This retrospective study was conducted to investigate the impact of using instituted standard criteria for on-site assessment of specimen adequacy on fine-needle aspiration (FNA) diagnosis of thyroid nodules. The study included a total of 1,031 thyroid FNAs that were performed and assisted with on-site adequacy assessment using instituted standard criteria from July 2006 to March 2009. Adequate specimens require the presence of at least six groups of follicular cells in total on Diff-Quik stained smears with a minimum of 10 cells in each group. Agreement on specimen adequacy between on-site and final assessment, nondiagnostic rate, distribution of cytologic diagnoses, and cytohistologic concordance for cases with surgical follow-up was evaluated. Implementing the instituted standard criteria resulted in 93% level of agreement on specimen adequacy between on-site and final assessment. Nondiagnostic rate upon final assessment was 10.7%. Cytohistologic concordant rate reached 93.9% and 82.3% for nonneoplastic and neoplastic lesions, respectively. Most importantly, this approach to standardization not only provided diagnostic consistency among cytopathologists, but also minimized confusions and enhanced effective communication. Thus, high satisfactions have been achieved from endocrinologists/radiologists who utilized our on-site assessment service and/or participated in the management of thyroid nodules.

Key Words: FNA; thyroid nodules; on-site adequacy assessment; instituted standard criteria

It has been well known that various adequacy criteria have been utilized while evaluating permanent smears of fine-needle aspiration (FNA) of thyroid nodules with or without on-site adequacy assessment. Benefits of on-site adequacy assessment for thyroid FNA have been well demonstrated previously. Accordingly, on-site adequacy assessment not only effectively decreased nondiagnostic rate at the time of final cytologic evaluation, but also provided efficient sample triage for ancillary studies. To the best of our knowledge, there are no criteria set forth for on-site adequacy assessment performed on rapid stained smears. In our institution, the vast majority of thyroid FNAs have been performed with on-site cytopathologist’s assistance. The lack of uniform criteria for assessing specimen adequacy resulted in diagnostic inconsistency among the cytopathologists and difficult communications with clinicians. Thus, a standard criteria for on-site adequacy assessment was developed, distributed, and explained to all involved parties including pathologists, endocrinologists, radiologists, and surgeons, and then implemented in our practice in 2005. On-site assessment reports including status of specimen adequacy and provisional diagnosis have been incorporated into our final cytology reports since 2006. The current retrospective study was conducted to assess the impact of using the instituted standard criteria on FNA diagnosis of thyroid nodules.

Materials and Methods

Through a Computer SNOMED Search from the file at The University of Michigan Hospital between July 2006 and March 2009, we retrieved a total of 1,031 thyroid FNAs with on-site adequacy assessment performed by
cytopathologists based on instituted standard criteria. The instituted standard criteria defined specimens as adequate by the presence of at least six groups of follicular cells in total on Diff–Quik (D–Q) stained smears with a minimum of 10 cells in each group. All FNAs were performed under ultrasound guidance by endocrinologists or radiologists. For each pass, a drop was put on a plain slide and smeared by a positively charged slide. One smear was air-dried, stained with D–Q stain and immediately evaluated. The other smear was quickly fixed with Sprayfix™ and later stained with Papanicolaou stain before final examination. The needle was then rinsed in Cytolyt® solution from which a ThinPrep® and/or a cell block was prepared as deemed appropriate. At the end of on-site assessment, location of the nodule, estimated size of the nodule, number of passes performed, status of specimen adequacy along with provisional diagnosis (for adequate specimen) was recorded. Both provisional and subsequent final diagnoses were established based on the previously described eight FNA diagnostic categories for thyroid nodules.⁶

Agreement on specimen adequacy between on-site and final assessment, nondiagnostic rate, and distribution of final cytologic diagnoses were evaluated. Further, cytohistologic concordance (neoplasia vs. nonneoplasia) was assessed on 221 cases that were followed up by surgical resection. Cytohistologic rereview was then performed for cytohistologic discordant cases to investigate causes of the discordance.

