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Original Research Article

Evaluation of solitary thyroid nodule by clinical presentation, fine needle aspiration cytology and thyroid scan

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ABSTRACT

Background: The solitary thyroid nodule, defined as a palpable discrete swelling within an otherwise apparently normal gland, is usually a benign lesion. However, patients and physicians alike are typically concerned about the possibility of thyroid cancer. This study describes a strategy for the treatment of clinically euthyroid patients who have a solitary thyroid nodule that prevents unnecessary testing while identifying the few patients who require therapy.
Methods: This is a prospective study of randomly selected patients with clinically palpable, solitary thyroid nodule diagnosed and treated at Al-Karama Teaching Hospital from September 2015 till December 2018. Initially 176 patients were diagnosed by clinical examination to have solitary thyroid nodule but after investigation and operative finding, 42 patients were found to have multinodular goiter and all excluded from the study.
Results: All the 134 patients included in the study (21 males and 113 females) have been evaluated by clinical examination; thyroid scan and fine needle aspiration, ultrasound and the results of the evaluation have been correlated with operative histologic diagnosis. The study was undertaken to obtain information on the usefulness of the above measures for predicting or ruling out malignancy in solitary thyroid nodule.
Conclusions: The incidence of malignancy seems to be higher among male, presented with hard nodule at palpation, those associated with hoarseness or palpable cervical lymph nodes. A cytological diagnosis of malignant tumor is reliable and provides sufficient basis of definitive surgery for thyroid cancer.

Keywords: Evaluation, Fine needle aspiration, Solitary thyroid nodule

INTRODUCTION

Thyroid nodules are common, with up to 8% of the adult population having palpable nodules. With the use of ultrasound, up to 10 times more nodules are likely to be detected. They are found in 4%–8% of adults by palpation and in 13%–67% when ultrasound detection is used. In autopsy studies, they have a prevalence of approximately 50%.[1, 2]

Solitary thyroid nodule is a common presentation of thyroid disease and is defined as a palpable discrete swelling within an otherwise normal gland and is usually benign. The prevalence of thyroid nodules which are solitary at palpation in general population is high, reported rate ranges from 0.8 to 6.4%, being lowest in males and highest in middle aged women.[1] The concern with thyroid nodules is the possibility of malignancy. Thyroid cancers are rare, accounting for only 1.0% of all cancers in most populations and 0.5% of all cancer

deaths.[3] Nonetheless, thyroid cancers occur in approximately 5% of all thyroid nodules independent of their size. The management of thyroid nodules has changed over the past two decades. As with all assessments, a thorough history and examination is required in patients who present with a thyroid nodule. Most nodules are asymptomatic and are often discovered serendipitously by the patient or their primary medical practitioner when being examined for another problem.[4] With the increasing use of diagnostic imaging, thyroid nodules are not infrequently detected as an incidental finding on ultrasounds and computed tomography (CT) scanning.

Exposure of the thyroid gland to ionizing radiation is known to contribute to a higher incidence of both benign and malignant thyroid nodules, with malignancy rates in a palpable nodule in a previously irradiated thyroid in the range of 20%-50%.[5]

Thyroid carcinomas are classified according to the cell type from which they develop. The majority are non-medullary thyroid cancers (NMTCs), which arise from the thyroid epithelial cells and comprise 95% of malignancies. Medullary thyroid cancers (MTCs) arise from the calcitonin-producing parafollicular cells of the thyroid and account for about 5% of all thyroid malignancies.[6]

The diagnosis of familial non-medullary thyroid cancer (FNMTC) is made when thyroid cancer occurs in two or more first-degree relatives.[7] Compared with sporadic NMTC, patients with FNMTC appear to present at an earlier age, have more benign thyroid nodules, have multifocal disease, and have a higher rate of locoregional recurrence.[7-9]

Since the clinical features alone are not conclusive, (hard, irregular mass, fixed to surrounding tissues with associated lymphadenopathy); various form of investigations have been used to solve this problem but still each have its own limitations.[10]

Thyroid scintigraphy has a limited role in the evaluation of a solitary thyroid nodule. It has been relied upon in the past to assist in risk stratification of nodules as being benign or malignant based on their ability to take up isotope. Depending on the pattern of uptake, nodules are classified as hyperfunctioning (hot), hypofunctioning (cold), or normal functioning (warm).[11-14]

Ultrasound is an inexpensive, readily available, and noninvasive investigation. The superiority of ultrasound examination of the thyroid over clinical examination has been described, with one study showing ultrasonography leading to a change in management of 44% of patients who had been referred for a solitary nodule on physical examination.[15-18]

Nodule size in not predictive of malignancy. It helps guiding the need for FNAB. The lower size limit of a nodule that should be biopsied is currently under debate, but nodules <10 mm with associated microcalcifications or a history of neck irradiation should undergo FNAB.[19-21]

FNAB is the most crucial step in the evaluation of a thyroid nodule and is the procedure of choice in the workup of thyroid nodules.[22,23] It is able to provide specific information about the cellular composition of a nodule that directs subsequent management decisions.

