3
Approach to Thyroid FNA Cytopathology: An Overview

In this book, we present a practical, algorithmic approach to the diagnosis of thyroid fine needle aspirations (FNAs) (Figure 3.1). This approach uses a combination of low-magnification assessment of cellular components, evaluation of cytoarchitectural patterns, and high-magnification scrutiny of nuclear features. This approach will also enable the placement of FNAs into diagnostic categories that have recently been developed from a National Cancer Institute (NCI) conference on thyroid FNA termed the Bethesda System for Reporting Thyroid Cytopathology (BSRTC).

Assess Adequacy

The first step in the evaluation of a thyroid FNA is a rapid, low-magnification review of all specimen slides to assess adequacy. The precise criteria for thyroid FNA adequacy have been frequently debated but not rigorously studied. Although experts agree that the presence of follicular epithelial cells is the critical feature for a specimen to be adequate, the number of required epithelial cells varies. The most stringent guidelines require ten groups of follicular cells, with at least 20 cells in each group. Other guidelines suggest a minimum of 5–6 groups of follicular cells, each group containing ten cells. Some experts suggest that

D.P. Clark and W.C. Faquin, *Thyroid Cytopathology*,
Essentials in Cytopathology 8, DOI 10.1007/978-1-4419-5954-6_3,

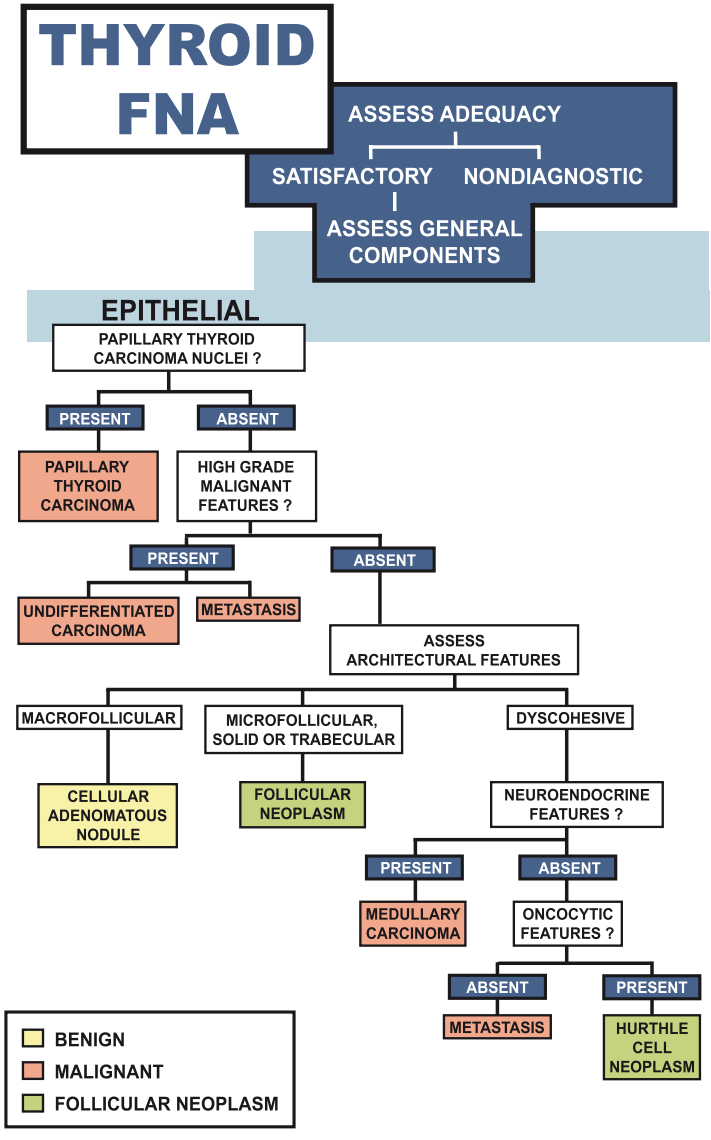

FIGURE 3.1. Algorithmic approach to thyroid fine needle aspiration (FNA) diagnosis.

