Med. J. Cairo Univ., Vol. 88, No. 5, December: 2229-2235, 2020
www.medicaljournalofcairouniversity.net

Diagnostic Value of Conventional Fine Needle Aspiration Cytology in Cervical Lymphadenopathy

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Abstract

Background: Lymphadenopathy is a common clinical presentation in outpatient clinics. Fine needle aspiration cytology (FNAC) of the enlarged lymph node is an easy and simple tool for clinical management. This is because it is fast and minimally invasive with minimal complications.

Aim of Study: To evaluate the reliability and validity of conventional FNAC of cervical lymphadenopathy.

Patients and Methods: This prospective study was carried out on 50 patients with cervical lymphadenopathy. The cytopathological diagnoses obtained by FNAC were compared with the histopathological results of the ongoing excised nodes.

Results: Fifty four percent of our cases were females. Seventy four percent of our cases were less than 40 years. The cytological diagnoses were benign in 29 cases (58%) and malignant (diagnostic or suspicious for malignancy) in 21 cases (42%). The sensitivity, specificity, positive predictive value, and negative predictive value were 84%, 100%, 100%, and 86.2%, respectively. The overall diagnostic accuracy was 92% (46/50), while the overall discordance rate was 8% (4/50).

Conclusions: FNAC is a reliable method for diagnosis of tuberculous lymphadenitis. It shows a high specificity for malignant cervical lymphadenopathy and provides the physician with valuable information for patient management. The sensitivity of FNAC in detection of malignancy is relatively low in cases of lymphoid neoplasm owing to missing Hodgkin's cells in the aspiration of Hodgkin's lymphoma and to difficulty in cytodiagnosis of low-grade lymphoma without use of flow cytometry.

Key Words: *Cervical lymph nodes – FNA morphology – Reliability and accuracy.*

Introduction

LYMPHADENOPATHY is one of the commonest clinical presentations in outpatient clinics. Lymphadenopathy has many underlying causes either benign or malignant. Fine needle aspiration cytology (FNAC) of lymph node is essential in the management of lymphadenopathy cases. This is because FNAC is a fast, simple and minimally invasive procedure with minimal complications **[1]**. FNAC has also been targeted as a useful method in comparison to more expensive surgical excision biopsies in developing countries **[2]**. It almost offers an accurate diagnosis for the etiology and it can avoid the use of excisional biopsy and allows rapid onset of treatment **[3]**.

The diagnosis of metastatic tumor to the lymph node on cytological smear is crucial and highly reliable. This would be the only indication to search for the primary tumor, especially with occult carcinoma **[4]**. The primary tumor is clinically known in most of these cases and FNAC is used for follow-up. Most of metastatic carcinoma can be identified by their cytomorphological characteristics alone. There are some situations where features of different metastatic tumors can overlap and the accurate diagnosis of the primary tumor remains obscure [5]. In such cases, immunocytochemistry can be used to identify the primary site of metastatic tumor [6].

FNAC is useful in diagnosis of lymphoid malignancies as well as in the recognition of the residual or recurrent lymphoid malignancies **[7]**. The cytology is also used for the evaluation of surgically inaccessible deep lymph nodes with primary lymphoma or for patients unfit for surgery **[8]**.

The aim of this study was to evaluate the diagnostic value of FNAC in diagnosis of cervical lymphadenopathy. The efficacy of FNAC was determined by comparing the cytologic diagnosis with final ongoing histological results in a prospective study.

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Patients and Methods

Study design: This was a prospective study.

Study frame: This study was conducted at the General Surgery Department, Assiut University Hospital from January 2016 to January 2017.

Study population:

This study was limited to the selected cases that had undergone FNAC from the enlarged cervical lymph nodes, followed by subsequent excisional biopsy of the same neck node with definitive histopathological diagnosis.

