Thyroid Cytology Comes to Bethesda

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DOI: 10.1309/AJCPJFDUQRJ3NGDQ

As outlined, the Bethesda system for reporting gynecologic cytopathology (TBS) has been taken as a model for consensus building and reporting in thyroid-fine needle aspiration (FNA) cytology.1 The history of this process is reviewed in the article in this issue of the Journal by Cibas and Ali.2 In parallel with the evolutionary path taken by the gynecologic materials, the current effort has been the subject of an international conference, comment periods, and multiple iterations of a summary statement, as well as the anticipation of future meetings and refinements. All who work in the field of thyroid cytology will welcome this effort at standardization.

As with past TBS initiatives, it involves not only cytopathologists, but also specialists in medical imaging and interested clinicians. The result is a patient care–oriented effort relevant to all who work in this area. Since much of this effort is hosted by the National Cancer Institute (NCI)—in this case headed by Andrea Abati, MD—the term TBS seems to have become generalized as an important imprimatur for consensus efforts in clinically oriented cytopathology. I am confident that we will come to call the various versions of this evolving document TBS-Thyroid (TBST). Largely of historic interest in most of our practices is a similar consideration of breast FNA.3

A key feature of this and other NCI summary statements in cytopathology is a clear effort to link reliable cytopathologic criteria to diagnostic terminology that accurately reflects outcome expectations that are, in turn, facilitated by consensus-derived patient management guidelines.

I am pleased to have been asked to comment on the current iteration of TBST in this issue of the Journal. This framework document mirrors that of the text/atlas that has or will soon appear in print, as well as online. It is stylistically telegraphic and does not address many details found in the much longer NCI document or in the text/atlas. Many interested practitioners will want to consult both or either of the latter.1 My own perspective is that of an individual in a very busy private practice; I see a great many thyroid FNAs that have been collected in a variety of clinical settings by individuals who range from quite skilled to apparently somewhat unschooled in FNA technique and in specimen preparation.

Before considering the current methods and nosology of thyroid cytopathology, it may be useful to observe a clinical trend noted in my own practice and prominent in the experience of others (John Abele, Outpatient Pathology Associates, Sacramento, CA, personal communication). In the past, thyroid FNA was directed at palpable lesions that often seemed solitary. It was in that setting that many still-useful criteria for specimen adequacy and sample diagnoses were created. This is also the history that brings us the authors’ statement that “a ‘benign’ result is obtained in 60% to 70% of thyroid FNAs.”

Today, many thyroid nodules are found incidentally or actively sought through sensitive imaging modalities. The size of the lesions studied by FNA has decreased, even as their number has increased. It is now common to see from two to several image-guided samples from a gland showing relatively little palpable abnormality. By these means, in some practices, the fraction of thyroid FNAs seen that is clearly benign now well exceeds 90% (John Abele, Outpatient Pathology Associates, Sacramento, CA, personal communication). Of course, one’s biopsy practices and referral patterns can significantly alter the local distribution...
of diagnoses; pathologists working in specialized referral centers may not share this private-practice experience.

Not addressed in the current article or the atlas but given expansive consideration in the NCI document are the niceties of FNA technique and specimen preparation. Officially, this conference confers legitimacy on direct smears and liquid-based preparations (LBPs) and highlights different clinical settings in which one may be logistically preferable to the other. It then goes on to give a carefully referenced comparison of these methods and seems to conclude that the data regarding LBPs are as yet incomplete, especially when the LBP is used as the sole preparatory method. We can all agree that reliance on LBPs requires special knowledge of the "new" face that is given to samples previously presented as smears.

This new consideration of smears vs LBPs seems to have taken the center of the specimen preparation stage. Our earlier considerations of air-dried vs wet-fixed smears seems not to enter the current discussion, as both methods are given equal footing. Our own experience continues to show that, unless a pathologist or cytotechnologist is present at the procedure, it can be very difficult to get fixed smears without substantial air-drying artifact. This is one reason for unsatisfactory samples in TBST. In many clinical settings, dried smears may be preferable because drying a slide amounts to doing nothing to an extent that can be achieved by most operators. Regardless of one’s preferred methods, high-quality material is needed for accurate interpretation, so it is fitting that we reflect on these issues at the time a new atlas is about to appear.

