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ASSOCIATION BETWEEN FINE NEEDLE ASPIRATION AND POSTOPERATIVE HISTOPATHOLOGY IN THYROID LESIONS OF JORDANIAN PATIENTS

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ABSTRACT

Background: Thyroid lesions are one of the most common issues that are encountered by a physician. Assessment of these lesions is collectively done with the aid of ultrasound, thyroid function tests, and cytology through FNA, which shows that up to 60% of the general population might be spotted with a thyroid lesion with an incidence of 20% to 25% of indeterminate significance and a malignancy rate of 5%, which is usually confirmed by the final histology report. Fine needle aspiration has false negative and false positive outcomes. Fine needle aspiration is the first-line confirmation investigation to assess thyroid lesions, aiming to diagnose benign lesions and decrease unnecessary operations. Fine needle aspiration is the sole main precise and cost-effective technique. **Goal:** To associate fine needle aspiration before surgery and histopathology after surgery in thyroid lesions. **Methods:** Our retrospective investigation included 247 patients with thyroid lesions, single or multiple, aged 20–80 yrs. and of both sexes, at King Hussein hospital, King Hussein medical city, Amman, Jordan, during the period Feb 2018–Feb 2022. Fine needle aspiration was used before surgery and was followed by histopathology after surgery. Confirmation classification of 247 thyroid lesions was done according to fine needle aspiration and histopathology. A correlation was done between fine needle aspiration before surgery and surgical specimen results after surgery, including confirmation of FNA results and malignancy rates. Fine needle aspiration results were based on the Bethesda System of the Royal College of Pathologists (RCPath) classification. In general, classification is divided into six categories: Bethesda category I (non-diagnostic), Bethesda category II (benign), Bethesda category III (Atypia of undetermined significance/Follicular lesion of undetermined significance; AUS/FLUS), Bethesda category IV (follicular neoplasm), Bethesda category V (suspicious for malignancy) and Bethesda category VI (malignant). The examined specimens were classified into Bethesda categories (III–VI). The examined FNA specimens included a minimum of an air-dried slide and an alcohol-fixed slide and were prepared using Papanicolaou and Romanowsky-type stains. Following fine needle aspiration, all patients were scheduled for surgery. The thyroidectomy specimen was assessed by histopathological examination. Surgical specimens were fixed in formalin, processed by automated tissue processors and stained using hematoxylin and eosin. **Results:** Fine needle aspiration showed that 80.97% (200/247) lesions were benign, and 19.03% (47/247) were malignant. In benign lesions, 31.6% (78/247) of patients were follicular. In malignant lesions, 19.03% (47/247) of patients had papillary carcinoma. Histopathology demonstrated that 64.8% (160/247) of lesions were benign, and 35.2% (87/247) were malignant. In benign lesions; 38.1% (94/247) of patients had a multinodular goiter. In malignant lesions, 25.9% (64/247) of patients had papillary carcinoma. Regarding men, there was a complete match of multinodular goiter (4) between fine needle aspiration and histopathology. Regarding women, there was complete matching of multinodular goiter (6) and papillary carcinoma (34) between fine needle aspiration and histopathology. **Conclusions:** Fine needle aspiration is a safe and cost-effective investigation for thyroid lesions, but histopathology is diagnostic.

KEYWORDS: Thyroid lesions; Fine needle aspiration; Histopathology.

INTRODUCTION

Thyroid disorders are the most frequent endocrine conditions according to ultrasonography, computed tomography, thyroid function tests, and fine needle aspiration.[1] None of these are exact. Fine needle aspiration was the sole best screening investigation because it distinguishes between benign and malignant lesions. Fine needle aspiration of thyroid lesions is safe and precise with a sensitivity of 65–98%, a specificity of

72–100%, a false positive of 1–8%, and a false negative of 1–11%.[2]

There are some disadvantages to fine needle aspiration, such as improper sampling and inter-examiner differences. Histopathology is the cornerstone of confirmation. The typical nuclear aspect of malignancy is easily distinguished from benign follicular epithelium with variable colloid. The frozen section might decrease radical operations. They might help plan lymph node dissections in the case of occult lesions.

