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Evaluation of thyroid histologic changes
following fine needle aspiration

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Author:

Dr. Mehrangiz Ghafari

Supervisor:

Dr. Noushin Afshar Moghaddam
(assistant professor)

Dr. Diana Taheri
(assistant professor)

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Abstract

Title: Evaluation of thyroid histologic changes following fine needle aspiration.

Introduction: Due to the introduction of fine needle aspiration (FNA) cytology to the routine clinical preoperative examination surgical pathologists are faced with thyroid gland specimens with FNA-induced secondary changes. These changes can cause diagnostic difficulties and be a source of incorrect diagnosis. This study investigates worrisome histologic alterations following FNA of thyroid (WHAFFT).

Methods: This study was performed on the samples of thyroid resection over a 2- year period. 142 cases in two groups one with history of previous FNA and another without FNA were selected. The histologic sections of these cases were studied for WHAFFT lesions.

Results: WHAFFT lesions were present in 40.8% of cases with history of previous FNA. Acute lesions were seen in 22 and chronic in 36 cases. The common lesions were hemorrhage and fibrosis. Atypical changes, like nuclear atypia, vascular changes, capsular pseudoinvasion and metaplasia were present in 28 (48.2%) of cases. In the control worrisome histologic changes were seen in 4.2%.

Conclusion: Considering the large number of FNA and reduction in the number of thyroid excisions, the advantages of FNA are manifold as compared to few diagnostic problems. Misdiagnosis can be avoided with awareness of WHAFFT lesions.

Key words: thyroid neoplasms, thyroid diseases, Fine needle aspiration, worrisome histologic alterations following FNA of thyroid.

Introduction

Of all endocrine gland diseases, those of the thyroid gland are the most common (1). About 40-50% of thyroids removed of autopsy contain nodules and less than 5% of them are malignant (2 - 4), therefore surgical excision of all thyroid nodules seems unreasonable.

Fine needle aspiration (FNA) cytology has emerged as a valuable, popular and routine investigation that differentiates between benign and malignant nodules, with minimal clinical complications (5). However a few cases of excised thyroid nodules have had changes suggestive of malignancy (1, 6-9). These are lesions produced by preoperative FNA. Livolsi and Merino applied the term *worrisome histologic alterations following FNA of thyroid (WHAFFT)* to these changes (1).

WHAFFT lesions include hemorrhage , granulation tissue , siderophages , necrosis , mitoses , granuloma , capsular distortion and pseudoinvasion , nuclear clearing and atypia , cyst formation , papillary degeneration and calcification (6).

Regarding the previous study on this subject a research by Pandit and Phulpagar, demonstrated 38.44% of these changes (6). Similar changes were also described following FNA of breast (10-12) and parotid (13-16).

These secondary changes can cause diagnostic difficulties and be a source of incorrect diagnosis. Capsular distortion and nuclear clearing can be misdiagnosed with follicular and papillary carcinoma(6-9) . Misdiagnosis can be avoided with awareness of WHAFFT losions.

The purpose of the present study was to determine the incidence of WHAFFT lesions in our materials and to investigate the various type of lesions.

Materials and methods:

This descriptive study was performed on the samples of thyroid resection at the hospitals affiliated with Isfahan university of medical sciences between 2002 and 2004.

Based on history of FNA, two groups with history of previous FNA and without FNA were selected. The number of cases in each group were 142 and the sampling method was simple non successive. At the beginning data consisting of age, sex, hormonal status and interval between FNA and surgery were noted from clinical history of patients. Gross examination of each specimen was done. Four random sections from the subcapsular area and one from the central portion were submitted for histopathologic examination. The paraffin sections of these cases were studied and the following changes were sought: acute (interval

between FNA and surgery ≤ 3 weeks) and chronic (interval between FNA and surgery >3 weeks).

In present study specimens including massive or multifocal tumoral lesions, Hashimoto's thyroiditis and graves' disease were excluded.

Results:

The study group comprised 142 cases in which thyroid resection was done. The age ranged from 10 to 76 years (average 40). There were 120 women (84.5%) and 22 men (15.4%). The interval between FNA and surgery was less than three weeks in 56 cases and more than three weeks in 86 cases.

