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Fine Needle Aspiration Cytology of Thyroid: Role as a first line investigation in children and young adults - A 5-year experience at a Medical College Teaching Hospital

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Abstract

Introduction: Thyroid nodules are an unpredictable group of lesions, incidence of which increases with age. Due to an increased incidence of malignancy in children as compared to adults, an aggressive approach to diagnose and manage these lesions is warranted.

Aims & Objectives: The objective of present study was to evaluate the frequency of the various thyroid lesions by FNAC in children and young adults and correlate these findings with the histopathological features and thyroid hormone status.

Results: The 5-year study included 280 cases, of which most were in the age group of 16-24 years (81.7%) with a female preponderance (93.9%). The benign lesions were more common with nodular colloid goitre being the most common lesion. Among the neoplastic lesions, follicular neoplasms were most common. Hormonal status was available for 250 cases, with most being euthyroid. Cyto-histopathological correlation was available in 15 cases, with 11 displaying positive correlation. The sensitivity of FNAC was 62.5%, specificity was 85.7%, diagnostic accuracy was 73.3% and positive predictive value was 83.3%.

Conclusion: Currently, many investigations including diagnostic imaging studies, serological tests as well as histopathological techniques are available to evaluate thyroid lesions. However, FNAC is a reliable diagnostic procedure in children and young adults for evaluating and managing thyroid lesions.

Keywords: Nodular colloid goitre, Follicular neoplasms, Paediatric, Cyto-histopathological correlation

Introduction

Thyroid nodules in childhood and adolescence are rare, with an estimated prevalence ranging from 0.05% to 1.8% and are more often malignant (up to 25% of cases) compared with those observed in adulthood, therefore requiring a careful evaluation and a more aggressive diagnostic approach. Due to the challenge of collecting large cohorts of patients in this age group, the clinical and etiological characterization of thyroid nodular disease has not been extensively explored in childhood.[1] Several risk factors are associated with the development of thyroid nodules in children, including iodine deficiency, prior radiation exposure, a history of antecedent thyroid disease, and several genetic syndromes.[2]

As written in the book of Abu Al-Qasim, thyroid sampling by using needles is one of the oldest techniques in the medical history since 936-1013 AD.[3] Martin and Ellis first reported using fine-needle aspiration (FNA) to study the thyroid in 1930, but it was commonly used first in Sweden during the 1950s and 1960s. They established its utility in the diagnosis of thyroid problems and its correlations with clinical manifestations.[4] FNA has been shown to be the safest and most accurate of diagnostic tools in thyroid lesions with a sensitivity as high as 93.4%, a positive predictive value of malignancy of 98.6%, and a specificity of 74.9%; its use has simultaneously diminished the number of surgeries done for benign lesions and increased the proportion of malignancies in surgically resected thyroids.[5] However, there are limitations due to the reported pitfalls related to specimen adequacy, sampling techniques, the skill of the physician performing the aspiration, the experience of the pathologist in interpreting the aspirate and overlapping cytological features between benign and malignant follicular neoplasm.[6]

The aim of this study was to evaluate the frequency of thyroid lesions in children and young adults and to correlate the cytological findings with histopathology and hormonal status of the patient.

Methodology

A retrospective study was done in the Department of Pathology of a teaching hospital from May 2010 to April 2015 after taking permission from the institutional ethical committee. The child labour (Prohibition & Regulation) act, 1986 of India defined "children" as the individuals below the age of 14 years. World health organization defined "youth" as individuals between 15 years and 24 years of age.[7] Thus, patients in the age group of 01 to 24 years presenting with palpable thyroid nodules were examined at the time of presentation for fine needle aspiration cytology (FNAC) to the Department of Pathology. The clinical details were collected from the guardian (in case of a minor) or from the patient (in case of a major).

After consent of the patient (or the guardian/parent, in children less than 18 years of age, whichever

applicable), using aseptic precautions FNAC was performed by aspiration and non-aspiration technique by 23-gauge needle with 10 ml syringe. If the swelling was cystic, the cyst fluid was collected in the syringe for the preparation of smears after centrifugation. The smears were either air-dried or alcohol fixed (95%). Air-dried smears were stained by May Graunwald Giemsa stain while alcohol fixed smears were stained by Haematoxylin & Eosin (H&E). The results of serological estimation of T3, T4, and TSH using enzyme linked fluorescent assay (ELFA) by VIDAS Biomeriuex, which was already done on clinician's directions, were collected from the patient record at the time of FNAC. Histopathological correlation of the cytological findings was done, wherever possible.

