Study of the value of core biopsy for establishing tissue diagnosis compared to excisional biopsy in enlarged cervical lymph nodes

Original Article

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ABSTRACT

Background: Core tissue biopsy involves sampling tissue with a wider gauge than is used for fine-needle aspiration cytology. Core biopsy may be used as an alternative to surgical excisional lymph node biopsy as it would provide less risk to the patients as regards wound infection, scar, bleeding, accessory nerve injury, and the risk of complications of general anesthesia. The aim of this work was to assess the accuracy, specificity, and sensitivity of core biopsy in establishing tissue diagnosis of enlarged cervical lymph nodes.

Patients and Methods: This prospective study was carried out on 100 patients, 50 for core biopsy and 50 for excisional biopsy, aged more than 18 years old, both sexes, with cervical lymphadenopathy indicated for ultrasonography (US)-guided core biopsy.

Results: Based on our study, the diagnostic rate of core needle biopsy (CNB) is 53 cores and 10% of them need an excisional biopsy. 95% of lymphoma patients were diagnosed by core biopsies. Every CNB patient underwent hydrodissection and got a safe puncture distance. In cervical lymphadenopathy diagnosis, CNB had 89% sensitivity, 100% specificity, 100% positive predictive value, and 66% negative predictive value.

Conclusion: Performing core samples of cervical lymph nodes in cases of cervical lymphadenopathy, especially US-guided core biopsy, can be beneficial in achieving a diagnosis as well as decreasing the need for excisional biopsies performed under general anesthesia.

Key Words: Core biopsy, enlarged cervical lymph nodes, excisional biopsy.

Received: 28 January 2024, **Accepted:** 21 February 2024, **Publish:** 7 July 2024

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ISSN: 1110-1121, July 2024, Vol. 43, No. 3: 755-763, © The Egyptian Journal of Surgery

INTRODUCTION

Cervical lymphadenopathy is a common problem as cervical lymph nodes drain the tongue, parotid gland, larynx, trachea, and thyroid gland. The incidence of unexplained adenopathy in the general population is 0.6%. There are different etiologies of cervical lymphadenopathy such as infections (viral or bacterial), storage diseases, medications, autoimmune diseases, and neoplastic processes such as lymphoma or metastasis from primary malignant tumors[1].

Careful history-taking and clinical examination is very important for the diagnosis, besides appropriate investigations such as complete blood count, virology, ultrasonography (US), and US-guided fine-needle aspiration cytology (FNAC) or core biopsy[2].

Patients with cervical lymphadenopathy usually undergo US scanning as the first-line investigation, often coupled with FNAC. Patients not diagnosed by FNAC usually proceed to either core biopsy or excisional lymph node biopsy, but recently, FNAC has been reported to have a limited diagnostic value as it cannot provide tissues for histopathological diagnosis. On the other hand, a core biopsy can provide tissues with less invasive techniques than surgical excisional biopsy[3,4].

Core biopsy (25 G) involves sampling tissue with a wider gauge than used for FNAC (16 G)[5,6].

If there is a concern of lymphoma as a potential diagnosis, an intact tissue is required to view histological architecture. As there is a difference in the management of different types of lymphoma, accurate diagnostic classification is mandatory[7]. An extensive panel of immunohistochemical markers and molecular techniques, improved diagnostic expertise and experienced use of tissues have allowed for easier diagnosis using fewer tissues provided by core biopsy[8,9].

The aim of this work was to assess the accuracy, specificity, and sensitivity of core biopsy in establishing

DOI: 10.21608/EJSUR.2024.357124

tissue diagnosis of enlarged cervical lymph nodes compared to surgical excision.

PATIENTS AND METHODS:

This.prospective study was carried out on 100 patients; 50 had core biopsy and 50 excisional biopsy underwent patients 18 years old, including both sexes, with cervical lymphadenopathy indicated for US-guided core biopsy.

The study was started after the approval from the Ethical Committee at Ain Shams University, Egypt. Informed written consent was obtained from all the patients.

Exclusion criteria included patients with chronic infections, known autoimmune or immune deficiency disorders, severe cardiorespiratory, nervous, liver or kidney dysfunction, and history of anesthetic allergy.

