthrie in 1921. This initial report was soon followed by reports from Forkner, Loseke and Craver. Cytodiagnosis of Hodkin's disease is usually based on the demonstration of Hodgkin cells and Reed Sternberg cells among appropriate reactive cellular components. Based on these features the overall diagnostic accuracy of FNA cytology ranges from 83 to 98%[5].

Although highly useful in clinical management, there are a number of potential pitfalls in the use of FNAC lymph node. Accurate cytological interpretation may be difficult in the inflammatory disease. Lymphoma and metastatic undifferentiated carcinoma may be cytologically indistinguishable. Aspiration of necrotic material from centre of a metastatic lymph node may give false negative results. The benign hyperplastic lymph node may be difficult to distinguish from lymphoma[6]. Kline also stated that no single pathognomonic feature could be relied on to distinguish these two entities. Mixed large cell and small cell lymphomas can also be difficult to distinguish from benign conditions. Further more nonhaematolymphoid malignancies such as small cell undifferentiated carcinoma and malignant melanoma can be misinterpreted as lymphoma. Other possible sources of false negative error are fibrosis, inflammatory reaction of lymph node and previous radiotherapy. At times the size of the lymph node, the number of sampling and the technical limitations can also effect the diagnostic accuracy[7].

Material and Methods

The patients were evaluated for fine needle aspiration cytology in the Department of Pathology, King Edward Medical College & Allama Iqbal Medical College, Lahore. A thorough history of the illness was taken. It was followed by general and systemic examination. The site, size and all other relevant information regarding the lesions were recorded. Relevant laboratory investigations and radiological findings were also noted. Any important finding in the past history, family history or related to previous treatment were also recorded. All these informations were noted in the relevant proformas.

Specimen collection

A. Collection of Aspirate Specimen

Instrumentation:

The aspiration was done using 10cc disposable syringe with 21-22 gauge needle. No local anaesthesia was used. The aspirate was expressed on six glass slides and the slides were fixed in air as well as in 95% alcohol.

Aspiration procedure

1. Immobilization of lesion

The lesion was immobilized by the nondominant hand. The skin over the lesions was stretched with two fingers so that the needle may reach its target by the shortest possible route and not get enmeshed in subcutaneous tissue. The aspiration across the large muscles like sternocleidomastoid was avoided.

2. Sterilization of field

The skin was cleaned with alcohol or spirit soaked gauze.

3. Penetration of lesion

The syringe with well fixed needle was grasped by the dominant hand and introduced through the skin into the lesion. The angle and depth of entry was planned according to the lesion. For larger lesion, off center part of the lesion was aspirated to avoid the necrotic center. Entrance into the lesion was felt by the changes in tissue consistency.

4. Creation of vacuum

The piston of the syringe was withdrawn upto 3ml to create the air vacuum.

B. Collection of Biopsy Specimen

Fixation

All biopsy specimens were collected and fixed in 10% buffered formation jar after the operation. The jars were sent to the pathology departments.

1.Obtaining the material

With the piston of the syringe in the vacuum position, the needle was rapidly moved back and forward in the same plane to loosen up the target. Tiny tissue fragments dislodged by the needle top were aspirated into the lumen of needle. Depending on the target lesion three to ten movements of the needle were performed. In case of parotid lymph gland sdeep pricks were avoided.

2. Changing the direction of needle

The needle under vacuum was withdrawn to the level of subcutaneous tissue and then redirected to secure sample from more than one area of the lesion.

3. Release of vacuum and withdrawal of needle

The piston of the syringe was returned to normal i.e., non vacuum position before withdrawal of the needle. In case of cystic lesion, the cystic content was aspirated fully and then centrifuged to make a smear.

Preparation of smear

After completion of the aspiration procedure, the syringe was disconnected from the needle, filled with air, and reconnected. the material in the needle was expelled on to a glass slide, with care to deposit it as a single drop at one end. The deposited material on the glass slide was first inspected visually. The aspirate was then spread along the slide by the use of flat pressure of another glass slide. Three of these slides were immediately fixed in 95% alcohol while the other three were air dried.

Results

One hundred and seventy eight patients were aspirated from superficial lymph nodes of head and neck region but the smears of 26(14.60%) patients were not suitable for cellular interpretation.

Out of one hundred and fifty two patients eighty two cases(53.94%) underwent surgical biopsy, 88(57.89%) patients were men with age range between five to seventy years and 64(42.10%) were women between nine to seventy five years old.

