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Original Article

Feasibility of fine-needle aspiration biopsy and its applications in superficial cervical lesion biopsies

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Abstract: The aim of the study was to investigate the feasibility and value of clinical application of fine-needle aspiration histological biopsy via ultrasound-guided thyroid nodule and enlarged cervical lymph node fine-needle aspiration histological biopsy. Fine-needle aspiration cytological and histological biopsies and surgical treatments were performed on 982 patients with thyroid nodule and 1435 patients with enlarged cervical lymph nodes. A comparative study of the histological and cytological examination results and post-surgical etiology results was subsequently conducted. Among the 982 thyroid nodule patients, the acquisition rates were 89.8% (882/982) for fine-needle aspiration histological biopsy and 96.2% (945/982) for cytological biopsy, while among the 1435 patients with enlarged cervical lymph nodes, the acquisition rate for fine-needle aspiration cytological biopsy was slightly higher than that for histological biopsy, with values of 95.7% (1374/1435) and 91.4% (1312/1435), respectively. For the thyroid nodule patients, when the acquired histological and cytological biopsy results were compared with the post-surgical etiology results, the sensitivity, specificity, and accuracy of the histological results were 98.5%, 100%, and 98.9%, respectively, whereas those of the cytological results were 86.8%, 82.9%, and 85.6%, respectively; the differences between the 2 biopsy methods were statistically significant ($P < 0.05$). For the patients with enlarged cervical lymph nodes, when the acquired histological and cytological biopsy results were compared with the post-surgical etiology results, the sensitivity, specificity, and accuracy of the histological results were 96.3%, 99.8%, and 97.6%, respectively, whereas the those of the cytological results were 76.8%, 92.1%, and 82.2%, respectively; again, the differences between the 2 methods were statistically significant ($P < 0.05$). In conclusion, Fine-needle aspiration histological biopsy is a reliable and highly accurate examination method. It is simple and feasible, thus facilitating the discrimination of malignant and benign thyroid nodules and enlarged cervical lymph nodes and playing an important role in the establishment of reasonable clinical therapeutic regimens.

Keywords: Thyroid nodule, cervical lymph node, fine-needle aspiration histology, fine-needle aspiration cytology

Introduction

Thyroid nodules and enlarged lymph nodes are superficial goiters that are commonly observed in the cervical area; thyroid diseases are frequently occurring diseases in this area in the clinical setting. With the popularization of medical examinations and ultrasonography, the clinical discovery rate of thyroid nodules is increasing, and approximately 5-15% of the population is found to have palpable nodules during medical examinations; among those who undergo cervical ultrasonography, the nodule discovery rate can reach 20-75% [1]. Although the application of ultrasound technology has improved the thyroid nodule diagnostic rate, nodule characteristics are still difficult to distinguish clinically. Patients who experience enlarged cervical lymph nodes as their initial symptom also have quite complex etiological factors. The timely and clear pathological diagnosis of enlarged lymph nodes is clinically significant with regard to therapeutic therapy determinations, therapy evaluations, and tumor progression monitoring. Cervical lymph node incision biopsy is a common clinical etiological diagnostic method, but it is complicated with the risk of serious surgical trauma and high expense and is thus not the most suitable clinical method. In contrast, the ultrasound-guided fine-needle aspiration technique uses a fine-gauge needle to puncture the lesion and negative pressure to

aspirate and collect a pathological sample for diagnosis. Because of its minimally invasive and secure nature and easy accessibility, this technique has gradually attracted more attention in the clinic. This article evaluated the feasibility of ultrasound-guided fine-needle aspiration histological biopsy and its clinical value for discriminating malignant and benign thyroid nodules and enlarged cervical lymph nodes by performing fine-needle aspiration histological and cytological examinations of thyroid nodule patients and patients with enlarged cervical lymph nodes, combined with a comparative study of the biopsy and post-surgical etiological results for each case.

Materials and methods

All participants signed informed written consent prior to participation and each study was approved by the Institutional Review Board for Human Subjects at the participating institutions: Zhejiang Cancer Hospital and Zhejiang Xiaoshan Hospital.

