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The Comparison of Fine Needle Aspiration Cytology and Histopathology Results in Hypoactive Solitary Thyroid Nodule

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ABSTRACT

Objective: Fine-needle aspiration (FNA) is currently the primary diagnostic procedure in diagnosing thyroid malignancy and guides surgeons on patient selection for thyroidectomy for thyroid nodules. Based on the cytology findings, patients can be followed in cases of benign diagnosis or subjected to surgery in cases of malignant diagnosis thereby decreasing the rate of unnecessary surgery. Purpose of the present study was to correlate the fine needle aspiration cytology (FNAC) findings with histopathology of excised specimens.

Materials and Methods: A comprehensive view of hospitalization records was performed that have assessed the sensitivity of FNA for detecting thyroid malignancy in hypoactive solitary thyroid nodules. This was a prospective study conducted on 62 consecutive patients between December 2001 and June 2008. All patients with clinically diagnosed solitary thyroid nodule who were clinically, radyologically and biochemically hypothyroid were included for study. Patients with multinodular goitre, euthyroid and hyperthyroid were excluded from the study.

Results: The sensitivity, specificity, accuracy, false positive rate, false negative rate, positive predictive value, and negative predictive value of FNAC for the diagnosis of neoplastic hypoactive solitary thyroid nodules were 80,7 %, 88,8 %, 85,4 %, 11,1%, 19,2 %, 80,7 %, and 88,8 %, respectively. The most common malignancy detected was papillary carcinoma of thyroid in 8 patients.

Conclusion: Fine needle aspiration cytology is a simple, easy to perform, cost effective, and easily repeated procedure for the diagnosis of thyroid cancer. It is recommended as the first line investigation for the diagnosis of hypoactive solitary thyroid nodule.

Key Words: *Hypoactive solitary thyroid nodule, Fine needle aspiration cytology, Histopathology.*

ÖZET

Hipoaktif Soliter Tiroid Nodüllerinde İnce İğne Aspirasyon Sitolojisi ve Histopatolojik Sonuçların Karşılaştırılması

Amaç: İnce iğne aspirasyonu tiroid malignensilerinin teşhisinde halen ilk akla gelen bir yöntemdir ve tiroid nodülü bulunan, tiroidektomi yapılacak olan hastaların seçiminde cerraha yol gösterir. Sitolojik bulgulara göre, hastalar benign olarak teşhis edildiklerinde takip edilebilir veya malign olarak tehis edildiklerinde opere edilebilirler. Böylece gereksiz cerrahiden kaçınılmış olur. Bu çalışmanın amacı ameliyat materyallerinin histopatolojisi ile ince iğne aspirasyon sitolojisi bulgularının ilişkisini araştırmakdır.

Gereç ve Yöntem: Hipoaktif soliter tiroid nodüllerinde tiroid maliğnensilerinin tespiti için hastane kayıtları kapsamlı bir şekilde gözden geçirilerek tiroid ince iğne sensitivitesi değerlendirildi. Bu 2001 Aralık'tan 2008 Haziran'a kadarki ardışık 62 hasta üzerinde yapılan bir prospektif çalışmaydı. Klinik olarak soliter tiroid nodülü teşhis edilen, klinik, radyolojik ve biyokimyasal olarak hipotiroidik olan tüm hastalar çalışmaya dahil edildi. Multinodüler guatr, ötiroid ve hipertiroidli hastalar çalışmaya dahil edilmedi.

Bulgular: Neoplastik hipoaktif soliter tiroid nodüllerinin teşhisi için yapılan ince iğne aspirasyon sitolojisinin sensitivite, spesifite, doğruluk oranı, yalancı pozitiflik, yalancı negatiflik, pozitif kestirim değeri ve negatif kestirim değeri sırasıyla 80,7 %, 88,8 %, 85,4 %, 11,1%, 19,2 %, 80,7 %, ve 88,8 % idi. Sekiz hastada tespit edilen en sık malignite tiroidin papiller karsinomu idi.

Sonuç: İnce iğne aspirasyon sitolojisi tiroid kanserlerinin teşhisinde basit, kolay yapılan, etkili ve kolay tekrarlanan bir yöntemdir. İnce iğne aspirasyon sitolojisi hipoaktif soliter tiroid nodüllerinin malignite açısından teşhis edilmesinde ilk olarak akla getirilmelidir.