Plan of data analysis: Those cases which were found to be malignant by cytology as well as by histopathology were labelled as true positive (TP). False positive (FP) were those diagnosed as malignant on cytology and turned to be benign on histopathology. True negative (TN) were benign on both cytology and histopathology. False negative (FN) were negative on cytology but positive for malignancy on histopathology. Sensitivity was defined on the basis of thyroid cancer detection using FNAC and specificity was defined on the basis of detection of benign thyroid disease. Diagnostic accuracy represents the combination of sensitivity and specificity.

Sensitivity = True Positives / True Positives + False Negatives x 100

Specificity = True Negatives / True Negatives + False Positives x 100

Accuracy = True Positives + True Negatives / Total No of Patients x 100

Descriptive statistics were assessed using SPSS 20.

Results

The 5-year study was conducted following permission from the Institutional ethical committee and included a total of 280 cases of children and young adults presenting with palpable thyroid nodules. Most of the patients in our study were females (263/280; 93.9%). The age ranged from 8 to 24 years, with a mean age of 18.9 years. Most of the patients were in the age group of 16-24 years (81.7%). Most of the smears were satisfactory in our study for evaluation (98.9%) (Table 1).

Cytological assessment revealed non-neoplastic lesions to be more common (265/280; 94.6%) in our study, of which most common was nodular colloid goitre (112/265; 41.5%), followed by hashimoto's thyroiditis (97/265; 36.6%) (Fig. 1). While correlating age with the cytological diagnosis of non-neoplastic lesions, goitre was more common in the age group of 16-20 years, whereas, hashimoto's thyroiditis was more common in the age group of 21-24 years (43/97; 44.3%). There were 12 neoplastic lesions in our study. Of these, most common were follicular neoplasm (08/12; 66.7%) followed by papillary carcinoma (Fig. 2) (02/12; 16.6%). We also observed single case each of medullary carcinoma and hurthle cell neoplasm (Fig. 3). While correlating age with cytological diagnosis among the neoplastic lesions, most of the cases (08/12; 66.7%) were in the age group of 21-24 years followed by 03 cases in the age group of16-20 years and 01 case in the age group of 11-15 years. (Table 1)

Table 1: Age distribution of various thyroid lesions

Cytological diagnosis	Age group (in years)				Total
	5-10	11-15	16-20	21-24	
Non-neoplastic (n=265) (94.6%)					
Nodular colloid goitre (42.3%) (NCG)	10	19	47	34	112
Hashimoto's thyroiditis (36.6%) (HT)	05	10	39	43	097
Lymphocytic thyroiditis (9.4%) (LT)	01	02	16	06	025
Colloid cyst (4.9%) (CC)	00	00	04	09	013
MNG with Adenomatous hyperplasia (5.3%)	00	01	04	09	014
Primary hyperplasia (1.5%) (PH)	00	00	02	02	004
Neoplastic (n=12) (4.3%)					
Follicular neoplasm (66.7%) (FN)	00	00	03	05	008
Hurthle cell neoplasm	00	01	00	00	001
Papillary carcinoma (16.6%) (PC)	00	00	00	02	002
Medullary carcinoma (8.4%) (MC)	00	00	00	01	001
Unsatisfactory (1.1%)	00	01	00	02	003
Total	16	35	115	114	280

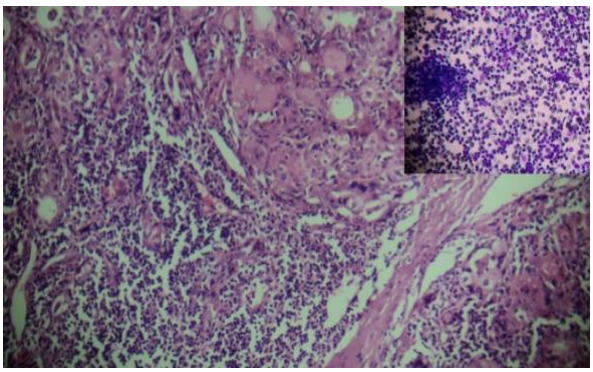

Fig. 1: Microphotograph of tissue section showing destruction of thyroid follicles by lymphocytic infiltration and hurthle cell change in hashimoto's

thyroiditis (H&E, x10); Inset: FNAC smear showing polymorphic lymphoid population (MGG, x10)