Study population

Between October 2009 and September 2013, the study subjects were selected from patients who visited the hospital because of cervical goiters and were found to have tumors suspected of malignancy via palpation and ultrasonography for thyroid nodules or enlarged cervical lymph nodes. We selected 982 cases of thyroid nodules and 1435 cases of enlarged cervical lymph nodes, among which 1025 cases were observed in men and 1392 cases were observed in women. The age range of the patients was 18-78 years and the average age was 44.15 ± 17.54 years. The thyroid nodules were 0.84 ± 0.77 cm in size, and the enlarged cervical lymph nodes were all located in the cervix II/III/IV/V area, with a size 1.87 ± 1.14 cm. All cases were hospitalized after admission to the surgical department. Informed consent was obtained from all patients before they participated in our study. The study was approved by the Institutional Review Board.

Instruments and methods

An Esaote MyLab 90 (Esaote Group, Genova, Italy) and GE Logiq 9 color ultrasonic scanner (GE Corporation, Fairfield, CT, USA) were used; the equipment had a linear array probe frequency of 5-12 MHz, and predetermined thyroid conditions were applied for all cases. Patients maintained a supine or side-lying position while undergoing 2-dimensional gray-scale and Doppler ultrasonic scanning to observe and record the characteristics of the thyroid nodules or lymph nodes, including the locations, sizes, internal echoes, and blood distribution.

Observed thyroid nodules and lymph nodes were selected for ultrasound-guided fine-needle aspiration histological and cytological examinations. A 21-gauge vacuum aspiration biopsy needle C1 needle (Bracco Eisai, Co., Tokyo, Japan) was used to puncture the nodules. All of the aspirates were examined in general-smear histological and cytological examinations according to the multiple-spot multiple-puncture principle. After the histological and cytological results were released, the nodules and lymph nodes were surgically removed.

Statistical analysis

The SPSS 13.0 software package (SSPS, Inc., Chicago, IL, USA) was used for statistical analyses. Comparisons of enumeration data were performed with the χ^2 test, and a P-value < 0.05 was considered to be statistically significant.

Results

All thyroid nodule and enlarged cervical lymph node patients underwent fine-needle aspiration histological and cytological examinations, as well as surgical treatments. Among the thyroid nodules, the post-surgical etiological results showed that there were 689 malignant cases, accounting for 70.2% of the punctured nodules; these included 598 papillary carcinoma cases, 54 follicular carcinoma cases, 23 medullary carcinoma cases, 11 undifferentiated carcinoma cases, and 3 other cases. Additionally, there were 293 benign cases, accounting for 29.8% of the nodules; these included 227 nodular goiter cases, 17 adenoma cases, 45 thyroiditis cases, and 4 other cases. Among the enlarged cervical lymph nodes, the post-surgical etiological results showed that there were 863 malignant cases, accounting for 60.1% of the punctured nodules; these included 604 metastatic carcinoma cases and 259 malignant lymphoma cases.

Table 1. Thyroid nodules: comparison of histological and cytological examination

Examination Method	Total Cases	Positive Cases	Negative Cases	True Positive	False Positive	True Negative	False Negative
Histology	882	657	225	657	0	215	10
Cytology	945	621	324	572	49	237	87

Table 2. Enlarged cervical lymph nodes: comparison of histological and cytological results

Examination method	Total cases	Positive cases	Negative cases	True positive	False positive	True negative	False negative
Histology	1312	773	539	772	1	509	30
Cytology	1374	724	650	686	38	443	207

There were also 572 benign cases, accounting for 39.9% of the nodules; these included 505 chronic lymphadenitis cases and 17 lymphatic tuberculosis cases.

After the fine-needle aspiration histological and cytological examinations, the acquisition rate of the histological results for the 982 thyroid nodule cases was 89.8% (882/982), while that of the cytological results was 96.2% (945/982). The acquisition rates among the 1435 enlarged cervical lymph node cases were 91.4% (1312/1435) for the histological results and 95.7% (1374/1435) for the cytological results. The acquisition rate for cytology was slightly higher than that for histology, but there was no statistical difference between the 2 methods ($P > 0.05$).

Among the thyroid nodules, when the acquired histological and cytological etiology results were compared with the post-surgical etiology results, the sensitivity, specificity, and accuracy of the histological etiology results were found to be 98.5%, 100%, and 98.9%, respectively, whereas those of the cytological etiology results were 86.8%, 82.9%, and 85.6%, respectively; the detailed results are shown in **Table 1**. The sensitivity, specificity, and accuracy of the histological examination were all better than those of the cytological examination; the differences between the 2 methods were statistically significant ($P < 0.05$).