Anahtar Kelimeler: *Hipoaktif soliter tiroid nodülü, İnce iğne aspirasyon sitolojisi, Histopatoloji.*

Nodular thyroid disease is considered to be a common clinical problem. But its diagnosis and management have remained controversial for more than two decades (1–5). Thyroid nodules are solid or complex (mixed solid and cystic in variable proportion) (5). Solitary thyroid nodule is defined clinically as localized thyroid enlargement with apparently normal morphology in the rest of the gland. Solitary thyroid nodule is a common entity. Majority of these nodules are benign. The main goal of evaluating these nodules is to identify nodules with malignant potential. A multitude of diagnostic tests like ultrasound, thyroid nuclear scan, and fine needle aspiration cytology (FNAC) is available to the clinician for evaluation of thyroid nodules. FNAC is the most accurate diagnostic test for differentiating benign from malignant thyroid nodules (3–7). FNAC is simple, cost effective, readily repeated, and quick to perform procedure in the outpatient department with excellent patient compliance. Important factor for the satisfactory test includes representative specimen from the nodule and an experienced cytologist to interpret findings. It is often used as the initial screening test for diagnosis of thyroid nodules (8). The prevalence of thyroid nodules ranges from 4% to10% in the general

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adult population and from 0.2% to 1.2% in children (9). The majority of clinically diagnosed thyroid nodules are nonneoplastic; only 5%–30% are malignant and require surgical intervention (10). FNAC is, however, not without limitations; accuracy is lower in suspicious cytology and in follicular neoplasms. The main aim of FNAC is to identify nodules that require surgery and those benign nodules that can be observed clinically and decrease the overall thyroidectomy rate in patients with benign diseases.

In this report we correlated the FNAC findings with histopathology of patients with hypoactive solitary thyroid nodule who underwent surgery.

MATERIALS AND METHODS

A comprehensive review of hospitalization records was performed that have assessed the sensitivity of FNA for detecting thyroid malignancy in hypoactive solitary thyroid nodules. This was a prospective study conducted on 62 consecutive patients between December 2001 and June 2008. All patients with clinically diagnosed solitary thyroid nodule who were clinically, radyologically and biochemically hypothyroid were included for study. Patients with multinodular goitre and who were euthyroid or hyperthyroid were excluded from the study. All patients were evaluated by thorough clinical examination followed by routine investigations including haemogram, renal function tests, liver function tests, chest X-ray, lateral neck X-ray, thyroid function tests and, FNAC. FNAC was performed with 23 gauge needle, smears were fixed with ether-95% alcohol solution, and staining was performed using May-Grünwald-Giemsa (*MGG)* staining. After FNAC, all the patients were subjected to surgery after preoperative preparation and anaesthesia checkup. Thyroid specimens were fixed with 10% neutral buffered formalin solution. After 48 hours, each nodule was totally or subtotally sampled (with at least ten sections comprehensive of capsule) and embedded in paraffin. Thyroidectomy specimen was evaluated by histopathological examination. Specimens were processed in automated tissue processing units and staining was performed with routine haematoxylin and eosin stain. Correlation of histopathological findings was performed with FNAC. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were calculated for neoplastic and carcinomatous lesions.