TBST diagnoses begin with 1 of 6 general categories, as summarized in the authors’ Table 1. These may be supplemented with subcategories, explanatory notes, or a summary of the reported risk for malignancy associated with the selected category (Table 2). Adequacy criteria are discussed more fully in the NCI document and TBST text/atlas than in the present article. As reviewed in the former, the time-honored criterion of at least 6 groups composed of at least 10 benign follicular cells is still with us in this latest of opinions (although it is certainly no longer the end-all criterion). We remain indebted to Goellner and coworkers for developing this, our most commonly cited measure of specimen adequacy.

Another statement about specimen adequacy is made very clearly: “Any specimen that contains abundant colloid is considered adequate (and benign), even if 6 groups of follicular cells are not identified.” The longer NCI document spells this out in greater detail, when it describes, “Abundant thick or watery colloid that covers a significant portion of the surface of a slide and is readily identified as colloid (not serum or protein) is a reliable sign of benignity and not a feature reported to be associated with malignancy.”

In my opinion, pathologists who are less familiar with the details of thyroid cytology should still be warned that occasional aspirates of cystic papillary carcinomas, in addition to being paucicellular, may also show abundant colloid. In such cases, the colloid can be very thin and pale, rather than thick or watery. Another warning for pathologists who do not frequently interpret thyroid FNAs is that the celebrated cracking artifact in colloid is far from universal. Lots of colloid does not crack, and all that cracks is not colloid.

This brings up the importance of identifying colloid and, apparently, of finding it thick, watery, or otherwise. Pathologists who prefer to base thyroid FNA interpretations on air-dried slides often believe that colloid is easier to identify and quantitate on such preparations. Again, neither the current article nor the longer NCI document addresses the relative virtues of these 2 methods.

As with any cytodiagnostic scheme, there remains a group of indeterminate cases called atypia or undetermined significance or follicular lesion of undetermined significance. Additional alternative terms listed in the NCI document also include atypical follicular lesion, cellular follicular lesion, and rule out neoplasm. Based on the descriptions that follow, Cibas and Ali² note worrisome aspirates that do not quite fit into other categories and a number of sampling issues and preparatory artifacts. The key points seem to be that this entity is fairly uncommon and that various nonoperative clinical follow-up strategies (usually with repeated FNA) are often used. Exceptions involve repeated abnormal FNAs or enlargement of the lesion during follow-up. Perhaps this diagnosis will be used with those aspirates with which we are tempted to use more verbose and descriptive diagnoses.

Equally vexing are the cases in which a follicular neoplasm is suspected. Cibas and Ali² point out that the relatively simple (and common) findings of high cellularity or a minor microfollicular component in an otherwise benign sample should not prompt this diagnosis; most such lesions do not require surgery. The NCI document mentions the older diagnosis of "follicular lesion" as an alternative for such cases. I suspect that some will continue to use this well-established term because it has come to encompass the various diagnostic possibilities, including nonepithelial cellular nodules, adenomas, and carcinomas showing follicular patterns of growth. The terms follicular neoplasm and suspicious for follicular neoplasm, however, connote the same possibilities and would likely not be too confusing for clinical colleagues who may be unfamiliar with the terms.

This classification should also help with the lingering problem we sometimes have with requests for frozen sections of follicular thyroid nodules. Most cases for which there is a cytologic diagnosis of malignancy of a type suitable for surgery now seem to receive definitive treatment without intraoperative pathology consultations. Indeed, that
is usually our intention in making such interpretations. Thus, the only category for which frozen section has any but the most occasional utility would seem to be suspicious for malignancy. In practice, the vast majority of such cases will have been called “suspicious for papillary carcinoma” at the time of FNA. Categories III and IV in Table 1 encompass the spectrum of cytologically follicular lesions that are bothersome but that are often not clearly neoplastic. Frozen sections are not useful in most such cases.4

This classification should be helpful on a number of levels in the laboratory and in the clinic. It will also be helpful as a tool for pathologists learning thyroid cytopathology and for pathologists and others working to craft clinically relevant thyroid FNA reports. We look forward to reviewing the online and the print versions of the atlas.

References