

Fine-Needle Aspiration Cytology of the Thyroid Gland at Kanazawa University Hospital, 1989 to 1993

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ABSTRACT

From 1989 to 1993, 1115 fine-needle aspiration (FNA) biopsies of the thyroid gland were performed in 647 patients with thyroid nodule or goiter at the Department of Nuclear Medicine, Kanazawa University Hospital (Kanazawa, Japan). Of the total 647 aspirated thyroid lesions, 147 were investigated histologically after thyroidectomy, and were compared with the cytologic diagnoses to determine the accuracy of FNA cytology of thyroid lesions. When "suspicious" cytologic finding was considered as positive, FNA cytology had a diagnostic sensitivity of 82.3%, aspecificity of 76.0% and an accuracy of 80.1%. Follicular cell tumors and chronic thyroiditis were relatively frequently misdiagnosed.

KEY WORDS

Thyroid gland, Fine-needle aspiration biopsy (FNA), Accuracy

INTRODUCTION

Fine-needle aspiration (FNA) cytology has been accepted as a preeminent preoperative diagnostic method of thyroid nodules. It provides an accurate and cost-effective method for identification of patients requiring surgery. However, false-negative and false-positive diagnoses or unsatisfactory specimens cannot be avoided, with this limitation of FNA largely depending on the skill of the operators and diagnosticians. Consequently the reported accuracy of the technique differs considerably among institutions^{1-3), 7), 11), 13-17), 21), 22)}.

This article presents our personal experience with FNA of the thyroid gland over a five-year period from 1989 to 1993. The problems associated with the

cytologic diagnosis of benign and malignant thyroid diseases are discussed.

MATERIALS AND METHODS

From 1989 to 1993, 1115 FNAs were performed on thyroid nodules in 647 patients. Five hundred ninety-five were women (92.0%) and 52 men (8.0%). The mean age was 50.6 years (range, 12-83 years). Of 647 patients, 147 (22.7%) underwent thyroidectomy, and the FNA diagnoses were compared with the histologic results to assess the accuracy of FNA of the thyroid nodules. FNA biopsy was performed by one nuclear medicine physician (T. M.) using a disposable 22-gauge needle and a 10 ml syringe attached to a holder under real-time ultrasound guid-

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Table 1. Results of FNA Diagnosis

Cytologic Diagnosis	No. of Specimens	No. of Patients	
		Total	With Operation
Benign (Class I, II)	810	467	55
Suspicious (Class III)	56	23	10
Malignant (Class IV, V)	218	132	81
Unsatisfactory Specimen	31	25	1
Total	1115	647	147

Table 2. Correlation Between Fine-Needle Aspiration and Surgical Diagnoses

Fine Needle Aspiration Diagnoses	No. of Opera- tions	Chro- nic Thyroi- ditis	Graves' Disease	Multi- nodu- lar Goiter	Adenoma	Cyst	Other Benign Disea- ses	Papi- llary Carci- noma	Follic- ular Carci- noma	Ana- plastic Carci- noma	Medu- llary Carci- noma	Malignant Lymh- oma	Other Malignant Diseases
Benign	55	1	2	4	26	4	1	14	1		1	1	
Suspicious	10	1		1	4			4					
Malignant	81	3			2		1	68	2	2	1		2
Papillary carcinoma	75	2			2		1	67	1	1			1
Follicular carcinoma	2								1				1
Anaplastic carcinoma													
Medullary carcinoma	1										1		
Malignant lymphoma	1	1											
Other malignant diseases	2							1		1			
Unsatisfactory specimen	1								1				
Total	147	5	2	5	32	4	2	86	4	2	2	1	2

TP: true positive; FP: false positive; TN: true negative; FN: false negative; sensitivity: $(TP/TP+FN)$; specificity: $(TN/TN+FP)$; positive predictive value: $(TP/TP+FP)$; negative predictive value: $(TN/TN+FN)$; accuracy: $(TP+TN/TP+FP+FN+TN)$

ance. Each aspirate was injected onto a glass slide, and the smears were either dried or fixed in 95% alcohol. Air-dried smears were stained with the May-Grunwald-Giemsa method, while alcohol-fixed specimens were stained with the Papanicolaou method. The FNA findings were reported as malignant (Class IV and V), benign (Class I and II) and suspicious

(Class III). Specimens with either no diagnostic element or insufficient cells for a cytologic diagnosis were classified as "unsatisfactory".

