Original Article

Investigation of the value of ultrasound-guided core needle biopsy from pathologic lymph nodes to the diagnosis of lymphoma

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Abstract

Introduction: In recent years, techniques with minimally invasive have been gradually developed and used in the diagnosis of lymphoma. Among minimally invasive techniques, core needle biopsy (CNB) has been widely accepted as an effective tool for the diagnosis of malignant lymphoma, carcinoma and deep tumors that are only accessible via CT or endoscopic-guided. This study was conducted to investigate of diagnostic value of ultrasound guided CNB in the diagnosis of lymphoma in all parts of the body compared to surgical excisional biopsy (SEB). **Materials and Methods:** This is an descriptive epidemiological study that was performed on patients with suspected lymphoma referred to the intervention ward of Golestan Hospital in Ahvaz in 2019. For all patients with suspected lymphoma, CNB of lymph nodes was performed by ultrasound-guided. Finally, the final diagnosis of CNB was compared with the results of surgical biopsy in the studied specimens. **Results:** In this study, 40 patients were evaluated with suspected lymphoma. At initial diagnosis with CNB, 12 (30%) had NHL, 19 (47.5%) had Hodgkin's lymphoma, and 2 had high-grade lymphoma. Of the 40 patients examined, 29 required IHC to confirm the diagnosis. In 8 cases, the final diagnosis was done using SEB. Final diagnosis in 9 (22.5%) patients was confirmed by CNB only. The CNB along with the IHC also led to the final diagnosis in 23 (57.5%) patients. However, another 8 patients required biopsy to confirm the diagnosis by SEB. **Conclusion:** The findings of this study indicated that US-CNB is a highly efficient method of diagnosis of lymphoma with high specificity, in the fastest possible mode and with the least complications.

Keywords: CNB, diagnostic value, lymphoma, surgical biopsy

Introduction

Lymphoma are a heterogeneous group of cancers with diverse epidemiology, etiology, clinical manifestations, treatment, and outcomes that are caused by the proliferation of lymphocytes.[1] Scientific advances in the field of laboratory and imaging have increased the diagnostic accuracy of different types of lymphoma. More than 50 specific types of this group of cancers have been identified and classified by the WHO.[2] Lymphomas are divided into two main subgroups: Hodgkin's (HL) and nonHodgkin's (NHL) lymphona, based on the presence or absence of ReedSternberg cells.[3] The annual prevalence rates of the NHL and HL are 6.7 and 2 (per 100,000, respectively) worldwide.[4] Taken together, lymphoma neoplasms are the fourth most common cancer and the sixth leading cause of cancer deaths in the United States, with 135,000 new cases in 2016.[3,5]

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As different types of lymphoma have very different clinical presentation, treatment and progression rate, early diagnosis and histologic classification are essential in determining treatment plan.[6] Surgical biopsy of the lymph node is accepted as the gold standard for accurate diagnosis of these neoplasms.[7,8] But this invasive procedure for biopsy not only increases the patient's pain but also is costly, time consuming, and has complications.[6] Therefore, in recent years, minimally invasive techniques have been used to diagnose lymphoma. Among minimally invasive techniques, core needle biopsy (CNB) has been widely accepted as an effective tool for the diagnosis of malignant lymphoma, carcinoma, and deep tumors that are only accessible by CT or endoscopic-guided.[8,9] For patients with manifestations of peripheral lymphadenopathy also fine-needle aspiration cytology (FNA) is using as a diagnostic tool, but the diagnostic capabilities of this technique are limited and provide only cytomorphological information.[8,10] In addition, although sono-fine needle aspiration cytology (US-FNA) is useful in the diagnosis of lymphadenopathy, FNA, especially in patients with lymphoma, has a high false-negative rate and is unable to accurately classify lymphoma.[11] Therefore, CNB is increasingly used as a subcutaneous sampling technique and is a cheap, fast, simple and well tolerated method.[12] The CNB not only helps in the diagnosis and differentiation of benign or malignant lymphoproliferative diseases but also helps in definitive diagnosis of HL and NHL.[13,14]

Han *et al.* (2018) in China conducted a study entitled "Effectiveness of ultrasound-guided CNB in cervical lymphadenopathy". In this retrospective study, the efficacy and factors affecting the diagnostic accuracy of ultrasound-guided CNB (US-CNB) were evaluated. This study examined the reports of 6603 lymphadenopathy patients who underwent 6695 US-CNB operations during 20042017. The results showed that the overall accuracy of US-CNB for differentiating malignant from benign lesions was 91/70%. Success or failure of US-CNB in diagnosis was significantly associated with size, nature (malignant or benign), location and depth of penetration, but there was no significant relationship between US-CNB diagnostic accuracy with needle size, number of core tissues, or history of malignancy taken. As a result, the US-CNB is a safe and effective method for the diagnosis of cervical lymphadenopathy.[15]

