



Application of the Bethesda Thyroid System in the Pediatric Population



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BACKGROUND

- Few studies have analyzed the Bethesda System for reporting pediatric thyroid nodules.
- The incidence of thyroid nodules in children is not as common as in adults. However, thyroid nodules in children are more likely to be malignant.
- The usefulness of molecular testing in the pediatric age group has been reported in few studies.
- This study aims to evaluate the usefulness of the Bethesda System and molecular testing in pediatric thyroid nodules.

METHODS

- All thyroid fine needle aspirations (FNAs) from patients 21 years of age or younger were collected from the pathology files at Yale University between the years of 2008-2012.
- Nearly all FNAs were performed under ultrasound guidance.
- The cytologic diagnoses were reviewed and retrospectively correlated with molecular testing results and histologic results in cases with surgical follow-up.
- Most cases were reviewed by at least two cytology board certified pathologists.
- All cases of FLUS, suspicious for PTC and positive for PTC were ordered for BRAF mutation test.
- BRAF mutations are tested by PCR-SSCP on FNA washing fluid.
- PCR primers target V600E mutation.

RESULTS

- 234 FNAs from 225 patients were identified, with 69 (31%) cases having histologic follow up and 17 (7.5%) cases having molecular analysis.
- The distribution of the ages of boys and girls is similar and the ratio of incidence of thyroid nodules in girls to boys was 4:1 (see **Table 1**).
- All malignant cases are papillary thyroid carcinoma (PTC).
- Not all cases of cytologically diagnosed malignancy had the surgery in our institute and eight of such patients were lost follow up.
- Two-third of surgical patients had thyroid neoplasm (10.2% were follicular adenoma and 56.5% were PTC) (see **Table 3**).
- The unsatisfactory rate in pediatric population (4.7%) is lower than the rate in adults (8-12%) (see **Table 2**).
- Of the 17 cases sent for mutational analysis, 10 (58.8%) cases were positive for the BRAF mutation.
- One case was diagnosed as FLUS cytologically and BRAF test showed the mutation. It was proved as PTC histologically without repeat FNA.
- All cases with BRAF mutation were diagnosed as PTC histologically.
- Boys (26.2%) have a higher incidence of malignancy than girls (12.5%) (see **Table 4**).
- The sensitivity and specificity of thyroid FNA in pediatric population is 100% and 94.7%, respectively.

Table 1. Distribution of Gender in Pediatric Thyroid nodule FNA

	Age	FNA No	Repeat
Boys	17±3.2	42	2
Girls	17±3.1	183	7

Table 3. Cytological Diagnosis Correlated with Histological Diagnosis in 69 Surgical Cases

	Neg	Flus	FN	Suspicious	Malign
Neg	18	3	1	1	0
FN	3	0	4	0	0
Malign	0	4	1	7	27
%	0	57.1	16.7	87.5	100

Table 2. Cytological Diagnosis of Thyroid FNA Based on Bethesda System

Unsat	Neg	Flus	FN	Suspicious	Malign
11	156	10	10	12	35
4.7	66.7	4.3	4.3	5.1	15.0

Table 4. Cytological Diagnosis of Thyroid FNA in Gender Distribution

	Unsat	Neg	Flus	FN	Suspicious	Malign
Boys	2	26	3	0	2	11
%	4.8	61.9	7.1	0	4.8	26.2
Girls	9	130	7	10	10	24
%	4.7	67.7	3.6	5.2	5.2	12.5

DISCUSSION

- Bethesda System is very sensitive and specific in diagnosing pediatric thyroid nodules.
- PTC is the most common malignancy in pediatric thyroid nodules.
- Thyroid FNA in children is more likely to harvest enough specimen for making a definitive diagnosis than in adults.
- Thyroid nodules in children are more likely to be malignant than those in adults.
- Thyroid nodules in boys have higher incidence of malignancy than those in girls.
- Follicular adenoma is more likely to occur in girls than boys.
- All cases with BRAF mutations have PTC.
- BRAF test is a sensitive and predicative tool for managing pediatric thyroid nodules.
- BRAF mutation in FLUS cases can avoid repeat FNA.

CONCLUSIONS

- This studies have the largest population in pediatric thyroid cytopathology.
- Bethesda System is as sensitive and specific in diagnosing pediatric thyroid nodules as in adults.
- BRAF mutation has the diagnostic and predictive value in managing pediatric thyroid nodules.
- More data is required to understand the BRAF pathogenesis in thyroid nodules of pediatric population.