Thyroid Cytology

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KEYWORDS

• Cytopathology • Bethesda • Immunohistochemistry • Follicular • Atypia
• Carcinoma • Panels

KEY POINTS

- This article reviews the Bethesda System for Reporting Thyroid Cytology, with the diagnostic criteria for atypical and indeterminate categories reviewed.
- Having a unified way of reporting thyroid cytopathology is important for pathologists and clinicians alike.
- Although significant progress has been made in the discovery of new immunohistochemistry and molecular markers that indicate malignancy, no test can be used as stand-alone test in the diagnosis of thyroid malignancy.
- Various immunohistochemistry and molecular panels have entered the daily practice, either as a rule-in or as rule-out malignancy.
- These are commercially available panels with high positive or negative predictive value in detecting malignancy but more work is necessary.

INTRODUCTION

It is estimated that 4% to 7% of the adult population in the United States has a clinically palpable nodule, a number that increases significantly when imaging studies of the neck region performed for other indications are included. Combined incidence of clinically palpable and incidentally discovered nodules reaches 50% of the adult population of the United States.

In this context, over the past few decades, fine-needle aspiration (FNA) has developed as the most reliable and cost-effective method for the evaluation of a thyroid nodule, and it became the standard of care for the initial work-up of patients. Because of the extremely large number of benign thyroid nodules relative to malignant ones, FNA is used not only as a diagnostic test but also, in many cases, primarily as a screening test, which is used in conjunction with clinical findings and family history to guide patient management. FNA reduces unnecessary surgery for patients with benign nodules and triages patients with malignant nodules for surgical intervention.

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The goal of FNA is to provide pathologists with an adequate specimen that allows a meaningful interpretation. This implies a specimen with enough cellularity to yield a specific diagnosis and to minimize the number of false-negative results. Adequacy criteria are abundant in the literature; in the authors' practice, criteria suggested by the Bethesda System for Reporting Thyroid Cytology are used (ie, presence of at least 6 groups of well-preserved follicular cells with more than 10 cells per cluster). Generally, 2 to 3 passes with on-site adequacy evaluation by a cytopathologist are enough for an adequate specimen. Cellularity/adequacy is dependent not only on the technique of the aspirator but also on the inherent nature of the lesion (solid vs cystic).

In general, FNA results fall into 1 of 4 major diagnostic categories, with the relative frequency of diagnosis in parentheses: benign (70%), indeterminate or suspicious (10%–15%), malignant (5%), and nondiagnostic/unsatisfactory (10%–15%).[1]

It is critical that the cytopathology diagnosis is precise, unambiguous, and clinically helpful. In the past, terminology for thyroid FNA has varied significantly from one laboratory to another, creating confusion and preventing sharing of clinically meaningful data among multiple institutions.[2,3] To address the terminology and to establish strict diagnostic criteria for thyroid FNA samples, the Bethesda System for Reporting Thyroid Cytopathology established in 2008 offers a 6-category scheme, with the predicted probability of malignancy increasing from category II to VI: Bethesda I—nondiagnostic/unsatisfactory, Bethesda II—benign, Bethesda III—atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS), Bethesda IV—follicular neoplasm or suspicious for follicular neoplasm (FN/SFN), Bethesda V—suspicious for malignancy (SFM), and Bethesda VI—malignant.

The indeterminate categories (Bethesda III to V) have an approximate cancer risk of 5% to 15%, 15% to 30%, and 60% to 75%, respectively.[2,4,5]

The goal of this article is to provide nonpathology clinicians with a summary of the most important concepts and categories of the Bethesda System for Reporting Thyroid Cytology and briefly describe the main cytologic criteria for the most common benign and malignant thyroid lesions.

NONDIAGNOSTIC SPECIMEN

The Bethesda I (nondiagnostic/unsatisfactory) category describes a specimen that fails to meet the adequacy criteria. The following scenarios describe nondiagnostic cases: fewer than 6 groups of well-preserved, well-stained follicular cells; poorly prepared, poorly stained, or obscured follicular cells (excessively bloody specimens); cyst fluid with or without histiocytes; and fewer than 6 groups of 10 follicular cells (**Fig. 1**).[4]

There are a few points that should be emphasized in this category. Adequacy criteria apply only to follicular cells and exclude macrophages or inflammatory cells. Therefore, in inflammatory conditions of the thyroid, such as lymphocytic thyroiditis, abscess, and granulomatous thyroiditis, follicular cells may be sparse and there is no minimum requirement for adequacy for follicular cells when inflammation predominates.

Cases of solid nodules with cytologic atypia—if the sample contains significant cytologic atypia—are never considered nondiagnostic. A comment describing scant cellularity is usually inserted in the report.

BENIGN THYROID LESIONS

The Bethesda II (benign) category includes benign follicular nodules and thyroiditis.