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Original Research

Cervical lymphadenopathies: A Retrospective Single-Center Analysis of Patients Undergoing Excisional Biopsy

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Abstract

Objectives: The aim of this retrospective study was to evaluate and compare cervical ultrasound findings, fine needle aspiration biopsy (FNAB) results and excisional biopsy results in the diagnosis of patients presenting with cervical lymphadenopathy and to reveal the most common causes.

Methods: A total of 137 patients who underwent cervical ultrasonography and FNAB before excision were included in the study. Demographic data, cervical ultrasonographic findings, FNAB pathology results and final pathology results after excisional biopsy were analysed.

Results: The pathological results indicated that reactive follicular hyperplasia was diagnosed in 33.6% (n=46) of the patients. A diagnosis of non-Hodgkin lymphoma (NHL) was made in 27.7% (n=38) of cases, while 13.1% (n=18) were diagnosed with Hodgkin lymphoma. Malignant pathology was diagnosed in 66 patients. In the FNAB results of patients diagnosed as malignant, 57 were interpreted as non-diagnostic and suspicious, while 9 were interpreted as benign. Of these, 8 had a pathological examination of lymph node excision that revealed non-Hodgkin lymphoma (NHL), and in one patient with a benign FNAB result, the result of lymph node excision was reported as malignant.

Conclusion: Especially in cervical lymphadenopathies in patients over 40 years of age, the possibility of malignancy increases significantly. In lymphoproliferative diseases and in cases accompanied by clinical suspicion, it would be rational to use the direct excisional biopsy option. Although prior fine needle aspiration biopsy may provide significant guidance in metastatic diseases, it should be kept in mind that false negative rates may increase in the diagnosis and staging of lymphoma.

Keywords: Cervical lymphadenopathies, excisional biopsy, fine needle aspiration biopsy, lymphoma, metastasis ve reactive follicular hyperplasia

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Lymphadenopathy (LAP) is a condition characterised by an enlargement and structural abnormality of lymph nodes, typically defined as nodes exceeding one centimetre in size.[1] It may be a presenting symptom of a range of diseases, including infectious, immunological, neoplastic and metabolic disorders. The prevalence of LAP is estimated to be between 0.5 and 0.6% in the general population, affecting individuals of all age groups, including children and adults.[1, 2] G. Since one-third of the lymphatic system is located in the neck, cervical lymph nodes are the most

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common site for peripheral LAP.[3] A study of a pediatric population revealed that 98% of lymph nodes were located in the cervical region.[4]

Despite its frequently benign nature, lymphadenopathy necessitates a comprehensive clinical evaluation, including detailed history-taking, physical examination, laboratory testing, and cervical ultrasonography, to accurately distinguish between benign and malignant etiologies. Although excisional lymph node biopsy (ELB) is often considered the definitive method for diagnosis, fine needle aspiration biopsy (FNAB) remains a valuable tool when combined with ultrasonographic evaluation for determining the underlying etiology. Furthermore, it is particularly effective in the assessment of various pathological conditions, including those with metastatic potential. In cases where a diagnosis cannot be reached through FNAB and clinical suspicion persists, or in instances of lymphoproliferative diseases, direct ELB may be the preferred option when larger sample sections are required for histopathological evaluation.[5,6]

Excisional lymph node biopsy (ELB) is a more invasive procedure compared to fine needle aspiration biopsy (FNAB). Excision can be performed under local anaesthesia, although general anaesthesia may be preferred, particularly in paediatric patients and in cases where the cervical LAP is deeply located.

One of the major challenges of this procedure is navigating the complex cervical anatomy, which increases the risk of adverse outcomes. Another potential issue is the formation of scars on the skin in the cervical region. Despite all these risks, ELB has the highest sensitivity especially in the diagnosis of lymphoma. The availability of sufficient tissue allows for the analysis of lymph node structure and the classification of lymphoma.[2]

The primary question in this context is which patients require ELB. In recent years, direct ELB has been recommended as an alternative to diagnosing each cervical lymph node with FNAB due to the increasing prevalence of medical-legal concerns. Consequently, the objective of this retrospective study was to evaluate and compare the diagnostic accuracy of cervical ultrasound, FNAB pathology, and excisional biopsy in patients presenting with cervical lymphadenopathy and to determine the optimal timing for surgical excision.

