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Introduction and Clinical Aspects

The second edition of this book incorporates the recent terminology and reporting guidelines for thyroid fine needle aspirations (FNAs), the Bethesda System for Reporting Thyroid Cytopathology (BSRTC) that emerged from a multidisciplinary National Cancer Institute (NCI) Thyroid FNA State of the Science conference (2007). A major challenge in the application of FNA to the diagnosis of thyroid lesions has been the inconsistent use of terminology for reporting results of thyroid FNAs both within laboratories and between different institutions. Not only has this hindered the sharing of information between different institutions, but it has created difficulties for clinicians managing patients with thyroid disease. Throughout this second edition, we will use a simple algorithmic approach, which we have modified to incorporate the BSRTC, to explain how to evaluate thyroid FNAs.

Over the past 3 decades, FNA has developed as the most accurate and cost-effective initial method for guiding the clinical management of patients with thyroid nodules. The purpose of this book is to describe the application of FNA to the assessment of thyroid nodules, with particular emphasis on the key cytologic features that can be used to diagnose FNA specimens based on a simple algorithmic approach.

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The clinical application of FNA as a primary diagnostic tool for thyroid nodules is widespread, because thyroid nodules are common. Within the general population, palpable thyroid nodules are present in 4–7% of adults, and subclinical (nonpalpable) nodules are present in up to 70% of individuals. Of these thyroid nodules, 90–95% are benign, and include a wide variety of lesions such as adenomatous nodules, simple thyroid cysts, colloid nodules, follicular adenomas, and inflammatory and developmental conditions, among others.

Benign Causes of Thyroid Nodules

- Adenomatous nodule
- Colloid nodule
- Follicular adenoma
- Simple thyroid cyst
- Graves disease
- Chronic lymphocytic thyroiditis
- Focal subacute thyroiditis
- Developmental conditions

The extremely large number of benign thyroid nodules and the small number of admixed malignant ones creates a clinical dilemma: how to manage the many patients with a detectable thyroid enlargement that is most likely benign? FNA has emerged as the most effective method for dealing with this problem. As a screening test for thyroid carcinoma, FNA assists in guiding the clinical management of patients by helping to select those individuals who are more likely to have a malignancy and need surgical management from the larger group of patients with benign nodules that can be managed without surgical intervention.

FNA is now generally accepted by endocrinologists and thyroid surgeons as a safe, cost-effective, and accurate means of evaluating a thyroid nodule. Widespread use of FNA has reduced the number of patients requiring thyroid surgery by more than 50%, it has increased the yield of malignancies at thyroidectomy by two to three times, and it has decreased the overall cost of managing a thyroid nodule by more than 25%.

Benefits of Using FNA to Evaluate Thyroid Nodules

- Reduces number of patients requiring thyroid surgery by 50%
- Increases the yield of thyroid malignancies at thyroidectomy by two to three times
- Decreases the cost of managing thyroid nodules by more than 25%

Incidence and Subtypes of Thyroid Carcinoma

In 2009, it is estimated that there will be over 37,000 new cases of thyroid cancer reported, and more than 1,500 deaths due to thyroid cancer. The rate of new cases of thyroid cancer has been increasing, in part due to the increased detection of small papillary thyroid carcinomas. Overall, thyroid cancer accounts for approximately 2% of the total number of new cancer cases for all anatomic sites and 0.5% of the total number of cancer-related deaths per year. Worldwide, the incidence of thyroid cancer varies from 0.5 to 10 per 100,000 individuals. It is the sixth most common form of cancer in women. Although the majority of thyroid cancers are well-differentiated tumors that have a very favorable prognosis, included within this group of malignancies is one of the most aggressive cancers affecting humans, undifferentiated thyroid carcinoma, with a mean survival of just 2–6 months.

Among the various types of thyroid carcinomas that may be encountered by FNA, the most common is papillary thyroid carcinoma, representing 60–80% of all thyroid malignancies. This incidence is distantly followed by follicular carcinoma (15–25%) and medullary carcinoma (5–10%) (Table 1.1).

Accuracy of Thyroid FNA

Thyroid FNA is widely accepted as an accurate means of evaluating a thyroid nodule, and it is considered by some to be the most sensitive and most specific nonsurgical thyroid cancer test available. For certain tumors, such as papillary thyroid carcinoma, FNA has

Table 1.1. Relative percentage of thyroid malignancies.