Procedure techniques:

Fine needle aspiration cytology:

This aspiration was performed using 22-gauge needle without local anesthesia under ultrasound image guide. The lymph node was visualized with aid of ultrasound imaging and the needle was advanced into the target lymph node. The cellular material was obtained by needle aspiration, and then the specimen was expelled onto a microscope slide. Smears were immediately processed by dry fixation and stained with Giemsa stain for rapid on site evaluation of cellular adequacy. Other slides were prepared for wet preparation and Papanicolaou stain. When on site evaluation revealed granulomas, another fine needle pass was done for preparation of additional slides submitted for special microbial stains.

Ethical consideration:

All Ethical requirements followed were according to the ethical standards of Ethical Committee of Faculty of Medicine, Assiut University and with the Helsinki Declaration of 1975, as revised in 2008. All the patients gave their written consent for participation in the study.

Statistical analysis:

Statistical analysis was performed using statistical package for the social sciences (SPSS-version 14): The results were expressed as mean ± SD or frequency. The overall diagnostic sensitivity, specificity, positive predictive value, negative predictive value, the overall diagnostic accuracy and the overall discordance also have been calculated.

Results

The demographic characteristic of the study group was shown in Table (1). Twenty-seven cases (54%) were females and 23 cases (46%) were males with male: female ratio of about 1:1.2. Fourteen cases (28%) were in pediatric age group (1-19 years). Twenty-three cases (46%) were in age group from 20 to 40 years. Thirteen cases (26%) were above 40 years.

Table (1): The demographic characteristic of the study group.

Variable	Number of cases
Gender:	
Males	23 (46%)
Females	27 (54%)
Age:	
Age groups:	
1-19	14 (28%)
20-40	23 (46%)
>40	13 (26%)
Total	50 (100%)

Fine needle aspiration cytology results:

The cytological diagnoses were found to be benign in 29 cases (56%) (Figs. 1,3) and malignant in 21 cases (42%) (Figs. 5,7) (Table 2). Regarding malignant cases, nine cases were metastatic carcinoma (18%), one case was diagnostic for non-Hodgkin's lymphoma (NHL) (2%), one case was diagnostic of Hodgkin's lymphoma (HL) (2%), two cases were suspicious for NHL (4%) and nine cases were suspicious for HL (18%).

Among benign cases, reactive hyperplasia, tuberculous lymphadenitis, chronic granulomatous lymphadenitis and suppurative lymphadenitis were 18 cases (36%), nine cases (18%), one case (2%) and one case (2%) respectively (Table 2).

Table (2): Results of cytologic diagnosis.

Cytologic diagnosis	Number of cases
Benign cases:	29 (58%)
Reactive hyperplasia	18 (36%)
Tuberculosis	9 (18%)
Granulomatous lymphadenitis	1 (2%)
Suppuration	1 (2%)
Malignant and suspicious cases:	21 (42%)
Diagnostic of NHL	1 (2%)
Suspicious for NHL	2 (4%)
Diagnostic of HL	1 (2%)
Suspicious for HL	8 (16%)
Metastatic carcinoma	9 (18%)
Total	50 (100%)

NHL: Non-Hodgkin's lymphoma.
HL : Hodgkin's lymphoma.

The majority of reactive hyperplasia cases were below 40 years old with striking male predominance (12 male patients (24%) and six female patients (12%). Regarding tuberculous lymphadenitis, the majority of cases were females (seven cases were female (14%) while two cases were males (4%).

After surgical excision of cervical lymph nodes, the ongoing histopathologic results were compared with the preoperative cytologic diagnoses (Table 3). Regarding the 29 benign cytologic cases, 25 cases were proved to be benign in histopathology (true negative: 86.2%) (Figs. 2,4) while four cases were malignant in histopathology (false negative: 13.8). The contradiction between benign cytologic and histopathologic results was in group of reactive hyperplasia. Only four cases out of 18 cytologically diagnosed as reactive hyperplasia proved by histopathology to be Hodgkin's lymphoma (22.2%). All of the 21 cytologically diagnosed or suspicious for malignant cases were proved to be malignant in histopathology (100%) (Figs. 5,8).

