

## Original Research Article

# Macrocalcification in thyroid nodule

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### ABSTRACT

**Background:** The thyroid is one of the largest endocrine organs. The prevalence of palpable thyroid nodules increases with age and is 4-7% in a middle-aged population. Objective of present study was to understand if thyroid malignancy is associated with macrocalcification.

**Methods:** 34 cases were with thyroid nodules were evaluated initially with sonography and then with FNAC, the results of which were given on the basis of Bethesda system.

**Results:** On USG, 23 (67.6%) nodules had macrocalcifications, 5 (14.7%) had microcalcifications and 6 (17.6%) had both micro as well as macrocalcifications. Cytology of 23 nodules with macrocalcification were non-diagnostic in 8.7%, benign 73.9%, suspicious for malignancy in 8.7% and malignant in 8.7%. Only 2 lesions with macrocalcification and 1 with both macro and microcalcification came out to be non-diagnostic. 17 lesions with macrocalcification were diagnosed as benign, 2 as suspicious for malignancy and 2 as malignant. While 3 lesions with microcalcification were diagnosed as malignant on FNAC and 2 as benign.

**Conclusions:** Macrocalcification is not a good indicator for malignancy.

**Keywords:** Macrocalcification, Thyroid nodule, Ultrasonography

### INTRODUCTION

The thyroid is one of the largest endocrine organs. The prevalence of palpable thyroid nodules increases with age and is 4-7% in a middle-aged population.<sup>1</sup> The annual incidence of thyroid carcinoma is 1-2 per 100,000 population which accounts for 90% of malignancies of the entire endocrine system.<sup>2</sup> Thyroid nodules are common in clinical practice. Besides clinical examination and above investigations, FNAC is most frequently used method for evaluation of thyroid lesions and is now considered the diagnostic test of choice for the pre-operative evaluation of thyroid lesions and selection of patients for thyroid surgery. Calcifications, often described in sonography reports, can be detected in both

benign and malignant thyroid nodules.<sup>3</sup>

In this study, we aimed to evaluate FNAC results of thyroid nodules with parenchymal and peripheral macrocalcification and macrocalcifications. Also, to find out if macrocalcifications are associated with thyroid carcinoma.

### METHODS

It's an Observational study performed in Department of Otorhinolaryngology, I.G.M.C, Shimla, India. The samples for cytological examination were collected from indoor/outdoor patients with thyroid swelling attending the departments of ENT and Surgery IGMC, Shimla over

a period of one year (from June 2015-2016). Complete clinical data was recorded and proforma were filled out after taking a written informed consent from the patient.

**Ultrasonography**

USG was performed with a color Doppler ultrasonography using a superficial probe (5.5 - 12.5 MHz) in all patients with patient in supine with neck in extension.

Nodule location, diameters, volume, echogenicity (isoechoic, hypoechoic or hyperechoic), texture (solid, mixed or cystic), presence of hypoechoic halo, presence and type of calcification (microcalcification, parenchymal macrocalcification, peripheral macrocalcification) and vascularization pattern were recorded for all nodules evaluated with FNAC.

Calcifications <2 mm were labeled as microcalcification and ≥2 mm in diameter and with an acoustic shadow as macrocalcification

**FNAC**

FNAC was performed after cleaning the skin in the area of the procedure with spirit, with a 23-25-gauge needle attached to a disposable 20 ml syringe. An average of 2-5 passes was made and atleast 4 smears were prepared. If the FNAC came out to be inadequate or opinion not possible then USG guided FNAC were done and again a minimum four smears were prepared. Thyroid tissue sample Specimens were sent to department of pathology, I.G.M.C, Shimla in 10% formalin for analysis. The Bethesda System for Reporting Thyroid Cytology (TBSRTC) was employed: I Non-diagnostic or Unsatisfactory, II Benign, III Atypia of undetermined significance or follicular lesion of undetermined significance, IV Follicular neoplasm or suspicious for a

follicular neoplasm Specify if Hurthle cell (oncocyctic type), V Suspicious for malignancy, VI Malignant.

**RESULTS**

It is a well-known fact that thyroid lesions are more common in females as compared to males. This fact was reconfirmed by the present study. The female to male ratio being 5.8:1.

Majority of patients presented with swelling in front on neck. 2 cases presented with lymphadenopathy at level 2 and 3. one of which was medullary carcinoma on FNAC and the other one was papillary carcinoma. One patient complained of pain in swelling, and was diagnosed as Hashimoto thyroiditis on FNAC.

