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Original Research Article

Follicular neoplasm of the thyroid: can clinical, ultrasonographical and cytological factors be used to predict carcinoma and determine extent of surgery

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ABSTRACT

Background: The optimal management of cytologically indeterminate thyroid nodules in follicular neoplasm is controversial. We examined the prevalence of malignancy within cytologically indeterminate follicular thyroid lesions in an attempt to predict malignancy based on clinical, sonographic and cytologic features.
Methods: Retrospective study was done in between April 2017 to July 2019 of 46 patients having a diagnosis of follicular neoplasm on fine needle aspiration cytology.
Results: A total of 46 patients (8 men, 38 women; mean age 47 year) with indeterminate cytology underwent thyroidectomy and had histopathological diagnoses. The prevalence of malignancy in patients was 34.7%. The size of nodules and ultrasonographic feature were significant predictor of malignancy with p value <0.05.
Conclusions: Author can predict malignancy in follicular neoplasm of thyroid with indeterminate nodule by using clinical and sonographic feature for the best compromise between the risk of missing carcinomas and the need for reducing unnecessary surgical procedures and cost benefit of the patients.

Keywords: Follicular neoplasm, Indeterminate lesions, Sonography, Fine needle aspiration cytology

INTRODUCTION

It has been estimated that palpable thyroid nodules are present in 4-7% of the population, but when examined by ultrasound (US), Incidental thyroid nodules are an increasingly common finding because of the expanding use of imaging studies US is safe non-invasiveness, nonradioactive, and effectiveness.[1-3] Presently high resolution real time US not only detect the presence, site, number and size of thyroid nodule but also clearly shows the characteristic of thyroid nodule. However, the US differentiation between benign and malignant nodule is not well describe. As many as 50-70% of subjects with no history of thyroid disease have been found to have incidentally discovered thyroid nodules by US.

In addition, nodular thyroid disease is more common in the elderly, population subgroup, which is steadily increasing.[8] Fine-needle aspiration biopsy (FNAB) examination and cytology are sensitive and accurate for most nodular thyroid lesions, however, a subgroup of patients have indeterminate cytology which is present in 11%-32% of cases. The routine application of this method has reduced the number of thyroid operations for benign disease and increased the percentage of thyroid cancers in surgical series. These indeterminate lesions

represent a source of much patient anxiety and can be diagnostic dilemmas. Because the incidence of malignancy within indeterminate lesions ranges varies greatly, there are no clear guidelines for the management of these lesions. Reports place the malignancy rate within indeterminate lesions between 3% and 51%.[9-11] To avoid misdiagnosing thyroid carcinoma, surgery is recommended for these patients. The risk of malignancy in indeterminate nodules is 12% to 30%.[12-18] This means that up to 70% of these patients are undergoing surgery for a benign disease. This potentially places a large economic burden on the health care system. Besides the increased costs, these patients face the risk of complications. Of note, frozen section is essentially worthless for most of these patients.

Author aim was to evaluate clinical and ultrasonographic features to predict malignant neoplasms in patients identified as having follicular neoplasm by fine needle aspiration cytology (FNAC). Patients with cytological indeterrminate lesion or follicular neoplasm with more than 18 years were included in this study.

METHODS

This was a retrospective study done in between April 2017 to July 2019 in the department of general surgery with the collaboration of department of Otorhinolaryngology in Pacific Institute of Medical Sciences, total 46 patients were included in this study.

Exclusion criteria

- Patient age less than 18 were excluded.
- Patient FNAC report other than follicular neoplasm was excluded.

The clinical and ultrasonographic features of the patients with thyroid nodules. All patients underwent FNAB, which was performed on a solitary nodule or a dominant nodule in a multinodular goiter and were diagnosed as having follicular neoplasm on FNAC findings.

All patients were queried for symptoms and had a physical examination. According to protocol, author documented the clinical finding and ultrasonographic features of these patients. All patients underwent surgery. Ultrasonography of the thyroid was performed using high-frequency 7.5 to 15 MHz linear transducers. Ultrasonographic findings were assessed for nodular status (solitary or multinodular), nodule size, presence of microcalcifications, structure (cystic, solid, or mixed), and echo-genicity (isoechoic, hypoechoic, hyperechoic, or mixed). Fine-needle aspiration biopsies were performed using a 20 to 22-gauge needle attached to a 10 or 20-mL syringe and was aspirated at least 2 times; usually 4 smears were used. Diagnostic cytopathological examination of FNAB specimens was performed and reported the specimen was labelled as diagnostic if it contained a minimum of 6 groupings of thyroid epithelial cells, consisting of at least 10 cells per group. A cytological diagnosis of follicular neoplasm was defined by abundant follicular cells arranged in microfollicular aggregates in a background of scanty or absent colloid. A total thyroidectomy or lobectomy was performed in all patients and findings from histologic examination of the nodules showed them to be the same as the index nodule, which was confirmed by a clinician, a surgeon and a pathologist. Informed consent was obtained from all patients. The institutional review board of our hospital approved the study design.