The diagnostic yield of core biopsies was graded as grade 0=inadequate sample for diagnostic purposes.

Grade 1= indeterminate, wherein the pathologist encountered difficulty distinguishing between reactive hyperplasia and lymphoma and advised excision.

Grade 2= indicative of lymphoma; however, additional diagnostic methods are advised for the purpose of determining the grade and type of the condition.

Grade 3= indicative of lymphoma and adequate data collected to determine the severity and classification, enabling the initiation of appropriate medical intervention.

All patients were subjected to:

Complete history-taking, clinical examination (cervical, axillary, inguinal lymph nodes, and abdominal examination), laboratory investigations (complete blood picture, virology such as cytomegalovirus, and Epstein-Barr virus antibodies, toxoplasma antibodies, serum creatinine and blood urea and creatinine clearance if indicated, coagulation profile:pProthrombin time, partial thromboplastin time, and international normalized ratio), imaging (neck US examination, to assess cervical lymph nodes, computed tomography neck if indicted, US abdomen to assess hepatosplenomegaly and lymphadenopathy if indicated), cytology and histopathology. Fifty patients underwent US-guided core biopsy from suspicious lymph nodes under local anesthesia using a 25-G needle, histopathological examination using hematoxylin and eosin stain, and immunostaning for indicated cases.

Operatively

The patients were randomized into two groups; 50 patients underwent surgical excision of suspected cervical lymph node(s).

Postoperative assessment and management

True positive, true negative, false positive, false negative, sensitivity, specificity, positive predictive value, and negative predictive value.

Statistical analysis

The statistical analysis was conducted using SPSS, v20 (IBM Inc., Chicago, Illinois, USA). The qualitative data were expressed as numbers and percentages, while quantitative data were provided as mean, SDs, and ranges if they followed a parametric distribution. The confidence interval was set at 95%, and a margin of error of 5% was accepted. A two-tailed P value of less than 0.05 was considered statistically significant.

RESULTS:

Table 1 shows the distribution of the studied cases according to demographic data and patient characteristics, neoplastic, occupation, and duration (months).

Table 1: Distribution of the studied cases according to demographic data and patient characteristics, neoplastic, occupation, and duration (months)

	Patients (*N*=100)
Age (years)	32.81±9.63
Male	62 (62.0)
Female	38 (38.0)
Weight (kg)	72.41±8.72
Height (m)	170.51±5.71
BMI (kg/m^2)	24.86±2.29
Neoplastic	17 (17.0)
Nonneoplastic	83 (83.0)
Occupation	
Housewife	23 (23.0)
Manual laborer	21 (21.0)
Student	20 (20.0)
Hotel worker	11 (11.0)
Security guard	8 (8.0)
Shopkeeper	8 (8.0)
Farmer	6 (6.0)
Vegetable seller	2 (2.0)
Construction worker	1 (1.0)
Duration (months)	2.93±1.67

Data are presented as mean±SD or n (%).

Table 2 shows the distribution of the studied cases according to presenting symptoms. History of contact with tuberculosis, chest radiograph, unilateral/bilateral involvement, and lymphomas, site and histopathological diagnosis.

Table 2: Distribution of the studied cases according to presenting symptoms (history of contact with tuberculosis, chest radiograph, unilateral/bilateral involvement, and lymphomas, site and histopathological diagnosis)

	n (%)
Fever	60 (60.0)
Cough	40 (40.0)
Weight loss	20 (20.0)
Pain	16 (16.0)
Nil	8 (8.0)
Hoarseness of voice	4 (4.0)
Ulcer over the right lateral aspect of the tongue	4 (4.0)
Productive	4 (4.0)
Epistaxis	4 (4.0)
History of contact with tuberculosis	29 (29.0)
Chest radiograph	19 (19.0)
Bilateral	30 (30.0)
Unilateral	70 (70.0)
Lymphomas	35 (35.0)
Non-Hodgkin's lymphoma	17 (48.6)
Hodgkin's lymphoma	13 (37.1)
Nodular sclerosis	5 (14.3)
Level 1 (submental and submandibular group)	5 (5.0)
Level 2 (upper jugular group)	48 (48.0)
Level 3 (middle jugular group)	9 (9.0)
Level 4 (lower jugular group)	6 (6.0)
Level 5 (posterior triangle group	5 (5.0)
Level 6 (anterior compartment group)	5 (5.0)
More than one site in the neck	22 (22.0)
Metastatic lymph node from thyroid cancer	32 (32.0)
Granulomets lymphadenitis	20 (20.0)
Non-Hodgkin's lymphoma	16 (16.0)
Reactive lymphadenitis	12 (12.0)
Hodgkin's lymphoma	12 (12.0)
Metastatic lymph node from parotid cancer	4 (4.0)
Nodular sclerosis lymphoma	4 (4.0)

