Original Article

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Thyroid Nodules in Childhood: a Single Institute Experience

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Abstract

Objective: Thyroid nodules are rare in children. Multiple diagnostic modalities are used to evaluate the thyroid mass. The aim of this study was to determine results of management of thyroid nodules in children with special attention to the role of fine needle aspiration biopsy (FNAB) in diagnosis.

Methods: Thirty-two children who underwent surgery for thyroid nodules in Mofid Children's Hospital within 10 years (1996to 2005) were retrospectively studied. From clinical records we obtained data about demographic characteristics, clinical manifestations, ultrasonography (USG) findings, and FNAB results, pathological reports, surgical therapy and complications. Data was analyzed statistically for association with thyroid cancer.

Findings: Twenty-five patients (78.1%) were girls, and 7 (21.9%) boys. Mean age was 10.9 (range 8 to 14) years. 24 (75%) patients had benign and 8 (25%) malignant tumors. 18 (56.25%) nodules were located in the right lobe. Statistical analysis revealed sensitivity, specificity, accuracy, and positive and negative predictive values as follows: 80%, 65%, 63%, 25%, and 86% for USG; 35%, 41%, 40%, 18%, and 66% for RNS; 91%, 94%, 90%, 74%, and 96% for FNAB respectively.

Conclusion: Clinical judgment as determined by serial physical findings with USG continues to be the most important factor in the management of thyroid nodules in children. FNAB is the most accurate method of investigation and its accuracy is improved by USG guidance.

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Introduction

Thyroid nodules are rare in children affecting 1% to 2% of the pediatric population[1,2]. These nodules are less common in children than in adults, but are more often malignant; they are in children 26% malignant while in adults the rate

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of malignancy is 5-10%[3-4]. Management of these lesions tends to be more aggressive owing to a perceived increased risk of malignancy in the pediatric population, particularly for younger patients with thyroid nodules [5].

Five categories of thyroid nodules classify this broad spectrum of pathology - hyperplasic, colloid, cystic (containing fluid), inflammatory, and neoplastic, with the last being the most feared [6]. As the thyroid nodules are uncommon in prepubertal children (1.5% or less), any nodule discovered in this age group is suspicious and the diagnostic approach should be evaluated more aggressively [7].

Recently single photon emission CT and CT (SPECT-CT) can determine and locate the spread of metastases in regional lymph nodes, and plays a major role in treating the disease [8].

Ultrasonography (USG) can be successfully used for screening and early detection of thyroid nodules in children, mostly those with a maximum diameter of 15 mm and smaller. And also can be useful in helping to determine which nodules can be aspirated rather than should be followed-up. (Nodules larger than 15 mm may require cyto-histologic evaluation). Fine needle aspiration biopsy (FNAB) is basic in the evaluation of solitary nodules, cysts and dominant nodules within multinodular goiters. If the procedure is performed properly, it should have very low false negative and positive results with the accuracy ranging between 69% and 93% [9].

Some consider this procedure of limited usefulness in children because of its discomfort and the rate of side effects. Those less than 10 years of age should preferably undergo exisional biopsy under general anesthesia instead of FNAB [9]. Recently thyroid scintiscaning has been less frequently used in the initial routine evaluation, because most benign and malignant nodules show reduced concentration of radioisotope [9]. Renewed interest in the recent literature has focused on diagnostic modalities especially ultrasound-guided FNAB (UG-FNAB), and FNA cytology for diagnosis [10-12].

The aim of this study was to determine the result of management of thyroid nodule in children with special attention to the role of FNAB in diagnosis.

Subjects and Methods

The study group consisted of 32 children who underwent surgery for thyroid nodules in Mofid Children's Hospital within 10 years (1996 to 2005). From clinical records we obtained data about demographic characteristics, clinical manifestations, thyroid function tests, diagnostic imaging results [USG and Radionuclide Scan (RNS)] findings, and FNAB cytology results, pathological reports, surgical therapy and complications. Data was analyzed statistically for association with thyroid cancer.

Thyroid function tests and diagnostic imaging were performed in all patients. All aspirates were performed by expert surgeon; two to five separate aspirates were carried out for each patient.

FNAB Technique: Under aseptic technique, the nodule is localized between USG probe, and a gauge 25 needle passed into the solid part of the nodule. It is aspirated only if fluid is obtained. Then the needle contents is emptied into a liquid preservative (such as Cytolyt), alternately the sample can be smeared directly on to glass slides. When lymphoma is suspected, a sample is sent in cell culture medium for flow cytometry; this may be very helpful in obtaining the diagnosis.

Once the fluid component is removed, the nodule is reassessed by palpation or with USG and aspiration is repeated if there is any residual mass. Care is taken not to contaminate the sample with the USG gel when using USG guidance.

There are several risk factors for malignant thyroid nodules, but in this study we considered age, duration of symptoms, and physical characteristics. Indications for surgery in our group of patients consisted of clinical characteristics of nodules, increase in size, and diagnostic modalities findings.

FAN-cytology results were categorized as benign, malignant, suspicious, or insufficient. Risk factors differentiating children with benign and malignant pathology were assessed for each group.