In the study of Huang *et al.* (2018), the studied samples included 471 cases of lymphoma, 12 atypical lymphoid hyperplasia (ALH), 136 cases of suspected lymphoma, 372 benign lesions, 22 descriptive diagnoses. 53.1% of CNB tumor specimens had ≥4 tissues and 40.4% had a length of <2 cm. 104 CNB cases that had a surgical biopsy included 45 carcinoma (non-metastatic), 32 lymphomas for treatment observations. 217 cases of CNB biopsies were performed in subsequent CNB biopsies (70 cases) or surgically (147 cases) with lymphoma diagnosis. As a result, CNB of lymph node have specific clinical indications, although they are limited to the diagnosis of lymphoproliferative disorders. Tissue biopsy should be performed for suspected lymphoma and ALH diagnosed by CNB. For benign lesions diagnosed by the CNB, additional biopsy is not necessary for further examination of the lesion.[16]

Kiliçarslan *et al.* (2017), in a study aimed to determine the diagnostic value of CNB and to compare it with surgical biopsy among 291 cases of CNB biopsy from lymph nodes, included 60 cases of patients who received pathologic lymph nodes after CNB. The results showed that CNB is a noninvasive, low cost and low side effect procedure that can be used as a surrogate for surgical biopsy. However, the sensitivity of CNB is less than its specificity, and because of high false-negative cases (7 cases), biopsy of the lymph node by surgical method recommended in cases of suspected neoplasms.[17]

It is well-established that CNB is increasingly being used as a valid biopsy and accepted to diagnose of lymphoma as replacement for surgical biopsy because of its lower cost, less invasive features, and fewer complications than surgical. However, some studies have focused only on particularly isolated areas, such as superficial or deep masses, or only one or two organs. In addition, the effect of different lesion sizes on the diagnostic accuracy of lymphoma and its variants via CNB has not yet been determined. The aim of this study was to evaluate the diagnostic value of ultrasound-guided CNB in the diagnosis of lymphoma in all parts of the body compared to biopsy by surgical procedure.

Materials and Methods

The present study is an descriptive epidemiological study that was performed on patients with suspected lymphoma referred to the intervention ward of Golestan Hospital of Ahvaz in 2019. All eligible individuals were selected according to the inclusion and exclusion criteria and after providing explanations by the researchers about the purpose and method of implementation of the project and were entered into the study with written and informed consent.

Inclusion criteria were included: Patient consent to participate in the study, performing ultrasound-guided CNB, clinical suspicion of lymphoma and lymphadenopathy is present anywhere in the body where CNB can be done. Exclusion criteria were primary metastasis or recurrence of metastasis except for lymphoma, unwillingness to participate in the study and malignancy except for lymphoma.

For all patients with suspected lymphoma, ultrasound-guided core needle biopsy from lymph node was performed. Patients' demographic information (age and sex), sonographic results and pathologic diagnosis included superficial location (neck, axillary, groin, breast, vertical muscle, and waist) and abdominal mass (abdominal cavity, peritoneum), length of lesion (max of its diameter on ultrasound and length of the CNB tissue), Subtypes lymphoma, and benign or malignant lesion in all specimens were recorded. The type of lymphoma

was determined according to the WHO classification.[18] Results of surgical biopsy were also recorded in patients who did not diagnose CNB lymphoma. Finally, the final diagnosis of CNB was compared with the results of surgical biopsy in the studied specimens. In this study, using Groneck *et al.* (2015) the sample size was obtained (8) through the following equation: 35 persons.

$$n = \frac{Z^2P(1-P)}{d^2}\frac{Z^2P(1-P)}{d^2} = 18/35 \cong\cong 35$$

SPSS software version 24 was used for statistical analysis. Mean, standard deviation, frequency, and percentage of frequency are used to describe the data. Chi-square and Fisher exact tests, Mc Nemar tests, and MannWhitney and KruskalWallis tests were used for data analysis. Significance level was set at 0.05.

Results

In this study, 40 patients with suspected lymphoma were evaluated. The mean age of participants was 49.4 years. Also 55% of patients, including 22 persons, were female. In most cases (50%) the neck was sampled, followed by axillary and abdominal sampling. At initial diagnosis with CNB, 12 cases (30%) had NHL, 19 (47.5%) had HL and 2 cases had high grade lymphoma. In total, the CNB was able to detect 33 cases of lymphoma. In 7 other cases, the exact type of disease was not detectable by CNB while the lymphoproliferative disease was detected. Of the 40 patients examined, 29 required IHC to confirm the diagnosis. In 8 cases, the final diagnosis was performed using SEB.

Final diagnosis in 9 (22.5%) patients was done by CNB only. The CNB along with the IHC also led to the final diagnosis in 23 (57.5%) patients. However, another 8 patients required biopsy to confirm the diagnosis by SEB [Table 1].