Table (3): Histopathologic diagnosis of excised lymph nodes.

Cytologic diagnosis	No. of cases	Histopathology	
		Benign	Malignant
Benign cases:	29 (58%)	25 (86.2%): TN	4 (13.8%): FN
Reactive hyperplasia	18 (36%)	14 (77.8%): TN	4 (22.2%): FN
Tuberculosis	9 (18%)	9 (100%): TN	0
Granulomatous	1 (2%)	1 (100%): TN	0
Suppuration	1 (2%)	1 (100%): TN	0
Malignant and suspicious cases:	21 (42%)	0: FP	21 (100%): TP
Diagnostic of NHL	1 (2%)	0	NHL: 1 (100%): TP
Suspicious for NHL	2 (4%)	0	NHL: 2 (100%): TP
Diagnostic of HL	1 (2%)	0	HL: 1 (100%): TP
Suspicious for HL	8 (16%)	0	HL: 8 (100%): TP
Metastatic carcinoma	9 (18%)	0	Metastatic carcinoma 9 (100%): TP
Total	50 (100%)		

NHL: Non-Hodgkin's lymphoma. TN: True negative. TP: True positive.
HL : Hodgkin's lymphoma. FN: False negative. FP: False positive.

The overall diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of cytological diagnoses were 84%, 100%, 100%, and 86.2% respectively. The overall diagnostic accuracy was 92% (46/50), while the overall discordance rate was 8% (4/50) (Table 4).

On focusing on cytologic diagnosis of reactive lymphoid hyperplasia, the diagnostic accuracy was 77.8% as four out of 18 diagnosed cases were proved by histopathology to be Hodgkin's lymphoma.

The diagnostic accuracy of cases diagnosed as tuberculosis, granulomatous disease and suppuration was 100% as all diagnoses were confirmed by histopathology.

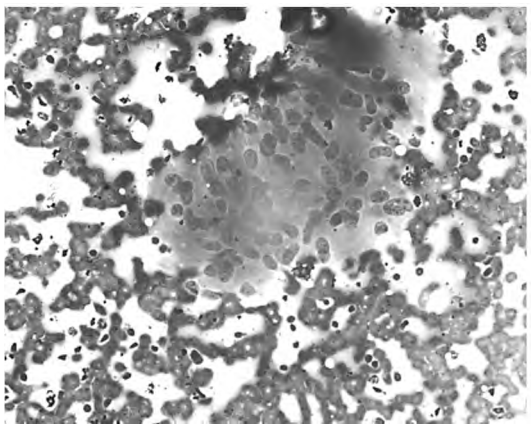

Fig. (1): Granulomatous lymphadenitis: Epithelioid cell granuloma showing syncytium filled with carrot shaped nuclei (Giemsa stain, 400x).

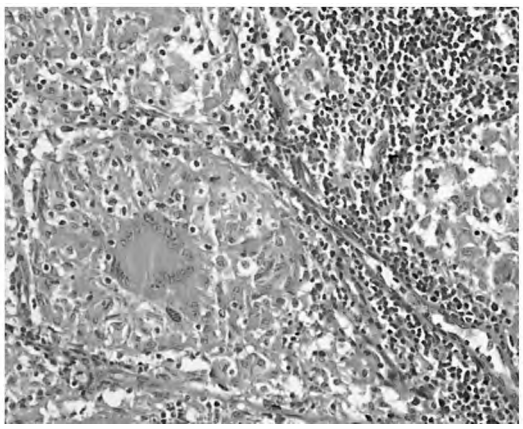

Fig. (2): Granulomatous lymphadenitis: Histologic section of lymph node showing epithelioid cell granuloma with multinucleated giant cells (H&E 400x).