Thyroid lesions are one of the most common issues that are encountered by a physician. Assessment of these lesions is collectively done with the aid of ultrasound, thyroid function tests, and cytology through FNA, which showed that up to 60% of the general population might be spotted with a thyroid lesion with an incidence of 20% to 25% of indeterminate significance (Thy 3a and Thy 3f), not possible to distinguish between benign, malignant, or doubtful lesions, and a malignancy rate of 5%[3] which is usually confirmed by the final histology report. For some of these indeterminate lesions, confirmation removal of the affected lobe is indicated with potential progression to completion thyroidectomy following histopathology with some benign lesions as Thy3 or Thy4 being over treated with hemithyroidectomy or a high false-negative rate with Thy2 cytology might cause missed cancers and progression. Fine needle aspiration has false negative and false positive outcomes. Fine needle aspiration is the first-line confirmation investigation to assess of thyroid lesions, aiming to diagnose benign lesions and decrease unnecessary operations. Fine needle aspiration is the sole main precise and cost-effective technique.

The goal of our investigation was to associate fine needle aspiration before surgery and histopathology after surgery in thyroid lesions.

METHODS

Our retrospective investigation enrolled 247 euthyroid patients, aged 20–80 years., of both genders and with thyroid lesions, single or multiple, at King Hussein hospital, King Hussein Medical City, Amman, Jordan, during the period Feb 2018–Feb 2022, after obtaining approval from our local ethical and research board review committee of the Jordanian Royal Medical Services. Patients with a history of head and neck irradiation, obstructive features, and toxic goiter were ruled out.

Evaluation investigations before surgery included fine needle aspiration, ultrasound, CT scan, and thyroid function tests (T3/T4/TSH/FT3/FT4) with an association between fine needle aspiration before surgery and histopathology after surgery. Correlations were done between fine needle aspiration before surgery and surgical specimen results after surgery, including confirmation of FNA results and malignancy rates. Fine needle aspiration results were based on the Bethesda System of Royal College of Pathologists (RCPath) classification. In general, classification is divided into six categories: Bethesda category I (non-diagnostic); Bethesda category II (benign); Bethesda category III (Atypia of undetermined significance/Follicular lesion of undetermined significance; AUS/FLUS); Bethesda category IV (follicular neoplasm); Bethesda category V (suspicious for malignancy); and Bethesda category VI (malignant). The examined specimens were classified into Bethesda categories (III-VI). The examined FNA specimens included a minimum of an air-dried slide and an alcohol-fixed slide and were prepared using Papanicolaou and Romanowsky-type stains. Following fine needle aspiration, all patients were scheduled for surgery. The thyroidectomy specimen was assessed by histopathological examination. Surgical specimens were fixed in formalin, processed by automated tissue processors and stained using hematoxylin and eosin.

The grading system had six confirmation categories, as it divided the possible neoplasm category (Thy3) into Thy3a (neoplasm possible-atypia/non-diagnostic) and Thy3f (neoplasm possible, suggestive of follicular neoplasm). Thyroid cysts were subcategorized within the Thy1 and Thy2 grades as Thy1c and Thy2c, respectively. The RCPath system is similar to the six Bethesda Systems for Reporting Thyroid Cytopathology.[4] If a patient had a pathological aspirate from more than one nodule, the most pathological result was used for the study. Fine needle aspiration was done using a 23-gauge needle, and smears were fixed with ether-95% alcohol solution.

RESULTS

The thyroid lesions were more frequent in women than in men (70.4[174/247] % and 29.6% [73/247], respectively). In our investigation, one patient was less than 20 years old (0.4% [1/247]), 6.5%(16/247) of patients were in the 20–30 year age group, 18.2%(45/247) of patients were in the 31–40 year age group, 22.7%(56/247) of patients were in the 41–50 year age group, 26.3%(65/247) of patients were in the 51–60 year age group, 14.97%(37/247) of patients were in the 61–70 year age group, 10.1%(25/247) of patients were in the 71–80 year age group, and two patients were over the age of 80 years (0.8% [2/247]). Table I. Women with thyroid lesions were more in all age groups than men. Any thyroid lesion of 0.5 to 1.0 cm can be palpated. In this investigation, the size of the least thyroid lesion was 10×9 mm, and the size of the biggest lesion was 9×7 cm.

Benign fine needle aspirations were in 80.97% of patients, and malignant fine needle aspirations were in 19.03% of patients. In benign lesions, 31.6% (78/247) of patients were follicular. In malignant lesions, 19.03% (47/247) of patients were papillary carcinoma. Table II. According to histopathology, 64.8% of lesions were benign, and 35.2% of lesions were malignant. In benign lesions, 38.1% (94/247) of patients had a multinodular

goiter. In malignant lesions, 25.9% (64/247) of patients had papillary carcinoma. Table III. The most frequent malignant type in fine needle aspiration and histopathology was papillary carcinoma. Regarding men, there was a complete match of multinodular goiter (4) between fine needle aspiration and histopathology. Table IV. Regarding women, there was a complete match of multinodular goiter (6) and papillary carcinoma (34) between fine needle aspiration and histopathology. Table V. All patients were exposed to different surgical procedures. A total of 113 had total thyroidectomy, 100 had hemithyroidectomy, 30 had completed thyroidectomy, and four had thyroidectomy with neck dissection. Based on histopathology, 87 thyroid cancer and 160 benign thyroid lesions were identified. 27/73 males with thyroid cancers were younger than 45 yrs. old (11/27) and more than 45 years old (16/27), 60/174 females with thyroid cancers were younger than 45 years old (20/60) and more than 45 years old (40/60).

