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Original research article

Assessment of cytomorphological features of thyroid lesions through the utilization of many cytochemical staining techniques

Dr. Plabita C Mohan
Assistant Professor, Department of Pathology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India

Corresponding Author:
Dr. Plabita C Mohan

Abstract

Objectives and Background: In order to investigate the cytomorphological characteristics of thyroid lesions, a diverse range of cytological staining techniques will be employed. Both single thyroid nodules and multinodular goitres are similarly prevalent in non-cancer regions, and they possess a comparable likelihood of developing malignancy.
Methods: This study represents a prospective experimental investigation conducted at the Department of Pathology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India throughout the specified time frame of February 2009 to January 2010. After getting the requisite consent from the Institutional Ethical Committee, a total of 80 cases with sufficient aspirates were taken into consideration.
Results: This study used H&E, Pap, and Wright Giemsa stains to assess the cytomorphological characteristics of individual thyroid lesions. These three stains are commonly utilized in numerous cytology institutions. This study involved a sample of twenty-two individuals diagnosed with Hashimoto's thyroiditis.
Conclusion: In our perspective, the utilization of diverse fixation and staining techniques significantly enhances the process of diagnosing thyroid lesions. Therefore, in cases when a sufficient amount of tissue is accessible, the utilization of varied cytological staining techniques in fine aspiration cytology of thyroid lesions can effectively mitigate the occurrence of both false positive and false negative outcomes.
Keywords: Cytomorphological, thyroid lesions, cytochemical staining methods.

Introduction

Thyroid lesions are an often encountered clinical concern. The utilization of fine-needle aspiration (FNA) for cytologic investigation of thyroid lesions was first introduced by Martin and Ellis from the New York Memorial Hospital for Cancer and Associated Disorders in 1930. Currently employed globally, fine-needle aspiration (FNA) of the thyroid has demonstrated itself as the most economically efficient and reliable minimally invasive diagnostic method currently accessible [1].

The likelihood of cancer development in a single thyroid nodule is comparable to that in a multinodular goitre, and both conditions are similarly prevalent in locations where the disease is not endemic. The identification of a benign lesion prior to surgery is of utmost importance in order to mitigate the occurrence of unnecessary surgeries. The sensitivity of FNAC in detecting thyroid lesions can reach up to 93.4%, while its positive predictive value for malignancy is 98.6% and its specificity is 74.9%. Accurate detection of thyroid abnormalities is crucial as it directly influences the type of thyroidectomy performed on a patient [2-4].

FNAC involves two methods for staining samples: air-drying followed by staining with a Romanowsky stain such as May Grunwalds Gimsa (MGG), Jenner-Gimsa (JG), Wright's stain (WT), or Diff-Quik, or alcohol-fixation followed by staining with Papanicolaou (Pap) or hematoxylin and eosin (H&E). Both approaches have advantages and disadvantages [5]. Both procedures are beneficial as some attributes of cells, cell products, and stroma are more effectively demonstrated by one way than the other. Integrating the morphological characteristics of various stains is an effective method to enhance diagnostic accuracy. The combination of thyroid function testing, antibody profiling, and fine-needle aspiration (FNA) is mutually beneficial [6]. In recent years, thyroid cytological material has been analyzed using several immunocytochemical and molecular markers to improve the accuracy of diagnosis and guide treatment

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processes.

Materials and Methods

This study represents a prospective experimental investigation conducted at the Department of Pathology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India throughout the specified time frame of February 2009 to January 2010. After getting the requisite consent from the Institutional Ethical Committee, a total of 80 cases with sufficient aspirates were taken into consideration.

Inclusion criteria

Samples of fine needle aspirates from individuals with thyroid lesions were obtained from the cytology outpatient clinic of the Hospital.

Exclusion criteria

A patient who exhibits a lack of cooperation.
Insufficient data is accessible regarding FNA.

Results

Table 1: Distribution of lesions

Sr. No.	Lesion	Number of cases	Percentage of cases
1.	Hashimotos thyroiditis	24	34.2%
2.	Lymphocytic thyroiditis	5	7.14%
3.	Nodular colloid goiter	27	38.5%
4.	Nodular colloid goiter with cystic degeneration	11	15.71%
5.	Follicular neoplasm	6	8.5%
6.	Suspicious of papillary carcinoma of thyroid	2	2.8%
7.	Papillary carcinoma of thyroid	5	7.14%
	Total	80	100