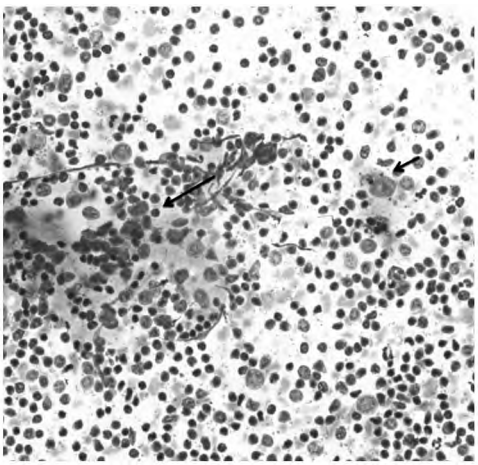

Fig. (3): Reactive lymphoid hyperplasia: Lymphohistiocytic aggregate is shown in left side (long arrow) and tingible body macrophage on right side (short arrow) (Giemsa stain, 400x).

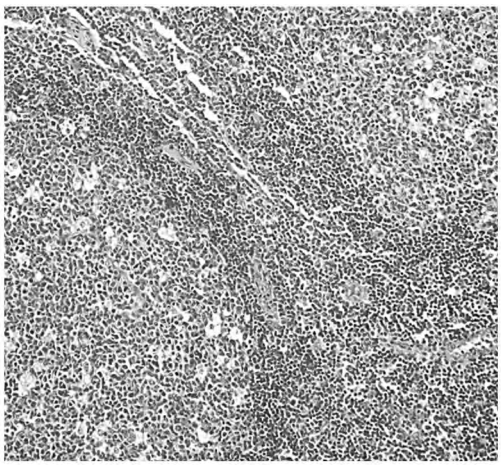

Fig. (4): Reactive lymphoid hyperplasia: Histologic section showing preservation of lymph nodal architecture, lymphoid follicles with reactive germinal center (H&E, 200x).

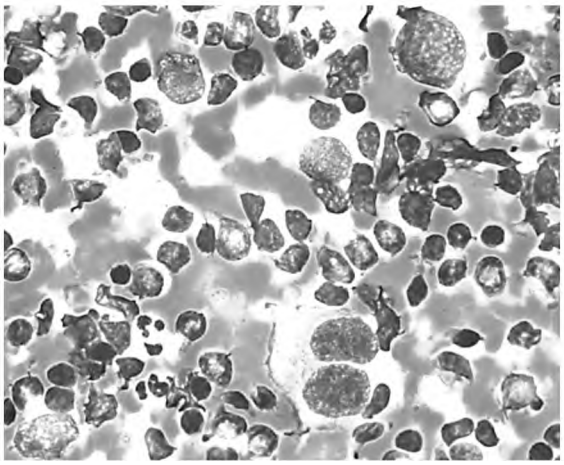

Fig. (5): Hodgkin's lymphoma: Large atypical mono and binucleated cells proved by following immunostaining on histologic section to be Hodgkin's cell (Giemsa stain, Oil immersion).

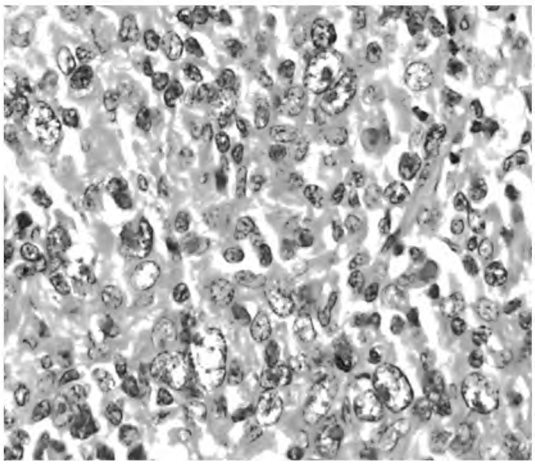

Fig. (6): Hodgkin's lymphoma: Histologic section shows large mono and multinuclear atypical cells on background of polymorphous lymphoid infiltrate. Cells stained with both CD30 and CD15 (H&E, Oil immersion).