For enlarged cervical lymph nodes, when the acquired histological and cytological examination results were compared with the post-surgical etiology results, the sensitivity, specificity, and accuracy of the histological results were 96.3%, 99.8%, and 97.6% respectively, whereas those of the cytological results were 76.8%, 92.1%, and 82.2% respectively; the detailed results are shown in **Table 2**. The sensitivity, specificity, and accuracy of the histological examination were all better than those of the cytological examination; the differences between the 2 were statistically significant ($P < 0.05$).

Discussion

Thyroid nodules are a common clinical disorder, and the ultrasonic technique is the most common examination method used to diagnose thyroid diseases. Although the development of ultrasonic techniques has provided a basis for the differential diagnosis of thyroid nodules, some diseases such as thyroid neoplasm are difficult to confirm solely with imaging examinations. Furthermore, the blood vessel-enriched thyroid is not suitable at any point for surgical removal to yield etiological examinations. Thus, a simple, safe, and reliable examination method that could clearly determine the nature of a thyroid nodule and simultaneously provide effective guidance for clinical treatment is currently an imperative challenge. Similarly, enlarged cervical lymph nodes are also a common clinical disorder with a complex etiology; for example, if a lymphatic metastasis from a malignant tumor in another area of the body occurs, there is a chance that the tumor will metastasize to the cervix and cause lymph node enlargement. A clear definition of the pathological characteristics of enlarged cervical lymph nodes is crucial to etiological determinations and can provide guidance for clinical diagnoses, treatments, and prognoses. However, surgical biopsies of cervical lymph nodes have limited clinical applications because of the high cost and serious associated trauma.

The fine-needle aspiration biopsy technique has become increasingly popular in the clinic. This technique is advantageous because of its simplicity, safety, and reliability, as it yields less trauma and fewer complications, with fast diagnoses and high accuracy [2]. It has already become a reliable method for discriminating malignant and benign nodules and is presently recognized as the preferred diagnostic method for early-stage thyroid nodules [3], but is applicable to all types of thyroid nodule for which unnecessary surgical treatment should be avoided. For enlarged cervical lymph nodes, fine-needle aspiration biopsy is also a simple, safe, and effective examination method. For cases that present with enlarged lymph nodes as the initial symptom without apparent primary lesions, a fine-needle aspiration biopsy can be combined with the lymph node convergence to suggest the location of the primary lesion; this is more commonly observed with nasopharyngeal cancer [4]. Furthermore, for lymph nodes located beside the main cervical vessels and in the supraclavicular area, which are very close to the blood vessels and nerves, an ultrasound-guided fine-needle aspiration biopsy could effectively avoid damage to the surrounding nerves and vessels and thus increase the diagnostic accuracy.

The accuracy of the etiological results obtained with the fine-needle aspiration biopsy technique is based on a massive collection of pathological samples and is largely dependent on the operator's skills. Each nodule should be examined according to the multiple-spot, multi-direction puncture method, and a negative pressure needle should be used simultaneously whenever possible; with the multiple-spot, multi-direction puncture method, it is wrong to randomly stir the puncture needle within a nodule. Instead, negative pressure should be implemented after the puncture needle enters the nodule, and a lifting-thrusting or rotor-cutting motion should be maintained in the same direction to facilitate the uptake of cells or tissue into the stylet, after which the needle should be withdrawn and another puncture implemented in a second direction in the nodule capsule. After the puncture, the operator must release the negative pressure before swiftly withdrawing the needle and subsequently spray the sample in the stylet onto a glass slide with the help of air pressure. Valid samples can only be obtained to increase the positive diagnosis rate when the apparatus is operated with strict adherence to the standardized procedure.

Among the 982 thyroid nodule cases and 1435 enlarged cervical lymph node cases in this study, the acquisition rates after fine-needle aspiration histological and cytological examinations were 89.8% and 91.4%, respectively, for the histological results and the 96.2% and 95.7%, respectively, for the cytological results. The acquisition rate for cytology was slightly higher than that for histology. The 21-gauge negative pressure aspiration biopsy needle is more conducive to the acquisition of cells, but there was no statistical difference between the 2 methods. Histological and cytological misdiagnoses are mainly due to the inaccurate positioning of a puncture, thus rendering the needle unable to aspirate valid pathological samples and bleeding that occurs during the puncture process, thus affecting the observation of pathological samples after smearing. Studies in the literature have reported [5, 6] that the sample acquisition rates for the fine-needle aspiration technique were relatively low, ranging only from 43-65%. Ultrasound-guided repetitive puncture can increase the diagnostic accuracy rate by 15-25% to offset the limitations of the sample [7]. However, the acquisition rates of the histological and cytological results in our study were superior to those previously reported in the literature, mainly because of the use of multi-spot, multi-direction, and negative pressure aspiration techniques.

