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Clinical Characteristics and Predictive Factors for the Detection of Thyroid Cancer in Children with Thyroid Nodules

Junghwan Suh, Han Saem Choi, Ah Reum Kwon, Hyun Wook Chae, Ho-Seong Kim

Department of Pediatrics, Severance Children's Hospital, Endocrine Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea

INTRODUCTION

• Thyroid nodules in children are less common than adults, but pediatric thyroid nodules have higher rate of malignancy compared with adults, and also have increased risk of lymph node metastasis and recurrence.

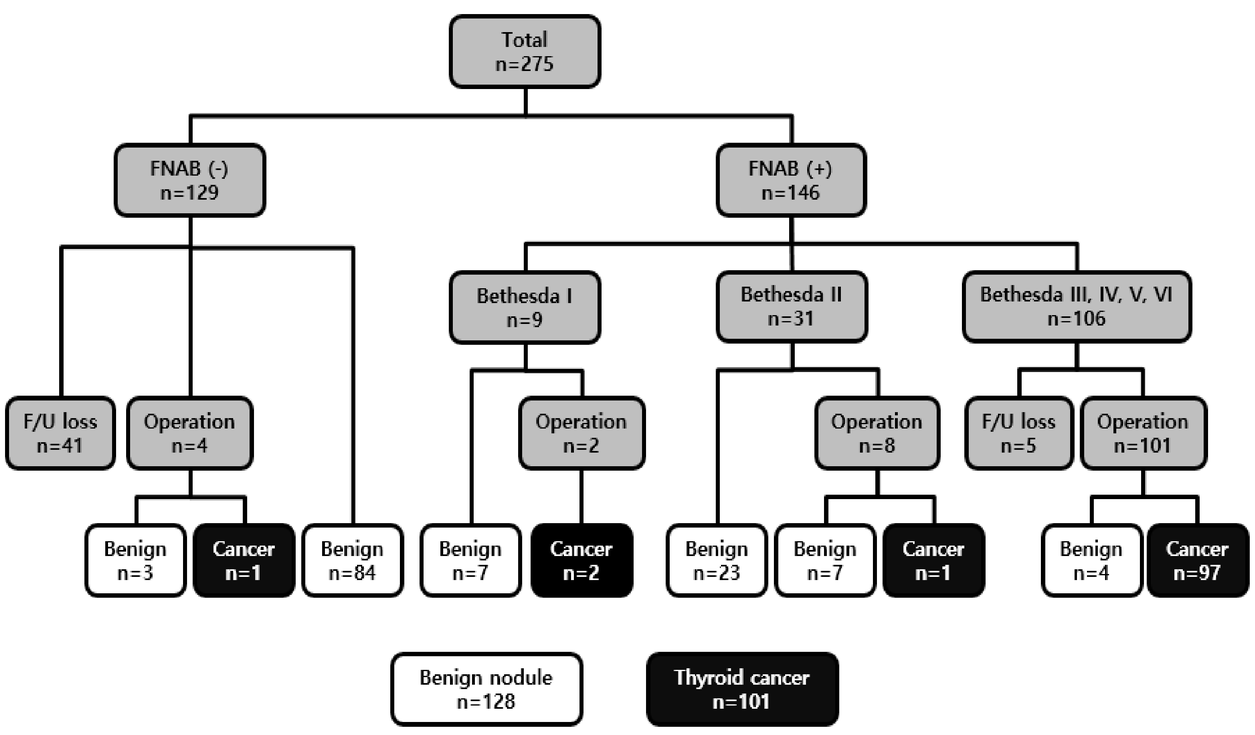
• Investigating risk factors of thyroid cancer is crucial in making a decision for when to perform fine-needle aspiration biopsy (FNAB), which is very important in early diagnosis and management of pediatric thyroid nodules.

• We analyzed clinical features, laboratory findings, and thyroid ultrasound (US) of children with thyroid nodules to determine predictive factors of thyroid cancer.

METHODS

• Total 229 patients under 18 years of age with thyroid nodule whom visited Severance Children's Hospital from January 2005 to May 2017 were retrospectively reviewed.

• Patients were divided into thyroid cancer group and benign nodule group, and clinical, laboratory, US data had been compared.



RESULTS

Table 1. Comparison of clinical characteristics in patients with benign nodules or malignancy