At the end of study, we calculated the sensitivity, specificity, accuracy, and positive

Table1: Characteristics and risk factors in 32 patients with thyroid nodule

Risk factors	Malignant (n=8)	Benign (n=24)
Mean age (years)	12.5	10.5
Symptoms duration (weeks)	208	50
Physical characteristics	Tender Multiglandular Fixed	Non-tender Soft Movable

predictive values (PPV) and negative predictive values (NPV) of USG, RNS, and FNAB results in the diagnosis of thyroid nodules of children. We derived these figures using the final histopathological diagnosis as the golden standard.

Findings

Totally 32 children with thyroid nodule underwent surgical treatment in Mofid Children's Hospital. Twenty-five (78.1%) patients were girls and seven (21.9%) boys. Female to male ratio was 3.5 to 1. Mean age was 10.9 (range 8-14) years. None had history of receiving ionizing irradiation to neck, or goitrogen ingestion. Nine (28.1%) patients had family history of goiter and Grave's disease.

Twenty-four (75%) patients had benign, and 8 (25%) malignant tumor, all the patients were euthyroid. Thyroid nodules were located in: right lobe 18, left lobe 5, bilateral 7, and central 2.

Benign tumors had mostly soft, nontender, movable, and nonfixed solitary nodules. 23% had multinodular goiter, 19% palpable lymphadenopathy, and 11% a nodule fixed to adjacent tissue. The clinical characteristics and risk factors of benign tumors compared to malignant nodules are shown in Table 1. USG revealed 21 (65.6%) solid, 8 (25%) cystic and 3 (9.4%) complex masses. Six Malignant nodules had solid characteristics, and 2 had predominantly cystic findings on USG evaluation.

RNA studies revealed 27 (84.4%) cold, 4 (12.5%) hot and one (3.1%) warm nodules. In warm and hot nodules there was no change after prolonged medical therapy. Results of FNAB examination were as follow: Twenty (62.5%) benign, 5 (15.6%) malignant, 4 (12.5%) suspicious and 3 (9.4%) insufficient type nodules (Table 2 and 3).

Table 2: Comparison of FNA cytology with histological diagnosis in 32 children with thyroid nodules

Cytology	Patients (No)	Finding		Histology	
		Type	No	Type	No
Benign	**20**	Follicular cells	14	Follicular adenoma	14
		Epithelial cells	2	Follicular adenoma	2
		Hurtle cells	2	Hurtle cell adenoma	2
		Lymphocytic cells	1	Papillary cancer	1
		Adenomatoid nodule	1	Papillary cancer	1
Malignant	**5**	Papillary cancer	5	Papillary cancer Mixed cancer	4 1
Suspicious	**4**	Papillary cells	4	Colloid goiter Papillary cancer	3 1
Insufficient	**3**	-		Follicular adenoma Lymphocytic thyroidtis	2 1

Table 3: Characteristic pathological findings in 32 children with thyroid nodules

Characteristic	Type	N0
Benign 24 (75%)	Follicular adenoma	18
	Colloid nodular goiter	3
	Lymphocytic thyroiditis	1
	Hurtle cell adenoma	2
Malignant 8 (25%)	Papillary carcinoma	7
	Mixed cancer	1

Benign nodules were managed with lobectomy and isthmectomy in 20 patients and Subtotal thyroidectomy in 4 cases with multinodular goiter, and malignant nodules Underwent total thyroidectomy. Complications were more commonly in total thyroidectomy patients (transient hypocalcaemia 2, wound keloid formation one). There was no mortality in our study, and patients were in follow-up for a period of 3 years. FNAB has the highest sensitivity and specificity in the diagnosis of thyroid nodules as well as the highest PPV and NPV. Table 4 shows sensitivity, specificity, accuracy, and PPV and NPV of USG, RNS and FNAB.

Table 4: Statistical analysis of the results of USG, RNS, and FNAB results in the diagnosis of thyroid nodules of children

Parameter	USG	RNS	FNAB
Sensitivity	80%	35%	91%
Specificity	65%	41%	94%
Accuracy	63%	40%	90%
PPV	25%	18%	74%
NPV	86%	66%	96%

USG: Ultrasonography/ RNS: Radionuclide Scan/ FNAB: Fine needle aspiration biopsy/ PPV: Positive Predictive Value/ NPV: Negative predictive value

Discussion

Although thyroid nodules in children are uncommon, the risk of malignancy within these lesions has been estimated to be 4-fold higher than adults [4, 13]. Based on this information, it may not be reasonable to align the treatment regimens of thyroid malignancies in children and youth with adult protocols. Recently the incidence of thyroid malignancy has leveled near 20% to 30%, and this reduction has been attributed by others to the effect of eliminating unnecessary radiation to the head and neck area during early childhood [14].

Other factors associated with malignancy are goitrogen ingestion, endemic region, and history of familial thyroid disease [15, 16]. None of above factors was found in our study group. Usually girls outnumbered boys, in our study there were 78% females and 21% males same as Nidziela et al [7] series and Drozd et al [14] study.

