The evaluation of ultrasound-guided core biopsy in detection of abnormal cervical lymph nodes

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Summary

Objective: To assess the value of routine ultrasound (US) imaging and histopathological results of ultrasound-guided core needle biopsy (US-CNB) of abnormal cervical lymphadenopathy. *Subject and method:* From September 2022 to August 2023, a total 112 patients with clinical suspected cervical lymph nodes (CLNs) and/or have suspected signs on US (width ≥ 5mm, round in shape and absent hilus of CLNs) underwent US-CNB at 108 Military Central Hospital. *Result:* Among 112 patients, there were 56 metastatic lymph nodes, 10 lymphomas, 10 tuberculous and 32 nonspecific inflammatory lymph nodes. Level IV nodes included benign and malignant lesions was predominant. In the group of malignant CLNs: Irregular margin, absence of hilum and hypoechogenicity were found in 65.7%, 70% and 94.3% respectively, these proportions were significantly greater than that of benign group, with $p<0.05$. Comparison of US and histopathology of CLNs diagnosis: The sensitivity, specificity, positive predictive value, negative predictive value were 88.6%, 66.7%, 81.6%, 77.8%, respectively, when there were ≥ 2 suspected signs. *Conclusion:* Ultrasound is often considered as the first imaging diagnostic and valuable tool for detecting suspicious CLNs due to its convenience, non-invasiveness and cost-effectiveness, to helps reduce unnecessary interventions for benign lymph nodes. US-CNB is a minimally invasive technique that allows accurate diagnosis of the lymph node's histopathology.

Keywords: Ultrasound, core needle biopsy, lymph node.

I. Background

Metastatic cervical lymphadenopathy is quite common in patients with head and neck cancers or cancers outside this region. For patients with squamous cell carcinoma of the head and neck, the presence of metastatic CLNs reduces the 5-year survival rate to 50% and contralateral CLNs metastasis decreases the 5-year survival rate to 25%[1]. Therefore, evaluating metastatic CLNs plays a crucial role in cancer patients, aiding in prognosis and optimal treatment. Treatment and prognosis depend on the histopathology and stage of the cancer. Additionally, cervical lymphadenopathy is also a common site for lymphoma, tuberculosis and other benign CLNs disorders such as Kikuchi's disease, Kimura's disease and Rosai-Dorfman disease[1].

Historically, the primary method for diagnosing and evaluating CLNs relied on clinical examination, which often led to the oversight of small or deep-seated nodes. US, utilizing high-frequency probes, has emerged as a non-invasive and flexible diagnostic approach. Through US, we can assess the size, structure, interrelationships between nodes and adjacent structures, vascularization and capsule disruption... Therefore, US not only plays a crucial role in distinguishing between benign and malignant but also monitors the effect of radio-

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chemotherapy of metastatic nodes as well as for the detection of recurrent lymph node metastases in the neck. The recent reports have demonstrated that US and US-CNB of CLNs are simple and safe procedures for detecting and diagnosing abnormal CLNs[2]. In Viet Nam, there are a number of studies of thyroid cancer but there is a few of reports study about other malignant CLNs. So we performed this study was to assess the value of routine ultrasound imaging and histopathological results of ultrasound-guided core neede biopsy in the diagnosis of abnormal cervical lymphadenopathy.

II. SUBJECT AND METHOD

2.1. Subject

A total 112 patients with abnormal CLNs on clinic and on US examinations, were performed US-CNB. Clinical suspicions include stiff, irregular margin and unmovable lymph nodes. According to Vassallo P et al., ultrasound signs of suspected CLNs include: Width ≥ 5mm, a round shape (width/length ratio ≥ 0.5) and the absence of a hilum structure of the lymph node[3].

