Original Article

Association of Ultrasonographic Characteristics with the Malignancy in Cold Nodules of Thyroid.

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Objective: To determine association of ultrasonographic findings with malignancy in patients with cold nodule of thyroid.

Methods: This was a observational study, conducted in Department of ENT, Jinnah Postgraduate Medical Center, Karachi. The study duration was six months, ie. from 15th April to 15th October, 2015. Patients with diagnosis of palpable nodule in thyroid gland on physical examination were enrolled. Detailed histories and physical examination was recorded. All patients underwent 99mTc-pertechnetate scintigraphy and patients with cold nodule were eligible for study after fulfilling inclusion/exclusion criteria. Thyroid ultrasonography was performed and findings such as size, shape, calcifications and echogenicity of nodule were recorded. FNA biopsy was performed under ultrasound guidance. Final diagnosis of malignancy was based on histopathologic examination. Data was analysed by SPSS and association was established between ultrasonographic characteristics and frequency of malignancy in cold nodules of thyroid gland.

Results: Out of total 188 patients of cold nodule, 17 were positive for malignancy. On analysis of association of various factors with malignancy, 04 patients of age less than 40 years while 13 of age 40 and above had malignancy (P=0.235). Ten males and 7 females had malignancy (P= 0.514). Seven patients with tumor size <2cm, while 10 patients with tumor size >2cm had malignancy (P=000). Fourteen patients with abnormal shape (irregular margins, infiltrative, microlobulated) while 03 patients without abnormal shape had malignancy (p=.036). Seven patients with calcification (microcalcifications) while 10 patients without calcification had malignancy (P=0.209). Seven patients with hypoechogenicity while 10 patients without hypoechogenicity had malignancy (P=0.533).

Conclusions: Majority of patients with malignancy are male of above 40 years of age. Tumor size above 2 cm and abnormal shape on ultrasound of thyroid gland are strongly associated with increased chances of malignancy in cold nodules of thyroid.

Keywords: thyroid malignancy, cold nodule, ultrasonography, FNA biopsy, tumor histopathology.

Introduction

A thyroid nodule is defined as a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid parenchyma.[1] Thyroid nodules are frequently discovered in clinical practice, either during physical examination, but also incidentally, during various imaging procedures. [2] The prevalence of thyroid nodules in the general population goes up to 76% when evaluated with ultrasound instead of clinical examination.[3] The risk of malignancy in nodular thyroid disease varies depending on factors such as gender, age, and personal and family history. Increased suspicion is associated with male gender, age < 15 or > 45 years, nodule size > 4 cm, history of radiation exposure, and personal or family history of conditions known to be associated with thyroid cancer. [4] On thyroid scanning solitary nodules are further classified as hot, warm, or cold. Since thyroid carcinoma usually does not concentrate radioiodine as well as normal tissue, malignant thyroid nodules commonly appear as hypofunctioning or nonfunctioning areas on the radioactive iodine scan of the thyroid represented as cold nodule on isotope scanning. Therefore most malignancies are found in cold rather than in hot or functioning nodules.[5] About 80% of solitary nodules are cold, but only 4.6% prove to be malignant. Cold nodules of thyroid are extremely common but most of them are benign.[6] Ultrasound is the preferred imaging modality for thyroid nodules. A number of studies have assessed various sonographic characteristics as predictors of thyroid cancer. Ultrasonographic findings associated with an increased risk of cancer include larger nodule size, presence of calcifications, hypoechogenicity, solid composition, absence of a halo, and irregular margins. Ultrasound guided, fine

needle aspiration (FNA) biopsy is the preferred method of tissue sampling for cold nodules.[7] Its sensitivity is 6598% with a specificity of 72100%.[8] FNA biopsy, particularly when performed under ultrasound guidance, is the most cost-effective and accurate way to evaluate a thyroid nodule. Biopsy samples are evaluated histopathologically for final diagnosis.[9] Detection of a malignant thyroid nodule is an important task. Ultrasonographic findings can be significantly helpful in differentiating malignant from benign nodules of thyroid gland, even before the FNA biopsy was performed. Surgery in benign conditions is better avoided, whereas malignant lesions are successfully treated surgically. Ultrasonography can identify more suitable candidates for FNA biopsy early in the course of evaluation that will help in better management of patients presenting with cold nodule. Objective of our study was to determine association of ultrasonographic findings with malignancy in patients with cold nodule of thyroid.

Methods

The study was conducted in Department of ENT, Jinnah Postgraduate Medical Center, Karachi, during six months period, ie. from 15th April to 15th October 2015. It was an observational case series study in which a total of 188 patients were recruited in this study by non-probability consecutive sampling technique. Patients were selected from OPD and ward of department of ENT, Jinnah Postgraduate Medical Centre, Karachi. An informed consent was taken from the patient. All patients with a palpable nodule in thyroid gland on physical examination underwent a 99mTc-pertechnetate scintigraphy using a pinhole collimator. Patients with cold nodule were eligible for study after fulfilling inclusion/exclusion criteria. Thyroid ultrasonography was performed by radiologist, with special expertise in thyroid sonography. Sonographic characteristics such as size, shape, calcifications and echogenicity of nodule were recorded. FNA biopsy was performed under ultrasound guidance. Final diagnosis of malignancy was based on histopathologic examination. Frequency of malignancy was recorded. A database was developed on SPSS-17. Mean±SD was calculated for age. Frequency and percentages were calculated for gender and sonographic characters of nodule. Effect modifier were controlled through stratification of age, gender and sonographic characteristics of nodule, to see effect of these on outcome variable, by applying chi square test. Association was established between ultrasonographic findings and results of FNA biopsy/histopathological reports. P value <0.05 was taken as significant.