Results

A total of 1,031 aspirates included in the study were prepared from 723 patients (596 female and 127 male). The nodules measured from 0.5 to 10 cm with median size of 1.9 cm. Number of passes performed ranged from 1 to 12 with a median of six passes.

Table I shows agreement on specimen adequacy between on-site and final assessment. Among 853 specimens that were interpreted as adequate on-site, 851 (99.8%) remained concurrent at the time of final assessment while 2 (0.2%) were reversed to nondiagnostic due to on-site misinterpretation of histiocytes as follicular cells. With regard to 178 specimens that were interpreted as inadequate on-site, 70 (39.3%) were converted to adequate specimens upon final assessment because of the presence of additional follicular cells in Papanicolaou stained conventional and/or ThinPrep smears. Final assessment identified 921 adequate and 110 inadequate specimens. Consistent results on specimen adequacy (final vs. on-site) were revealed in 851/921 adequate specimens and 108/110 inadequate specimens. Overall, 93.0% level of agreement (final vs. on-site) on specimen adequacy was achieved. A final nondiagnostic rate was 10.7%.

Distribution of cytologic diagnoses among 921 adequate specimens along with surgical follow-up is presented in Table II. Proportion of nonneoplastic lesions, follicular/Hurthle cell lesion of undetermined significance (FL/HL), and neoplastic lesions comprising the adequate specimens was: 722 (78.4%), 116 (12.6%), and 83 (9.0%), respectively. Majority of the nonneoplastic lesions were nodular hyperplasia and less were chronic lymphocytic thyroiditis. Diagnosis of papillary thyroid carcinoma was rendered in more than half (54.8%) of neoplastic lesions, followed by follicular/Hurthle cell neoplasm (34.5%). The remainder 10.7% was comprised of the less common neoplasms, including medullary thyroid carcinoma, lymphoma, metastatic squamous cell carcinoma, and intrathyroidal parathyroid adenoma. Surgical follow-up was available in 24.0% of the adequate specimens, including 9.1% (66/722) of nonneoplastic lesions, 75% (87/116) of FL/HL, and 81.9% (68/83) of neoplastic lesions. Rate of cytohistologic concordance (neoplasia vs. nonneoplasia) reached 93.9% (62/66) and 82.3% (56/68) for nonneoplastic and neoplastic lesions, respectively. Overall cytohistologic concordance reached 88.1% (118/134). Among 14 cytohistologic discordant cases that were cytologically diagnosed as follicular/Hurthle cell neoplasm, follow-up histologic examination showed six follicular cell adenomas, two follicular/Hurthle cell carcinomas, and six follicular variant of papillary thyroid carcinomas.

Of 16 cytohistologic discordant cases, slides were available for rereview in 13 cases. Sampling error contributed to four false-negative cases. False-positive results were associated with over-interpretation of nonspecific cytologic findings. For example, cytologic diagnosis of papillary thyroid carcinoma was rendered in four cases
due to the finding of occasional intra-nuclear grooves, while five cases were misinterpreted as follicular neoplasm due to the presence of a minor population of microfollicles in the setting of predominantly honeycomb- ing tissue fragments, consistent with nodular hyperplasia.

Follow-up histologic examination of 87 FL/HL revealed 21 (24.1%) neoplasms, including 13 follicular/Hurthle cell adenomas, three follicular/Hurthle cell carcinomas, and five conventional papillary thyroid carcinomas. When the data were reanalyzed including the indeterminate diagnostic category with definitive nonneoplasia and neoplasia categories, and only the 21 histology-confirmed neoplasms were considered cytohistologic concordant, overall cytohistologic concordance dropped to 62.9% (139/221).

Of the 110 inadequate aspirates, 11 had histology follow-up that revealed eight nodular hyperplasia, one follicular carcinoma, one papillary thyroid carcinoma, and one intrathyroidal parathyroid gland.