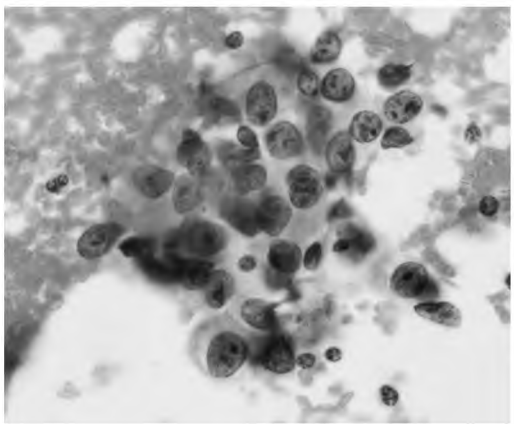

Fig. (7): Metastatic adenocarcinoma: A single 3D cellular group with typical cellular cohesion, perceptible cyanophilic delicate cytoplasm, cellular disarray and anisonucleosis. (Pap stain, Oil immersion).

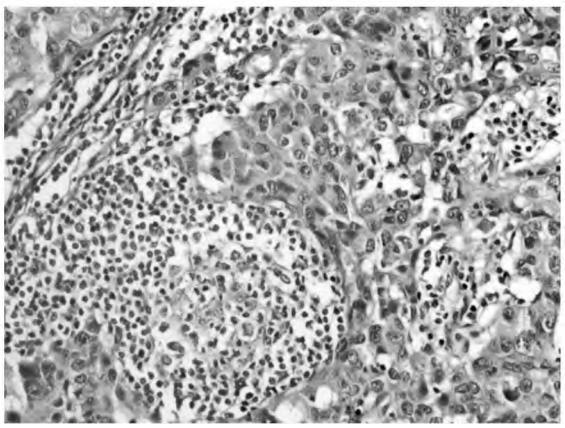

Fig. (8): Metastatic adenocarcinoma: Section from lymph node showing nests and acini of pleomorphic epithelial cells on lymphoid background (H&E, 400x).

Table (4): Validity values of cytologic diagnosis of cervical lymphadenopathy.

Cytologic diagnosis	Number of cases
Specificity	100%
Sensitivity	84%
Positive predictive value	100%
Negative predictive value	86.2%
Diagnostic accuracy	92%
Discordance rate	8%

Discussion

Enlarged palpable cervical lymph nodes are common and worrying clinical presentation in adults as well as in children **[9]**. Seventy four percent of cases in the present study were less than 40 years. Fourteen cases (28%) were in the pediatric age group (between 0 and 19 years). In the present study, out of a total 50 studied cases, 21 cases (42%) were malignant or suspicious for malignancy and 29 cases (58%) were benign. These findings correlated with the other studies **[1,10,11]**.

In this study, benign cytologic diagnosis constitutes a significant proportion of studied cases (58%), of which reactive lymphoid hyperplasia were more than half of benign cases (62%). These figures are compatible with previous studies **[10-12]**. In other previous studies, the ratio between malignant and benign cases was reversed where the percentage of malignant cases was higher than benign cases **[13,14]**. Steel et al. (1995) found malignant and benign cases forming 59% and 41% respectively. They explained these percentages by the fact that the western countries, where their study was carried out, show predominance of malignant lesions over the benign conditions **[14]**. Hafez and Tahoun (2011) found malignant cases constituting 69.4% and benign cases were 30.6%. They explained the higher percentage of malignancy in their study by the fact that they selected their cases that had undergone lymph node excision after FNAC either due to clinical, radiological, or cytological suspicion **[13]**.

In Egypt, tuberculous infection is relatively common. All nine cases in this study diagnosed as tuberculous based on presence of epithelioid cell granuloma and positive acid fast stain. The specificity of cytologic diagnosis of tuberculous lymphadenitis in this study was 100% owing to that all tuberculous cases showed positive staining with Ziehl Nelseen stain. Ahmed et al. (2005) found slightly lower specificity (97.5%). This slight difference was attributed to the fact that they diagnosed tuberculous lymphadenitis based on presence of epithelioid cell granuloma or/ and necrotic granular debris even if acid fast stain was negative. Ahemd et al. (2005) found that 33 out of 35 cytologically diagnosed tuberculous cases were proved to be tuberculous in histopathology. The other two cases were revealed to be lymphoma in histopathology **[10]**.