Thyroid tumor type	Relative percentage (%)
Papillary	60–80
Follicular (including Hurthle cell)	15–25
Medullary	5–10
Undifferentiated	1–10
Lymphoma	<1
Metastasis	<1

Table 1.2. Accuracy of thyroid fine needle aspiration (FNA).

Statistical measurement	Percentage (%)
Accuracy for satisfactory specimens	>95
False-negative rate	0.7–11
False-positive rate	0–7
Positive predictive value	89–98
Negative predictive value	94–99
Sensitivity	43–98
Specificity	72–100

even been reported to be superior to frozen section diagnosis. Other modalities for evaluating thyroid nodules such as serum tests, sonography, and scintigraphy have been largely overshadowed by FNA.

Based on several large studies, the accuracy of thyroid FNA has usually been reported as greater than 95% for satisfactory specimens, with positive predictive values of 89–98% and negative predictive values of 94–99% (Table 1.2). These values, however, are dependent upon several factors including how the indeterminate and suspicious groups of lesions are used in the calculations, the skill of the person performing the FNA, and the expertise of the cytopathologist interpreting the specimen. In addition, the accuracy of a thyroid FNA classified as "Benign" is difficult to assess, since so many patients in this group do not have surgery. The wide range of sensitivities and specificities for thyroid FNA that have been reported reflects the influence of these various factors. False-negative and false-positive FNA diagnoses occur, but in most studies, they are very uncommon, and are usually less than 1%.

The only caveat to these values is that the reported false-negative rates are based only upon those patients who undergo surgical resection of their aspirated nodules, and thus the calculations may be an underestimate; approximately 18% of patients who have an FNA are actually treated surgically.

Classification of Follicular-Derived Thyroid Carcinomas

Although the most important clinicopathologic predictors of aggressive clinical behavior for thyroid carcinomas are patient age, tumor size, and tumor stage, cytologic and histologic features that we recognize in daily practice can be used to divide neoplasms of thyroid follicular cells into three general categories that differ in clinical aggressiveness: well-differentiated, poorly differentiated, and undifferentiated carcinoma.

Well-differentiated thyroid carcinomas, representing the majority of thyroid cancers, have an excellent overall prognosis with mortalities in the range of 3–6%. In contrast, undifferentiated thyroid carcinoma, at the opposite end of the spectrum, is an extremely aggressive malignancy associated with greater than 90% mortality and a mean survival of only 2–6 months. Poorly differentiated carcinomas, insular carcinoma being the classic example, are characterized by a clinical behavior and mortality rate intermediate between that of the well-differentiated and undifferentiated thyroid carcinomas. These three groups of thyroid carcinomas, particularly the poorly differentiated ones, are continuing to be defined by advances in our understanding of their biologic behavior, as well as by their molecular features and their cyto- and histomorphologies. The recent Tourin Proposal (2007) provided a unified series of diagnostic criteria that have further defined the poorly differentiated subset of thyroid carcinomas. Some cases of less-differentiated carcinoma may arise by progression from better-differentiated thyroid carcinomas; however, other cases of poorly differentiated and undifferentiated carcinoma possibly arise de novo because they do not exhibit microscopic evidence of such a progression (Figure 1.1).

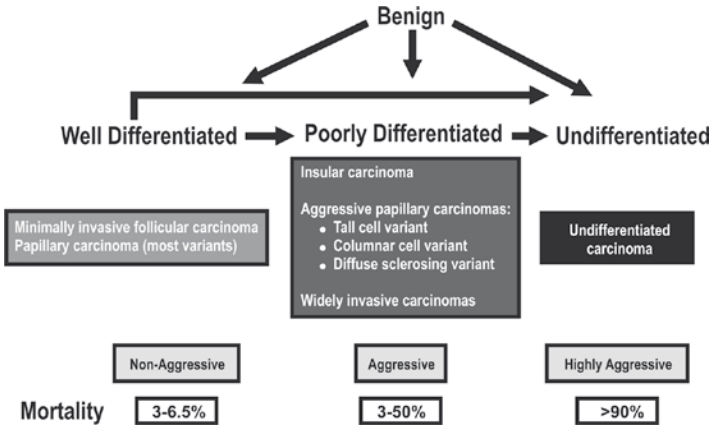

FIGURE. 1.1. Classification of follicular-derived carcinomas.

Suggested Reading

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