Methods

In this study, a total of 312 patients who underwent excisional biopsy for cervical LAP at the Istanbul Medeniyet University Goztepe Prof Dr Suleyman Yalcin City Hospital Otorhinolaryngology clinic between November 2015 and June 2024 were evaluated. A total of 137 patients who had undergone fine-needle aspiration biopsy (FNAB) at our clinic or an external centre and had undergone cervical ultrasonography prior to excision were included in the study. The study was approved by the Istanbul Medipol University Non-Interventional Ethics Committee (decision number: 768-01.08.2024). This study was conducted in accordance with the Declaration of Helsinki. Due to the retrospective nature of the study, it was not necessary to obtain patient consent. The indication for biopsy was established in cases where the lymph node was unresponsive to empirical medical treatment and presented with at least one suspicious ultrasonographic feature, such as a short-axis diameter greater than 1 cm, presence of intranodal necrosis, a round shape, absent or displaced echogenic hilum, irregular, blurred, or spiculated margins and peripheral or mixed vascularity patterns. All patients underwent lymph node excision under general or local anaesthesia according to their age and lymph node location. The largest lymph node with pathological lymph node appearance on ultrasonography was surgically excised. Histopathological evaluation of the excised lymph nodes was performed.

The data set comprised demographic information, cervical ultrasonographic findings, results of FNAB, and pathological results following ELB. The ultrasonography reports were classified according to whether they indicated a reactive or pathological finding. The results of FNAB were classified and evaluated as follows: benign, suspicious, and non-diagnostic. The final pathological results of ELB were compared with the ultrasonography and FNAB pathological results.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) 24.0 (Armonk, New York: IBM Corp.) programme was used for statistical analyses. Descriptive statistical methods (Number, Percentage) were used to evaluate the study data. Pearson Chi-Square test was used for group comparisons. Significance was evaluated at $p<0.01$ and $p<0.05$ levels.

Results

The numbers and ratios of the patients who underwent FNAB followed by LAP excision according to age ranges are given in Table 1.

In terms of gender distribution, 59.9% (n=82) and 40.1% (n=55) of the patients who underwent FNAB and subsequent LAP excision were male and female, respectively.

Table 2 presents the distribution of diagnoses according to ELB pathological results. The pathological results indicated that reactive follicular hyperplasia was diagnosed in 33.6% (n=46) of the patients. A diagnosis of non-Hodgkin lympho-

Table 1. Number of patients who underwent FNAB and LAP excision according to age distribution

Age Range	Number	%
0-20	20	14.6
21-30	22	16.1
31-40	11	8.0
41-50	19	13.9
51-60	26	19.0
61-99	39	28.5
Total	137	100.0

Table 2. Distribution of diagnoses according to pathology results

Diagnosis	Number	%
Reactive follicular hyperplasia	46	33.6
Non-Hodgkin Lymphoma	38	27.7
Hodgkin Lymphoma	18	13.1
Tuberculosis	16	11.7
Metastasis	10	7.3
Sarcoidosis	3	2.2
Cat-scratch disease	3	2.2
Ebstain-Barr Virus	2	1.5
Toxoplasma	1	0.7
Total	137	100

ma (NHL) was made in 27.7% (n=38) of cases, while 13.1% (n=18) were diagnosed with Hodgkin lymphoma. Malignant pathology was diagnosed in 66 patients. Patients diagnosed as malignant were mostly in the 41-99 age range. A statistically significant difference was found between age groups according to ELB results (p=0.001; p<0.01). Patients diagnosed as malignant were mostly in the 41-99 age range. No statistically significant difference was observed between the ELB and FNAB results (p>0.05). No statistically significant difference was observed between the ELB diagnosis results and USG results (p>0.05). Detailed comparison of ELB results with ultrasonography, FNAB pathological results and age distribution is given in Table 3.