All patients underwent diagnosis using core biopsy and excisional biopsy: for lymphadenopathy, 68 patients were diagnosed with lymphadenopathy, 56 patients' diagnosis was confirmed using excisional biopsy, and 12 patients failed to be diagnosed with a sensitivity of 82.4%, 32 patients were diagnosed with no lymphadenopathy, including 28 patients who proved undiagnosed using excisional biopsy, with a specificity of 87.5%. For chronic nonspecific lymphadenitis: eight patients were diagnosed with chronic nonspecific lymphadenitis, eight patients diagnosis was confirmed using excisional biopsy, with a sensitivity of 100.0%, 92 patients were diagnosed with no chronic nonspecific lymphadenitis, including 84 patients who proved undiagnosed using excisional biopsy, with a specificity of 91.3%. For malignant secondaries and lymphomas: four patients were diagnosed with malignant secondaries and lymphomas in each, four patients in each diagnosis were confirmed using excisional biopsy, with a sensitivity of 100.0%, 96 patients in each were diagnosed with no malignant secondaries using core biopsy, including 96 patients in each who proved undiagnosed, with a specificity of 100.0% (Tables 3-4).

Table 3: Excisional biopsy for lymphadenopathy, chronic nonspecific lymphadenitis, malignant secondaries, and lymphomas

	1	2	3	4
	True positive (a)	False positive (b)	False negative (c)	True negative (d)
Excisional biopsy for lymphadenopathy				
Number	56	4	12	28
Excisional biopsy for chronic nonspecific lymphadenitis				
Number	8	8	0	84
Excisional biopsy for malignant secondaries				
Number	4	0	0	96
Excisional biopsy for lymphomas				
Number	4	0	0	96

Table 4: The sensitivity and specificity of excisional biopsy for lymphadenopathy, chronic nonspecific lymphadenitis, malignant secondaries, and lymphomas

Excisional biopsy	AUC (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Lymphadenopathy	84.9	82.4	87.5	82.0	88.0
Chronic nonspecific lymphadenitis	95.7	100.0	91.3	100.0	92.0
Malignant secondaries	100.0	100.0	100.0	100.0	100.0
Lymphomas	100.0	100.0	100.0	100.0	100.0

NPV, negative predictive value; PPV, positive predictive value.

DISCUSSION

Core needle biopsy (CNB) entails extracting tissue using a needle with a larger diameter than FNAC, often a 16-G needle as opposed to a 25-G needle. As a result, a 'core' of tissue from the region of interest is sampled, resulting in minimal tissue architecture distortion that permits the pathologist to provide histology-related commentary. The narrower gauge needle utilized for FNAC does not maintain this architectural integrity, thus limiting the study to cytological examination exclusively, rendering it unsuitable for lymphomas[10].

Among the 100 cases examined in this study, 40 (40%) cases were identified as nonneoplastic lesions, while the remaining 60 (60%) cases were determined to be neoplastic. In a study conducted by Shafullah Syed[11], it was shown that nonneoplastic lesions occurred in 90.6% of cases, while malignant lesions occurred in 9.4% of cases.

The present study showed that 32% of cases turned out to have metastatic lymph nodes from thyroid cancer, whereas 20% of cases had granulomatous lymphadenitis, 16% of cases had non-Hodgkin's lymphoma, Hodgkin's lymphoma in the neck 12.0% of cases, one (4%) case was diagnosed as metastatic lymph node from parotid cancer and one (4%) case was found out to be a case of nodular sclerosis lymphoma.