2.2. Method

The design of our study was a cross-sectional descriptive study. Before the biopsy, we performed US of CLNs by the GE Voluson S8 machines with a 5-12MHz linear transducer. Using US to evaluate the location, size, echogenicity, calcification, necrosis, hilum and vascularization of CLNs. US-CNB was performed by interventional radiologists free-handed with a 13cm-long manual 14-18G needle (US Biopsy, Franklin, IN, Japan). US was used to point the biopsy location, carefully identifying the needle path, avoiding major blood vessels and nerve structures. The skin was disinfected. The physician washed their hands, put on gloves and prepared a sterile drape with a hole for the biopsy site, covering the probe with a sterile endoscopy nylon. Local anaesthesia was administered by using 1% lidocaine. The biopsy needle was passed through the lymph node's capsule. Then, the inner cutting needle was withdrawn while simultaneously advancing the cutting needle to obtain the tissue sample. At least 3-6 tissue specimens were placed in a specimen container. Potential bleeding was stopped by compression. The puncture site was disinfected and pressure dressing was applied. To assess any procedure-related complications, US imaging was performed again 30-45 minutes after the biopsy. Furthermore, patients were encouraged to communicate with the clinical physician or directly contact the biopsy-performing physician regarding any signs of pain or swelling at the intervention site[4].

2.3. Statistical analysis

The data were collected and processed using SPSS 20.0 software. Statistical analysis was performed using Chi-square Tests and Fisher's Exact Test. The significance level was set at $p<0.05$. Base on three characteristics (margin, echogenicity and absent of hilum of lymph node) and histopathology report, we calculated the sensitivity, specificity, positive predictive value and negative predictive value of ultrasound.

2.4. Ethical standards

Consent was obtained from all participants through written informed consent after providing detailed explanations before the biopsy.

III. RESULT

3.1. Patient's general characteristics

Table 1. Patient's general characteristics

Characteristics		Value	
Age		52.9 ± 16.2	Min 12
			Max 87
Gender	Male	75 (67%)	
	Female	37 (33%)	

In our study, the patient's average age was 52.9 ± 16.2 years old. Majority of patients were male with the rate of 67%.

3.2. Ultrasound image characteristics of cervical lymph node

Table 2. Correlation of characteristics of cervical lymph node ultrasound with histopathological results

Characteristics \ Pathology		Malignant CLNs	Benign CLNs	Sum	p
Width	<8mm	8 (11.4%)	10 (23.8%)	18 (16.1%)	0.11
	≥ 8mm	62 (88.6%)	32 (76.2%)	94 (83.9%)	
Shape	Width/Long < 0.5	15 (21.4%)	13 (31%)	28 (25%)	0.27
	Width/Long ≥ 0.5	55 (78.6%)	29 (69%)	84 (75%)	
Margin	Regular	24 (34.3%)	38 (90.5%)	77 (68.8%)	0.00
	Irregular	46 (65.7%)	4 (9.5%)	35 (31.2%)	
Echogenicity	Hypoechoic	49 (70%)	25 (59.5%)	39 (34.8%)	0.00
	Hyperechoic	14 (20%)	1 (2.4%)	50 (44.6%)	
	Heterogeneous echo	7 (10%)	16 (38.1%)	23 (20.5%)	
Calcification	No	67 (95.7%)	42 (100%)	109 (7.3%)	0.29
	Yes	3 (4.3%)	0 (0%)	3 (2.7%)	
Necrosis	No	63 (90%)	32 (76.2%)	95 (84.8%)	0.06
	Yes	7 (10%)	10 (23.8%)	17 (15.2%)	
Hilum	Absent	66 (94.3%)	26 (61.9%)	92 (82.1%)	0.00
	Present	4 (5.7%)	16 (38.1%)	20 (17.9%)	
Vascularization	No angiogenesis	50 (71.4%)	33 (78.6%)	83 (74.1%)	0.23
	Central	3 (4.3%)	4 (9.5%)	7 (6.2%)	
	Peripheral	8 (11.4%)	1 (2.4%)	9 (8%)	
	Central and peripheral	9 (12.9%)	4 (9.5%)	13 (11.6%)	

p<0.05 is considered significant. Chi-square and Fisher Exact tests were used for analysis.