The use of FNAB has led to a reduction in the number of patients requiring surgery and increased the diagnostic yield of cancers at thyroidectomy.[24-26]

METHODS

The study comprised 134 patients (21 males and 113 females) who met the requirements of our study. From September 2015 till December 2018, (176) patients were diagnosed clinically to have solitary thyroid nodule, however, after scanning and operation, 42 (22%) patients found to have multinodular goiter and all of them excluded from the study.

Each patient was interviewed and examined in accordance with a standardized form. Thyroid scan had been done to all patients and the results of the scan were classified into cold, warm and hot nodules. The researcher performed the fine needle aspiration biopsies. The cytological examination performed and the results were then grouped as follows:

- Benign: Where the aspirate revealed normal thyroid epithelial cells with various amount of RBC or colloid.
- Malignant: Where the smears revealed high cellularity with variations in cellular shape, size and nuclear structures. In certain smears, the type of malignancy could also be found.
- Suspicious: Where the smears revealed high cellularity with sheets of follicular cells that of nuclear variability; malignancy was suspicious in these cases.
- Inadequate: Where the aspirate was insufficient for cytological diagnosis.

All 134 patients have been treated surgically and the results of final histological diagnosis were with the results of fine needle aspiration biopsy. All data were entered and analyzed using Statistical Package for Social Sciences(SPSS) version 22. a probability of less than 0.05 is considered significant for Chi-square test.

Equations of sensitivity, specificity and efficiency have been used for evaluation of the results of the fine needle aspiration.

RESULTS

The age and sex distributions are shown below. The highest incidence of the solitary thyroid nodule occurred in the age group 21-30 (39.1%). Females 113/134 (84.3%) were more frequently affected than males 21/134 (15.7%) (Table 1).

Table 1: Age and sex distribution of 134 patients with solitary thyroid nodule.

Age (years)	Male	Female	Total	%
10-20	1	20	21	16.4
21-30	8	44	52	39.1
31-40	5	31	36	28.1
41-50	4	15	19	12.9
51-60	2	3	5	3.9
61-70	1	0	1	0.7
Total	21	113	134	100

Table 2: Clinical profile of 134 patients presented with solitary thyroid nodule.

Variable	No. of patients	%
Clinical findings		
History of deep X-ray therapy	1	0.78
Family history of benign goiter	32	24.9
Family history of malignant goiter	0	0
Nodules present >6 months	98	76
nodules enlarged in the past 6 months	33	25.5
Nodules >3 cm in size	39	28
Nodules hard on palpation	11	8.3
Dysphagia	24	19.2
Hoarseness	5	3.9
Palpable cervical lymph nodes	5	2.8
Symptoms and signs of thyrotoxicosis	9	6.4
Thyroid scan		
Cold	116	88.2
Hot	13	8.5
Warm	5	3.1
Type by malignancy		
Benign	121	89.8
Malignant	13	10.15
Histopathological types		
Papillary carcinoma	9	7
Follicular carcinoma	3	2.3
Anaplastic carcinoma	1	0.7
Follicular adenoma	24	17
Colloid adenoma	95	71
Hashimoto's thyroiditis	2	1.5
Fine needle aspiration		
Malignant	3	2
Benign	88	66
Suspicious	17	13
Insufficient	26	19

The overall clinical presentation and finding of investigations are shown below. The highest reported presentation was nodule enlargement in last 6 months followed family history of benign Goiter and dysphagia.

Isotope scanning of the nodules showed 116 cold nodules, 13 hot nodules and 5 warm nodules. By the fine needle aspiration, 96 (71.8%) of the nodules were solid while 38 (28.2%) of the nodules were cystic. Colloid adenoma was the commonest histopathological finding of the nodules (71%). Examination of two nodules revealed Hashimoto's thyroiditis and both cases were female patients. Among the malignant nodules, papillary carcinoma was the commonest and we had one case with anaplastic carcinoma that was 51 years old. The incidence of malignancy found to be 10.15% (Table 2).

The incidence of malignancy found to be the highest in the young age group with the peak incidence in the age group 21-30 (38.4%), while the incidence of benign found to be the highest in the same age group (21-30 years) (38.4%). Malignant nodules were significantly ($p<0.05$) more common in males (21%) than females (8.2%) (Table 3).

Table 3: Age distribution in relation to the final histologic diagnosis.