In the present study, all cytologically diagnosed or suspicious malignant cases were confirmed histopathologically as malignant. FNA offers very high positive predictive value of malignancy (100%) and diagnostic accuracy (100%). This is coming in close comparison to other studies **[5, 11]**.

On the other hand, four out of 29 cytologically benign cases were proved histopathologically to be Hodgkin's lymphoma (false negative cases) with a diagnostic accuracy of reactive hyperplasia equals 77.8%. This finding was lower than that of Keith et al. (2007). Who reported 88% diagnostic accuracy **[15]**. False negative diagnosis of Hodgkin's disease, in particular, as reactive hyperplasia is a common scenario and reported in many previous studies. This is because the diagnosis of Hodgkin's lymphoma based on presence of Reed Sternberg cells that could be, unfortunately, not sampled by the needle aspiration **[11,13]**.

Among 21 cytological malignant cases, nine cases were diagnosed as metastatic carcinoma and the diagnoses were confirmed histopathologically. Diagnostic accuracy of FNA in diagnosis of metastatic carcinoma in this study was 100%. This figure is perfectly in agreement with Ahmed et al. (2005) who found all of 40 cases cytologically diagnosed as metastatic carcinoma were confirmed by ongoing histopathology **[10]**. Hafez and Tahoun (2011) found the exact correlation as all of 31 metastatic carcinoma diagnosed by FNA was proved histopathologically **[13]**. This perfect diagnostic accuracy of FNA in metastatic carcinoma is attributed to the fact that the diagnosis is based on presence of malignant epithelial neoplastic cells which are different from lymphoid population in both cytological features as well as architectural arrangement.

One case of Hodgkin's lymphoma was diagnosed with FNA while nine cases were just suspicious for the Hodgkin's lymphoma. The diagnostic accuracy of FNA in Hodgkin's lymphoma in this study was 100% as all diagnostic and suspicious cases were proved histopathologically to be Hodgkin's lymphoma. This high diagnostic accuracy was in agreement with other studies **[13,16]**. On the other hand four cases of Hodgkin's disease in this study were misdiagnosed as reactive hyperplasia (false negative). False negative diagnosis of Hodg-

kin's disease is a commonly reported scenario **[11,13,17]**. This false negative diagnosis is usually attributed to sampling rather than diagnostic error. Diagnosis of Hodgkin's lymphoma needs presence of typical Reed Sternberg cells which is not always present in FNA sample.

Regarding NHL, only one case could be diagnosed as large cell NHL on cytologic examination. This is because the fact the large cell lymphoma is easily diagnosed by the presence of predominant large lymphoid atypical cells on background of lymphoglandular bodies. In the other two cases suspicious for NHL, the smears showed monotonous small lymphoid population which made complete exclusion of reactive hyperplasia difficult. Marked similarity between low grade lymphoma and reactive hyperplasia is reported by many authors **[11,17,18]**. In addition to the unavailability of flow cytometric analysis in our study, conclusive diagnosis of NHL with small cell morphology was difficult.

According to the histopathological diagnosis, the overall diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of FNAC of cervical lymph nodes in the present study were 84%, 100%, 100%, and 86.2%, respectively. The overall diagnostic accuracy was 92% while the discordance rate was 8%. Rakhshan and Rakhshan (2009) in their similar study reported sensitivity, specificity, positive predictive value, and negative predictive value of 75.8%, 96.6%, 94%, and 85%, respectively. It was found that the sensitivity in our study was higher than the sensitivity reported by them. This was attributed to the less false negative results in our study (4/50, 8%) compared to their study (15/151, 9.9%). However in Hafez and Tahoun (2011) **[13]** in retrospective study conducted on 157 selected patients with cervical lymphadenopathy. The overall diagnostic sensitivity, specificity, diagnostic accuracy of FNAC of cervical lymph nodes were 90.9%, 67.2%, 82.2% respectively. This study showed higher sensitivity, lower specificity and lower diagnostic accuracy in comparison to the current study (82.6%, 100% and 92% respectively).