Results

A total of 188 patients fulfilling the inclusion criteria were included in this study. The mean±standard deviation age of study population was 47.92±9.375 years. On analysis of demographics data it was observed 65 (34.6%) were below 40 years of age & 123 (65.4%) were of age 40 years and above. Out of 188 subjects, 115 (61.2%) were male and 73 (38.8%) were female. On analysis of sonographic characteristics, 112 (59.6%) had abnormal shape. Also 56 (29.8%) had

Table-1: Frequency of malignancy in patients with cold modules, according to different parameters.

Parameters	Categories	MALIGNANCY			P-level
		Yes (17)	No (171)	Total (188)	
Age	40 years and above	13	110	123	0.2352
	Below 40 years	04	61	65	
Gender	Male	10	105	115	0.514
	Female	07	66	73	
Size of Tumour	Less than 20cm	07	147	154	0.00
	20cm and above	10	24	34	
Sape of Tumour	Abnormal (irregular margins, infiltrative microllobulated)	14	98	112	0.036
	Normal (well defined regular margins)	03	73	76	
Calcification	Non calculated	10	122	132	0.209
	Calculated (mircocalcifications)	07	49	114	
Echogenicity	Echgenic, isocchoic	10	104	114	0.533
	Hypoechgenic	07	67	74	

calcification and 74 (39.4%) had hypoechogenicity. On analysis of frequency of outcome variables, 17 (9%) had malignancy. On analysis of association of various factors with malignancy, 04 patients of age less than 40 years while 13 of age 40 and above had malignancy (P= 0.235). Ten males and 7 females had malignancy (P= 0.514). Seven patients with tumor size < 2 cm while 10 patients with tumor size >2 cm had malignancy (P=0.00). Fourteen patients with abnormal shape while 03 patients without abnormal shape had malignancy (p=0.036). Seven patients with calcification while 10 patients without calcification had malignancy (P=0.209). Seven patients with hypoechogenicity while 10 patients without hypoechogenicity had malignancy (P=0.533). Stratification with respect to age, gender and sonographic characters like size, shape, calcification, and echogenicity is mentioned in **(Table-1).**

Discussion

Several thyroid diseases may present as nodules. According to population-based studies conducted with adults in iodine sufficient areas, approximately 4 to 7% of women and 1% of men exhibit palpable thyroid nodules [10, 11]. However, the prevalence of nodules indicated by ultrasound exams is substantially higher, reaching up to 68% of the population (such high frequencies are usually found among older women than 65. Although most thyroid nodules are benign, the possibility of a malignancy must be ruled out[12, 13] It has been reported that solitary, solid and large sized nodule possesses a different clinical and pathological significance for surgical evaluation.[14, 15] In this study we analyzed frequency of malignancy in patients with cold nodule of thyroid. High resolution ultrasound is the best imaging modality for objectively detecting size, number and cellular nature of the nodules.[16] In our series ultrasound imaging single large nodule and abnormal shape have more chances of development of malignancy. Solid nodule (less than 25% of cystic component) in ultrasound image, merit further careful evaluation and eventual indication for surgical intervention. On the other hand ultrasound has not the ability to establish functional status of the nodule. Nuclear imaging is a useful modality for the functional characterization of a thyroid nodule.[17] In our series, nuclear scanning was found useful to define functional status of solitary solid nodule. Larger hot spot and image of suppressed extranodular tissue in the thyroid scintigraphy has identified hyperactive nodule, and has established the diagnosis of toxic adenoma in our 20 patients. Cold spot in the remaining 24 cases has determined hypo or inactive (functional status of the) solid nodule. Hypoactive solid nodule in nuclear scanning points out increased risk of malignancy.[18] After imaging modalities FNAC is the preferred method for preoperative pathological evaluation. As a scintigraphic feature, cold spot significantly increases the risk of malignancy in a large solid nodule. Solitary hypoactive solid nodule in our patients has supported the indication of surgical intervention. Larger size, solitary nodule, hypoechogenicity of solid elements, microcalcification, irregular shape as features of echotexture determined by ultrasound, and hypoactive nodule (cold spot) by nuclear scan have been reported as marker of high risk for malignant development.[19] The rate of 29% (10/34) of malignancy in our patients has confirmed the increased risk of malignancy in larger hypoactive nodule. Previous studies have also reported similar rates of malignancy between 16% and 30% in solitary solid nodule.[20] On the other hand the malignancy rate was 8.5% in autopsy and surgical series including solitary and multinodular goiter cases.[21] Although the number of patients is relatively small for definitive conclusion, based on our findings we have concluded that large nodule has a considerable rate among patients with cold nodular goiter in endemic area. Ultrasound objectively defines cellular architecture of the nodule, and nuclear scan its functional status. Solitary hypoactive, abnormal shape and larger nodule possess high rate of malignant change.

Conclusion

Majority of patients with malignancy are male of above 40 years of age. Tumor size above 2 cm and abnormal shape including infiltrative microlobulated irregular margins, on ultrasound of thyroid gland are strongly associated with increased chances of malignancy in cold nodules of thyroid.

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