The detailed distribution of ELB pathology results according to FNAB results is given in Table 4. In the FNAB results of patients diagnosed as malignant, 57 were interpreted as non-diagnostic and suspicious, while 9 were interpreted as benign. Of these, 8 had a pathological examination of lymph node excision that revealed non-Hodgkin lymphoma (NHL), and in one patient with a benign FNAB result, the result of lymph node excision was reported as malignant. Final pathology results did not show a statistically significant difference according to the results of FNAB (p>0.05).

Discussion

Cervical lymphadenopathy may result from either benign or malignant etiologies, and determining the appropriate diagnostic approach is essential to achieving a timely and accurate diagnosis. Upon clinical presentation, a thorough history and physical examination are conducted to assess the pathological nature of the lymph node. Patient age is an important factor, as the likelihood of malignancy increases with advancing age. In our study, the incidence of malignancy was notably higher among individuals over 40 years of age. Similarly, Al Kadah et al.[1] identified a statistically significant correlation between age and malignancy in their study of 251 cases. It was reported that malignancy was detected in 95 of the 543 patients referred to a tertiary

Table 3. Comparison of results according to final pathology findings

	Final Pathology Results				[a]p
	Malign		Benign		
	Number	%	Number	%	
Age					
0-40	13	19.7	40	56.3	0.001**
41-99	53	80.3	31	43.7	
FNAB results					
Benign	9	13.6	9	12.7	0.513
Non-Diagnostic	28	42.4	24	33.8	
Suspicious	29	43.9	38	53.5	
USG					
Benign	18	27.3	28	39.4	0.132
Pathological	48	72.7	43	60.6	

[a]Pearson Chi-Square; **p<0.01. FNAB: fine needle aspiration biopsy; USG; Ultrasonography.

Table 4. Comparison of final pathology results according to FNAB results

Diagnosis	FNAB results						[a]p
	Benign		Non-Diagnostic		Suspicious		
	N	%	N	%	N	%	
Ebstain-Barr Virus	1	5.6	0	0.0	1	1.5	0.177
Hodgkin Lymphoma	0	0.0	7	13.5	11	16.4	
Cat-scratch disease	0	0.0	2	3.8	1	1.5	
Metastasis	1	5.6	6	11.5	3	4.5	
Non-Hodgkin Lymphoma	8	44.4	15	28.8	15	22.4	
Reactive follicular hyperplasia	7	38.9	18	34.6	21	31.3	
Sarcoidosis	1	5.6	1	1.9	1	1.5	
Tuberculosis	0	0.0	3	5.8	13	19.4	
Toxoplasma	0	0.0	0	0.0	1	1.5	

FNAB: fine needle aspiration biopsy.

cancer centre in the UK with peripheral lymphadenopathy.[7] In the same study, it was reported that advanced age was a risk factor for malignancy, with each 10-year increase in the patient's age increasing the risk of malignancy by a factor of 1.64. Additionally, male gender, lymph node size, and especially lymph nodes in the supraclavicular region were identified as risk factors for malignancy. Celenk et al.[5] also reported that advanced age was associated with malignancy.

In the presence of clinically suspicious lymph nodes and pathological lymph nodes according to ultrasound findings, further investigations are required to reach a definitive diagnosis. In our study, patients who underwent both FNAB and ELB were selected. Our clinical approach is to perform ELB directly in patients who are referred especially in the presence of clinical suspicion. However, recently, especially in internal medicine, ELB has been recommended as a primary treatment for lymph nodes that have not responded to medical therapy without the need for additional examination such as FNAB. In the present study, the patients who underwent FNAB prior to ELB were evaluated. Of the 137 patients included in the study, 46 (33.6%) were diagnosed with reactive follicular hyperplasia. Of the 46 patients with reactive follicular hyperplasia, 7 had benign FNAB results, while the remaining 39 had non-diagnostic or suspicious results. The necessity of surgery in these patients is a matter of debate.

While the accuracy of FNAB diagnosing metastatic carcinoma in the lymph nodes is over 90%, this rate is approximately 70% for primary lymphoma.[8,9] Gupta et al.[10] found that when FNAB diagnosis was combined with ultrasound findings, sensitivity increased from 72.7% to 95.4% and specificity increased from 82.1% to 92.3%. In addition, Lioe et al.[11] investigated the role of FNAB in the diagnosis of superficial LAP and found the specificity of this method to be high and found false negativity in 7 patients out of 157 patients. In the same study, it was highlighted that the most challenging aspect was differentiating between reactive hyperplasia and low-grade lymphoma. Excluding lymphomatous cases resulted in a decreased false negativity rate.

