OMICS Journal of Radiology
ISSN: 2167-7964

Djekidel et al., OMICS J Radiol 2014, 3:3
DOI: 10.4172/2167-7964.1000162

Research Article Open Access

Correlation of Hot Nodules and Cytopathology: Nine Years at an Academic Institution

Mehdi Djekidel[1]*, Guoping Cai[2], Rafay Ahmed[1] and Constantine Theoharis[2]

[1]*Department of Diagnostic Radiology, Yale University School of Medicine, USA*
[2]*Department of Pathology, Yale University School of Medicine, USA*

Abstract

Background: Thyroid nodules are frequently diagnosed in everyday clinical practice. Strategies for the evaluation of their potential malignant risk and clinical management approaches have been widely developed by multiple endocrine and surgical societies. These guidelines are dynamically changing and the malignant potential of a hot thyroid nodule has become a matter of debate.

Methods: All thyroid scans (n=137) performed at our institution over nine years (January 2003 to December 2012), for which a cytopathology result was available for review were retrospectively reanalyzed by an experienced nuclear medicine physician. 65 scans demonstrated clearly hot nodules and were correlated with cytopathology results.

Results: Only one of sixty-five nodules (1.5%) was found to be malignant: a Hürthle cell carcinoma. An additional papillary thyroid carcinoma was found incidentally in another patient, however corresponding to a cold nodule in the contralateral lobe to the hot nodule.

Conclusions: A hot nodule on a thyroid scan likely confers an overall low but non-negligible risk for malignancy. Further studies on larger datasets pooled from various centers would be valuable.

Keywords: Hot nodule; Malignancy; FNA; Cytology; Thyroid scan

Introduction

Benign thyroid nodules are frequent in the general population, however, thyroid cancer, the most common endocrine malignancy, has been increasing in incidence over the last few decades throughout the Western World [1-4]. Imaging has assessed noninvasively the malignant risk of thyroid nodules either be solitary nodules or part of a multinodular goiter. If they exhibit suspicious characteristics on ultrasound, or appear "cold" i.e. non-functioning (without uptake) on a thyroid nuclear scan, they have been associated with a higher risk of malignancy [5,6]. Suspicious nodules traditionally undergo fine needle aspiration for cytology review and/or surgical resection. A hemi or total thyroidectomy will then be performed [7]. On the other hand, autonomous hyperfunctioning nodules i.e. that show uptake and appear "hot" on a nuclear thyroid scan have been regarded as having a very low but undefined malignant risk [8]. However, there have been a few recent reports describing a possible malignant association with hot nodules on a thyroid scan [9-13]. We conducted a retrospective analysis in order to better ascertain the potential malignant risk of a hot nodule.

Methods

The archives of the Yale Department of Diagnostic Radiology were reviewed and all thyroid nuclear medicine scans performed over the past nine years (January 2003 to December 2012) were extracted and reanalyzed. A total of 137 thyroid nodules were identified for which cytopathology FNA correlation existed. 137 scans were then retrospectively re-analyzed by an experienced nuclear medicine physician. Final cytopathology diagnoses were then reviewed and correlated to the nodules identified on the thyroid scan. Procedure dates, biopsy sites, cytologic FNA findings and/or surgical specimen histology were additionally recorded and correlated with the thyroid nuclear scan findings.

Thyroid scans were performed as per a routine protocol. A 100-microcurie dose of ^{123}I was used for 24 hour uptake measurements. Immediately following the iodine uptake measurement, a thyroid scan was performed 20 minutes after the injection of 10 mCi of ^{99m}Tc-pertechnetate. This protocol offering the best image quality, most accurate uptake measurement and lowest radiation dosimetry compared to a higher dose iodine only uptake and scan protocol.

Fine-needle aspiration biopsies were performed almost entirely via ultrasound. Each sample was evaluated via smears stained with either the Diff-Quik stain or via the Papanicolau method. Needle washes were performed and evaluated via ThinPrep processing.

Surgical histologic samples were processed via conventional buffered formalin preservation and Hematoxylin/Eosin staining.

Results

Our patient population was overwhelmingly female (61:4). Mean age was 50.9 ± 16.7. Table 1 describes the results. 65 of the 137 nodules (47%) were hyper-functioning "hot" nodules. Of our 65 scans with hot nodules, 14 (21%) of them additionally had a cold nodule usually in the contralateral lobe.

53 (81%) of patients additionally showed evidence of definite suppression of the remainder of their thyroid gland. The average uptake value was 25% (± 13%).