Statistical analysis

Data analysis was done by comparative percentage, Chi square test and Fisher exact test.

RESULTS

A total of 46 consecutive patients with follicular neoplasm on FNAC (8 men and 38 women) were included in the study in which 16(34.78%) were malignant and 30 were benign (p value=0.523). Age range were 18 to 76 year with the mean age 47, p value=0.161 which is insignificant. Nodular size were significant with the size of >3 cm having more chances of malignancy. Number of nodules was insignificant with the p value 0.208. Solid consistency was present in 63.8% in benign and 36.1% malignant. Multiple nodule with malignancy was present in 41% patients and single nodule malignancy in 21% patients (p value=0.208). 36.1% patients showed malignancy with solid consistency and 30% malignancy in cystic consistency (p value 0.72, margin and shape were not showed significance. Lymphadenopathy was present in 33.3% malignant patient (Table 1).

Radiological assessment

On radiological assessment size were significantly more frequent in malignant lesions than in benign nodules (26.3 vs. 73.68%; p<0.009. solid cystic and mixed echo structure in malignant vs. benign (66.63% vs. 33.33%, 4.54% vs. 95.45% and 50% vs. 50%) with p value <0.001. micro calcification 63.63% vs. 36.36% with p value 0.021. Echogenicity like in hypoechoic, were 60% vs. 40%, in hyperechoic 16.66% vs 83.33% and in isoechoic 27.72% vs. 72.72% with the p value 0.038 (Table 2).

Cytological assessment

On cytological assessment of tissue follicular with atypia showed 25% malignant with 75% benign nodule and follicular without atypia showed 10% malignant nodule and 90% benign and atypical cells were present in 43.7% malignant nodule and 56% benign nodule with total combined p value=0.135 which is not a significant value (Table 3).

Table 1: Clinical assessment of follicular neoplasm.

Clinical feature	Total number	Benign nodule	Malignant nodule	P value
Gender				
Male	8	6 (75%)	2 (25%)	0.523
Female	38	24 (63.15%)	14 (36.8%)	
Age (in years)				
<45	10	8 (80%)	2 (20%)	0.161
>45	36	20 (55.5%)	16 (45.5%)	
Size of nodule				
<3 cm	35	26 (74.2%)	9 (25.8%)	0.021*
>3 cm	11	4 (36.3%)	7 (63.6%)	
Solitary nodule	14	11 (78%)	3 (21%)	0.208
Multiple nodule	32	19 (59%)	13 (41%)	
Consistency				
*Solid	36	23 (63.8%)	13 (36.1%)	0.720
*Cystic	10	7 (70%)	3 (30%)	
Margin				
Irregular	14	10 (71.4%)	4 (28.5%)	0.699
Regular	32	21 (65.6%)	11 (34.3%)	
Shape				
Tall	6	3 (50%)	3 (50%)	0.334
Wide	28	22 (78.5%)	6 (21.4%)	
Lymphadenopathy	12	8 (66.6%)	4 (33.3%)	

Table 2: Radiological assessment of follicular neoplasm.

Radiological feature	Total number	Benign nodule	Malignant nodule	P value
Size	38			
<4 cm	8	28 (73.68%)	10 (26.3%)	0.009
>4 cm		2 (25%)	6 (75%)	
Echo structure				
solid	18	6 (33.33%)	12 (66.66%)	
cystic	22	21 (95.45)	1 (4.54%)	<0.001
mixed	6	3 (50%)	3 (50%)	
Microcalcification				
present	11	4 (36.36%)	7 (63.63%)	0.021
absent	35	26 (74.28%)	9 (25.71%)	
Echogenicity				
Hypoechoic	21	10 (40%)	11 (60%)	
Hyperechoic	6	5 (83.33%)	1 (16.66.%)	
isoechoic	8	8 (100%)	0 (0.00%)	0.038
mixed	11	8 (72.72%)	3 (27.27%)	

Table 3: Cytological assessment of follicular neoplasm.