Table I: Patients demographics.

Age group(yrs.)	Men (no,%)	Women (no,%)	Overall (no,%)
<20	--	1; 0.4	1; 0.4
20–30	4; 1.6	12; 4.9	16; 6.5
31–40	7; 2.8	38; 15.4	45; 18.2
41–50	12; 4.9	44; 17.8	56; 22.7
51–60	29; 11.7	36; 14.6	65; 26.3
61–70	7; 2.8	30; 12.1	37; 14.97
71–80	12; 4.9	13; 5.3	25; 10.1
>80	2; 0.8	--	2; 0.8
Overall(no,%)	73; 29.6	174; 70.4	247

Table II: Fine needle aspiration.

Males				**Females**			
Benign	**No.**	**Malignant**	**No.**	**Benign**	**No.**	**Malignant**	**No.**
Follicular lesion	**16**	**Papillary carcinoma**	**13**	**Follicular lesion**	**62**	**Papillary carcinoma**	**34**
Atypia with unknown significance	10			Atypia with unknown significance	13		
Colloid lesion	14			Colloid lesion	18		
Hurthle lesion	5			Hurthle lesion	19		
Multinodular goiter	4			Multinodular goiter	6		
Others	11			Others	22		
Overall	60		13	Overall	140		34
Overall	73				174		
Overall	247						

Table III: Histopathology.

Males				**Females**			
Benign	**No.**	**Malignant**	**No.**	**Benign**	**No.**	**Malignant**	**No.**
Multinodular goiter	34	Papillary carcinoma	12	Multinodular goiter	60	Papillary carcinoma	52
Benign tissue	9	Follicular carcinoma	11	Benign tissue	28	Follicular carcinoma	6
Thyroiditis	3	Medullary cancer	1	Hurthle adenoma	7	Hurthle carcinoma	2
		Hurthle cancer	2	Follicular adenoma	1		
		Anaplastic cancer	1	Thyroiditis	18		
Overall	46		27		114		60
Overall	73				174		
Overall	247						

Table IV. Matching between fine needle aspiration and histopathology in 73 men.

FNA		Histopathology	
Lesion	**No.**	**Lesion**	**No.**
Atypia with unknown significance	10	Papillary carcinoma	1
		Follicular carcinoma	3
		Multinodular goiter	4
		Benign tissue	2
Colloid	14	Papillary carcinoma	1
		Multinodular goiter	13
Follicular	16	Papillary carcinoma	1
		Follicular carcinoma	7
		Medullary cancer	1
		Multinodular goiter	7
Hurthle	5	Hurthle cell cancer	2
		Multinodular goiter	3
Multinodular goiter	4	Multinodular goiter	4
Papillary carcinoma	13	Papillary carcinoma	9
		Follicular carcinoma	1
		Multinodular goiter	3
Others	11	Anaplastic cancer	1
		Benign tissue	7
		Thyroiditis	3

Table V: Matching between fine needle aspiration and histopathology in 174 women.

FNA		Histopathology	
Lesion	**No.**	**Lesion**	**No.**
Atypia with unknown significance	13	Papillary carcinoma	3
		Follicular carcinoma	4
		Multinodular goiter	6
Colloid	18	Papillary carcinoma	2
		Multinodular goiter	16
Follicular	62	Papillary carcinoma	9
		Follicular carcinoma	2
		Hurthle cell carcinoma	2
		Multinodular goiter	21
		Benign tissue	28
Hurthle cells	19	Hurthle cell adenoma	7
		Follicular adenoma	1
		Multinodular goiter	11
Multinodular goiter	6	Multinodular goiter	6
Papillary carcinoma	34	Papillary carcinoma	34
Others	22	Papillary carcinoma	4
		Thyroiditis	18