Distribution of cases

There were a total of 80 instances identified, out of which 62 (77.1%) were classified as Bethesda group II, indicating benign lesions. There were 24 patients diagnosed with Hashimoto's throiditis, 6 patients diagnosed with lymphocytic thyroiditis, 27 patients diagnosed with nodular colloid goitre, 6 patients diagnosed with category IV (Follicular neoplasm), 2 patients diagnosed with category V (suspicious for malignancy) - suspicious for papillary carcinoma of thyroid, and 5 patients diagnosed with category VI (Malignant). All four patients had papillary carcinoma of thyroid, with one of them being the Hurthle cell variant. Excluded were cases that were classified as Bethesda category I (Non-diagnostic or Unsatisfactory). No examples in the current investigation were identified to exhibit Atypia of Uncertain Importance or Follicular Lesion of Uncertain Significance.

Histopathological correlation

Table 2: Histopathological correlation

Sr. No.	Lesion	Total no. of cases	Cases with histopathological correlation
1.	Hashimotos thyroiditis	24	4
2.	Lymphocytic thyroiditis	6	2
3.	Nodular colloid goiter	27	6
4.	Nodular colloid goiter with cystic degeneration	11	4
5.	Follicular neoplasm	6	3
6.	Papillary carcinoma of thyroid	6	2

Out of the 80 examples examined in this analysis, only one had a histologic association. Histopathological correlation was observed in three cases of Hashimoto's thyroiditis, one case of lymphocytic thyroiditis, five cases of nodular colloid goitre, three cases of nodular colloid goitre with cystic degeneration, two cases of follicular neoplasm, and one case of papillary carcinoma of the thyroid. Histological findings were consistent with cytological diagnosis in 22 of the instances. The diagnosis of follicular carcinoma was confirmed through histopathology in three patients who were initially

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diagnosed with follicular neoplasm. Thyroid lesions observed by the utilization of H&E, Pap, and Wright Giemsa stains exhibit distinct cytomorphological characteristics.

Hashimoto's Thyroiditis / Lymphocytic Thyroiditis

Wright Giemsa stain

A substantial augmentation in cellular dimensions was observed. Hurthle cells had diminutive nuclei and possessed delicate granular amphophilic cytoplasm. The cells were positioned either centrally within the cell or slightly peripherally. The cytoplasm of follicular cells exhibited a whitish appearance and lacked clear demarcation, while the nuclei displayed a tiny and spherical shape, characterized by densely packed chromatin. The populations of lymphocytes and plasma cells exhibit a significant degree of heterogeneity.

Papanicolou stain

The smears were observed to contain Hurthle cells, which exhibited distinct features including a nucleus situated either centrally or eccentrically, thin chromatin, a substantial amount of deep eosinophilic cytoplasm, and notable anisokaryosis. Pap staining detected intranuclear inclusions in three samples. The characterization of the nuclei, cytoplasm, and nucleoli of follicular cells was found to be lacking. The background was infiltrated by lymphocytes.

Hematoxylin and eosin stain

The H&E-stained slides exhibited a significant presence of eosinophilic cytoplasm, evident anisokaryosis, and a densely packed nucleus located either centrally or peripherally. The cytoplasm of follicular cells had a lack of distinct demarcation, while the nuclei displayed a diminutive and spherical shape, characterized by densely arranged chromatin. The background was infiltrated by lymphocytes. The cytoplasmic granularity of Hurthle cells and the polymorphous population of lymphocytes and plasma cells were observed using the Wright Giemsa stain. By employing Pap stain, we successfully observed the presence of anisokaryosis in Hurthle cells. Pap staining detected intranuclear inclusions in three samples.

The nuclei of stripped follicular cells resemble those of lymphocytes, which makes it difficult to distinguish between different diagnoses. The nuclei of follicular cells exhibit a more homogeneous distribution of chromatin and a more compact nuclear rim compared to lymphocytes, which possess a more pronounced basophilic cytoplasmic fringe. The lymphocytes in Romanowsky stained smears exhibited greater visibility compared to the nuclei of the naked follicular cells.

In order to distinguish between Hurthle cell neoplasm and Hurthle cells in Hashimoto's thyroiditis, it is imperative to possess a comprehensive comprehension of the cytological attributes associated with these two disorders. Patients with thyroiditis exhibited the presence of sizable, atypical, pleomorphic oncocytes. However, the cellular composition of a Hurthle cell neoplasm typically exhibits uniformity. The utilization of the Papanicolou stain, which is subsequently fixed with alcohol, facilitated the clear visualization of anisokaryosis.