Most common diagnosis on USG was multinodular goitre (n=11), 2<sup>nd</sup> most common was colloid nodule (n=10). Other diagnosis was solitary thyroid nodule (n= 9) and malignancy (n= 4). The size of the nodule varied from 1.5x1.5 to 8x8 cm.

The other major finding on USG was calcification. Now, calcification of size ≤2mm were defined as microcalcification and calcification of size >2mm were defined as macrocalcifications. 23 (67.6%) nodules macrocalcifications, 5 (14.7%) had microcalcifications and 6 (17.6%) had both micro as well as macrocalcifications. Of the 23 nodules with macrocalcification, 9 (39.1%) were benign, 5 (21.7%) were solitary nodules, 8 (34.8%) were colloid nodule and 1 (4.3%) were malignant on USG. Of the 5 nodules with microcalcification, 1 (20%) was solitary nodule, 2 (40%) were colloid nodule and 2 (40%) were malignant. The nodules showing micro as well macrocalcification were diagnosed as MNG in 2 (33.3%), solitary nodule in 3 (50%) and malignant in 1 (16.7%) cases (Table 1).

**Table 1: Relationship between USG diagnosis and calcification.**

Calcification	Total no	MNG	STN	Colloid nodule	Malignant
Macro-calcification	23	9 (39%)	5 (21.7%)	8 (34.7%)	1 (4.3%)
Micro-calcification	5	0	1 (20%)	2 (40%)	2 (40%)
Micro+macro	6	2 (33.3%)	3 (50%)	0	1 (16.6%)

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The nodules showing micro as well macrocalcification were diagnosed as MNG in 2 (33.3%), solitary nodule in

3 (50%) and malignant in 1 (16.7%) cases (Table 1). Vascularity was increased in 11 cases only 3 (27.3%) of which were malignant on USG. Rest 4 were MNG, 3 STN and 1 was colloid nodule.

In present study, on FNAC, out of total 34, 3 nodules were non-diagnostic, 19 were benign, 1 was follicular neoplasm, 4 were suspicious of malignancy and 7 were malignant.

Cytology of 23 nodules with macrocalcification were non-diagnostic in 8.7%, benign 73.9%, suspicious for malignancy in 8.7 % and malignant in 8.7%.

Only 2 lesions with macrocalcification and 1 with both macro and microcalcification came out to be non-diagnostic. 17 lesions with macrocalcification were

diagnosed as benign, 2 as suspicious for malignancy and 2 as malignant. While 3 lesions with microcalcification were diagnosed as malignant on FNAC and 2 as benign (Table 2).

2 lesions with both types of calcification were diagnosed as suspicious for malignancy and 2 as malignant.

**Table 2: Relationship between FNAC and calcification.**

FNAC		Calcification			Total
		Macrocalcification	Microcalcification	Microcalcification+macrocalcification	
Non-diagnostic	Count	2	0	1	3
	% within FNAC	66.7%	0.0%	33.3%	100.0%
	% within calcification	8.7%	0.0%	16.7%	8.8%
Benign	Count	17	2	0	19
	% within FNAC	89.5%	10.5%	0.0%	100.0%
	% within calcification	73.9%	40.0%	0.0%	55.9%
Follicular neoplasm	Count	0	0	1	1
	% within FNAC	.0%	0.0%	100.0%	100.0%
	% within calcification	.0%	0.0%	16.7%	2.9%
Suspicious for malignancy	Count	2	0	2	4
	% within FNAC	50.0%	0.0%	50.0%	100.0%
	% within calcification	8.7%	0.0%	33.3%	11.8%
Malignancy	Count	2	3	2	7
	% within FNAC	28.6%	42.9%	28.6%	100.0%
	% within calcification	8.7%	60.0%	33.3%	20.6%
Total	Count	23	5	6	34
	% within FNAC	67.6%	14.7%	17.6%	100.0%
	% within calcification	100.0%	100.0%	100.0%	100.0%

**DISCUSSION**

Thyroid lesions are of great importance because most are amenable to medical or surgical management. The differential diagnosis of thyroid lesions is crucial as malignancy necessitates surgery while follow up is necessary in case of benign lesions. FNA is a well-established diagnostic test that is often used as an initial screening test for patients with thyroid nodules.