RESULTS

A total of 62 patients with hypoactive solitary thyroid nodule were identified: 3 (4,8%) were male and 59 (95,2%) were females. Age of the patients ranged from 24 to 67 years with mean age of 41,4 years. Characteristics of the patients were shown in Table 1. Thirty six (58%) patients were from plain areas and 26 (42%) were residents of hilly areas. Commonest presentation was neck swelling in 56 (90,3%) of the patients. FNAC results revealed 37 (59,6%) cases as benign lesions, 4 (6,4%) as hurthle cell tumours, 11 (17,7%) as follicular neoplasm, 2 (3,2%) as suspected of malignancy, and 8 (12,9%) cases as papillary carcinoma. Histopathological examination of excised specimens showed 34 (54,8%) cases as nodular hyperplasia, 10 (16,1%) as follicular adenoma, 2 (3,2%) as follicular carcinoma with capsular invasion, 10 (16,1%) as papillary carcinoma, 2 (3,2%) as hurthle cell adenoma, 2 (3,2%) as hurthle cell carcinoma with capsular invasion and, 2 (3,2%) as Hashimoto's thyroiditis. Comparison of FNAC with histopathological findings was performed. Thirty seven cases were diagnosed benign lesions by FNAC. Thirty two of these cases were nonneoplastic lesions, 2 as follicular adenoma, 1 as follicular carcinoma and 2 as papillary carcinoma in histopathological examination (Table 2). Twenty five cases were diagnosed as neoplastic lesions (hurthle cell tumours, follicular neoplasm, suspected malignancy, and papillary carcinoma) by FNAC. Two of these cases were nonneoplastic lesions, 10 were benign neoplastic lesions, 11 were carcinoma, and 2 cases of suspected malignancy were diagnosed as Hashimoto's thyroiditis on histopathological examination (Table 3). False positive and false negative results were shown in Table 4. Statistical analysis of neoplastic lesions (Table 5) showed sensitivity, specificity, accuracy, false positive rate, false negative rate, positive predictive value, and negative predictive value of FNAC to be 80,7%, 88,8%, 85,4%, 11,1%, 19,2%, 80,7%, and 88,8%, respectively. Whereas statistical analysis of carcinomatous lesions (Table 6) showed sensitivity, specificity, accuracy, false positive rate, false negative rate, positive predictive value, and negative predictive value of FNAC to be 78,5%, 95,8%, 91,9%, 4,16%, 21,4%, 78,5%, and 95,8%, respectively. A total of 14 cases of solitary thyroid nodules were diagnosed as malignant and the most common malignant lesion detected was papillary carcinoma, 10 out of 14 (71,4%).

Table 1. *Characteristics of the patients presented with clinically hypoactive solitary thyroid nodule.*

Characteristic	Total patients (*n* = 62)
Age (in years)	
20–29	2
30–39	28
40–49	25
50–59	4
60–69	3
Sex	
Male	3
Female	59
Demography	
Plains	36
Mountains	26
Presenting complaint	
Neck swelling	56
Neck pain	3
Neck discomfort	3
Site of swelling	
Right lobe	30
Left lobe	26
Isthmus	6

Table 2. *Nonneoplastic lesions diagnosed by FNAC and their comparison with histopathological diagnosis.*

FNAC report	Number of patients (*n* = 37)	Histopathological report	Number of patients (*n* = 37)	Remarks
Benign lesions	37	Nodular hyperplasia	32	True negative
		Follicular adenoma	2	False negative
		Follicular carcinoma	1	False negative
		Papillary carcinoma	2	False negative

Table 3. *Benign or suspicious neoplastic lesions diagnosed by FNAC and their comparison with histopathological diagnosis.*

FNAC report	Number of patients (*n* = 25)	Histopathological report	Number of patients (*n* = 25)	Remarks
Hurthle cell tumours	4	Hurthle cell adenoma	2	True positive
		Hurthle cell carcinoma	2	True positive
Follicular neoplasm	11	Follicular adenoma	8	True positive
		Follicular carcinoma	1	True positive
		Nodular hyperplasia	2	False positive
Suspected malignancy	2	Hashimoto thyroiditis	2	False positive
Papillary carcinoma	8	Papillary carcinoma	8	True positive

Table 4. *Summary of false positive and false negative results of FNAC.*

FNAC finding	Histopathology result
False positive	
Follicular neoplasm	Nodular hyperplasia
Suspected malignancy	Hashimoto's thyroiditis
False negative	
Benign lesions	Follicular adenoma
Benign lesions	Follicular carcinoma
Benign lesions	Papillary carcinoma

Table 5. *Statistical analysis for neoplastic lesions.*

Test being evaluated (FNAC)	Reference standard test (Histopathology)	
	Positive	Negative
Positive + suspicious	21	4
Negative	5	32

**Sensitivity= 80,7 %, Specificity= 88,8 %, Accuracy= 85,4 %, False positive result= 11,1 %, False negative result = 19,2 %, Positive predictive value= 80,7 %, Negative predictive value= 88,8 %.*

Table 6. *Statistical analysis for carcinomatous lesions.*

Test being evaluated (FNAC)	Reference standard test (Histopathology)	
	Positive	Negative
Positive + suspicious	11	2
Negative	3	46