Wright Giemsa stain

The cytoplasm of follicular cells exhibited a white appearance and lacked clear demarcation, while the nuclei displayed a spherical shape with exposed chromatin. The colloid exhibited a bluish violet coloration as observed using Wright Giemsa staining. The thick colloid exhibited evident indications of breaking. Additionally, the utilization of Wright Giemsa staining on air-dried smears facilitated the identification of the delicate colloid. In a patient with pre-existing hyperthyroidism, the presence of paravacuolar granules was detected in a case of nodular colloid goitre.

Papanicolou stain

The thyroid follicular cells exhibited nuclei of comparable size to that of a red blood cell, accompanied by a minimal presence of cytoplasm. The colloid exhibits a range of colors, varying from a faint greenish blue to shades of pink and orange, which are determined by its thickness. Follicular cells exhibited anisokaryosis.

Hematoxylin and eosin stain

The thyroid follicular cells displayed a minimal amount of cytoplasm and nuclei that were characterized by their spherical shape and rich chromatin content. The H&E-stained smears exhibited a colloid-like appearance resembling eosinophilic material. The anisocortic nature of follicular cells was demonstrated. The cytologic characteristics of diffuse and nodular goitres exhibited a high degree of similarity. Serum may be mistaken for colloid, particularly in cases of Pap stains, where aspirates exhibit a high degree of bloodiness. The issue was resolved by employing Romanowsky stains, such as Wright Giemsa / MGG, to visually detect thin colloid as a watery blue on air-dried smears. Clear evidence of anisokaryosis was observed in both the Pap test and the H&E staining.

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Nodular colloid goiter with cystic degeneration

Wright Giemsa stain

The smears were stained with Wright Giemsa, which showed that macrophages of cysts had dark grey cytoplasm. On the other hand, follicular cells exhibited pale, poorly defined cytoplasm and a spherical nucleus with compacted chromatin.

Papanicolou stain

Macrophages and benign follicular cells were observed to be suspended within a fluid or colloid milieu. Follicular cells exhibited anisokaryosis.

Hematoxylin and eosin stain

The colloid exhibited a clustering of follicular cells in both microfollicles and macrofollicles, accompanied by the presence of cyst macrophages. The anisocortic nature of follicular cells was demonstrated. Cystic macrophages with vacuolated cytoplasm were observed in the H&E stained smears. The smears that were stained with H&E demonstrated the presence of macrophages containing hemosiderin in a single patient.

Clear evidence of anisokaryosis was observed in both the Pap and H&E stained smears. Through the utilization of Pap stain, it was observed that cyst macrophages exhibited the engulfment of colloid within their cytoplasm. The determination of the age of cystic degeneration is facilitated by this.

Follicular Neoplasm

Wright Giemsa stain: The microfollicular architecture of thyroid follicular cells was seen to be quite intact in Wright Giemsa stained smears, exhibiting nuclear crowding and overlapping in certain regions. The delineation of cytoplasmic borders in follicular cells was seen to be pale and lacking clarity. The size of the nuclei is greater, exhibiting irregular shapes that vary from circular to oval, and containing chromatin that is coarse and granular in nature.

Papanicolou stain

The hypercellular aspirate exhibits a notable presence of microfollicular architecture and three-dimensional clusters. Follicular cells typically exhibited a sleek, round nucleus and a light, indistinct cytoplasm. Bleeding without any clumping substance in the background.

Hematoxylin and eosin stain

The H&E-stained smears exhibited recurring microfollicular patterns and three-dimensional clusters characterized by a uniform cell population, indicating the presence of hemorrhage.

Distinguishing microfollicular focal nodular goitre from follicular neoplasm can provide a challenge. The quantity of colloid in the background is a critical determinant for distinguishing them. The presence of colloid was minimal in follicular neoplasms, while nodular goitres had a high concentration of the substance. The presence of much blood in smears facilitated the detection of follicular neoplasms due to their high vascularity. Furthermore, anisokaryosis is a notable characteristic that distinguishes it from others. The presence of an aberrant chromosome has been associated with nodular goitre, thyroiditis, and other non-neoplastic disorders of the thyroid. The wet fixed Pap stained smears exhibited indications of anisokaryosis, even at a mild level.

Papillary Carcinoma of Thyroid

Wright Giemsa stain

In Wright Giemsa stained smears, the thyroid follicular cells were organized into papillary clusters and monolayered groups, with unusually large nuclei and cytoplasms. The presence of cytoplasmic inclusions within the nucleus of the cells was observed.