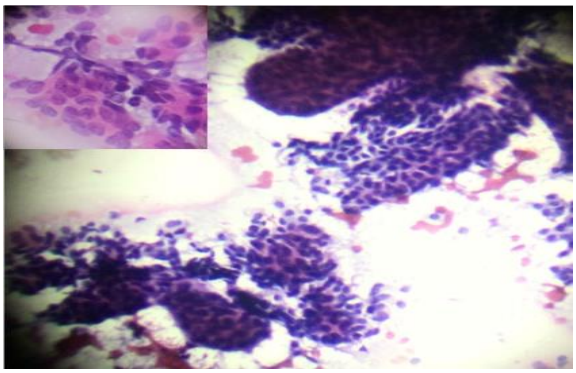

Fig. 2: Microphotograph of FNAC smear showing Papillary structures (MGG, x10); Inset: Nuclei displaying chromatin clearing, intranuclear inclusions and nuclear grooves (H&E, x40)

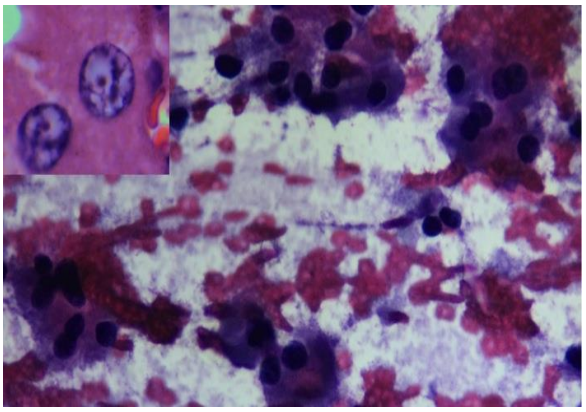

Fig. 3: Microphotograph of FNAC smears showing groups and microfollicular pattern of hurthle cells in Hurthle cell neoplasm (MGG, x10); Inset: Hurthle cells showing abundant eosinophilic granular cytoplasm and vesicular nucleus with prominent nucleolus (MGG, x40)

Cyto-histopathological correlation was available in 15 cases. Of the 15 cases, 08 were neoplastic and 07 were non-neoplastic. Among the neoplastic cases, most common were follicular lesions (03 cases of follicular adenoma, 01 case each of follicular adenoma with hashimoto's thyroiditis and follicular carcinoma). In our study, we also had 02 cases of papillary carcinoma and 01 case of medullary carcinoma (Fig. 4). Among the non-neoplastic cases, most common was multinodular goitre (5/7; 71.4%), followed by single case each of hashimoto's thyroiditis and multinodular goitre with adenomatoid nodule.

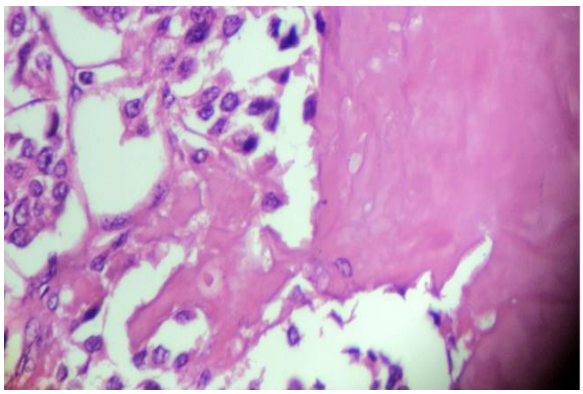

Fig. 4: Microphotograph of tissue section showing tumour cells and amorphous pink amyloid in medullary carcinoma (H&E, x40)

Positive histopathological correlation was available in 11 cases. Among the rest of the cases, one case of follicular adenoma with hashimoto's thyroiditis (Fig. 5) was diagnosed as hashimoto's thyroiditis only, one case of follicular carcinoma was diagnosed as multinodular goitre with adenomatous hyperplasia, one case of papillary carcinoma with multinodular goitre (Fig. 6) was diagnosed as multinodular goitre only and one case of dyshormonegenetic goitre was diagnosed as follicular neoplasm on cytology (Table 2).

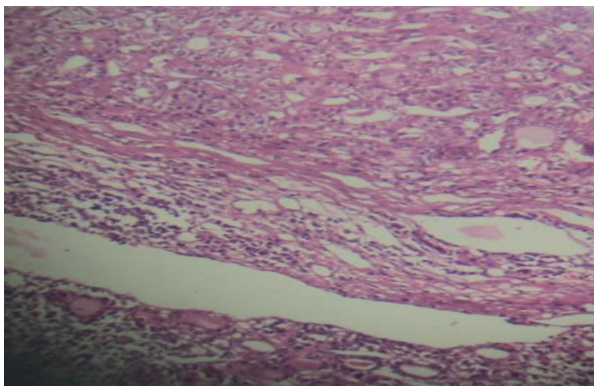

Fig. 5: Microphotograph of tissue section showing Follicular adenoma associated with Hashimoto's Thyroiditis (H&E, x10)