DISCUSSION

In this investigation, the thyroid lesions were more frequent in women than in men (70.4% and 29.6%, respectively), which is comparable, to Shenbagavalli S. (2019) (85% and 15% in females and males, respectively)[5] and Kamal M. (2002) (86.5% in females).[6] There were patients confirmed as having colloid goiter in fine needle aspiration and who appeared to have other diagnoses on histopathology.[7] In Shenbagavalli S., the mismatch was 3.84% of patients disconfirmed as a colloid in fine needle aspiration when confirmed as a follicular adenoma in histopathology. The mismatch was 1.92% of patients disconfirmed as a colloid in fine needle aspiration when confirmed as papillary carcinoma on histopathology[5], and two patients were disconfirmed as a colloid in fine needle aspiration when found malignant on histopathology.[5]

Fine needle aspiration has a relatively increased rate of inadequate samples, requiring repetition and the inability to differentiate between benign and malignant lesions sometimes. False-positive confirmation of malignancy may lead to unimportant thyroid surgery with a 2%–10% risk of long-term morbidity after surgery. The RCPath-Thy grading system enhanced clarity for patient management and attained the anticipated risk of malignancy. Inadequate sample preparation, mostly from cystic lesions, is a factors in increased rates of non-

diagnostic aspirates. Cystic modifications and degenerative processes in thyroid lesions may lead to florid atypia with the potential for false-negative and malignancy in 14%–17% of Thy1c and 4%–33% of Thy2c lesions. Fine needle aspiration must be repeated for all Thy1 and Thy2 with doubtful clinical or ultrasonographical outcomes.

Fine-needle aspiration biopsy is important for the assessment of single thyroid lesions but less efficient for multinodular thyroid glands. A false-negative outcome rarely occurs if the aspect of cancer in a multinodular goiter is missed but occurs in multinodularity of the thyroid gland when fine needle aspiration is done on a benign nodule and malignancy is found after surgery in another nodule. It is possible to plan the extent of surgery and further treatment based on the results of this evaluation. The most important data point of fine needle aspiration is whether a nodule has a neoplastic pattern. A thyroid lesion with anteroposterior diameter greater than its transverse one is more likely to be malignant than benign. Thyroid lesions with microcalcifications are more correlated with malignancy than those with coarse or no calcifications. Central vascularity is pathognomonic of malignancy, but peripheral vascularity is correlated with benign lesions. The rate of spotting of incidental thyroid carcinoma postoperatively in benign multinodular goiter is 3–16.6%. Of the total cases, 33% of thyroidectomies for multinodular goiter needed a further operation. Thyroid cancer is usually seen in a euthyroid patient, but features of hyperthyroidism or hypothyroidism can be correlated with a metastatic well-differentiated tumor. Thyroid lesions are important if found in people younger than 20 years. The traditional cytologic confirmations are benign (negative), suspicious (indeterminate), malignant (positive), or unsatisfactory (nondiagnostic). The new Bethesda has six.

The sensitivity of Islam was 76.68%, and that of Sreeramulu was 74%. The specificity was in Sreeramulu and Sengupta at 100% and 97.26%, respectively.[7,8–9] The malignant to benign ratio of this investigation was 1:1.8, which is not comparable to Sengupta (1:5.5), Sreeramulu (1:6.1), and Safirullah (1:7.6).[7,9–10] In our investigation, there was a discrepancy between fine needle aspiration and the histopathology of thyroid lesions. Although fine needle aspiration is less accurate than histopathology, it is fast and easy to achieve and could exclude the requirement for extensive and risky operations.

Confirmation of hemithyroidectomy for Thy4 lesions is according to the RCPath protocol, noting a 30%–35% possibility of benign disease and excluding the potential long-term morbidity of total thyroidectomy. In centers with a malignancy rate of more than 90% for Thy4, total thyroidectomy is indicated in patients with larger lesions (more than 4 cm) to exclude a second completion hemithyroidectomy. Malignancy is always histologically confirmed in Thy5, explaining the standard practice of therapeutic hemi- or total thyroidectomy with central compartment neck dissection.[11]

The limitations of this investigation include a heterogeneous population. As ours was retrospective, it was difficult to make sure that a histologically confirmed malignant lesion was the same one aspirated for FNA before surgery. There are multiple factors, such as discrepancies in thyroid cancer prevalence, differences in lesion choice for aspiration, the skill of the aspirators, and the experience of the cytopathologists.

CONCLUSION

Fine needle aspiration of the thyroid is crucial in the primary assessment of a thyroid lesion. Lesions doubtful of malignancy before surgery must be sent to the histopathologist as frozen histology. Histopathology is the cornerstone for the assessment of any lesion prognosis, radioiodine management, and follow-up.

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