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RESEARCH PAPER

Retrospective evaluation of frozen section use for thyroid nodules with a prior fine needle aspiration diagnosis of Bethesda II–VI: The Weill Cornell Medical College experience

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Abstract *Objective:* To evaluate the Weill Cornell Medical College (WCMC)/New York Presbyterian Hospital (NYPH) experience with intraoperative frozen (IOF) section in the management of thyroid nodules with a fine needle aspiration (FNA) diagnosis of Bethesda II–VI and to analyze the cost and pathology benefit it provides.
Methods: The surgical and cytopathology files at WCMC/NYPH were searched within the time period of January 2008 to May 2013. A total of 435 thyroid specimens were identified for which both an FNA and subsequent IOF section was performed. The FNA was correlated with the locations of the resected nodule and the nodule frozen for intraoperative diagnosis. The results of the FNA were compared to the IOF section diagnosis and final diagnosis (FD).

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Results: Among 435 cases, the FNA diagnosis was Bethesda II: 149 cases, Bethesda III: 170 cases, Bethesda IV: 91 cases, Bethesda V: 19 cases, and Bethesda VI: 6 cases. There were a total of 83 carcinomas identified on FD, which included 69 papillary thyroid carcinomas (PTCs), 12 follicular carcinomas, and 2 poorly differentiated carcinomas. The preoperative FNA diagnosis for these carcinomas was as follows: Bethesda II, 11/149 (7.4%), Bethesda III, 24/170 (14%), Bethesda IV, 26/91 (29%), Bethesda V, 16/19 (84%), and Bethesda VI, 6/6 (100%). IOF section contributed to the diagnosis of malignancy in 16/429 (4%) cases: 1/149 (0.7%) Bethesda II, 5/170 (3%) Bethesda III, 2/91 (1.1%) Bethesda IV, and 8/19 (42%) Bethesda V. The diagnosis of malignancy was confirmed in the 6 Bethesda VI cases by IOF section. There were no false positives on IOF section. IOF had a sensitivity and specificity of 26% and 100%, respectively.
Conclusion: The role of IOF section is limited in the evaluation of thyroid nodules. IOF section is most useful for nodules with an FNA diagnosis of Bethesda V lesions. The diagnosis of follicular variant of PTC remains difficult on frozen section.

Introduction

Affecting 4%—7% of the general population, palpable thyroid nodules are common.[1] The incidence of thyroid cancer has nearly tripled from 4.9 to 14.3 per 100,000 individuals over a thirty-five year period ending in 2009.[2] Such a high incidence mandates a cost-effective and efficient method for the preoperative evaluation of thyroid nodules. Fine needle aspiration (FNA) has emerged as a cornerstone modality in the preoperative management of thyroid lesions because of its reported high accuracy, specificity, cost-utility and low false negative rate. The widespread utilization of FNA has driven a significant reduction in unnecessary thyroidectomies worldwide as well as a decrease in the use of intraoperative frozen (IOF) sections.[3] In many cases, FNA provides a definitive benign or malignant diagnosis and effectively facilitates the planning of surgical and therapeutic treatment. Among thyroid nodules that undergo FNA, about 65% are classified as benign, 8% as malignant, and 3% as suspicious for malignancy.[4]

Nevertheless, there are several limitations of thyroid FNA due to the nature of the procedure, the large variety of pathologies that may arise in the thyroid gland—some of which cannot be diagnosed based on cytologic features alone—and the subjectivity inherent to the interpretation of samples. Inspired by the Bethesda system for reporting cervical cytology widely used for reporting Pap smear results, the Bethesda Criteria for Reporting Thyroid Cytopathology were published in 2009 in order to help standardize FNA reporting (Table 1).[5] Importantly, the system also recommends supplemental studies such as immunohistochemistry and molecular analysis that may aid in diagnosis, links each of the six diagnostic categories to an implied risk of malignancy, and provides clinical management guidelines ranging from clinical surveillance to near-total thyroidectomy.[5]

Although FNA is most often the diagnostic modality of choice in the management of thyroid nodules, the results are indeterminate (classified as "unsatisfactory", "atypical cellular lesions", "follicular neoplasm", or "suspicious for malignancy") in about 30% of cases.[4] FNA is especially inadequate at distinguishing between follicular adenoma and follicular carcinoma because the determination of malignancy for follicular lesions requires histologic evidence of vascular and/or capsular invasion.[6] In cases of thyroidectomy, IOF section is often used to aid further

Table 1 The Bethesda system for reporting thyroid cytopathology, adapted from Cibas and Ali.[5]

Bethesda category
I Nondiagnostic or unsatisfactory
Cyst fluid only
Virtually acellular neoplasm
II Benign
Benign follicular nodule (adenomatoid nodule, colloid nodule, etc.)
Lymphocytic (Hashimoto) thyroiditis
Granulomatous (subacute) thyroiditis
III Atypia of undetermined significance or Follicular lesion of undetermined significance
IV Follicular neoplasm or Suspicious for a follicular neoplasm
Hürthle cell (oncocytic) type
V Suspicious for malignancy
Suspicious for papillary carcinoma
Suspicious for medullary carcinoma
Suspicious for metastatic carcinoma
Suspicious for lymphoma
VI Malignant
Papillary thyroid carcinoma
Poorly differentiated carcinoma
Medullary thyroid carcinoma
Anaplastic carcinoma
Squamous cell carcinoma
Carcinoma with mixed features
Metastatic carcinoma
Non-Hodgkin lymphoma