Conclusion:

FNAC is a reliable method for diagnosis of tuberculous lymphadenitis. It shows a high specificity for malignant cervical lymphadenopathy, and provides the physician with valuable information for patient management. The sensitivity of FNAC in detection of malignancy is relatively low in cases of lymphoid neoplasm owing to missing Hodgkin's cells in the aspiration of Hodgkin's lymphoma and to difficulty in cytodiagnosis of low grade lymphoma without use of flow cytometry.

Funding:

There is no funding.

Conflict of interests:

None of the authors have any financial or scientific conflicts of interests in relation to the data and conclusions presented in this manuscript.

References

1- HIRACHAND S., et al.: Evaluation of fine needle aspiration cytology of lymph nodes in Kathmandu Medical College, Teaching hospital. Kathmandu Univ. Med. J. (KUMJ), 7 (26): p. 139-42, 2009.

2- DAS D.K.: Value and limitations of fine-needle aspiration cytology in diagnosis and classification of lymphomas: A review. Diagn. Cytopathol., 21 (4): p. 240-9, 1999.

3- HOWLETT, D.C., et al.: Diagnostic adequacy and accuracy of fine needle aspiration cytology in neck lump assessment: Results from a regional cancer network over a one year period. J. Laryngol. Otol., 121 (6): p. 571-9, 2007.

4- KOLLUR S.M. and EL HAG I.A.: Fine-needle aspiration cytology of metastatic nasopharyngeal carcinoma in cervical lymph nodes: Comparison with metastatic squamous-cell carcinoma, and Hodgkin's and non-Hodgkin's lymphoma. Diagn. Cytopathol., 28 (1): p. 18-22, 2003.

5- AL-MULHIM A.S., et al.: The role of fine needle aspiration cytology and imprint cytology in cervical lymphadenopathy. Saudi Med. J., 25 (7): p. 862-5, 2004.

6- HAQUE M.A. and TALUKDER S.I.: Evaluation of fine needle aspiration cytology (FNAC) of lymph node in Mymensingh. Mymensingh Med. J., 12 (1): p. 33-5, 2003.

7- RAGHUVEER C.V., et al.: Fine Needle Aspiration cytology versus Fine Needle Sampling without aspiration. A prospective study of 200 cases. Indian J. Med. Sci., 56 (9): p. 431-9, 2002.

8- SHAKYA G., et al.: A study of fine needle aspiration cytology of cervical lymph nodes. J. Nepal. Health Res. Counc., 7 (14): p. 5, 2009.

9- KHADKA S. and SHRESTHA D.: Evaluation of fine needle aspiration cytology of cervical lymphadenopathy in Bir Hospital. Journal of College of Medical Sciences-Nepal., 11 (1): p. 4, 2015.

10- SHAMSHAD AHMAD S., et al.: Study of Fine Needle Aspiration Cytology in Lymphadenopathy with Special Reference to Acid-fast Staining in Cases of Tuberculosis. Vol. 7, 2005.

11- RAKHSHAN, M. and Rakhshan A.: The Diagnostic Accuracy of Fine Needle Aspiration Cytology in Neck Lymphoid Masses. Iranian Journal of Pathology, 4 (4): p. 147-150, 2009.

12- SERRANO EGEA A., et al.: Usefulness of Light Microscopy in Lymph Node Fine Needle Aspiration Biopsy. Acta. Cytologica, 46 (2): p. 364-368, 2002.