Discussion

To the best of our knowledge, there are no criteria set forth for preliminary on-site assessment of adequacy in FNA cytologic diagnosis of thyroid nodules. Our data demonstrate that implementation of the instituted standard criteria for preliminary on-site adequacy assessment preformed on D–Q stained smears resulted in over 90% level of agreement on specimen adequacy between on-site and final assessment. Nondiagnostic rate and cytohistologic concordant rate revealed by this study are compatible with that of published literatures.5,9 Most importantly, this approach to standardization not only provided diagnostic consistency among cytopathologists, but also minimized confusions and enhanced effective communication. Thus, high satisfactions have been achieved from endocrinologists/radiologists who utilized our on-site assessment service and/or participated in the management of thyroid nodules.

With regard to nondiagnostic rate, it has been shown that operator’s experience in performing FNA plays an important role.9 Since all FNAs included in the current study were performed in a setting of a teaching institution, operator’s experience varied, although experienced faculty members routinely performed the first pass and supervised performance of consecutive passes. A few studies have addressed the optimal number of FNA passes for obtaining diagnostic materials with the presence of on-site adequacy assessment. Accordingly, need of four to six passes per thyroid nodules has been suggested in order to establish diagnostic certainty.7,10 The vast majority of the FNAs in this study were well-tolerated and the operators routinely performed three or four consecutive passes and then waited for cytopathologist’s assessment of adequacy. If needed, additional two to four passes might be performed. Rarely, less than two passes (due to poor tolerance) or more than eight passes were performed. As a result, a median number of six passes per nodule were performed, which is in agreement with the previously reported studies. It is noteworthy to mention that intrinsic nature of thyroid lesions should also be taken into considerations. For example, aspiration of lesions that are mainly composed of colloid or cyst contents may reveal none or less than optimal number of follicular cell. We thus used number of follicular cells as a general but not sole measuring tool while assessing specimen adequacy.

While in the original cytology reports, follicular and Hurthle cell lesion/neoplasm was specified in the diagnosis, Hurthle cell lesion/neoplasm and follicular lesion/neoplasm were grouped into one category in this study as a previous study conducted in our institution has indicated that Hurthle cell lesion/neoplasm did not predict more malignant potential compared to follicular lesion/neoplasm.11 Among the cytoplogically diagnosed follicular/Hurthle cell neoplasms, follow-up histology revealed follicular variant of papillary thyroid carcinoma in nearly 50% of the cases. The finding, similarly to previous studies,9,12 demonstrate limitations and challenges of utilizing FNA in distinguishing follicular variant of papillary thyroid from follicular neoplasm. Not surprisingly, false-negative and false-positive diagnoses identified in this study were results of sampling error and over interpretation of nonspecific cytologic findings, respectively.

Indeterminate lesion (FL/HL) constituted 11.2% of all FNAs included in this study. The finding is compatible with the results reported by the other investigators.13,14 Histology-confirmed carcinomas were revealed in 9% cases categorized into the indeterminate group. The data are in agreement with the risk of malignancy (5–10%) presented at NCI Thyroid FNA State of the Science Conference.15

Carcinomas were identified in 2 of 11 nondiagnostic FNAs that were followed-up by surgical interventions. The result further supports the opinion that nondiagnostic FNAs carry malignant potentials,7,16–18 and further investigation is needed for these cases.

In summary, this study confirms that specifying six groups of follicular cells as the threshold for adequacy at the time of on-site assessment is appropriate and provides diagnostic accuracy compatible with the literatures. In addition to providing compatible diagnostic accuracy and consistency, our approach to standardization of criteria for preliminary on-site adequacy assessment enhanced effective communication that further resulted in high satisfactions from endocrinologists/radiologists who utilized our on-site assessment service and/or participated in the management of thyroid nodules.

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