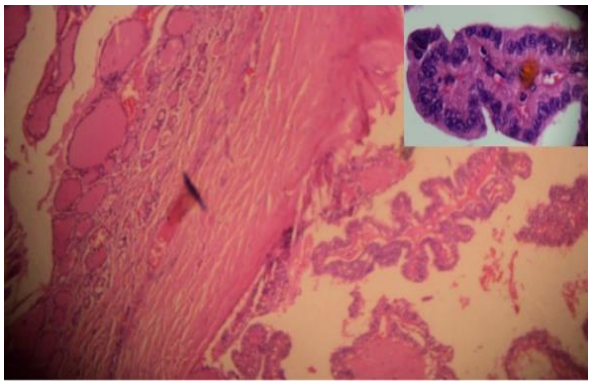

Fig. 6: Microphotograph showing section with focus of papillary carcinoma in nodular colloid goitre

(H&E, x10); Inset: Single papilla with fibrovascular core lined by tumour cells displaying nuclear chromatin clearing (H&E, x40)

Hormonal status was available in 250 cases in our study, of which 246 were non-neoplastic and 04 were neoplastic lesions. Of the 250 cases, most cases were euthyroid (149/250; 59.6%) in our study. Among the non-neoplastic lesions, most cases of nodular goitre were euthyroid (94/108; 87.3%), whereas, most cases of hashimoto's thyroiditis were hypothyroid (61/86; 70.9%). Furthermore, most of the cases (62.5%) of lymphocytic thyroiditis and adenomatoid hyperplasia (85.7%) were euthyroid. Among the neoplastic lesions, all four cases of follicular neoplasm were euthyroid. (Fig. 7)

Table 2: Cytohistological correlation (n=15)

FNAC	Histology		Total
	Neoplastic	Non-neoplastic	
Neoplastic	05	01	06
Non-neoplastic	03	06	09
Total	08	07	15

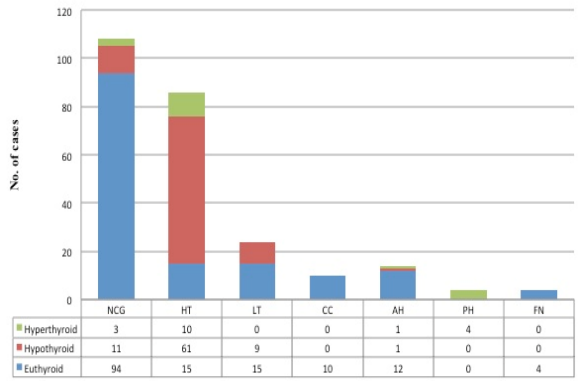

Fig. 7: Correlation of cytological diagnosis with hormonal statue

In our study the sensitivity, specificity and diagnostic accuracy of FNAC was 62.5%, 85.7% and 73.3% respectively. The positive predictive value (PPV) was 83.3% and negative predictive value (NPV) was 66.7%.

Discussion

Thyroid lesions are rare in paediatric age group, increasing in incidence linearly with age with an average of 0.08% per year.[3] Although multiple studies have been done regarding thyroid lesions in adults, their number is limited in the paediatric and young adult population. Among the few studies done to address thyroid lesions in this age group, there is no uniformity in terms of the upper age limit of the patients included in the study, with most studies maintaining 21 years as the upper age limit. In our study, however, we considered patients from 01 to 24 years of age (as per definition of children and young adults). In a span of 5-years, we received 280 cases with palpable thyroid nodules in the respective age group with a mean age of 18.9 years. Studies which have considered cases till 21 years of age, have found similar findings with most of them observing a mean age of 17 years.[8,9,10]

In the present study, most (81.7%) of the cases were in the age group of 16-24 years with a female preponderance (93.9%). The gender disparity is perhaps explained by the hormonal influences of both oestrogen and progesterone, as increasing nodule size and new nodule is related to pregnancy and multiparity.[11] In our study, we had a high satisfactory rate (98.9%) of the smears. This could be attributed to the fact that all the aspirates were collected by a cytopathologist.

Since Ellis introduced FNAC in 1930, it has been widely used for evaluation of thyroid nodules in adults. But it is under-utilised in young and paediatric patients probably due to the possibility of complications and need for sedation. There is also concern regarding maintenance of correct posture during the procedure by the child.[8]

Thyroid nodular disease can include different entities: a solitary nodule, multinodular goitre (MNG), goitre observed in autoimmune diseases like Hashimoto's thyroiditis and Grave's disease, and non-palpable thyroid nodule. In our study of palpable thyroid nodules, most of the lesions were benign (94.6%) with nodular colloid goitre being the most common diagnosis. This is similar to studies done by other authors.[8,12] We had 97 cases of Hashimoto's thyroiditis and it was more common in the age group of 21-24 years (44.3%).