Cytological feature	Total number	Benign nodule	Malignant nodule	P value
Follicular with atypia	4	3 (75%)	1 (25%)	0.135
Follicular without atypia	10	9 (90%)	1 (10%)	
Atypical cells	32	18 (56%)	14 (43.7%)	

DISCUSSION

It has been estimated that palpable thyroid nodules are present in 4-7% of the population, but when examined by US, as many as 50-70% of subjects with no history of thyroid disease have been found to have incidentally discovered thyroid lesions, many of which are not palpable.[1-7] Many studies have been published on the risk

of malignancy in patients with thyroid nodules; these studies show that the risk of malignancy is low, approximately 5%, unless the patient has an underlying risk factor, such as a history of external neck irradiation.[8-11] FNAC is the most reliable test for the diagnosis of thyroid nodules, but it is not cost-effective to submit all these lesions to FNAC.[19-24] The definition of clinical feature, sonographic finding with cytological assessment as risk of malignancy should help to determine optimal management of these lesions, by reducing the unnecessary surgery and the cost of healthcare.

The incidence of clinically significant carcinoma in patients with an indeterminate FNAB was 13%, because of the inability of FNAB to distinguish a benign and malignant follicular and the limited value of frozen section examination, clinical and radiological factors have been investigated for their potential value in predicting carcinoma and determining the needed extent of thyroidectomy.[25-26] Davis et al, found that patients with a follicular carcinoma were more likely to be over 50 years old, have a nodule size greater than 3 cm, and a history of neck irradiation than patients with a follicular adenoma of the thyroid gland.[25] They concluded that these clinical parameters were useful in planning the appropriate extent of thyroidectomy. The clinical findings associated with a malignant index nodule were tall and larger diameter, fixation of the mass, and old age with multiple solid nodule of the patient. Other authors, however, suggest that clinical factors are inaccurate in predicting cancer. Intralesional vascular pattern is one of the features that correlates with the suspicion of malignancy. In the current study, none of the clinical parameters was of value in predicting malignancy except one which was size of nodule >3 cm having more chances towards malignant lesion. Layfield et al, investigated the correlation of clinical variables with the benign and the malignant nature of follicular neoplasms and found that only large size correlated with malignancy.[27] Many investigators have attempted to point out ultrasonographic features to identify the lesions with a higher risk of malignancy.[20-23,26] The value of ultrasonography for predicting malignant neoplasms is still controversial, but in this study the presence of larger size, solid hypoechoic features with microcalcification is usually considered to be the most reliable predictor for the malignancy with statically significant value. In another study by Koike et al, a nodule's margin, shape, echo structure, echogenicity and presence of calcification were not reliable indicators of malignancy. Here we show that thyroid FNAB examination is sufficiently sensitive to categorize thyroid nodules as benign or malignant in the majority of nodular thyroid lesions. However, the category of indeterminate follicular lesions continues to present a challenging clinical dilemma. Indeterminate follicular thyroid lesions comprise 10% to 30% of cytopathologic diagnoses.[12] Indeterminate lesions accounted for 34% of thyroid cytology in this study population. This is consistent with other reports, but represents a large volume of patients because of the high prevalence of thyroid lesions in the general population and the widespread use of thyroid FNA.[9,10] This potentially places a large economic burden on the health care system and by generating additional testing (FNA and/or imaging) it may heighten patient anxiety, because the prevalence of cancer in indeterminate lesions varies widely, uniform clinical guidelines are elusive. Further, there are no uniform clinical, radiological or cytologic criteria to determine the prevalence of malignancy in these lesions accurately in some studies, male sex, age, and nodule size are risk factors for malignancy in indeterminate follicular lesions.[9-13] However, others have found that clinical factors are inaccurate in predicting cancer.[14] Cytologic features such as nuclear with atypia and without atypia and atypical cells increase the index of suspicion for malignancy; however, their predictive value is also widely variable.[9,10] Thyroid cancer was most common in the subgroup with atypical cells. This is consistent with reports by Goldstein et al, who showed that atypia within thyroid FNA was associated with malignancy in up to 44% of patients compared with 7% without atypia.[9] Similarly, another study identified a malignancy rate of up to 60% in the presence of nuclear atypia.[15] These findings strongly suggest a need for thyroidectomy in patients with cytologic atypia.

CONCLUSION

The risk for malignancy in cytologically indeterminate thyroid lesions is high. Clinical and cytological features are inaccurate predictors of malignancy, although clinically nodular size and cytological atypical features in follicular neoplasm and radiologically four features (size, echo structure, microcalcification and echogenicity) were statically significant for the prediction of malignancy. But still we cannot confirm the prediction of malignancy on the basis of clinical, radiological and cytological finding except few positive findings because malignant follicular cells having tendency to invade the cellular and vascular structure which is only be detected by histopathologically.

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