	Total	Histologic finding	
		Benign (n=121)	**Malignant (n=13)**
Age (in years)		**N (%)**	**N (%)**
10-20	21	18 (16.5)	3 (23.0)
21-30	52	47 (38.2)	5 (38.4)
31-40	36	34 (28.6)	2 (15.3)
41-50	19	17 (12.1)	2 (15.3)
51-60	5	4 (3.4)	1 (7.6)
61-70	1	1 (0.8)	0
Sex			
Male	21	17 (79)	4 (21)
Female	113	104 (91.8)	9 (8.2)

All patients with positive family history of benign goiter had either nodule that proved histologically to be benign. Nodules that were hard on palpation, associated with hoarseness or with palpable cervical lymph node were more frequently malignant than benign and to a statistically significant level ($p<0.05$). 11.5% of the cold nodules were malignant while all hot and warm nodules found to be benign nodules.

Results of the fine needle aspiration biopsy related to the final histologic diagnosis. All 3 cytological diagnosed malignant nodules proved histologically to be malignant. Out of 88 nodules diagnosed cytological as benign nodules, one proved histologically to be malignant, thus we had one false negative cytological result. The sensitivity of fine needle aspiration cytological diagnosis was found to be 75%, specificity was 100% while efficiency was 98% (Table 4).

Table 4: Association between selected variables and definite diagnosis.

Variable	Total	Histologic findings		P value
		Malignant (n=13)	Benign (n=121)	
		N (%)	N (%)	
Clinical findings				
Family history of benign goiter	32	0	32 (21.8)	<0.05
Nodules present >6 months	98	8 (61.5)	90 (76.5)	NS
nodules enlarged in the past 6 months	33	5 (38.4)	28 (23.9)	NS
Nodules >3 cm in size	39	4 (30.7)	35 (26.0)	NS
Nodules hard on palpation	11	8 (46.0)	3 (2.6)	<0.05
Dysphagia	24	3 (23.0)	21 (20.0)	NS
Hoarseness	5	3 (23.0)	2 (1.7)	<0.05
Palpable cervical lymph nodes	54	5 (3.1)	0	<0.05
Symptoms and signs of thyrotoxicosis	9	0	9 (6.0)	NS
Thyroid scan				
Cold solitary nodules	116	13 (11.5)	103 (88.5)	
Hot solitary nodules	13	0(0)	13(100)	<0.05
Warm nodules	5	0(0)	5(100)	
Cytology diagnosis				
Malignant		3(100)	0(0)	
Benign		8(8)	87(92)	<0.05
Suspicious		1(10)	9(90)	
Insufficient		1(3)	25(97)	

NS: Not Significant.

DISCUSSION

The solitary thyroid nodule is a common form of thyroid disease, but the clinical diagnosis is not always confirmed by scanning with isotopes or with the operative findings. The clinically palpable nodule of a more generalized multinodular pathology and in our study there was 21% error between the clinical diagnosis and scanning confirmation. Series differ in reporting this error rate and a range of 25-48% have been reported.

The commonest age group affected by the solitary thyroid nodule in our study was the age group 21–30 with incidence of 39.1%. The incidence of the solitary nodule was decreasing with age in our study. Hathaway et al Found the thyroid nodules to be very uncommon in children and when present is more likely to be malignant.[27] Discrete nodules are also uncommon in the elderly due to the prevalence of multinodular goiter and again when present are likely to be malignant.[28]

Eighty six percent with solitary thyroid nodule were females while males constituted only 14% of our patients with female to male ratio about 6:1. Kneafsey et al found the female to male ratio of 5:4. Kumar et al reported a female to male ratio of 5.6:1 while Mengistu reported a female to male ratio of 7.12:0.14.[29-31]

Clinically, only one of our patients had a history of therapeutic head and neck irradiation. Family history of benign goiter obtained in 24.9% of our patients. Cervical lymph nodes were palpable in five of four patients. Clinically nine patients were having symptoms and signs of thyrotoxicosis and performing the thyroid scan a total of eleven patients found thyrotoxic and the thyrotoxicosis confirmed in all of them by thyroid function test.

Regarding the isotope scanning, 88.2% of nodules in our study were cold, 8.5% hot and 3.1% of the nodules were warm. In comparison with other studies, Kumar et al. reported 77.7% cold nodule, 12.4% hot and 8.5% warm nodules. Gonzales et al. and Hung reported the incidence of the cold nodule in their studies to constitute 62% and 77% respectively.[32,33]

In our study FNA revealed 96 (71.8%) of the nodules to be solid while 38 (28.8%) of the nodules were cystic. References reported that about 30% of solitary thyroid nodules contain fluid and are cystic or party cystic.

The results of the aspirate were malignant in 3 cases, two of which were solid nodules while the third one was cystic. In 26 cases, the aspirate was insufficient for cytological examination and the cystic swelling yielded more insufficient aspirates (22%) than the solid swellings where only 185 of their aspirates were insufficient for cytological diagnosis.