In group of malignant CLNs, irregular margin, absence of hilum and hypoechogenicity was found in 65.7%, 70% and 94.3% respectively, these proportions were greater than rates of benign group, the variance had statistical significance with p<0.05. The differences in nodal size, shape, calcification, necrosis and vascularization characteristics between benign and malignant CLNs were not statistically significant.

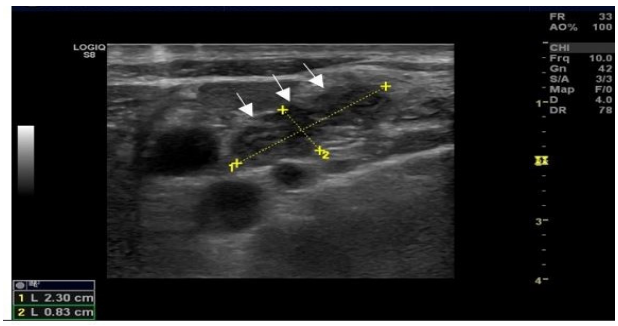

Figure 1. A hypoechoic mestastatic lymph node with oval in shape, absence of echogenic hilus, irregular margin (arrows).

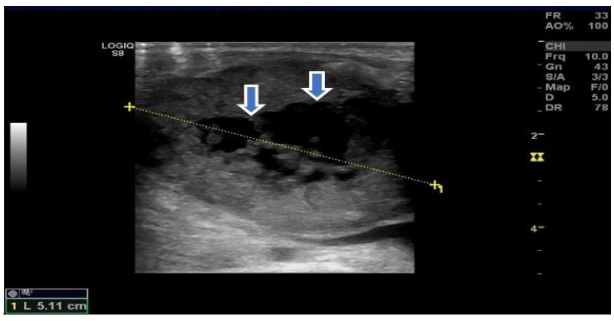

Figure 2. A hypoechoic mestastatic lymph node with round in shape, absence of echogenic hilus, irregular margin and necrosis (arrows)

3.3. Histopathological characteristics and ultrasound-guided cervical lymph node biopsy results

Complications of the ultrasound-guided cervical lymph node biopsy: There were no cases of bleeding, death, nerve damage or infection along the biopsy tract in our study.

Table 3. Histopathological results of patients

		Patients (n)	Percentage (%)	Sum (%)
Malignant lymph node	Metastase	56	50	62.5
	Lymphoma	14	12.5	
Benign lymph node	Tuberculosis	10	8.9	37.5
	Inflammatory	32	28.6	

In our study, metastatic CLNs were predominant, accounting for 50%, while the minority were cases of tuberculous lymph node accounting for 8.9%.

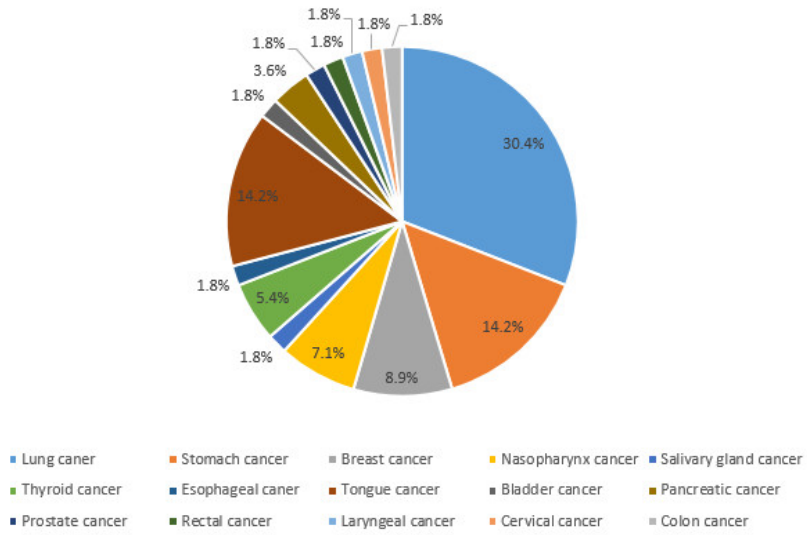

Chart 1. Distribution of metastatic cancers in cervical lymph nodes

Among the 112 patients included in the study, metastases originating from lung cancer were predominant, constituting 30.4% of cases.

