

Preface

The evaluation of glandular lesions in cervical cytology specimens can be vexing, even to the most experienced cytologist. The mere identification that a glandular lesion is present can be subtle during the screening process, and once a potential abnormality is detected, accurate classification can be even more challenging. Compared to the more prevalent squamous lesions, glandular lesions in cervical cytology specimens were not well recognized or fully classified until late. Endocervical adenocarcinoma in situ (AIS) was not fully described in the histopathology literature until 1953 [1], and it was not codified as a discrete cytologic entity until the second edition of the Bethesda Manual (TBS2) in 2001 [2]. Prior to that AIS was grouped under the descriptor of “atypical glandular cells of undetermined significance, favor neoplasia.” In the 1990s, a number of detailed publications that appeared defined the morphologic characteristics of AIS and showed that when applied correctly, these criteria were actually predictive when histologic specimens were obtained [3–5]. Extensive study of glandular lesions followed upon the publication of TBS2 such that a variety of conditions affecting glandular cells of the gynecologic tract became better recognized and the morphologic criteria for each became better defined.

It is fair to say that there has been an increased awareness that, although the test is not perfect, glandular lesions can

indeed be reliably identified in cervical cytology specimens. As with any newly emerging discipline, the ability to detect glandular lesions has had other effects. Patients now expect that, just like squamous neoplasia, glandular neoplasia can be perfectly identified when present. Many lawsuits alleging malpractice have involved this very subject. The unfortunate truth is that the Pap test is not as sensitive for endocervical as it is for squamous neoplasias. The anatomy of endocervical cell location and the plethora of reactive mimics make accurate detection difficult from both sampling and interpretation viewpoints, respectively. That being said, there is always room for improvement and that is the idea behind the present monograph.

At the Massachusetts General Hospital, we are fortunate to have access to the material from very active gynecologic oncology, colposcopy, and general screening services. In addition, there are a large number of outside consultation cases that are received for review by our subspecialty experts in gynecologic practice, both clinical and pathologic. In the writing of the text and collection of the illustrations, we have attempted to identify the key issues in the cytology of glandular lesions, to present the important demography and clinical features associated with them, and finally to describe and to illustrate the pertinent morphology of these lesions.

The monograph begins with a background discussion and illustration of the normal histology and cytology associated with glandular epithelia in the gynecologic tract. It then describes the prototypical endocervical and endometrial neoplasia spectrums. In addition, illustrations of malignant mimickers, namely metastatic adenocarcinomas, which can have appearances very similar to primary lesions will be presented, with the discussion focusing on the features that should help the observer to make a correct final interpretation. The latter morphologic chapters focus on the many mimickers of glandular neoplasia. Entities such as the large number of metaplastic processes, reactive endocervical cells caused by irritants such as polyps, intrauterine devices, prior biopsies, infectious disease, and many more will be detailed. These

benign entities are common and can actually be the underlying cause of many cases of interpretations of “atypical glandular cells (AGC).” It has been a “rule of thumb” for many years that the majority of cases of AGC will turn out to be either benign/reactive or unusual presentations of squamous intraepithelial lesions, with only a small minority actually representing true glandular neoplasias. Hence recognition and correct classification of these presentations as benign can lead to significant improvements in cervical cytology specificity and can help to avoid costly and stressful follow-up clinical investigations. Therefore accuracy in both directions, detection and false negativity, as well as classification and false positivity, are addressed by this monograph.

Aids to interpretation have become very important in histopathologic applications. When applied to cytologic preparations, the use of immunohistochemistry for markers associated with high risk HPV-associated neoplastic transformation and with types of differentiation has greatly aided again, both detection and classification. The principles behind their use and illustrations to aid in proper interpretation are presented in order to bring the reader up to speed with this newly emerging functionality.

Finally, the management of glandular lesions may seem like the clinicians’ domain. But it is extremely important for laboratory professionals to be aware of the published guidelines. These lesions are rare in the general screening population and the cytologist, because of their diagnostic role, may be in the best position to advise and guide the clinician trying to determine the best course of action. Therefore the newest management algorithms are presented to assist the cytologist in this important advisory role. In addition, appropriate quality assurance practices, such as prevalence monitoring, cytology–histology correlation, and HPV testing use are included as these will be important to the laboratorian.

We certainly hope that this monograph meets the needs of the cytology community and that the format and content is displayed in a manner that allows for easy access, adaptability to clinical situations, and ease of information transfer. It has

been our pleasure to “put down on paper” these subjects that we have studied and struggled over for the better parts of our careers. We hope that the knowledge and experience that we have gained will be useful to the reader.

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Cytopathology with Histologic Correlates

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