25% (16/63) of the patients had abnormal uptake values defined as

***Corresponding author:** Mehdi Djekidel, Department of Diagnostic Radiology, Yale University School of Medicine, 310 Cedar Street, New Haven, CT 06520, USA, Tel: 203-200-5180; E-mail: mehdi.djekidel@yale.edu

Received April 28, 2014; **Accepted** May 14, 2014; **Published** May 21, 2014

Citation: Djekidel M, Cai G, Ahmed R, Theoharis C (2014) Correlation of Hot Nodules and Cytopathology: Nine Years at an Academic Institution. OMICS J Radiol 3: 162. doi:10.4172/2167-7964.1000162

Sex	Age	Cold nodule	Hot nodule	Gland suppression	Uptake value%	FNA results: P/N	Surgery
Female	67	no	yes	yes	10.2	NONE	MNG
Female	46	no	yes	yes	11.3	Negative	NONE
Female	38	no	yes	yes	20.7	Atypical	NONE
Female	52	no	yes	0	33.8	Negative	Negative
Female	70	no	yes	0	28	Negative	NONE
Female	43	no	yes	yes	23.9	Negative	NONE
Female	48	no	yes	0	39.7	Negative	NONE
Female	69	no	yes	yes	29.6	Negative	NONE
Female	48	yes	yes	yes	31.6	Negative	NONE
Female	20	no	yes	yes	42	NONE	MNG
Female	51	no	yes	yes	28.5	Negative	NONE
Female	77	no	yes	yes	13	Negative	NONE
Female	65	no	yes	yes	7.2	Negative	NONE
Female	**38**	**yes**	**yes**	**yes**	**32.8**	**Suspicious PTC^T**	**PTC^T**
Female	15	no	yes	yes	NONE	Negative	NONE
Female	59	no	yes	yes	24.8	Negative	NONE
Female	45	yes	yes	yes	28	Follicular neoplasm	Follicular adenoma
Female	55	no	yes	yes	17	Negative	NONE
Male	86	no	yes	no	14.5	Negative	NONE
Female	23	no	yes	yes	19.4	Negative	NONE
Female	18	no	yes	yes	21.3	Negative	NONE
Female	59	no	yes	no	13.6	Negative	NONE
Female	63	yes	yes	no	13	Indeterminate	MNG
Male	79	no	yes	yes	24	Negative	NONE
Female	63	no	yes	yes	14.8	Negative	NONE
Female	36	yes	yes	yes	37.7	NONE	MNG
Female	58	yes	yes	no	8.2	Suspicious Follicular neoplasm	NONE
Female	70	yes	yes	yes	13.6	Hurthle cell nodule	Hurthle cell nodule
Female	59	yes	yes	no	37.2	Negative	NONE
Female	77	no	yes	yes	30	Negative	NONE
Female	55	no	yes	no	27.6	Negative	NONE
Female	54	yes	yes	no	NONE	Negative	NONE
Female	39	no	yes	yes	16.3	Negative	NONE
Female	68	no	yes	yes	25.2	Negative	NONE
Female	53	no	yes	yes	34	Negative	NONE
Female	46	yes	yes	yes	26.7	Negative	NONE
Female	34	no	yes	yes	36.3	Negative	NONE
Female	72	no	yes	yes	85.5	Negative	NONE
Male	22	no	yes	yes	35	NONE	Follicular adenoma
Female	46	yes	yes	yes	16.5	Negative	NONE
Female	42	yes	yes	yes	19	Follicular neoplasm	Follicular adenoma
Female	55	yes	yes	yes	25.4	Negative	NONE
Female	63	no	yes	yes	20	Follicular neoplasm	Follicular adenoma
Female	55	no	yes	yes	27.6	Negative	NONE
Female	79	no	yes	yes	6.6	Negative	NONE
Female	57	no	yes	yes	50.1	Negative	NONE
Female	37	no	yes	yes	28.6	Negative	NONE
Female	37	no	yes	yes	28.6	Negative	NONE
Male	73	yes	yes	yes	26	Negative	NONE
Female	**45**	**no**	**yes**	**yes**	**33.5**	**Hurthle cell neoplasia**	**Hurthle cell cancer**
Female	61	no	yes	yes	37.9	Negative	NONE
Female	49	no	yes	yes	28.6	Negative	Goiter-TT
Female	41	no	yes	yes	28.2	Negative	NONE
Female	42	no	yes	yes	27.9	Negative	NONE
Female	47	no	yes	yes	15	Negative	Goiter-TT
Female	49	no	yes	no	28.1	Negative	NONE
Female	74	no	yes	yes	22.9	Negative	NONE
Female	21	no	yes	yes	40.3	Negative	Goiter-Rt
Female	50	no	yes	yes	39.5	Negative	NONE
Female	49	no	yes	yes	15.3	Negative	NONE
Female	43	no	yes	yes	47.4	Negative	NONE
Female	21	no	yes	yes	16.7	Negative	Goiter-Lt
Female	32	no	yes	no	6	Negative	NONE
Female	34	no	yes	yes	28.3	Negative	NONE
Female	67	no	yes	yes	22.4	Negative	NONE

T PTC: Papillary Thyroid Cancer

Table 1: Summary of cytopathology correlation with thyroid scan results.