The most common presenting feature is the presence of a mass within the thyroid gland, and other symptoms are cervical lymphadenopathy, growth of mass, voice change, pain, hyper-thyroidism and fatigue [15]. Our children with malignancy were characterized by multi-glandular appearance, localized tenderness, and a nodule fixed to adjacent tissue, characteristics that were significant when compared with the benign group. Localized tenderness is thought to represent an acute bleeding episode inside a solid tumor with necrosis and cyst formation [17].

We performed USG for all our patients, and achieved 80% sensitivity, 65% specificity, 63% accuracy, and 25% positive and 86% negative predictive values. Lugo-Vicente et al achieved 86% accuracy, 80% sensitivity and 88% specificity for USG [18]. Arda et al achieved 60% sensitivity, 59% specificity, 59% accuracy, and 15% PPV and 92% NPV for USG [19].

RNS decided the functionality of nodule, but its accuracy was far from ideal [18]. We achieved 40% accuracy, 35% sensitivity and 41% specificity and 18% PPV and 66% NPV of RNS. In study of Lugo-Vicente et al, RNS showed 26% accuracy, 80% sensitivity and 11% specificity [18]. Arda et al achieved 30% sensitivity, 42% specificity, 39% accuracy, and 12% PPV and 68% NPV of RS [19].

Some consider FNAB procedure of limited usefulness in children because of its discomfort and the rate of side-effects. Those less than 10 years of age should preferably undergo exisional biopsy under general anesthesia instead of FNAB, as we have done in some of our patients [9, 20,21]. In children younger than 10 years, identified thyroid lesions are more likely to be

malignant, and also more likely to have recurrent cancer [22,23].

FNAB did not reduce the number of patients who underwent thyroidectomy in our study, and its best use was to help decide whether a more aggressive gland removal is needed in those cases found suspicious or frankly malignant. We believe that benign FNA finding should be viewed with caution, and patients should have close clinical follow-up[9].

FNA is a diagnostic test that needs the interpretation of the clinician, and with clinical findings of malignancy the patient should undergo surgery[21, 23]. The diagnostic accuracy in recognizing malignant nodules is highest for FNAB [9,24]. The accuracy of diagnosing malignancy in thyroid nodules of our 32 children was 63% for thyroid ultrasound (hypoechogenecity), 40% for thyroid scans, and 90% for FNAB.

One result from Italy revealed accuracy rate of 67% for thyroid US, 53% for thyroid scans (cold nodule), and 90% for FNAB[25]. The probability (sensitivity) that a malignant thyroid nodule had suspicious or frankly malignant cytology was 91%, and the probability (specificity) that a benign thyroid nodule had negative cytologic findings on FNAB was 94% in our series, the low sensitivity places the test in question, and the high specificity is the result of a higher number of patients with cytological findings of follicular cell in the aspirate. No attempt should be made to differentiate follicular adenoma from follicular carcinoma because capsular and vascular invasion cannot be adequately assessed by FNA aspiration alone.

24 cases of follicular adenoma in our group of patients, as in most series, represent the most common benign pathological finding[26-30]. Table 5 compares previous series with ours. Patients with malignant thyroid nodules were generally asymptomatic and euthroid [31] same as in our study.

Conclusion

Clinical judgment as determined by serial physical findings with USG continues to be the most important factor in the management of the thyroid nodules in children. FNAB is the most accurate method of investigation, and its accuracy is improved by USG guidance.

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Conflict of Interest: None

Table 5: Comparison of the childhood fine-needle aspiration series

Series		Our study	Arda et al[19]	Al-Shaikh et al[32]	Khurana et al[33]	Lugo-Vicente et al[18]	Degnan et al[11]	Raab et al[12]
No		32	46	41	57	24	18	57
Sex	Male	7 (22%)	9 (19%)	35 (85%)	11 (19%)	4 (17%)	4 (22%)	8 (14%)
	Female	25 (78%)	37 (81%)	6 (15%)	46 (81%)	20 (83%)	14 (78%)	49 (86%)
Age		11	9	13	17	15	14	13
FNA results	Benign	20 (63%)	38 (82%)	30 (73%)	36 (63%)	11 (61%)	7 (41%)	51 (77%)
	Malign	5 (16%)	3 (7%)	2 (5%)	7 (12%)	2 (11%)	2 (12%)	4 (6%)
	Suspicious	4 (12%)	3 (7%)	6 (15%)	14 (25%)	2 (11%)	7 (41%)	8 (12%
	Insufficient	3 (9%)	2 (4%)	3 (7%)	0	3 (17%)	1 (6%)	3 (5%)
Overall malignancy		25%	7%	5%	25%	21%	33%	18%
Statistical analysis	Sensitivity	91%	100%	87%	93%	60%	73%	80%
	Specificity	94%	95%	100%	81%	90%	80%	86%
	Accuracy	90%	95%	87%	84%	80%	75%	85%
	PPV	74%	67%	29%	62%	75%	89%	36%
	NPV	96%	100%	100%	97%	81%	57%	98%

PPV: Positive predictive value/ NPV, Negative predictive value

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