Table. Diseases diagnosed on FNAC

Diseases	Total Cases	With Histopa Thology	Without Histo-pathology
Reactive hyperplasia	23	17	6
Pyogenic lymphadenitis	9	00	9
Granulomatous lymphadenitis	87	46	41
Hodgkin's lymphoma	4	3	1
Non Hodgkin's lymphoma	4	3	1
Metastatitic	17	8	9
Suspicious for lymphoma	8	5	3
Total	152	82	70

Table. 2. Diseases diagnosed on histopathology

Diseases	Number of patients
Reactive hyperplasia	20
Pyogenic lymphadenitis	-
Granulomatous lymphadenititis	46
Hodgkin's lymphoma	5
Non-Hodgkin's lymphoma	4
Metastatic	7
Total	82

The cytological examination showed reactive hyperplasia in 23 patients, pyogenic lymphadenitis in 9 patients and granulomatous lymphadenitis in 87 lymph nodes.

Among the malignant cases FNAC diagnosed four cases each of Hodgkin's lymphoma and non-Hodgkin's lymphoma and metastatic in 17. Eight aspirates were suspicious for lymphoma.

Out of the 7 metastatic carcinoma, 2 patients had metastasis from the squamous cell carcinoma of tongue and one from the carcinoma thyroid. Two patients had metastatic deposits from the carcinoma of stomach and two cases were of unknown epithelial origin.

Histology confirmed the reactive hyperplasia in fifteen cases while two cases were diagnosed as a case of granulomatous lymph adenitits. Pyogenic cases were not biopsied. Cytological diagnosis was confirmed in forty three cases of granulomatous lymphadenitis while three

cases were declared as reactive , hyperplasia of lymph node.

Among the malignant cases biopsy confirmed the Hodgkin's lymphoma and non-Hodgkin's lymphoma in three cases each. One case of Hodgkin's lymphoma turned out to be a case of non-Hodgkin's lymphoma and the other discrepancy case was vice versa. One misdiagnosis occurred in the cytological diagnosis of matastatic carcinoma which turned out to be a case of tuberculous lymph adenitis, out of the five cases which were diagnosed as suspicious for lymphoma on cytology biopsy declared two of them as a case of reactive hyperplasia.

Table3. Cytological diagnosis versus histopathological diagnosis.

Diseases	Cytological Diagnosis	Histopathological Diagnosis	False +ve	False –ve
Reactive hyperplasia	17	15		2(TB)
Pyogenic Granulomatous	46	43		3(Reactive)
Hodkin's lymphoma	3	2	01 Non-Hodgkin	
Non-Hodgkin's lymphom	3	2	1 Non-Hodgkin	
Metastatic	8	7	1(TB)	
Suspicious of lymphoma	5	3	2Reactive 1-Non-Hodking's lymphoma	
Total	82	72	5	5

Table 4. Diagnostic discrepancies

Cytological Diagnosis	No.	Histopathological Diagnosis
Reactive hyperplasia	2	Granulomatous (Tuberculosis)
Granulomatous lymphadenitits	3	Reactive
Hodgkin's lymphoma	1	Non-Hodgkin's lymphoma
Non-Hodgkin's lymphoma	1	Hodgkin's lymphoma
Metastatic	1	Granulomatous
Suspicious for lymphoma	2	Reactive
Total	10	

Discussion

The diagnostic accuracy of FNA cytology in superficial lymph nodes is influenced by multiple factors including the size of lymph node, inflammatory reaction, fibrosis previous radiotherapy and technical limitations. The reported percentage of inadequate smears varies from 10% to 20%. Our results showed an inadequacy rate of 14.60%. The high rate of inadequate smears may be on one hand due to lack of personal experience and on the other hand due to nodal fibrosis and extensive necrosis secondary to tuberculosis as also reported by Kline et al, 1984[7]. The difficulties in interpretation of lymph nodes are known since the technique was introduced in 1930s. Stewart in 1993 wrote that "we found often times great difficulty in distinguishing or classifying lymph node lesions on cytology".

Two cases of tuberculous lymphadenitis were falsely diagnosed cytologically as cases of reactive hyperplasia. On review, the first case did not show any epitheloid cell but a mixed population of lymphoid cells with a predominance of small normal lymphocytes. So this misdiagnosis was due to sampling error as rightly pointed out by Lee et al (1987)[1,8] who wrote that false negative cases are more common and are generally based on sampling errors rather than interpretation errors. In the second case there was a necrotic background with a few lymphoid cells. With the increase in necrotic material, the number of cells appear to decrease and at times it becomes very difficult to visualize the pale staining epitheloid cells and Langhans giant cells[9]. This was the reason that in a research on Chinese patients, 11 cases of tuberculosis were misdiagnosed as reactive hyperplasia. The other three misdiagnosed cases of tuberculous lymphadenitis were confirmed on histology as cases of reactive hyperplasia. The smears of the cases showed lymphoid cells, few plasma cells and occasional epitheloid cells against thick necrotic background. Correlating these cytological features, with clinical history, diagnosis of tuberculosis was given.