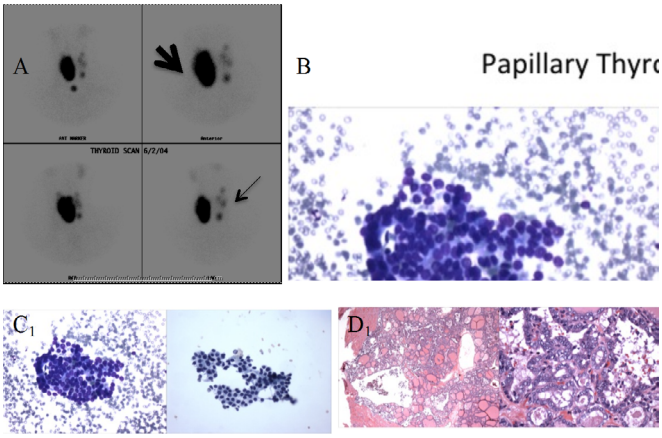

Figure 1: A. Thyroid uptake scan showing a large right sided hot nodule (thick arrow: found to be benign) and left sided cold nodule (thin arrow: found to be malignant). B. Gross pathology showing the corresponding 0.5-cm well-circumscribed encapsulated tan-white nodule located in the left lobe of the thyroid (arrow). C. Fine needle aspiration shows clusters of follicular cells with oval nuclei, nuclear grooves and rare intranuclear pseudo-inclusions (C_1. Diff-Quik stain, X400; C_2. Papanicolaou stain, X400). D. Microscopically the surgical histopathological specimen shows that the tumor is composed of follicles of variable sizes with focal papillary architecture (D_1. Hematoxylin-eosin stain, X40 D_2. X400). The tumor cells have oval nuclei, nuclear grooves, clear chromatin and small nucleoli. Cytologic and histopathologic features are consistent with papillary thyroid carcinoma.

≥ 30%. While 3% (2/65) of the patients had no uptake measurement performed.

Only 25% (16/65) of the cohort underwent surgical resection, usually for a Goiter. All except 4 patients had an FNA performed who instead underwent a surgical resection as the initial diagnostic step. 3% (2/65) of cases were malignant. However, in one case, we found that a papillary micro carcinoma involved a lobe contralateral to the hot nodule on the nuclear scan, so the cancer did not correlate to a hot nodule. It should be noted however that a second nodule, this one "cold" (nonfunctioning), had been identified in this same patient corresponding to the microcarcinoma as shown in Figure 1. The second patient found to have a malignancy had a surgical resection revealing Hürthle cell carcinoma corresponding to the hot nodule as seen in Figure 2. The tumor was large, at least 3 cm in size on postoperative histologic evaluation. Furthermore, the patient was found to be hyperthyroid with a low TSH, with abnormal values ranging between

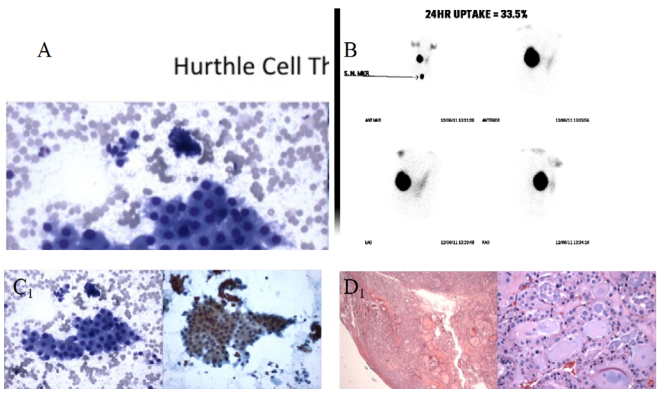

Figure 2: A. Gross pathology showing a 3-cm well-circumscribed encapsulated tan-brown nodule located in the right lobe of the thyroid (arrow: found to be malignant). B. Thyroid uptake scan showing a large right sided hot nodule. (thick arrow) C. Fine needle aspiration showing single and clusters of follicular cells with a granular cytoplasm, round nuclei and prominent nucleoli (C_1. Diff-Quik stain, X400; C_2. Papanicolaou stain, X400) D. Microscopically, the tumor is composed of follicles of variable sizes focally invading into the capsule (D_1. Hematoxylin-eosin stain, X40). The tumor cells have granular cytoplasm, round nuclei and prominent nucleoli (D_2. Hematoxylin-eosin stain, X400). Cytologic and histopathologic features consistent with Hurthle cell carcinoma.

0.005-0.0010 mIU/l (Normal: 0.5-4.5 mIU/l).