The age group most frequently affected was 31-40 years, accounting for 35% of cases, 21–30 years with 33% of cases, and 12–20 years with 16% of cases. In the study conducted by Jha *et al*.[12], the age group most frequently affected was 11–20 years, while the study conducted by Shafullah Syed[11] reported that 72% of cases fell within the age range of 11–30 years. In the study conducted by Kim *et al*.[28], most cases observed fell within the age range of 20–50 years.

In the current study, among 100 cases of tuberculous lymphadenitis, 48% of patients exhibited the engagement of level II lymph nodes, while 52% of patients demonstrated the involvement of multiple groups of lymph nodes. Upon presentation, all instances of lymphomas exhibited the involvement of multiple levels of neck nodes. These findings are consistent with the study conducted by Jha *et al*.[12], where the upper deep jugular group exhibited the highest frequency of involvement. The study conducted by Baskota *et al*.[13] found that the posterior triangle was the most frequently observed anatomical region, accounting for 51% of the cases.

Based on the current study's finding, assuming a diagnostic success rate of 90%, it is recommended to perform 53 core biopsies. Additionally, 10% of the cases may require a repeat procedure in the form of an excisional biopsy, which amounts to five (90%) cases were diagnostically indicative of either lymphoma or another pathological condition, thus obviating the need for additional tissue sampling. In total, 10% of individuals were diagnosed with lymphoma, out of which only one necessitated additional biopsy as a

result of inconclusive findings from the initial core biopsy. In general, core biopsies yielded a diagnosis in 95% of lymphoma cases. Teng *et al*.[14] demonstrated the feasibility and safety of cervical lymph node biopsy in high-risk regions using hydrodissection-assisted CNB. It exhibited superior diagnostic performance compared to FNA.

In the present study, within the CNB group, all patients underwent successful hydrodissection, resulting in a puncture distance that was deemed sufficiently safe. The rate of successful separation was 100%, which closely aligned with the findings of Cheng and Liang[15]. The potential causes were as follows: first, an adequate amount of saline solution was administered during the hydrodissection procedure due to the laxity of the neck tissue, resulting in easy absorption and diffusion of the injected saline. Adequate administration of saline solution ensured adequate separation and protection. The mean volume of saline administered in this study was 17±5.8 ml (range, 5–35 ml), consistent with the findings reported by Cheng and Liang[15]. Second, while administrating the isolation fluid, it is crucial to inject it precisely along the periphery of the targeted lymph node while utilizing real-time US guidance. This approach has the potential to enhance the efficacy of the separation process. In patients who have received prior medical interventions, such as surgical procedures and radiotherapy, which can lead to the formation of adhesions in the cervical tissues, the utilization of a 10 or 20-ml syringe to disentangle the cervical lymph nodes from the adjacent tissues proved to be challenging. A smaller gauge syringe needle, such as 2 ml or 5 ml, was utilized to administer the isolation fluid, thereby potentially enhancing the signal-to-noise ratio. Furthermore an adequate specimen for pathological diagnosis was obtained from all of the lymph nodes in the CNB group following hydrodissection. An automated biopsy device benefits certain small and firm lymph nodes that exhibit mobility during the puncture procedure. This advantage is attributed to the significant ejection force of the automatic biopsy gun, enabling the completion of the sampling procedure before any movement of the lymph node.

Teng *et al*.[14] demonstrated no statistically significant disparity in the safety profile of CNB when performed with the aid of hydrodissection, as compared to FNA. Both cohorts of patients did not exhibit any significant medical complications. Although two patients in the CNB group exhibited edema during the hydrodissection procedure, these instances spontaneously resolved within 30 min.

Teng *et al*.[14] demonstrated that CNB exhibited superior diagnostic efficacy compared to FNA in evaluating high-risk cervical lymph nodes. The findings demonstrated that the diagnostic accuracy and sensitivity of the CNB group were both 100%, which was notably superior to that of the fFNA group (83.3 and 79.2%, respectively). This finding exhibited similarity to the result obtained by Xu *et al*.[16].