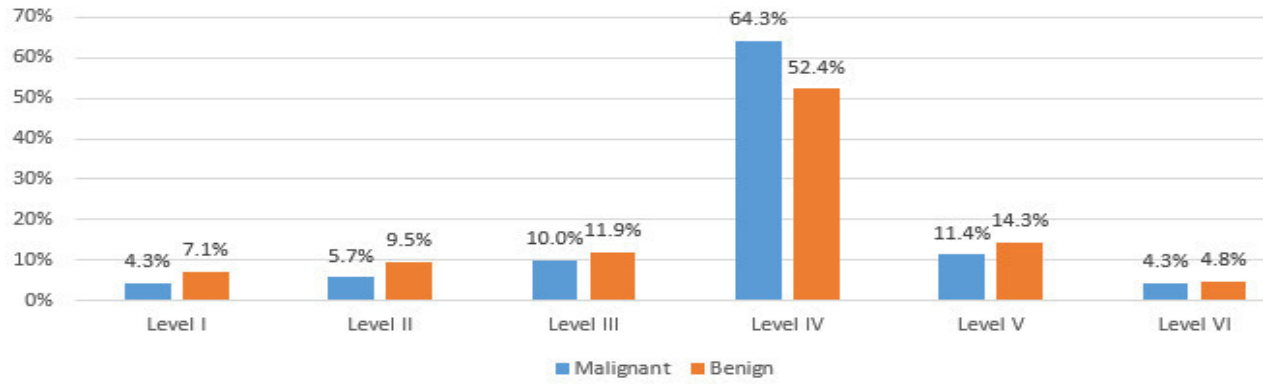

Chart 2. Distribution of cervical lymph node levels according to Robbins

Cervical lymph node level IV were predominant for both malignant and benign lymph nodes with the rate of 64.3% and 52.4% respectively.

3.4. The value of ultrasound in diagnosing abnormal cervical lymph nodes

Table 4. Sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) of ultrasound images

Value / Characteristic	Se (%)	Sp (%)	PPV (%)	NPV (%)
≥ 1 sign	100%	7.1%	64.2%	100%
≥ 2 signs	88.6%	66.7%	81.6%	77.8%
≥ 3 signs	41.4%	95.2%	93.5%	49.4%

To achieve both high sensitivity and high specificity, it was advisable to choose ≥ 2 suspicious signs.

IV. DISCUSSION

Regarding the high proportion of CLNs group IV it can be explained by the predominance of malignant CLNs, accounting for 50% in our study. These metastatic CLNs often involve various types of cancers. According to Ellison's research, CLNs level IV play a significant role in the lymphatic drainage of the chest, lungs, and esophagus...[5]. They are commonly affected by both malignant and benign CLNs. Among the metastatic group, lung cancer is the most common because it is the second most common cancer in Vietnam, following liver cancer, according to Globocan 2018 statistics. Regarding the nodal size and shape, although larger CLNs tend to have a higher likelihood of malignancy, reactive and tuberculous CLNs can also be large and appear round in shape. Moreover, even early-stage metastatic CLNs can be very small. It is similar to the findings of Ying M et al[6]. Therefore, nodal size plays a more crucial role in monitoring lymphadenopathy than differing benign or malignant nature. According to Vassallo P et al[3], eccentric cortical hypertrophy had been a useful sign for identifying CLNs with malignant potential before changing shape. This is due to early-stage cancer cells tend to develop in a specific region of CLNs, causing an eccentric shift in the axis, while inflammatory CLNs tend to spread diffusely. The presence of the hilum is often associated with benign CLNs; however, early-stage metastatic lymph node can also be present of hilum. In our study, presence of hilum was observed in 5.7% of malignant CLNs, which is consistent with the findings of other authors 4-51%[3,6-8]. In addition, tuberculous CLNs are typically associated with absent of hilum on ultrasound[1,9].