Discussion

Hot nodules are believed to possess a low risk of malignancy and ATA guidelines do not recommend an aggressive approach to management. Additionally patients with a low TSH (similar to our patient) are felt to also be of low risk [7]. Our data supports the hot nodule expectation as only 1 patient (1.5%) had a malignancy corresponding to a hot nodule in our cohort. This patient surprisingly also had a low TSH. The malignant potential of a hot nodule in our limited population (n=65) is therefore low. However, this low rate is not negligible, and a few authors have reported a possible malignant association of hot nodules [9-13]. Polyzos et al. also had found an incidental thyroid carcinoma in the contralateral lobe as in our series [11]. The ATA guidelines state that a hyperfunctioning or hot nodule on scintigraphy may be treated non-surgically if the patient is clinically hyperthyroid or euthyroid. Our single Hürthle cell cancer patient was hyperthyroid. The size of the nodule however was clinically concerning. Our patient's nodule was larger than 3 cm. This is noteworthy as this was also the case of several malignant hot nodules reported in the literature. The size of a hot nodule may be a satisfactory criterion to decide of its malignant potential. TSH status is not supported in our limited study.

Clinicians are frequently faced with the dilemma of thyroid nodule characterization and the estimation of a malignant risk. This risk can then be conveyed to the patient and translated into a medical management decision. Our data and the hot nodule literature support a low malignant risk. However, this risk may be altered in larger nodules.

Conclusion

A hot nodule on a thyroid scan may overall confer a low risk for malignancy (1.5%). Evaluation of size (>3 cm) may improve the diagnosis of malignancy in hot nodules in selected cases. Further studies on larger datasets pooled from various centers would be valuable.

References

1. Aschebrook-Kilfoy B, Ward MH, Sabra MM, Devesa SS (2011) Thyroid cancer incidence patterns in the United States by histologic type, 1992-2006. Thyroid 21: 125-134.
2. Hughes DT, Haymart MR, Miller BS, Gauger PG, Doherty GM (2011) The most commonly occurring papillary thyroid cancer in the United States is now a microcarcinoma in a patient older than 45 years. Thyroid 21: 231-236.
3. Leux C, Colonna M, Guizard AV, Uhry Z, Velten M, et al. (2009) Time trends in the geographic variation of thyroid cancer incidence by tumor size from 1983 to 2000 in France. Rev Epidemiol Sante Publique 57: 403-410.
4. Rego-Iraeta A, Pérez-Méndez LF, Mantinan B, Garcia-Mayor RV (2009) Time trends for thyroid cancer in northwestern Spain: true rise in the incidence of micro and larger forms of papillary thyroid carcinoma. Thyroid 19: 333-340.
5. Sarkar SD (2006) Benign thyroid disease: what is the role of nuclear medicine? Semin Nucl Med 36: 185-193.
6. Leidig-Bruckner G, Cichorowski G, Sattler P, Bruckner T, Sattler B (2012) Evaluation of thyroid nodules--combined use of (99m)Tc-methylisobutylnitrile scintigraphy and aspiration cytology to assess risk of malignancy and stratify patients for surgical or nonsurgical therapy--a retrospective cohort study. Clin Endocrinol (Oxf) 76: 749-758.
7. Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, et al. (2010) American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations. Endocr Pract 16: 468-475.
8. Pazaitou-Panayiotou K, Perros P, Boudina M, Siardos G, Drimonitis A, et al. (2008) Mortality from thyroid cancer in patients with hyperthyroidism: the Theagenion Cancer Hospital experience. Eur J Endocrinol 159: 799-803.
9. Ruggeri RM, Campennì A, Giovinazzo S, Saraceno G, Vicchio TM, et al. (2013) Follicular variant of papillary thyroid carcinoma presenting as toxic nodule in an adolescent: coexistent polymorphism of the TSHR and Gsα genes. Thyroid 23: 239-242.
10. Yalla NM, Reynolds LR (2011) Hürthle cell thyroid carcinoma presenting as a "hot" nodule. Endocr Pract 17: e68-72.
11. Polyzos SA, Goulis DG (2011) Coincidental thyroid papillary microcarcinoma in a patient treated for a toxic adenoma of the thyroid. Arch Iran Med 14: 149-151.
12. Hernán-Martínez J, Uzcategui M, Corder E, Castillo M, Sostre S, et al. (2010) Hyperthyroidism, hyperfunctioning thyroid nodule, and thyroid cancer in a young female: a rare and unusual coexistence. P R Health Sci J 29: 78-82.
13. Uludag M, Yetkin G, Citgez B, Isgor A, Basak T (2008) Autonomously functioning thyroid nodule treated with radioactive iodine and later diagnosed as papillary thyroid cancer. Hormones (Athens) 7: 175-179.