WHAFFT lesions were seen in 58 cases (40.8%). In this group, the average age was 39.3 ± 10.71 . There were 49 women (84.4%) and 9 men (15.5%). Table 1 and 2 show acute and chronic WHAFFT lesions respectively.

Table 1. Acute WHAFFT lesions (22)

Lesions	No. of cases	%
Hemorrhage	20	34.4
Granulation tissue	11	18.9
Siderophage	9	15.5
Poorly formed granuloma	1	1.72
Capsular distortion	7	12.6
Necrosis & Infarction	6	10.3
Vascular changes		
-Thrombosis & recanalization	7	12.6
-Hemangioma- like area	1	1.72

Percentage was calculated from 58 cases of WHAFFT lesions

Table 2. Chronic WHAFFT lesions (36)

Lesions	No. of cases	%
Granulation tissue	10	17.2
Siderophage	32	55.1
Hemorrhage	6	10.3
Linear fibrosis	24	41.3
Necrosis & Infarction	13	13.7
Vascular changes	1	1.72
Capsular pseudoinvasion & rupture	9	15.5
Hürthle cell metaplasia	4	6.89
Calcification	5	8.62
Papillary formation	5	8.62
Mitoses	1	1.72

Percentage was calculated from 58 cases of WHAFFT lesions

The histologic examination revealed nodular goiter in 15(25.8%), adenoma in 16 (27.5%) and papillary carcinoma in 27(46.5%). In general, 43 cases (74.1%) were neoplastic and 15 cases (25.8%) non- neoplastic lesions. Atypical changes were seen in 28 cases (48.2%), of these changes, 11(7.7%) were acute and 17(11.9%) chronic. The correlations between the type of lesions and histologic diagnosis are shown in Table3.

Table 3. Correlations of Histologic Diagnosis and WHAFFT lesions.

WHAFFT lesions	No.	Nodular goiter	Follicular adenoma	Hürthle cell adenoma	Papillary carcioma
Hemorrhage	26	10	4	2	10
Granulation tissue	21	7	1	1	12
Siderophage	41	13	7	4	17
Linear fibrosis	24	7	3	1	13
Vascular changes	8	4	1	2	1
Necrosis& Infarction	11	4	2	2	3
Capsular distortion	7	1	2	2	2
Nuclear atypia	8	5	3	0	0
Capsular peseudoinvasion or rupture	9	0	6	3	0
Calcification	5	2	0	0	3
Metaplasia	4	2	2	0	0
Poorly formed granuloma	1	1	0	0	0
Mitoses	1	1	0	0	0

Discussion

Results of this study showed that in acute WHAFFT lesions, hemorrhage was the most common (34.4%), followed by *granulation* tissue (18.9%) and *siderophages* (15.5%). Hemorrhage can be differentiated from spontaneous hemorrhage by its linear arrangement, perpendicular to the center of the nodule(1), therefore they did not pose a problem to histopathologist. *Capsular distortion* and *thrombosis* were the next common lesions (both 12.6%). Capsular distortion an excessive thickening or thinning of the capsule and indicates the point of the needle puncture. Necrosis (infarction) was seen in 10.3% of cases. Traumatic venous thrombosis is considered a possible cause of infarction (17) (Figure 1). Poorly formed granuloma composed of siderophages was present in one case. It may be a reaction to colloid, which follows rupture of follicles (1), due to a direct effect of FNA trauma.

In chronic *WHAFFT* lesions *siderophages* was the most change (55.1%) , followed by *linear fibrosis* (41.3%). Linear fibrosis can be distinguished from reactive change in the goiter by its perpendicular arrangement to the center of the nodule (Figure 2).

Nuclear atypia was seen in 8 cases; of the 8, 7 revealed large cells with large hyperchromatic nuclei and prominent nucleoli. Clear nuclei

with a ground glass appearance were seen in one case (figure 3). All these cases were of colloid goiter and the nuclear changes were present only in the vicinity of the needle track. To differentiate the ground glass appearance from papillary carcinoma, clues are the WHAFFT lesions do not show nuclear grooves or overlapping and are seen focally only in the vicinity of the needle track. Unfortunately only in a few cases we can detect the needle track. Absence of a mass on gross examination of the specimen and review of preoperative FNA smears supported the diagnosis WHAFFT lesions (6). Review of preoperative FNA smears in the present case did not reveal intranuclear inclusions.