13- HAFEZ N.H. and TAHOUN N.S.: Reliability of fine needle aspiration cytology (FNAC) as a diagnostic tool in cases of cervical lymphadenopathy. Journal of the Egyptian National Cancer Institute, 23 (3): p. 105-114, 2011.

14- STEEL B.L., SCHWARTZ M.R. and RAMZY I.: Fine needle aspiration biopsy in the diagnosis of lymphadenopathy in 1,103 patients. Role, limitations and analysis of diagnostic pitfalls. Acta. Cytol., 39 (1): p. 76-81, 1995.

15- VOLMAR, K.E., SINGH H.K. and GONG J.Z.: Fine-Needle Aspiration Biopsy of Lymph Nodes in the Modern Era: Reactive Lymphadenopathies. AJSP: Reviews & Reports, 12 (1): p. 27-35, 2007.

16- KOO, V., LIOE T.F. and SPENCE R.A.J.: Fine needle aspiration cytology (FNAC) in the diagnosis of granulomatous lymphadenitis. The Ulster Medical Journal, 75 (1): p. 59-64, 2006.

17- N A.A., et al.: Fine needle aspiration cytology versus histopathology in diagnosing lymph node lesions. Eastern Mediterranean health Journal, 2 (2): p. 320-325, 1996.

18- M M.-A.: Fine needle aspiration cytology of lymph nodes. Rev. Esp. Patol., 32 (3): p. 410-411, 1999.

القيمة التشخيصية للفحص التقليدى للخلايا المسحوبة بالابرة الرفيعة فى اعتلال العقد اللمفاوية فى العنق

المقدمة: ان اعتلال اللمفاوية هو شكوى صحية شائعة فى العيادات الخارجية. ويعتبر فحص الخلايا المسحوبة بالإبرة الرفيعة من العقدة الليمفاوية أداة سهلة وبسيطة كخطوة فى مجرى التشخيص والعلاج. وذلك يرجع إلى سرعته وقلة المضاعفات الناجمة منه.

الهدف من البحث: تقييم توثيقى لصلاحية الفحص التقليدى للخلايا المسحوبة بالإبرة الرفيعة من اعتلال العقد اللمفاوية فى عنق الرأس.

طريقة البحث: أجريت هذه الدراسة الاستطلاعية على ٥٠ مريضاً يعانون من اعتلال العقدة اللمفاوية فى منطقة العنق. وتمت مقارنة التشخيصات الخلوية التى حصلت عليها مع النتائج التشريحية للعقد بعد الاستئصال الجراحى.

النتائج: أربعة وخمسون فى المئة من الحالات لدينا من الإناث. كان أربعة وسبعون فى المئة من الحالات لدينا أقل من ٤٠ عاماً. كانت التشخيصات الخلوية حميدة فى ٢٩ حالة (٥٨٪) وخبيثة (مؤكدة أو مشتبهه للأورام الخبيثة) فى ٢١ حالة (٤٢٪).

كانت الحساسية والقيمة التخصصية والقيمة التنبؤية الإيجابية والقيمة التنبؤية السلبية ٨٤٪ و ١٠٠٪ و ١٠٠٪ و ٨٦.٢٪ على التوالى. كانت دقة التشخيص الشاملة ٩٢٪ (٤٦/٥٠)، فى حين كان معدل الخلاف العام ٨٪ (٤/٥٠).

الاستنتاجات: أن الفحص التقليدى للخلايا بالابرة الرفيعة هو وسيلة موثوقة لتشخيص إلتهابات وانفعالات الغدد اللمفاوية. وهو يظهر خصوصية عالية لاعتلال العقد اللمفاوية السرطانية فى منطقة العنق بينما أظهرت الدراسة أن الحساسية للفحص الخلوى التقليدى فى الكشف عن الاورام الخبيثة منخفضة نسبياً بسبب فقدان خلايا هودجكين فى الليمفوما ذات النوع هودجكين وصعوبة فى تشخيص الأورام اللمفاوية المتميزة بخلايا صغيرة الحجم دون استخدام قياس التدفق الخلوى.