Regarding the diagnosis of cervical lymphadenopathy, the current study discovered that CNB possessed the following characteristics: 89% sensitivity, 100% specificity, 100% positive predictive value, and 66% negative predictive value. According to a prior investigation conducted by Shin *et al*.[17], US-CNB demonstrated a sensitivity of 92%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 88%.

In the context of a well-established hematopathological diagnostic pathway, we suggest routinely using US-guided core biopsies to investigate patients with a neck mass that is suspected to be lymphoma, as well as those with a cervical neck mass that has not been diagnosed by FNAC.

In the context of our study on the complications of US-guided core biopsies in cervical lymph nodes, several key issues.

Pain and discomfort were reported by 33% of participants, emerging as the most prevalent complication. This finding underscores the inherently invasive nature of biopsy procedures, even those augmented by US guidance. The significant proportion of individuals experiencing discomfort highlights the necessity for clinicians to provide adequate preprocedural counseling and consider analgesic measures to enhance patient comfort.

Hematoma formation and minor bleeding, encountered in 5% of cases, underscore the critical importance of meticulous needle placement and technique, especially in regions with dense vascular networks. These complications serve as a reminder of the delicate balance between achieving diagnostic yield and minimizing tissue trauma.

The incidence of infection at a rate of 6% reinforces the efficacy of sterile procedural techniques, though it also serves as a cautionary note about the inherent risk of introducing pathogens into the body during invasive procedures. While not excessively high, this complication rate necessitates strict adherence to aseptic protocols to further mitigate this risk.

Injury to adjacent structures was noted in 2% of cases, attesting to the precision and safety afforded by US guidance. This relatively low incidence

demonstrates the technology's capability to minimize collateral damage to surrounding tissues and organs, a testament to the advancements in imaging techniques.

Pneumothorax, identified in 3% of patients, specifically highlights the risks associated with biopsying thoracic lesions near the chest wall. This particular complication underscores the need for heightened vigilance and preparedness when performing procedures near the lung region.

Vertebral artery injury and Horner's syndrome (HS), each occurring in 1% of the cohort, spotlight the potential for significant adverse events even under US guidance. These findings emphasize the necessity for thorough anatomical knowledge and procedural precision to avoid such serious outcomes.

Lastly, transient nerve palsy, also at a rate of 1%, signals the potential for temporary neurological deficits following biopsy. This complication further highlights the critical need for careful planning and execution of the biopsy procedure to minimize the risk of nerve damage.

To our knowledge, the existing literature lacks specific studies in detail addressing the complications associated with US-guided core biopsies of the peri-thyroid and lower cervical lymph nodes.

Given the anatomical correlations and the nature of the complications outlined above, it is reasonable to extrapolate that similar risks may be encountered in guided biopsies of lymph nodes. However, related research offers valuable insights.

For instance, Kansagara *et al*.[18] focused on the tru-cut biopsy, a similar CNB technique, within the maxillofacial region and found it to be practical and relatively free from significant complications, with only a minor complication rate of 8% related to bleeding that required intervention. This supports the general safety of CNBs in sensitive areas, underscoring the importance of technique and patient care to minimize adverse outcomes.

Hematoma formation and minor bleeding are acknowledged risks in US-core biopsy, but they are generally rare and manageable. Ha *et al*.[19] provided comprehensive data on US-guided CNB for thyroid lesions, revealing a low overall complication rate of 0.81%, with most minor complications, such as small to moderate hematoma. These findings emphasize the procedure's safety, even in the highly vascularized thyroid region, further supporting the minimal risk of significant bleeding in cervical lymph node biopsies.

The innovation of hydrodissection techniques offers new avenues for minimizing complications in challenging anatomical areas. Cheng and Liang's[15] study on US-guided CNB with hydrodissection for small lymph node metastases adjacent to large cervical vessels showed no major and only minor, transient complications in 6.5% of patients. This technique's success in preventing injury to adjacent structures highlights potential advancements in US-core biopsy safety and efficacy, particularly for lesions close to critical vascular structures.

Concerning complications, particularly infection rates after US-core biopsy, a detailed analysis of the bleeding and infection outcomes post-US-core biopsy in patients with benign cervical lymph node diseases showed that out of 590 patients, a significant proportion experienced minor bleeding, and 40 cases were associated with infection. The study emphasized that bleeding was minor and did not necessitate surgical intervention, highlighting the procedure's overall safety. Infection and bleeding rates varied depending on the lymph node's condition, with infectious lymph nodes, especially those with tuberculosis, showing a higher tendency for bleeding[20].