RESULTS

The cytologic diagnoses were summarized in Table 1. Eight hundred ten (72.6%) specimens obtained

Table 3. Fourteen Cases of Papillary Thyroid Carcinoma With False-Negative FNA Diagnosis

Case No	Tumor Size	Type of Error
1	1.2 cm	diagnostic
2	1.1 cm	sampling
3	1.5 cm	unsatisfactory
4	2.0 cm	sampling
5	2.5 cm	diagnostic
6	2.0 cm	unsatisfactory
7	1.0 cm	unsatisfactory
8	1.5 cm	diagnostic
9	0.2 cm	unsatisfactory
10	0.7 cm	unsatisfactory
11	0.6 cm	unsatisfactory
12	0.7 cm	diagnostic
13	1.5 cm	sampling
14	3.5 cm	diagnostic

Table 4. Statistical Analysis With False-Negative FNA Diagnosis

sensitivity	82.3%
specificity	76.0%
positive predictive value	86.8%
negative predictive value	69.1%
accuracy	80.1%

from 467 patients were diagnosed as benign, 56 (5.0%) specimens from 23 patients as suspicious and 218 (19.6%) specimens from 132 patients as malignant. Thirty-one (2.8%) specimens from 25 patients were unsatisfactory for diagnosis.

Surgical confirmation of the cytologic diagnoses was obtained in 147 of the 647 patients. Fifty-five (37.4%) lesions were histologically diagnosed as benign, 10 (6.8%) lesions as suspicious and 81 (55.1%) lesions as malignant. The correlation between cytologic and histologic diagnoses in these 147 lesions was detailed in Table 2.

Of the 81 malignant neoplasms diagnosed by FNA, 6 had a false-positive diagnosis (Three cases were diagnosed as chronic thyroiditis, 2 as follicular adenoma and 1 as other benign disease after surgery). Two of the 3 cases histologically proven as chronic thyroiditis demonstrated large follicular cells with atypical and hyperchromatic nuclei, interpreted as papillary carcinoma, in their cytologic specimens. The remaining one was misinterpreted as malignant lymphoma because of high lymphoid cellularity in the cytologic specimen. Two cases of follicular adenoma, which were misinterpreted as papillary carcinoma by FNA, demonstrated pseudopapillation in their smears. On the other hand, of the 55 cytologically benign lesions, 38 (69%) were histologically confirmed, but the remaining 17 were histologically proven to be

malignant (Fourteen cases were diagnosed as papillary carcinoma, 1 as follicular carcinoma, 1 as medullary carcinoma and 1 as malignant lymphoma after surgery). Of these 17 false-negative cases, 14 cases, which were proven histologically to be papillary carcinoma, were reviewed to determine whether errors could be attributed to unsatisfactorily aspirated material, sampling error or cytodiagnostic errors (Table 3). Sampling error was considered significant in 3 cases; on retrospective review of the smears, adequate cellular sample was present but tumor cells were not evident. In 6 other cases, the materials aspirated were insufficient for cytologic diagnosis. The cytodiagnostic error was considered significant in the remaining 5 cases. On reviewing the cytologic specimens of these 5 patients, the tumor cells did not show nuclear changes typical of papillary carcinoma or papillary clustering of the tumor cells was not evident rather with follicular structure. Histologically all these 5 cases were diagnosed as follicular variant of papillary carcinoma.

Of the 10 "suspicious" FNA cytologic results, 4 (40%) were histologically proven to be malignant and the remaining 6 (60%) benign. Analysis of the overall group was shown in Table 4. Considering cases of "suspicious" for malignancy as positive results, FNA cytology had a diagnostic sensitivity of 82.3%, a specificity of 76.0% and an accuracy of 80.1% in the diagnosis of malignancy of the thyroid lesions. If "suspicious" FNA results were included as benign, FNA cytology had a sensitivity of 78.1%, a specificity of 88.0% and an accuracy of 81.5%.

DISCUSSION

We found the diagnostic sensitivity of FNA at our hospital to be 82.3%, the specificity to be 76.0% and the accuracy to be 80.1%. To compare

Table 5. Review of the Literature on FNA of the Thyroid

	Year	No. of Patients	Accuracy (%)	Sensitivity (%)	Specificity (%)	Inadequacy (%)
Suen & Quenville. ²¹⁾	1983	79		97		
Akerman et al. ¹⁾	1984	420		57	98	3
Bugis et al. ⁷⁾	1986	198	83	80	83	3
Goellner et al. ¹¹⁾	1987	349		98	99	20
Asp et al. ³⁾	1987	155	73	100	47	
Hawkins et al. ¹³⁾	1987	415		86		
Jones et al. ¹⁵⁾	1990	82		92	85	14
Altavilla et al. ²⁾	1990	257	95	71	100	16
Hamming et al. ¹⁴⁾	1990	169	75	92	71	3
Klemi et al. ¹⁶⁾	1991	194	95	55	100	
Watters et al. ²²⁾	1992	120		86	85	
Okamoto et al. ¹⁷⁾	1994	252		80	98	
Present study		147	80	82	76	3