**Sensitivity = 78,5 %, specificity = 95,8 %, accuracy = 91,9 %, false positive result = 4,16 %, false negative result = 21,4 %, positive predictive value = 78,5 %, and negative predictive value = 95,8 %.*

DISCUSSION

In present study, the age of patients ranged from 24 to 67 years with mean of 41,4 years. This age range and mean incidence is similarity as compared with previous studies (10–12). We found that majority of patients (45,1%) were in their third decade of life. This is in accordance with the study by Dorairajan and Jayashree (13). Fine needle aspiration cytology is a well-established technique for preoperative investigation of thyroid nodules. The technique is a noninvasive, cost-effective, and efficient method of differentiating benign and malignant thyroid nodules (14-16). Many investigators have shown that fine needle aspiration cytology is the single most sensitive, specific, and cost-effective method in the investigation of solitary thyroid nodules (17, 18). Thyroid nodules are usually benign (19–21). However, the presence of a thyroid nodule in a patient immediately raises the question of its malignancy. This has been estimated in 5–10%, independent of how many nodules are present in the gland, and of their size (less or more than 10 mm) (3-6, 22-24). FNAC and sensitive ultrasonography are the methods used to distinguish benign from malignant nodules, and in selecting patients for surgery (5, 7, 21-23). Solitary thyroid nodules were 4–9 times more common in females as compared to males (13, 25). Our study showed that solitary thyroid nodules were 6 times more common in females than males. The false negative rate was 19,2% in cases of neoplastic lesions. It constitutes a serious limitation of this technique since these malignant lesions would go untreated. The incidence of false negative results is as low as 1% to as high as 30% (26, 27). The false positive rate was 11,1% for neoplastic lesions but none of these lesions were malignant. Comparison of results of present study with various previous studies is shown in Table 7.

Table 7. *Comparison of results of present study with previous studies.*

Study	Number of patients	Sensitivity	Specificity	Accuracy	Negative predictive value	Positive predictive value	Year
Present series	62	80,7 %	88,8 %	85,4 %	88,8 %	80,7 %	2008
Kessler et al. (30)	170	79	98.5	87	76.6	98.7	2005
KO HM et al. (21)	207	78.4	98.2	84.4	66.3	99	2003
Bouvet et al. (25)	78	93.5	75	79.6	88.2	85.3	1992
Cusick et al. (29)	283	76	58	69	64	72	1990

The methods used for the calculation of sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were similar to previous studies (28, 29). Sensitivity and accuracy of FNAC for detection of neoplasm were 80% and 84%, respectively, whereas they were 76% and 69%, respectively, in a study by Cusick et al. (29).

In the present study 14 cases were found to be malignant on histopathological examination (10 papillary carcinoma, 2 follicular carcinoma and 2 hurthle cell carcinoma). It is to be stressed that all cases of papillary carcinoma diagnosed by FNAC were also papillary carcinoma on histopathological examination. This is in accordance with previous studies (13, 30). The incidence of malignancy in this study was 22,5% which is in accordance with study by Dorairajan and Jayashree (13). The incidence of malignancy can be as high as 43.6% (25).

The incidence of papillary carcinoma in the present study was 71,4%. In the literature, incidence of papillary carcinoma varies from 50% to 80% (13, 25, 31). Brooks et al. found that preoperative FNAC had no direct impact on the selection of the surgical procedure and intraoperative frozen section added very little to surgical management (32).

Analysis of data from seven series showed a false-negative rate of 1% to 11%, a false-positive rate of 1% to 8%, a sensitivity of 65% to 98%, and a specificity of 72% to 100% (23). The results are consistent with this study.

FNAC provides useful information and may be used along with other clinical information to decide best form of treatment in a hypoactive solitary thyroid nodule. The use of FNAC has reduced the number of patients with solitary thyroid nodules undergoing unnecessary surgery and has led to proper planning of surgery in malignant cases. I concluded that FNAC diagnosis of malignancy is highly significant and such patients should be subjected to surgery. A benign FNAC diagnosis should be viewed with caution as false negative results do occur and these patients should be followed up and any clinical suspicion of malignancy even in the presence of benign FNAC requires surgery.

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