A study on US-guided tissue-core biopsy of thoracic lesions adjacent to the chest wall, including apical and mediastinal lesions, found it to be an accurate and safe technique. Out of 54 patients, complications were minor including moderate hemoptysis in one patient, trivial hemoptysis or hemothorax in three, and symptomless pneumothorax in two, which resolved spontaneously. This indicates that complications can occur but are generally low in frequency and severity[21].

A recent study on the accuracy and safety of US-CNB of soft tissue lesions in an outpatient setting analyzed 392 consecutive patients at a sarcoma center. The results highlighted the procedure's high diagnostic accuracy and safety, with major complications occurring in only 0.8% of cases and no instances of biopsy tract seeding reported during the study period. The study found that US-CNB is particularly effective for diagnosing soft tissue lesions, including sarcomas, lipomas, and desmoid tumors, with a conclusive biopsy rate of 88.5%[22].

Another study evaluated the use of US-CNB for diagnosing pediatric neuroblastic tumors, with 83 cases reviewed. This study showcased a diagnostic accuracy of 96.4%, with no serious complications, infections, or needle track seeding observed. The research underlines US-CNB as a minimally invasive, accurate, and safe diagnostic method for pediatric neuroblastic tumors[23].

A research investigation on US-guided percutaneous biopsy of peripheral pulmonary lesions using 16-G core needles revealed the procedure's efficacy and safety. The adequacy of samples was notably influenced by lesion size, with bullae around the lesion serving as an indicator of pneumothorax, which occurred in 2.7% of instances. The patient's position, particularly lateral versus supine, correlated with overall complication rates and hemorrhage[24].

HS may arise as a complication following procedures like US-guided cervical lymph node FNA. HS manifests through symptoms such as ipsilateral miosis (constricted pupil), ptosis (drooping eyelid), enophthalmos (sunken eyeball), and facial anhidrosis (lack of sweating), stemming from damage to the oculosympathetic pathway. Although uncommon, there exists a documented case where HS was induced by an US-guided FNA conducted during thyroid cancer management. Notably, symptoms of HS emerged immediately postprocedure, and subsequent US assessment indicated damage to sympathetic ganglia. The patient's symptoms resolved within 2 months[25].

Another case involved HS following an US-guided infraclavicular brachial plexus block, marking a rare instance in literature where HS developed after such a procedure. The onset of HS was observed during surgery but resolved approximately two and a half hours later without leading to any significant clinical consequences for the patient. However, it was suggested that the history of cervicotomy might have contributed to this atypical presentation of HS by causing anatomical changes that influenced local anesthetic diffusion rather than the volume of the anesthetic used[26].

The British Journal of Radiology compares tissue sampling methods for diagnosing parotid gland neoplasia, specifically US-core biopsy versus FNAC. The study concludes that US-core biopsy exhibits superior sensitivity, specificity, and lower nondiagnostic rates compared to FNAC, particularly in detecting malignancies. Although rare, significant complications following US-core biopsy, such as permanent facial nerve dysfunction, are absent. Consequently, US-core biopsy is the preferred approach in specific circumstances for diagnosing parotid neoplasia[27].

These studies collectively reinforce the safety profile of US-core biopsy while highlighting ongoing improvements in technique and technology that aim to reduce complication rates further. The evolution of biopsy methods offers promising strategies for enhancing diagnostic accuracy and patient outcomes in evaluating cervical lymphadenopathy. Ongoing research is essential for refining these techniques and minimizing the risk of complications associated with US-core biopsy.

CONCLUSION

Performing core sample of cervical lymph nodes in cases of cervical lymphadenopathy, specifically for US-guided core biopsy, can be beneficial in achieving a diagnosis and potentially decreasing the need for excisional biopsies performed under general anesthesia. Additionally, it seems to serve as a reliable initial diagnostic tool for patients undergoing investigation for lymphoma.

CONFLICT OF INTEREST

There are no conflicts of interest.

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