Among the malignant cases, there were four false positive diagnosis. One case was misdiagnosed as non-Hodgkin's lymphoma which on histology was confirmed as a metastatic carcinoma. The smear showed heavy cellularity of lymphoid cells, small and large with occasional cells having faintly eosinophilic cytoplasm and vesicular nuclei. Such a cytological pattern sometimes makes the specific diagnosis difficult between these two conditions, otherwise a high specificity has been reported in metastatic squamous carcinoma, adenocarcinoma and melanoma. The other false positive diagnosis was of tuberculosis diagnosed as metastatic carcinoma on cytology. Elongated epitheloid cells seen in the smear was the reason for this false diagnosis. This diagnostic problem was also highlighted by Klin 1984[7,10] that the epitheloid cells of tuberculosis sometimes mimic with those of metastatic carcinoma. Blotch has also mentioned the same diagnostic problem and so in the study of Chinese patients a case of tuberculosis was misdiagnosed as metastatic carcinoma. Granulomatous reaction due to metastatic carcinoma especially those of squamous cell carcinoma can also be a source of diagnostic error. One such case was misdiagnosed as tuberculosis[8,11].

The other two false positive cases were of reactive hyperplasia which were given suspicious for lymphoma. Separation of lymphoma cases from hyperplastic nodes by FNA cytology presents a challenge. No single pathognomic feature has been found to differentiate these two conditions. In some cases the distinction is impossible on cytology, particularly in low grade lymphomas, notably

the small cell and mixed cell subgroups[12]. .In the series of Kline et al 1984[7], ten cases of lymphoma were misdiagnosed as hyperplasia among 73 patients. Similarly in one series there were four false negative results but all were confirmed as malignant lymphoma. In the series of Cardillo (1989)[12], 13 FNA lymph nodes were reported as suspicious but 9 turned out to be of reactive hyperplasia. The reason for this usual discrepancy is that some features are equally common in hyperplasia and lymphoma. These include cell density and arrangement, nuclear membrane thickening and when smears contain large controblasts, they can be mistaken for Reed Sternberg cell. Lymphocytes of various degrees of differentiation often considered to be the cytological indicator of lymphoid hyperplasia, may also be found in the aspirates of lymphoma. On the other hand malignant cells of majority of lymphomas are indistinguishable from benign lymphoid cells on cytological examination[13]. The results of our study supports the point of view of Deelay 1874 who wrote that if a lymphoma was suspected clinically, it was preferable to remove the lymph node rather than attempting to make a diagnosis of FNAC.

References

1. Lee RE, Valts J. Kalis O, Sopian A, Sehultz E: Lymph node examination by fine needle aspiration in patients with known or suspected maoignancy. Acta Cytologica 1987; 3(5):563-572.
2. Kardos TF, Vinson JH, Behm GG, Frable WJ, Dowd GJ: Hodgkin's disease: diagnosis by fine needle aspiration biopsy. Am J Clin. Pathol 1986; 286-191.
3. Show JH F and Rumbal EM: Complications and local recurrence following lymphadenectomy. British Journal of Surgery 1990; 77: 760-764.
4. Cheng AT, Dorman B: Fine needle aspriation cytology: the Auckland experience 1992; 62(5): 368-72.
5. Shaha A, Webber C, Merill J, Brooklyn: Fine needle aspiration in the diagnosis of cervical lymphadenopathy. The American Journal of Surgery 1986; 152: 420-423.
6. Kline TS, Kannan W,. Kline JK: Lymphadenopathy and aspiration biopsy cytology, Cancer 1984"54: 1076-108.
7. Lau SK, Wei WI, Hsu C, Engzel UCS G: Efficacy of the needle aspiration cytology in the diagnosis of tuberculous cervical lymphadenopathy.The Joural of Laryngology and Ontology 1990; 104:24-
8. Arora B and Arora DR: Fine needle aspiration cytology in diagnosis of tuberculous lymphadenitis. Indian J Med Res(A) 1990; 9: 189-192.
9. Kline TS: Fine needle aspiration biopsy, past present and future. Arch Pathol Lab Med 1980; 104: 117.
10. Cardillo MR: Fine needle aspiration cytology of superficial lymph nodes. Diag cytopathology. Acta Cytological 1988; 32(6): 848-853
11. Cardillo MR: Fine needle aspiration cytology of superficial lymph nodes. Diag Cytopathology 1989; 5: 166-173.
12. Morton KD: Find needle aspiration cytology oflesions of the head and neck and factors affecting outcome. 1989; 34 (5): 523-5.
13. Hajdu S I, Melamed MR: Limitations of aspiration cytology in the diagnosis of primary neoplasms. Acta Cytologica 1984; 28: 337-345.