Papanicolou stain

The papillary architecture of Pap-stained smears is remarkably well-preserved. Demonstrating the presence of densely packed, overlapping nuclei, and abundant intranuclear cytoplasmic inclusions and grooves was straightforward. The utilization of Pap stained smears is highly advantageous in the examination of follicular cells, characterized by their thin granular chromatin (powdery chromatin) and diminutive, indistinct nucleoli.

Hematoxylin and eosin stain: The presence of papillary clusters consisting of follicular cells exhibiting minute granular chromatin was observed.

Other potential diagnoses to examine include hyalinizing trabecular tumor and papillary hyperplasia in other thyroid tumors. Diagnostic problems arise in cases of cystic transformation, lymphocyte infiltrate in papillary carcinoma, and the follicular type of prostate cancer, which in turn elevate the likelihood of erroneous positive or negative diagnoses. In instances of this nature, the utilization of wet fixed Pap

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stained smears facilitates a comprehensive analysis of nuclear attributes such as powdery chromatin, intranuclear cytoplasmic inclusions, and nuclear grooves, hence contributing to the enhancement of diagnostic precision.

Discussion

Aspiration using a superfine needle Thyroid lesion cytology is widely employed in contemporary practice because to its low-risk and cost-effective nature as an outpatient treatment. The interpretation of FNAC smears is significantly influenced by two essential parameters: sampling quality and staining quality. The expertise of a pathologist plays a significant role in determining the quality of a sample, whereas the quality of a stain is contingent upon the specific type of stain and the technique employed for its application. The selection of an appropriate stain for FNAC is the initial stage in achieving reliable and optimal outcomes. The incidence of both false negative and false positive results might be influenced by the selection and quality of stains, as indicated by previous studies [7].

The cytomorphologic properties of individual thyroid lesions are examined in this study using H&E, Pap, and Wright Giemsa stains. These three stains are utilized by numerous cytology laboratories. This investigation includes a total of twenty-two patients diagnosed with Hashimoto's thyroiditis. Nguyen G-K *et al*. observed the presence of oncocytic transformation in follicular epithelial cells, which were observed in sheets on a Pap stained smear, alongside benign lymphoid cells [8].

According to Krafts K *et al*., Romanowsky-type stains typically exhibit a high level of granule detail, which becomes advantageous in the identification of neoplastic cell differentiation. Romanowsky-type stains have been found to be more efficacious than wet fixed preparations in the analysis of hematolymphoid neoplasms derived from body fluid specimens. Papanicolaou and hematoxylin and eosin stains have been found to present challenges in distinguishing or observing specific characteristics of hematolymphoid cells [9]. In Pap stained smears, Hurthle cells demonstrate significant anisonucleosis, and in rare instances, the nucleus may exhibit cytoplasmic inclusions. Hurthle cells in Romanowsky stained smears display polygonal, abundant granular cytoplasm, a somewhat eccentric nucleus, fine granular chromatin, and Anisokaryosis [9].

The preservation of cellular architecture is notably high in wet fixed smears that have been stained with H&E and Pap in the context of Hashimoto's thyroiditis. Hurthle cells with a substantial eosinophilic cytoplasm and a centrally located nucleus were found to be more readily distinguishable in Pap smears that were stained with Pap stain as opposed to H&E. The utilization of a Pap stain reveals the presence of distinct indications of anisokaryosis in Hurthle cells. Pap staining detected intranuclear inclusions in three samples [10].

The cells exhibited a small increase in size when observed on air-dried slides stained with Wright Giemsa. Hurthle cells possess several tiny granules within their cytoplasm. The Hurthle cell's cytoplasm had an amphophilic coloration. The utilization of the Wright Giemsa stain effectively demonstrates the diverse characteristics of both lymphocyte and plasma cell populations. The findings of Nguyen G-K *et al*. and Krafts K *et al*. [10] align with the current research.

The present study included a total of 25 individuals who were diagnosed with nodular colloid goitre. The literature describes a color change from cyanophilic to eosinophilic and orangish when colloid is coupled with blood. In PAP-stained smears, a thin colloid exhibits a pale green or orange coloration, accompanied by the presence of apparent cracking artifacts. The thick colloid is represented by clumpy masses of dark green or orange material [11].

According to Krafts, KP, *et al*., Romanowsky stains possess unique folding and breaking patterns that can be utilized for the identification of thin colloid. These patterns give the stain a visually striking appearance reminiscent of "crazy pavement" or "broken glass," accompanied by a red-violet hue. The blue violet color and hyaline texture of the colloid in May Grunwalds Giemsa (MGG)-stained smears are advantageous as they help differentiate it from fibrillary collagen and deep magenta-staining amyloid, as explained by Orell *et al*. [11].