The prevalence of palpable thyroid nodules increases with age and is 4-7% in a middle aged population<sup>1</sup>. The annual incidence of thyroid carcinoma is 1-2 per 100, 000 population which accounts for 90% of malignancies of the entire endocrine system, 1% of total human malignancies and 0.5% of total deaths from malignancies.<sup>2</sup> In India, there are 21600 new cases of thyroid malignancy every-year.<sup>3</sup> Incidence of cancer among diseases of thyroid varies from 5.3% in Delhi to 32% in Jaipur.<sup>4</sup> Thyroid nodules may be solitary within a normal thyroid gland or dominant within a diffuse or multinodular goiter.<sup>5</sup> A solitary nodule is more likely to represent carcinoma (2.7-30%) than a dominant nodule

within a multinodular gland (1.4 to 10%).<sup>6</sup> Thyroid nodules are more frequent in women, iodine deficient regions, in older ages and with history of head and neck radiation in children. Any solitary or dominant nodule larger than 1cm should be subjected to FNAC.

Risk factors that increase the probability of malignancy in a thyroid nodule are age under 20 or over 60 years, males (8% vs 4% in females), history of head and neck irradiation in childhood and family history of medullary thyroid cancer (MTC) or multiple endocrine neoplasia (MEN) type-2. Thyroid nodules are uncommon in children and adolescents compared with adults, but the risk of malignancy is much higher in children (14- 40% compared with 5% in adults).<sup>6</sup>

Serum TSH measurement is recommended in all patients presenting with a nodule. Majority of the patients with benign or malignant thyroid nodule(s) are euthyroid. It has recently been reported that the risk of malignancy in a thyroid nodule increases proportionally to serum TSH concentrations at the time of presentation.<sup>7</sup> FNAC is most frequently used method for evaluation of thyroid lesions. Since its introduction, percentage of patients undergoing

thyroidectomies has decreased by 25-50%.<sup>8</sup> It is considered to be the “gold” standard in management of patients with thyroid nodules. Ultrasound guided FNA can detect even 1 mm sized nodules and is performed in non-palpable nodules >1cm, nodules palpable but <1.5cm, deep seated nodules in close vicinity to blood vessels and cystic or mixed nodules (if previous FNA is non-diagnostic).<sup>9</sup>

FNAC is now considered the diagnostic test of choice for the pre-operative evaluation of thyroid lesions and selection of patients for thyroid surgery. It is simple, inexpensive, safe, rapid, minimally invasive, can be carried out in outdoor patients with excellent patient compliance and considered to have a high sensitivity and specificity. Its sensitivity ranges from 80-98% and specificity from 58-100%.<sup>10</sup> However, it has some limitations in specimen adequacy, sampling technique, skill and experience of pathologist and inability to distinguish follicular lesions reliably, which includes hyperplastic nodule in goitre, follicular neoplasms and papillary carcinoma (follicular variant). It is rarely associated with complications like haematoma, massive intrathyroid haemorrhage, necrosis and local metastasis of malignancy from needle track seeding. Calcifications, often described in sonography reports, can be detected in both benign and malignant thyroid nodules. Although it is well known that microcalcifications are associated with thyroid malignancy, the results for macrocalcifications are controversial.<sup>9</sup> Recent studies have revealed a relationship between macrocalcification and malignancy, particularly in papillary thyroid carcinomas.<sup>10</sup> In addition, despite the general belief that peripheral macrocalcification indicates benign situations, it was shown that if it is irregular it can also be related with malignancy. Macrocalcification together with microcalcification in the same nodule or located in the middle of a hypochoic nodule have a higher probability of malignancy.

Thyroid nodular calcifications can be classified according to their diameter and location; calcifications <2 mm and without acoustic shadow at posterior are microcalcifications, calcifications  $\geq 2$  mm and with posterior acoustic shadow are macrocalcifications, and calcifications surrounding the nodule are peripheral (eggshell) calcifications. Pathologically, microcalcification is a psammoma body that contains 10-200  $\mu\text{m}$ , rough, smooth, bright, calcific aggregations.<sup>11</sup> Large and irregular bordered macrocalcification can exist secondary to tumor necrosis and it can be seen in both benign and malignant nodules. Peripheral calcifications are believed to occur secondary to chronic degenerative changes.

## CONCLUSION

So, to conclude present study, macrocalcification is not a good indicator for malignancy. It is noticed that nodules with macrocalcification have increased chances of

microcalcification in the same nodule which could be a reason that in other studies nodules associated with macrocalcification have come out to be positive for malignancy. Also, the study is required to be taken for a period with larger study group to reach at a conclusion.

The limitations of this study were that the sample size was limited (34 cases) and Histopathological confirmation was not obtained.

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