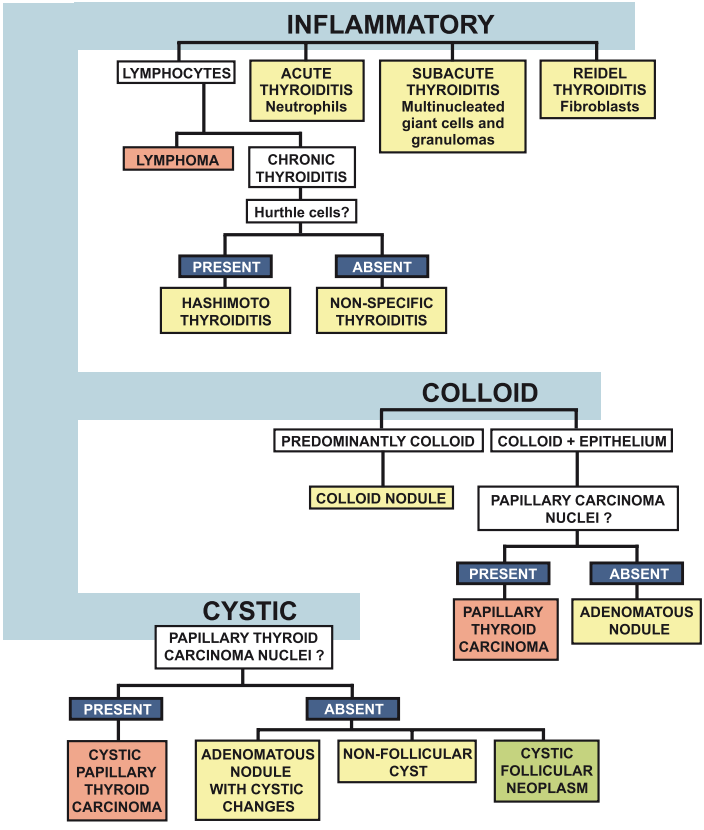

FIGURE 3.1. Continued

very large groups may be counted as multiple small groups of ten cells each. Another source also suggests a minimum of six groups, but indicates that they should be present on at least two of six passes. The BSRTC recommends a minimum of six groups of follicular cells each containing at least ten cells. Samples containing fewer than six groups of follicular cells, and minimal colloid, should be put into the nondiagnostic category. Cystic lesions that contain predominantly macrophages and cyst contents but an inadequate follicular component (less than six groups of follicular cells) should also be placed in the nondiagnostic category because of the risk of an occult papillary thyroid carcinoma (PTC) in these cystic lesions. Samples may also be considered inadequate due to obscuring blood, extensive air-drying artifact, or a thick smear with obscuring cellularity.

So how does one handle the specimen that contains fewer than six groups of follicular cells, each with ten cells, in the setting of abundant watery colloid? The guidelines of the Papanicolaou Society indicate that pathologists may report such specimens as "consistent with a benign colloid nodule," The BSRTC concurs with this and advises that such colloid-rich lesions be placed into the benign category and diagnosed as colloid nodules. Because of the clinical implications of placing a thyroid FNA into a benign category, the colloid in specimens with few follicular cells must be abundant and obvious on the slides. Scant colloid alone should not be considered sufficient for adequacy or placement in the benign category.

Guidelines for assessing thyroid FNA adequacy are as follows:

- A minimum of six groups of follicular cells, each containing ten cells.
- Specimens with abundant colloid but few follicular cells are considered benign colloid nodules.
- Specimens consisting of macrophages and cyst contents only are considered nondiagnostic.
- A nondiagnostic rate of greater than 20% may represent a technical procurement problem.
- Any sample containing atypical cells should not be considered nondiagnostic.

Assess General Components

Once the specimen is considered adequate, a low-magnification assessment of the components of the FNA should direct the cytotechnologist or pathologist to one of four major groups of the algorithm (1) colloid-predominant, (2) epithelium-predominant, (3) cystic, or (4) inflammatory and lymphoma (see Figure 3.1). The diagnostic criteria outlined in subsequent chapters will then permit the pathologist to determine the diagnostic category and the specific diagnosis within each group.

Colloid-Predominant (Discussed in Chap. 5)

Colloid is a proteinaceous substance (containing thyroglobulin and thyroid hormone) that is produced by thyroid follicular cells. The presence of abundant colloid within a thyroid lesion is generally a benign feature associated with adenomatous nodules and colloid nodules.

Epithelium-Predominant (Discussed in Chaps. 6, 7, 9–11)

Thyroid FNA samples that contain numerous epithelial cells relative to the amount of colloid raise the possibility of a neoplasm. Such samples should be carefully screened for nuclear features of papillary carcinoma (fine chromatin, nuclear grooves, nuclear pseudoinclusions). If these are absent, the differential diagnosis for these lesions includes a follicular neoplasm and a cellular adenomatous nodule, as well as other nonfollicular neoplasms.

Cystic (Discussed in Chap. 8)

Lesions that consist largely of macrophages indicate that the lesion is cystic. Most cystic lesions of the thyroid gland represent cystic degeneration of benign adenomatous nodules, but the differential diagnosis also includes cystic PTC. Consequently, it is important to sample the epithelial component associated with the cyst to exclude PTC.