In this study, when the pathological results obtained from cytological examinations of thyroid nodules were compared with the post-surgical etiology results, the sensitivity and specificity for the cytological results were 86.8% and 82.9%, respectively. This is consistent with results reported in the literature; the reported sensitivity and specificity of fine-needle aspiration cytological diagnosis for discriminating malignant and benign thyroid nodules range from 55-91.6% and 73.7-100%, respectively [8-10], whereas the sensitivity and specificity of the histological results are above 95% and are thus both higher than those for cytology. This is because the application of the fine-needle aspiration technique can acquire more valid histological pathology samples and thus the diag-

nostic results are more accurate. In comparison, cytological examinations are limited by the requirement for pathological samples and the smear technique, which affects the diagnostic accuracy. When the pathological results obtained from histological examinations of enlarged cervical lymph nodes were compared with the post-surgical etiology results, the sensitivity, specificity, and accuracy of the histology results were 96.3%, 99.8%, and 97.6%, respectively. According to a study by Kim [11], the etiological diagnostic sensitivity, specificity, and accuracy of ultrasound-guided biopsy needle aspiration are 97.9%, 99.1%, and 97.9%, respectively. These findings indicate that in cervical lymph nodes, the histological etiology results obtained from fine-needle aspiration were more consistent with the results obtained from coarse needle aspiration biopsies. The 21-gauge negative pressure aspiration biopsy needle is more flexible when puncturing the lymph node; further, it is secure, reliable, and has fewer contraindications and complications. It is easier for 21-gauge biopsy needles to reach their targets by avoiding blood vessels, especially in small lymph nodes (< 1 cm), active lymph nodes, and lymph nodes beside main cervical vessels and in the supraclavicular area. Similarly, for enlarged cervical lymph nodes, the sensitivity, specificity, and accuracy of fine-needle aspiration cytology are significantly lower than those for histology; in particular, the sensitivity of cytology is only 76.8%. Although this study did not conduct separate studies of the sensitivities of different etiological examinations with regard to lymph nodes, according to the literature, the sensitivity for a malignant lymphoma puncture is only 64% [12], while in this study, malignant lymphoma only accounted for 18.2% (259/1435) of the total cases. This discrepancy is likely the explanation for the relatively low sensitivity. These findings indicate that there are some existing difficulties with the use of fine-needle aspiration cytological examinations for the diagnosis of malignant lymphoma, and thus this technique cannot replace diagnostic histological etiology. These findings also reflect the profound significance of fine-needle aspiration histological examinations for the discrimination of malignant and benign enlarged cervical lymph nodes.

For thyroid nodules, when the acquired histological and cytological etiology results were compared with the post-surgical etiology results, the positive and negative predictive values were 100% and 95.6%, respectively, for the histological results and 92.1% and 73.1%, respectively, for the cytological results. For enlarged cervical lymph nodes, the positive and negative predictive values for the histological and cytological results were 99.9% and 94.4% and 94.6% and 68.2%, respectively. The positive predictive values for both the histological and cytological examinations were relatively higher, indicating that the fine-needle aspiration biopsy technique is more accurate and reliable in for positive diagnostic results. In comparison, according to an analysis of the high false-negative value, the inability of cytology to predict negative diagnostic results accurately is mainly due to insufficient samples, high blood content, over diluted cells, insufficient cells on smears, cellular degeneration, poor staining, and inaccurate puncture positioning, leading to a failure to acquire valid pathological samples.

The ultrasound-guided fine-needle aspiration histological biopsy technique is a simple and feasible method that provides an effective way to differentiate the diagnoses of thyroid nodules and enlarged cervical lymph nodes. This technique is safe and reliable, with a high diagnostic accuracy rate, a low complication rate, and operational simplicity. This method has important implications for focal discrimination, clinical therapeutic method selection, and therapy and prognosis evaluations, and thus can be used as a conventional preoperative diagnostic method.

Disclosure of conflict of interest

None.

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