	Benign nodule (n=128)	Thyroid cancer (n=101)	*p* value
Sex (Male/Female)	34(26.6%)/94(73.4%)	14(13.9%)/87(86.1%)	**0.019**
Age at diagnosis (year)	12.5 ± 4.3	15.0 ± 2.8	**<0.001**
BMI at diagnosis	19.86 ± 3.84	20.90 ± 3.62	**0.046**
BMI SDS at diagnosis	0.13 ± 1.18	0.08 ± 1.26	0.788
Symptom at first visit			
Goiter (≥ grade 2)	42/110 (38.2%)	10/60 (16.7%)	**0.004**
Palpable mass	26/110 (23.6%)	42/61 (68.9%)	**<0.001**
Goiter and palpable mass	3/110 (2.7%)	2/59 (3.4%)	0.809
Asymptomatic	45/110 (40.9%)	11/59 (18.6%)	**0.003**
Thyroid function test (n=206)			
T3 (ng/mL)	1.58 ± 0.93	1.28 ± 0.28	**0.003**
free T4 (ng/dL)	1.39 ± 1.22	1.27 ± 1.11	0.498
TSH (μIU/mL)	2.16 ± 2.51	1.98 ± 1.64	0.546
Anti-thyroglobulin antibody	17/76 (22.4%)	19/96 (19.8%)	0.680
Anti-TPO antibody	18/72 (25.0%)	17/62 (27.4%)	0.546

Table 2. Ultrasonographic features in patients with benign nodules or malignancy

	Benign nodule (n=128)	Thyroid cancer (n=101)	*p* value
Nodule size (mm)	14.1 ± 13.2	23.5 ± 12.3	**<0.001**
Echogenicity			
Hypoechoic	26/82 (31.7%)	29/64 (45.3%)	0.092
Isoechoic	5/82 (6.1%)	1/64 (1.6%)	0.171
Hyperechoic	7/82 (8.5%)	2/64 (3.1%)	0.177
Mixed	32/82 (39.0%)	7/64 (10.9%)	**<0.001**
Cystic	13/82 (15.9%)	2/64 (3.1%)	**0.012**
Spongiform	1/82 (1.2%)	0/64 (0%)	0.375
Solid	0/82 (0%)	5/64 (7.8%)	**0.010**
Microcalcifications	2/122 (1.6%)	36/72 (50.0%)	**<0.001**
Lymph node alterations	6/122 (4.9%)	59/95 (62.1%)	**<0.001**
Irregular margins	2/120 (1.7%)	22/84 (26.2%)	**<0.001**
Intranodular blood flow	2/120 (1.7%)	7/84 (8.3%)	**0.022**

Table 3. FNAB stage by Bethesda System and histopathologic results

Bethesda stage, n (%)	Surgical procedure	Final pathology	Malignant (%)
I. Non-diagnostic, n=9 (6.4%)	Total (n=2)	Papillary (n=2)	2 (22.2%)
II. Benign, n=31 (22.0%)	Total (n=2)	Medullary (n=1)	1 (3.2%)
	Partial (n=6)	Benign (n=7)	
III. Atypia of undetermined significance or follicular lesion of undetermined significance, n=12 (8.5%)	Total (n=7)	Papillary (n=7)	9 (75.0%)
	Partial (n=5)	Follicular (n=2)	
		Benign (n=3)	
IV. Follicular neoplasm or suspicious for a follicular neoplasm, n=2 (1.4%)	Partial (n=2)	Follicular (n=1)	1 (50%)
		Benign (n=1)	
V. Suspicious for malignancy, n=20 (14.2%)	Total (n=17)	Papillary (n=18)	20 (100%)
	Partial (n=3)	Follicular (n=1)	
		Medullary (n=1)	
VI. Malignant, n=67 (47.5%)	Total (n=57)	Papillary (n=65)	67 (100%)
	Partial (n=10)	Medullary (n=2)	

Table 4. Predictive factors for the detection of thyroid cancer

	Odds ratio (95% CI)	*p* value
Palpable mass	28.996 (1.392 – 604.080)	**0.030**
Nodule size	0.932 (0.844 – 1.029)	0.162
Mixed echogenicity	0.020 (0.001 – 0.463)	**0.015**
Cystic nodule	0.009 (0.000 – 16.855)	0.221
Microcalcifications	226.717 (5.030 – 10217.987)	**0.005**
Lymph node alterations	28.687 (2.244 – 366.736)	**0.010**
Irregular margins	5.732 (0.296 – 111.121)	0.248
Intranodular blood flow	18.084 (0.876 – 373.239)	0.061

Table 5. Surgical interventions

Type of operation	
Total thyroidectomy	83 (82.2%)
Right total thyroidectomy	6 (5.9%)
Left total thyroidectomy	2 (2.0%)
Right total left subtotal thyroidectomy	5 (5.0%)
Left total right subtotal thyroidectomy	5 (5.0%)
Pathology of specimen	
Papillary cancer	93 (92.0%)
Follicular cancer	4 (4.0%)
Medullary cancer	4 (4.0%)
Molecular mutation ($BRAF^{V600E}$ mutation)	16/26 (61.5%)
Lymph node involvement	75 (74.3%)
Radioactive iodine (I-131) ablation therapy	63/75 (84.0%)
Recurrence of cancer	6 (5.9%)
5-Year survival rate	60/60 (100%)

CONCLUSION

• Comprehensive assessment of parameters including physical exam, clinical features, laboratory tests, and US findings are necessary to evaluate pediatric thyroid nodules.

• Patients with palpable thyroid nodule, nodule with microcalcifications, and lymph node alterations are highly associated with thyroid cancer, so further evaluation including FNAB should be considered.