The present study identified 66 patients who were diagnosed with malignant pathology as a consequence of ELB. Of the total number of patients, only 9 were determined to have a benign diagnosis following FNAB. In the remaining 57 patients, the results of FNAB were interpreted as non-diagnostic and suspicious. The final pathology of eight patients with a benign FNAB result was Non-Hodgkin's Lymphoma, while the final pathology of one patient whose ELB result was reported as metastasis was interpreted as benign. In accordance with the results of this study and the existing literature, it can be concluded that, in addition to the high rate of false negativity of FNAB, particularly in cases of lymphoproliferative malignancies, a larger sample size is required for the typing of this disease. Therefore, ELB should be preferred as the gold standard in this group of patients.

In our study, metastatic lymph node diagnosis was reported in 7.3% (n=10) of the patients. In the study conducted by Metin et al.,[12] the incidence rate was 14.2% in patients under 40 years of age. In contrast, the rate doubled in patients over 40 years of age, and lymph nodes in the fourth and fifth neck regions were identified as a significant risk factor.

In considering the aetiology of infectious LAP, the prevalence of tuberculosis, which represents the most striking pathology, is observed to vary between countries and ethnic groups. In the present study, tuberculosis was observed in 11.7% (n=16) of the patients. This rate is higher

in developing countries, reaching a prevalence of 45.45%.[13] Conversely, the prevalence of tuberculosis in developed countries is reported to range between 1.9 and 4.5% (2, 6). In our study, 13 of the FNAB results of patients with a final pathology result of tuberculosis were interpreted as suspicious, while three were interpreted as non-diagnostic. Thus, FNAB demonstrates a lower false-negative rate in cases of tuberculosis compared to lymphoproliferative conditions. Among other infectious causes, 1.5% (n=2) Epstein-Barr virus, 2.2% (n=3) cat scratch and 0.7% (n=1) toxoplasma were observed in our study. These rates were similar to the results of Ozkan et al.[14]

This study has several limitations. Firstly, retrospective and single-centre design of the study is a key limitation, as it restricts the generalisability of the findings. It is recommended that future research adopt a multi-centre approach in order to enhance the external validity and broader applicability of the results. Consequently, the participants included in this study were selected based on specific criteria, which may have resulted in a bias towards malignancy and potentially influenced the outcomes. Additionally, some FNAB procedures were performed at external centers, which limited standardization. As both ultrasonography and FNAB are operator-dependent, performing them and interpreting the results by the same experienced clinician is recommended to reduce variability and enhance diagnostic accuracy. This study investigated the comparative outcomes of FNAB and excisional biopsy. A more comprehensive assessment of the patient's characteristics, clinical features and comorbidities would enhance the validity of the findings. Future research should include larger, prospective studies to yield more definitive conclusions.

Conclusion

Cervical lymphadenopathy (LAP) is a common pathology at all ages. However, in cases of cervical LAP over 40 years of age, the possibility of malignancy increases significantly. FNAB has limited sensitivity in diagnosing lymphoproliferative diseases and in cases accompanied by clinical suspicion, the direct ELB should be preffered to obtain sufficient tissue for histological subtyping. It should be noted that FNAB has a relatively high false-negative rate, particularly in the diagnosis and classification of lymphoma. FNAB demonstrates high diagnostic accuracy for metastatic carsinoma, especially when combined with ultrasonographic evaluation. İn patient with risk factors for metastatic disease, FNAB should be the initial diagnostic approach. In cases of infectious etiologies, such as tuberculosis, FNAB may be adequate. However, in cases where there is persistent concern, histopathological confirmation through excision is recommended.The selection of the optimal modality, between FNAB and ELB, must be made by a multidisciplinary team comprising radiologists, pathologists and clinicians to ensure that clinical, radiological and cytological data are integrated for the optimum patient management.

Disclosures

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