The current study revealed that in smears stained with H&E, the colloid exhibited eosinophilic characteristics.

The colloid exhibited blue green, pink, and orange hues as observed on the Pap stained slides. In Wright Giemsa-stained smears, the colloid exhibited a bluish violet hue. The thick colloid exhibited evident indications of breaking. Additionally, the utilization of Wright Giemsa staining on air-dried smears facilitated the identification of the delicate colloid. According to Sidawy and Costa *et al*., the presence of paravacuolar granules, which are indicative of lysosomes containing hemosiderin or lipofuscin pigments, is commonly detected in fine needle aspirates of the thyroid. Our current analysis revealed the presence of paravacuolar granules in one case of nodular colloid goitre, suggesting that the patient had hyperthyroidism [12].

In the present study, we examined four distinct instances of follicular neoplasm. E.A. Sinna *et al*. reported a case of follicular neoplasm, where they saw acinar-like structures in pap stained smears. These structures were seen in abnormal follicular cells with a high N/C ratio and nuclear pleomorphism. According to Marluce Bibbo *et al*., smears of follicular neoplasm are characterized by cellular structures,

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with tissue fragments showing significant crowding and overlap. The delineation of cytoplasmic borders in follicular cells was seen to be pale and lacking clarity. The Romanowsky dyed smears exhibit nuclei that are bigger and spherical in shape [12].

In the current study, wet fixed smears stained with hematoxylin and eosin and Pap stains revealed the presence of hypercellular aspirates characterized by a well preserved cellular architecture. There is a prominent microfollicular structure with groups of cells arranged in three dimensions. The follicular cells exhibited a diverse array of nuclear atypia. The Wright Giemsa stained smears revealed that the thyroid follicular cells displayed a relatively intact microfollicular architecture, characterized by nuclear crowding and overlap in certain areas. The delineation of cytoplasmic borders in follicular cells was seen to be pale and lacking clarity. The size of the nuclei is greater, exhibiting irregular shapes that vary from circular to oval, and containing chromatin that is coarse and granular in nature [13]. This investigation encompassed a total of five cases with thyroid papillary cancer. The present study presents a case of papillary cancer, as documented by E.A. Sinna *et al*. Parameters such as ground glass chromatin, intranuclear cytoplasmic inclusions, and prominent clefts in the nuclei are observed in Pap smears. The current analysis demonstrates exceptional preservation of papillary architecture through the use of H&E and Pap stained smears. Nuclear crowding, overlapping, and intracytoplasmic nuclear inclusions can be easily observed using H&E and Pap stained smears. In a particular instance [13], the H&E stained smear exhibited the presence of nuclear grooves. The utilization of Pap stained smears is highly advantageous in the examination of follicular cells, characterized by their thin granular chromatin (powdery chromatin) and diminutive, indistinct nucleoli. The thyroid follicular cells, as shown in Wright Giemsa stained smears, exhibited distinct features including enlarged nuclei, irregular nuclear contour, fine granular chromatin, and expanded cytoplasms. The presence of cytoplasmic inclusions within the nucleus of the cells was observed.

Conclusion

Thorough examination of diffuse or nodular enlargement of the thyroid is necessary in order to exclude the possibility of neoplasia. Prior to pursuing more invasive procedures, it is crucial to exclude FNAC and other unnecessary surgeries. The diagnostic accuracy of FNAC for neoplasms and thyroiditis is consistently high, however there are variances observed among studies and different stains. Wright The utilization of Giemsa staining effectively demonstrates the cytoplasmic features seen in the present study, encompassing cytoplasmic granularity, paravacuolar granules, and thin colloid. Wet fixed smears stained with H&E and Pap stains provide the most effective means of observing the sharpness of cell borders and nuclear features, such as chromatin pattern and intranuclear inclusions. The Papanicolaou stain has been extensively utilized in the field of cytopathology because to its capacity to effectively emphasize nuclear features such as chromatin pattern, intranuclear inclusions, and cell size. Many laboratories employ hematoxylin and eosin stain as an alternative to Pap stain due to its ease of application and ability to generate more intricate pictures of cell nuclei.

It is posited that the utilization of many stains and diverse fixation procedures may enhance the diagnostic precision of thyroid lesions. In the context of fine aspiration cytology of thyroid lesions, various cytological staining techniques can be employed to minimize the occurrence of false positive and false negative outcomes, given the availability of sufficient tissue.

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None.

Conflict of interest

Nil.

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