Necrosis was seen in 11 cases, necrotic areas are also seen in lymph nodes(18), breast (10), and salivary glands(14, 19). Infarction of the thyroid following FNA is seen commonly in neoplastic lesions. There are many case reports indicating infarction in neoplastic cases(20). This can be explained by the fact that vascular compromise occurs readily in neoplastic nodules rather than hyperplastic or colloid nodules (21). The infarction complicates the morphologic diagnosis due to extensive destruction of the lesion. Thus it is not possible to confirm the cytologic findings or establish the diagnosis (21). Hemangioma – like area was seen adjacent to capsular distortion in a case of follicular adenoma. Other

vascular changes in the form of angiosarcoma appearance, papillary endothelial hyperplasia were not seen in this study. (6, 8, 18, 22).

Capsular pseudoinvasion was present in 9 cases. This is a worrisome lesion. The points in favor of WHAFFT changes are: 1. linear pattern 2. association with hemorrhage and siderophages. 3. usually one focus only: and 4. never vascular invasion (1). Sometimes even plump, reactive endothelial cells from granulation tissue can be mistaken for invading lesional follicles.

Hürthle cell metaplasia was present in 4 cases. Squamous metaplasia was not observed. The metaplastic cells nest were seen at the periphery of an infarcted areas. Metaplasia associated with infarction has also been observed in salivary glands (13- 16) and breast (10-12) lesions. Its histologic significance is that may be misinterpreted as malignancy.

Calcification was present in 5 cases. In 4 it was seen amid a large area of fibrosis. The other case of a goiter revealed calcification in the media of a medium- sized blood vessel.

In the control group *worrisome histologic alterations* were seen in 6 (4.2%) cases; respectively: hürthle cell metaplasia (3 cases), nuclear atypia (2 cases) and papillary formation (1 case) In previous study by Pandit and Phulpagar these changes were not found in control group

However analogous changes have been seen in a goiter, and it may not be related to FNA.

The incidence of WHAFFT lesions in the present study is 40.8%. The reported incidences were 1.4% (23), 20.3% (7), 38.4% (6). The high incidence may be related to the technique of multiple passes and to the enthusiasm of our young physicians.

The most common changes were hemorrhage and fibrosis. As similar study *atypical worrisome lesions* were seen in a few cases, thus, with review of the Literature and in agreement with prior studies , we suggest the advantages of thyroid FNA are manifolds as compared to the few diagnostic problems of WHAFFT lesions.

We recommend using of syringe holder for reduction of incidence of WHAFFT changes.

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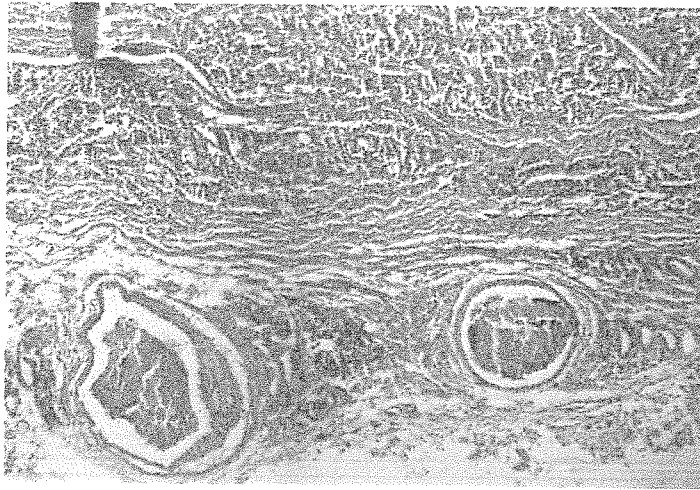


figure 1.photomicrograph of nodular goiter showing traumatic venous thrombus (H&E , X200)