Histopathological examination of the nodules showed the colloid adenoma as the commonest pathology of the nodules 71%. Malignancy found in 13 nodules

constituting an incidence of 10.5%. In comparison with malignancy incidence in other studies:

- Wong et al. reported an incidence of 10.2%.[34]
- Adwork reported an incidence of 15%.[35]
- Sabel et al. reported an incidence of 37%.[36]
- Abu-Eshy et al. reported an incidence of 15.2%.[37]

The prevalence of thyroid cancer has been compared in the different age groups of patients. The highest incidence of malignancy 38.4% found in the age group 21-30. We had one patient with malignant nodule in the age group 51-60 while the only who was 67 years old who proved to have a benign nodule.

Thyroid nodules are more likely to be malignant in the young and elderly patients.[27] The high malignancy rate of thyroid cold nodules in the young patients has been related to a previous head and mediastinal exposure to therapeutic irradiation, but in the absence of such exposure we still can find high malignancy rate in the young age group the reason of which still is not that clear. It may be due to increase susceptibility of the young thyroid tissue to various environmental factors (e.g. Viral, hormonal and increased background radioactivity other than therapeutic irradiation).

Among the patients with a family history of benign goiter, the final diagnosis was benign in all of them and to a statistically to a significant level. Nodules that were hard on palpation, those that are associated with hoarseness or with palpable cervical lymph nodes were more frequently malignant than benign and again to a statistically significant level ($p<0.05$). The proportion of patients with a final diagnosis of malignancy was not significantly influenced by known duration of goiter, by growth of the nodule during the six months immediately before surgery, by presence of dysphagia or by the size of the nodule. All our patients with symptoms of thyrotoxicosis had benign nodules; however, this didn't achieve a statistically significant level.

Out of 116 cold nodules in our study, only 13 (11.5%) proved histopathological to be malignant. All the 11 hot and 4 warm nodules proved to be benign.

Different rate of malignancy has been reported in scintigraphically cold nodules ranging from 10-30%. Svend et al. found 22% of the cold nodules to be malignant and all the hot nodules in his study were benign.[28] George reported a malignancy rate of 16% in the cold nodules, 9% in the warm and 4% malignancy rate of 16% in the hot thyroid nodules. In a study a study done by Hung et al, the incidence of malignancy in the cold nodules was 25.5%.[33] While no malignancy was present in the warm or hot nodules. Thus if the cold scan used alone as an indication of operation on the solitary thyroid nodule then about 70-90% of the operations will be done for a benign lesion since the scan is a poor discriminator between the malignant and benign nodules.

The results of FNA have been related to the final histologic diagnosis. The three lesions cytologically diagnosed as malignant, proved histologically to be papillary carcinoma one of which had a dominant cystic component, thus no false positive results were there in our study.

One patient with cytology report of benign lesion had histologic report of papillary cancer; the false negative result was cause by a small papillary carcinoma found within a large colloid nodule. The cytological diagnosis of all other nodules as benign nodules proved histologically to be benign too (follicular adenoma, colloid goiter or thyroiditis) thus the reliability of benign cytological findings for predicting histologically benign diagnosis was good an experience shared with other studies and this fact is of great importance since Excisional biopsy might then be avoidable.

12.6% (17 of 134) of aspirates reported as questionable or suspicious in our study. 53% (9 of 17) of these suspicious aspirates proved to be malignant by final histological diagnosis 3 of which were follicular carcinoma, one was anaplastic, while the remaining four were papillary carcinoma, thus all the follicular carcinomas in our study failed to be diagnosed as malignant lesion cytologically. Twenty-six aspirates in our study were insufficient for cytological examination and the histopathology proved to be benign in all except one of them proved to be a papillary carcinoma. Richard stated that most inadequate specimens are obtained from benign lesions since the malignant lesions are usually hypercellular and are unlikely to yield inadequate specimens, however, still some exceptions from this generalization exist and thus whenever possible the inadequate biopsies should be repeated unless decision has been made on clinical grounds to proceed with surgery.

In our study the FNA had a sensitivity of 75% a specificity of 100% and an accuracy of 98%. In comparison with other studies: Hamming et al, reported specificity of 99% and accuracy of 89%; Lopez et al, reported sensitivity of 90%, specificity of 99.8% and an accuracy of 99%; while Altavilla reported sensitivity of 71.4%, specificity of 100% and accuracy of 95%.[38-40]

Consequently, our study confirms the high specificity and accuracy of FNA and this is in agreement with those of other reports establishing that FNA of the thyroid gland is safe, reliable and effective for differentiating between benign and malignant thyroid nodules.[38-40]

CONCLUSION

The incidence of malignancy seems to be higher among male, presented with hard at palpation, those associated with hoarseness or palpable cervical lymph nodes. A cytological diagnosis of malignant tumor is reliable and provides sufficient basis of definitive surgery for thyroid cancer.

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