In adolescents and young adults, thyroid carcinoma represents approximately 7.5% of all malignancies in the 15-19 years of age group and 10.6% of all cancers in 20-24 years of age group. in children younger than 15 years of age, it is a much rarer malignancy.[13] In our study, there were 12 aspirates of neoplastic morphology, of which follicular neoplasm were more common (66.7%) than others. The incidence of neoplastic lesions increased with age, as most of theses cases were in the age group of 21-24 years (66.7%).

While evaluating thyroid lesions, hormonal status is an important step towards clinical management of the patients especially in managing the more commonly encountered benign lesions. In our study, hormonal status was available for 250 cases, with benign lesions dominating over the malignant. Among the cases with nodular colloid goitre, most were euthyroid as compared to cases with Hashimoto's thyroiditis wherein most were hypothyroid. In 1912, Hashimoto described four women with goiter and the apparent transformation of thyroid into lymphoid tissue (struma lymphomatosa). These patients usually present with diffuse and non-tender enlargement of thyroid gland.

As the disease progresses, subclinical and then clinical hypothyroidism appears, symptoms of which may be subtle, even with marked biochemical derangement. Growth and pubertal development may also be deranged. The childhood prevalence peaks in early to mid puberty.[14] However, most of our cases were >20 years of age, which could explain the increased incidence of hypothyroidism due to advanced stage of disease. In Hashimoto's thyroiditis, presence of goitre or high TSH levels should prompt the measurement of anti-TPO antibodies.[14] In our study, due to the limited resources we weren't able to screen for the antibodies.

In the present study, cyto-histopathological correlation was done. We observed sensitivity of 62.5%, specificity of 85.7%, diagnostic accuracy of 73.3% and a PPV of 83.3%. The diagnostic pitfalls which we encountered in our study were due to the presence of dual lesions and overlapping features seen in adenomatous nodule and follicular neoplasms. One case of follicular adenoma with Hashimoto's thyroiditis was diagnosed as only Hashimoto's thyroiditis on cytology. This could have been due to limited number of needle passes, inadequate sampling of multiple nodules and abundance of background inflammation. However, epithelial preponderance over inflammation, nuclear crowding, severe atypia and cell dyscohesion should raise the possibility of a neoplasm in spite of other features of Hashimoto's thyroiditis.[15]

One case of follicular carcinoma was diagnosed as multinodular goitre with adenomatous hyperplasia and another case of dyshormonegenetic goitre was diagnosed as follicular neoplasm on cytology. Even though, the definition of follicular lesions on FNAC is not clear enough, cellular aspirates with scanty amount of colloid composed of microfollicles in >50-70% cases are evaluated as follicular neoplasm. In our case, presence of good amount of colloid with microfollicular pattern was seen. Such cases are considered as either benign nodules or follicular lesions of unknown significance according to Bethesda system. Thus, for these lesions cytopathology turns out to be a screening test rather than a diagnostic tool. Dyshormonegenetic goitre and intrathyroid parathyroid adenoma are characterized by the presence of microfollicular pattern and lack of colloid. Thus, they can be falsely diagnosed as follicular neoplasm on cytology. However, microfollicular pattern without intrafollicular colloid is typical of dyshormonegenetic goitre along with the presence of anisokaryosis and large bizarre cells.[16] One case of papillary carcinoma with MNG was diagnosed as only MNG on cytology. Stromal degenerative fragments can mimic bubble gum type of colloid and large amounts of loose colloid may also be seen in papillary carcinoma, causing confusion in the diagnosis.[16]

In the past decade, there have been major advances in diagnostic modalities of thyroid lesion leading to establishment of various diagnostic and management algorithms. However, FNAC is important as an initial diagnostic and screening modality for assessing the benign or malignant nature of thyroid nodules. Nonetheless, there are diagnostic pitfalls encountered, which may be related to sampling technique, skill of cytopathologist and overlapping cytological features of different lesions.

Conclusion

Management of paediatric and young adults with thyroid nodules can be challenging. Due to a higher percentage of these patients harbouring malignancy requiring surgical intervention, accurate pre-operative diagnosis is of utmost importance. Pre-operative FNAC allows for better operative planning and minimizes the need for second surgery particularly in children who present with single thyroid nodule only.

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