the efficacy of FNA at our hospital with that at other centers, we reviewed the 12 series described in the literature as to the sensitivity, specificity and accuracy of the procedure, in which a total of 2690 patients underwent surgery. The sensitivity was 55 to 100% (mean, 82.8%), the specificity 47 to 100% (mean, 86.6%) and the accuracy 73 to 95% (mean, 84.2%) in differentiating benign from malignant disease^{1-3), 7), 11), 13-17), 21, 22)} (Table 5). In the present study, the frequency of false-positive cases was higher compared with that reported at other centers. Such false-positive cases were found in chronic thyroiditis and follicular adenomas. It has been reported that in chronic thyroiditis follicular cells tend to show considerable nuclear pleomorphism, occasionally leading to a misdiagnosis of papillary carcinoma^{8), 12), 19), 21)}. Special attention is required to discriminate atypical cells associated with chronic thyroiditis from malignant cells. The presence of atypical epithelial cells concomitant with lymphoid cells strongly suggests that the lesion is chronic thyroiditis.

Seventeen of the 55 cases diagnosed as benign by FNA cytology were histologically proven to be malignant after surgery. Of such 17 false-negative cases, 14 cases were papillary carcinoma. Cytodiagnostic errors contributed significantly to such false-negative results in 5 of these 14 cases of papillary carcinoma, and it appeared to be caused by the absence of discernible papillary fragments on the cytologic specimens. Histologic examination after surgery revealed that all these 5 cases were follicular variant of papillary carcinoma. Careful attention should be paid in the FNA diagnosis of follicular variant of papillary carcinoma.

Malignant lymphoma can be confused with severe chronic thyroiditis¹²⁾. In the present study, two such cases were noted; one case with an FNA diagnosis of malignant lymphoma was histologically proven to be chronic thyroiditis and the other case with an FNA diagnosis of chronic thyroiditis turned out to be malignant lymphoma after surgery. The latter case was a low-grade follicular lymphoma of the thyroid, and the diagnosis was difficult even with the

surgically resected specimen.

The most important limitation of FNA is the differentiation of encapsulated follicular carcinoma from follicular adenoma. FNA cannot distinguish them, since capsular or vascular invasion, essential to the diagnosis, cannot be determined from FNA specimens. In the present study, six of the 32 benign adenomas proven histologically were preoperatively diagnosed as suspicious or malignant with FNA based on the cytologic findings of high cellularity, considerable variation in nuclear size or abnormality in chromatin pattern. On the other hand, of 4 cases proven histologically as follicular carcinoma (all encapsulated type), one case had a preoperative FNA diagnosis of follicular adenoma based on the relatively uniform, round to oval nuclei with evenly dispersed chromatin and abundant colloid. Our results supported the view that FNA cytology cannot reliably classify individual follicular lesions of the thyroid. Accordingly all follicular cell tumors should probably be treated surgically^{5), 6), 9), 10), 13), 14)}.

Four of the 10 "suspicious" aspirates in the present study were proven after surgery to be obtained from cancer, while the remaining 6 were from benign lesions. Gharib, H. et al¹⁰⁾ found a 24% incidence of malignancy in their "suspicious" cases, and suggested that all lesions with FNA results of "suspicious" require operation. We also believe that "suspicious" results should be confirmed by repeat FNA or by surgery.

In conclusion, our results indicated that FNA cytology is an excellent method for the diagnosis and management of thyroid nodule. A small proportion of false-negative or false-positive FNA results cannot be avoided, and therefore knowledges of the clinical and laboratory findings as well as results of radiographic or ultrasound scan should be used complementarily to accurately evaluate the nature of the thyroid lesion^{4), 18), 20)}.

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金沢大学病院における甲状腺穿刺吸引細胞診の成績（1989－1993年）

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要 旨

金沢大学病院核医学科で、1989年より1993年の5年間に施行された甲状腺穿刺吸引細胞診（FNA）は計1115件（患者総数647名）であった。647名中、147名はその後甲状腺切除術が行われた。この147例について、FNAによる術前診断と手術後の病理診断との対比を行い、FNA診断の精度に関する検討を行った。“疑陽性”の結果を陽性群に算入した場合、FNAのSensitivity（感度）は82.3%、Specificity（特異性）は76.0%、Accuracy（正診率）は80.1%と良好な結果が得られた。FNAによる術前診断の困難な疾患はろ胞性腫瘍と慢性甲状腺炎であり、しばしば診断不一致例が認められた。