Inflammatory and Lymphoma (Discussed in Chap. 4)

This group includes aspirates characterized by a predominance of inflammatory cells. A range of entities may be encountered, from Hashimoto thyroiditis to subacute thyroiditis and Reidel thyroiditis. In FNAs containing a predominance of lymphocytes, particularly atypical lymphocytes, the possibility of lymphoma should be excluded.

Reporting Thyroid FNA Cytopathology

A thyroid FNA report should contain statements regarding adequacy, and the general diagnostic category, as well as a specific diagnosis. In some cases, a descriptive comment or a recommendation may also be included (Table 3.1).

Adequacy Statement

As discussed previously, the initial step in thyroid FNA analysis is an adequacy assessment that places the FNA into one of two categories: satisfactory or nondiagnostic.

TABLE 3.1. Sample report template.

Patient identification	
Location	(Right/left) lobe
	(Superior/mid/lower) pole; isthmus
Adequacy	Nondiagnostic
	Satisfactory
Category	Nondiagnostic
	Benign
	Malignant
	Suspicious for malignancy
	Atypia of undetermined significance
	Suspicious for a follicular neoplasm
Diagnosis	(See Table 3.2)
Comment	(Immunocytochemistry results, etc.)
Recommendation	

Diagnostic Categories

Next, the FNA should be assigned to a general diagnostic category, such as nondiagnostic, benign, atypia of undermined significance; suspicious for a follicular neoplasm (including Hurthle cell neoplasms); and suspicious for malignancy or malignant, based on the diagnostic criteria discussed in subsequent chapters (Table 3.2). Because of the spectrum of categories and diagnoses utilized by pathologists, communication with clinicians is essential to ensure optimal patient management.

Nondiagnostic

The nondiagnostic category has been reported to comprise 10–30% of cases; however, nondiagnostic rates of greater than 20% should elicit an evaluation of patient selection criteria, and procurement and processing techniques, as well as diagnostic criteria, to optimize the system.

Benign

The benign thyroid FNA category comprises approximately 70% of all thyroid FNAs. The majority of these nodules are adenomatous nodules or colloid nodules. Because the false-negative rate for malignancy in this category is low (less than 3%), most of these patients are managed without surgical intervention.

Malignant

Thyroid FNAs that fall into the malignant category represent approximately 5–10% of all cases, and most of these are PTC. Because of the low (1–3%) false-positive rate within the malignant category, patients in this category are usually managed surgically, often by near-total thyroidectomy.

Suspicious for Malignancy

The suspicious for malignancy category contains a heterogeneous group of lesions in which the risk of malignancy ranges from 60 to 75%. Because there is an increased risk of malignancy in this category, most patients are referred for surgical excision, either a lobectomy or a near-total thyroidectomy.

TABLE 3.2. Diagnostic categories of thyroid fine needle aspirations (FNAs).

Nondiagnostic	Benign	Atypia of undetermined significance	Suspicious for follicular neoplasm	Suspicious for malignancy	Malignant
Insufficient follicular epithelium	Adenomatous nodule	Cellular adenomatous nodule vs. follicular neoplasm	Follicular neoplasm	Suspicious for: • PTC • Medullary carcinoma	Papillary thyroid carcinoma
Obscuring blood	Colloid nodule	Atypical Hurthle cell proliferation	Follicular neoplasm with Hurthle cell features		Lymphoma
Extensive preparation artifact	Cellular changes c/w: • Hashimoto thyroiditis • Graves disease	Focal nuclear atypia			Anaplastic carcinoma Medullary carcinoma
Macrophages only	Thyroiditis (subacute, acute, Reidel)				Metastatic disease

Suspicious for a Follicular Neoplasm

FNAs in this category are cellular and composed predominantly of microfollicles. Alternatively they may be cellular aspirates composed predominantly of Hurthle cells. The risk of malignancy in this category ranges from 15 to 30%; consequently most of these patients are managed surgically with thyroid lobectomy. Histologic outcome in these patients is heterogeneous but includes follicular adenomas, adenomatous hyperplasia, and less commonly follicular variant of PTC and follicular carcinoma.

Atypia of Undetermined Significance

This is a new diagnostic category in the BSRTC that previously fell within the broad "indeterminate" category. It remains a heterogeneous category that should be used judiciously given the potential for overuse. Fewer than 7–10% of a laboratory's thyroid FNAs should be placed into this category. FNAs that might be placed into this category include, among others, FNAs with a prominent population of microfollicles, but that do not fulfill criteria for the suspicious for a follicular neoplasm category and FNAs with focal features of PTC that do not fulfill criteria for the suspicious for malignancy category. The risk of malignancy in this category has been reported between 5 and 15% and is typically managed with a repeat FNA in 3 months. For repeat FNAs that are benign, the patient will usually be followed clinically, while repeat FNAs that are atypical will usually be referred for lobectomy.

Suggested Reading

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