Malignant CLNs at an early stage, before capsule invasion or rupture, often have more distinct and well-defined borders similar to benign nodes. Because cancer cells infiltrate and disrupt the internal lymph node structure, causing a loss of echogenicity within the lymph node. When cancer cells invade and rupture the capsule, the margin may appear irregular. However, the nature of CLNs margin is not considered a definitive criterion for distinguishing between benign and malignant CLNs, according to Ahuja AT, Ying M[1,6].

Regarding calcification, our study encountered very few cases, primarily due to the low incidence of metastatic CLNs from thyroid cancer (only 3 cases). In contrast, metastatic CLNs from other cancers often exhibited coarser calcifications when there was a history of recurrent bleeding in CLNs. This can be attributed to the relatively low demand for biopsy in cases of thyroid cancer metastasis, as most clinicians rely on fine-needle aspiration combined with evidence of malignant changes in the thyroid gland for diagnosis. Moreover, the assessment of neovascularization in our study did not yield statistically significant results. This could be because malignant CLNs tend to generate new blood vessels as cancer cells produce angiogenic factors, leading to increased vascularity within CLNs. However, acute inflammatory lymph nodes can also exhibit numerous vascular signals. These values are crucial in assessing the diagnostic accuracy of US in detecting abnormal CLNs, helping clinicians make informed decisions regarding further evaluation and intervention. Therefore, using two out of the three

suspicious features on US (irregular margin, hypoechogenicity and absense of hilum architecture) in diagnosing malignant CLNs achieved a sensitivity of 88.6%, and specificity of 66.7%, which is consistent with the findings of Dang Thi Xuan[10], who reported a sensitivity of 81.2%. The specificity in our study is low because all 112 patients have lymphadenopathy on clinical and width ≥ 5mm, performed US-CNB. Hence, combining two of the three suspicious features on US can improve diagnostic specificity.

Abnormal CLNs has tradifionally been diagnosed by surgical excision biopsy, and this technique has represented the "gold standard" for diagnosis. It requires surgery, nursing, anaesthetic and theatre staff, adding considerable cost as well as anaesthetic and surgical risks. For these reasons, alternafive techniques have been tried to obtain tissue for diagnosis, including FNA and more recently core biopsy. FNA produces a cytological preparation, which allows cell identification to some degree but no ability to assess tissue architecture and immunohistochemistry. US-CNB is now a well established technique widely used in sampling CLNs. It represents an alternative approach to the established ways of tissue sampling and provides an intermediate step between FNA and surgical excision biopsy. US-CNB can be performed as an outpatient, under local anaesthetic, requiring only an ultrasound machine, a radiologist and nurse. US-CNB is regarded as being particularly useful in elderly people and in those with multiple comorbidifies. It allows direct needle visualisation to avoid adjacent structures and necrotic areas and also ensures that the tip of the biopsy needle traverses the lesion without penetrating deep to it. Multiple areas from CLNs can be sampled and non-palpable disease can be visualised and biopsied. US-CNB produces a histological preparation which allows cell identification, some assessment of tissue architecture and immunohistochemistry[4].

V. CONCLUSION

Ultrasound is often referred to as the first imaging diagnostic and valuable tool for detecting suspicious CLNs due to its convenience, non-invasiveness and cost-effectiveness, to helps reduce unnecessary interventions for benign lymph nodes. US-CNB is a minimally invasive technique that allows for accurate diagnosis of the lymph node's histopathology.

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