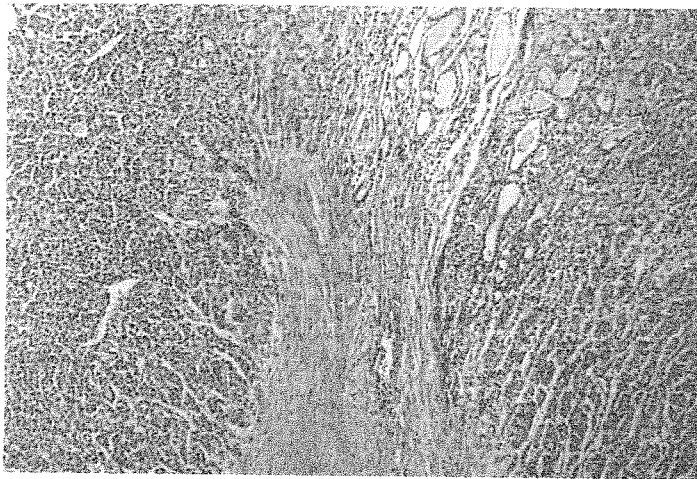


figure 2.photomicrograph of nodular goiter showing linear fibrosis (H&E , X40)

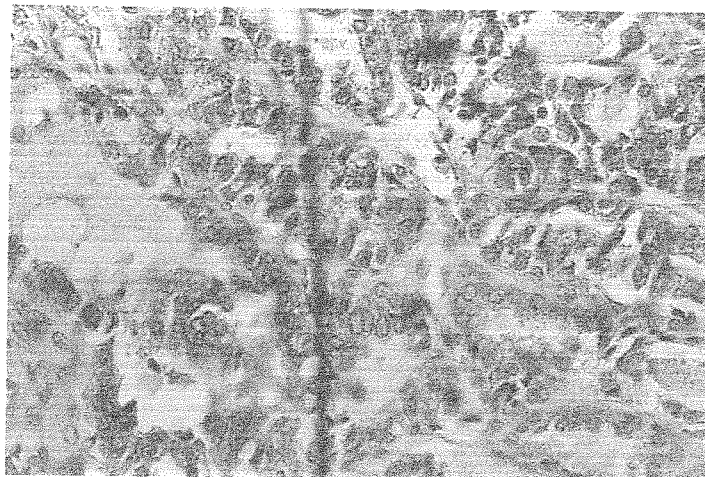


figure 3.photomicrograph of nodular goiter showing large and clear nuclei (H&E , X400)

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چکیده:

عنوان:

ارزیابی تغییرات هیستولوژیک تیروئید ناشی از آسپیراسیون سوزنی ظریف

مقدمه:

به دنبال معرفی آسپیراسیون سوزنی ظریف (FNA) به عنوان روش ارزیابی روتین در ندولهای تیروئید، با مواردی از تغییرات ثانویه به این روش، در نمونه های بعد از عمل جراحی مواجه می شویم. این تغییرات می توانند منجر به مشکلات تشخیصی و تشخیص های نادرست گردند. در این مطالعه تغییرات هیستولوژیک نگران کننده به دنبال FNA تیروئید (WHFFT) را بررسی خواهیم کرد.

روش ها:

این مطالعه توصیفی بر روی نمونه های جراحی تیروئید در مقطع زمانی سالهای ۱۳۸۱ تا ۱۳۸۳ در مراکز وابسته به دانشگاه علوم پزشکی اصفهان صورت گرفت. ۱۴۲ مورد برای هر گروه از افراد با سابقه و بدون سابقه FNA در نظر گرفته شد و برش های بافتی بیماران مذکور از لحاظ وجود تغییرات WHFFT ارزیابی شدند.

نتایج:

در گروه مورد (باسابقه مثبت FNA) تغییرات WHAFFT در ۸/۴۰٪ دیده شد. تغییرات حاد و مزمن به ترتیب در ۲۲ و ۳۶ مورد مشاهده گردید. شایعترین تغییرات، خونریزی و فیبروز بود. تغییرات آتیپیک شامل آتیپی هسته ای، تغییرات عروقی، تهاجم کاذب کپسول و متاپلازی در ۲۸ مورد (۲/۴۸٪) رویت گردید. در گروه کنترل (بدون سابقه FNA) تغییرات WHAFFT در ۲/۴۰٪ برآورد گردید.

بحث:

با توجه به استفاده زیاد از FNA و کاهش میزان اعمال جراحی تیروئید، مزایای FNA در مقایسه با مشکلات تشخیصی تغییرات WHAFFT چندین برابر است. با آگاهی از این تغییرات می توان از اشتباهات تشخیصی اجتناب نمود.

کلیدواژه ها:

تیروئید، آسپیراسیون سوزنی ظریف، تغییرات هیستولوژیک نگران کننده به دنبال FNA تیروئید.