Of the 7 LPD cases that were sampled with SEB, 3 cases were NHL, 2 were HL and the other 2 cases were not classified even by SEB method [Table 2].

Frequency and percentage of lymphoma diagnosis from patients with suspected lymphoma are listed in Table 3.

The incidence of side effects was compared in both sampling methods. All cases of SEB were associated with a complication; however, only 2 cases (5%) had an adverse event after CNB [Table 4].

Table1: Diagnostic methods in different lymphoma[1]

Diseases	CNB	CNB+IHC	CNB+IHC+SEB
NHL	2 (13.3%)	10 (66.6%)	3 (20%)
HL	6 (28.5%)	13 (61.9%)	2 (9%)
High grade lymphoma	1 (50%)	0 (0%)	1 (50%)
Total	9 (22.5%)	23 (57.5%)	6 (15.7%)

[1]NHL non-Hodgkin's lymphoma; HL Hodgkin's lymphoma; CNB core needle biopsy; IHC Immunohistochemistry; SEBsurgical excisional biopsy

Table 2: Relationship between SEB and CNB results

SEB	CNB	
	LPD	High grade lymphoma
NHL	3 (42.85%)	0
HL	2 (28.57%)	0
High grade lymphoma	0	1 (100%)
Unclassifiable (LPD)	2 (28.57%)	0

Table 3:Results from SEB evaluation

Diagnosis	Frequency	Percent (%)
NL	3	37.5
NHL	2	25
Unclassifiable	2	25
High grade lymphoma	1	12.5

Table 4: Incidence of side effects following biopsy

Adverse events	CNB	SEB
Pain	2 (5%)	8 (100%)
Hematoma	0	1 (12.5%)
Seruma	0	1 (12.5%)
Infection	0	0

Discussion

Due to the high prevalence of lymph node disease and the possibility of malignancy in some of them, it should be possible to differentiate benign and malignant tumors prior to surgery to prevent a large number of unnecessary surgeries, the most important diagnostic method for this purpose is the use of low invasive sampling methods such as CNB. There have been numerous studies to date on the ability of the CNB to diagnose lymphatic disease. The present study also using evaluate of 40 patients with lymphoma (suspected lymphoma), especially HL and NHL, showed that performing CNB in 80% of cases had eliminated the need for SEB. The ultrasound-guided core needle biopsy is a non-radiologic method that detects the accuracy of sampling through information obtained from the lesion's bloodstream.

In addition, in this method the obtained sample is unchanged and the cells do not become compressed, which is very important for pathological evaluation.[19]

Previous studies have shown that the success rate of ultrasound-guided CNB was significantly higher than that of FNB (37.6% success rate) as well as the CNB under CT scan guidance (success rate of 71.5%). Of the 7 LPD cases sampled with SEB, 3 cases with NHL, 2 with HL, and 2 cases with SEB were not classified. Thus, of the 8 cases which the CNB was unable to detect, 2 cases were not classified by the SEB. These findings are in line with other studies in this area. In a study, Oh *et al.* (2016) evaluated the efficacy of US-CNB in the diagnosis

of cervical lymphadenopathy and found that the success rate of CNB biopsy was 91.1%. The study also reported that the efficacy of CNB in lymphoma detection was much higher than in US-FNA (88.8% vs. 11.1%).[11] In another study by Groneck *et al.* (2016) US-CNB's performance in the diagnosis of lymphadenopathy and lymphoma was evaluated. The findings of the study showed that the US-CNB identified 121 of the 132 samples evaluated. In other words, the US-CNB has been able to diagnose the disease in 91.6%.[8]

So far, many studies have investigated the diagnostic accuracy of US-CNB in the diagnosis of lymphatic lesions. Kiliçarslan *et al.* (2017) in Turkey, studied potential of US-CNB for replacement for SEB and showed that CNB results had 90% and 100% sensitivity and specificity compared to surgical biopsy; positive predictive value (PPV) and the negative predictive value (NPV) was 100% and 0%, respectively, and the diagnostic accuracy was 86.5%.[17] Also, a study by Oh *et al.* (2016) showed that US-CNB performs well in distinguishing benign from malignant lymphadenopathy and its sensitivity, specificity, and diagnostic accuracy are 91.6%, 100%, and 98.6%, respectively.[11] Following CNB or surgical interventions, patients were evaluated for side effects and it was shown that, unlike SEB, which was completely associated with complications such as pain or hematoma, CNB was only associated with unbearable pain in one case. These findings are consistent with other studies.

Conclusion

It can be concluded that the US-CNB is a highly efficient method for the diagnosis of lymphoma, which enables high specificity, fastest possible, and with the least complications. One of the most important limitations of this study was the small sample size and non-calculation of diagnostic accuracy. Another limitation of this study was the lack of evaluation of US-CNB efficacy factors such as mass size. It is therefore recommended that future studies be conducted to address these limitations with longer-term multicenter studies and a larger sample size.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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