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REVIEW

What is atypia? Use, misuse and overuse of the term atypia in diagnostic cytopathology

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The term "atypical" was introduced by the founder of modern cytodiagnosis, Dr. George N. Papanicolaou, to convey a very low suspicion of (pre)malignancy. Despite controversies concerning its ambiguous and imprecise definition and its uncertain optimal use, the term "atypia" has continued to be used in cytopathology, and has recently been increasingly used in standardized nongynecologic cytopathology diagnostic reporting terminologies. Its increasing use suggests that "atypia" continues to be a useful category to fill the gap between what we can recognize as entirely normal (including reactive changes) and what we can recognize as clearly abnormal (premalignant or malignant). However, this diagnosis should be used parsimoniously, since the potential overuse of "atypia" diagnoses can lead to the erosion of clinicians' confidence in cytopathology, their misunderstanding of the cytopathology report, and to an increase the clinicians' diagnostic uncertainty, with negative consequences on patients' satisfaction and wellbeing, and on health care costs. A clinically meaningful, standardized cytodiagnostic category of "atypia" requires a narrow definition, quantitative criteria, agreed-upon reference images, a clear clinical meaning (likelihood of underlying malignancy or premalignancy) and, ideally, well-defined management options. The successful implementation of such a standardized "atypia" diagnostic category requires continuous education of cytology professionals and quality assurance efforts to monitor its use. The interobserver variability and potential excessive use of the diagnosis of "atypia" may be reduced by considering and addressing the major factors involved in its variable use, namely the quality of the sample, the definition of "atypia", the education/training of the cytologist/pathologist, and cytologist/pathologist-related "supracytologic" factors.

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This commentary expresses the author's personal views and opinions on "atypia" diagnoses in cytopathology. These opinions were developed during all-too-common encounters with difficult-to-classify cytologic specimens, while trying to apply the diagnosis that is both most accurate and most useful in the further management of the patient, through introspection, numerous discussions with cytotechnologists, colleagues, residents, fellows, and clinicians from both medical and surgical specialties. The hope underlying this commentary, which may at times be provocative, is that it will encourage reflection and an open discussion about the usefulness of this diagnostic term, its definition and place in our diagnostic vocabulary, its current use and potential future use, and about measures and strategies that may be useful to limit its use. The author believes that such a discussion is highly relevant at a time when efforts are under way to increase the standardization of nongynecologic cytopathology reporting, as attested by development of standardized reporting in thyroid[1] and pancreatobiliary[2] cytopathology and the current international collaboration that is under way to develop of a standardized reporting system for urinary tract cytopathology ("The Paris System").[3]

Like *dysplasia*, *atypia* is a term intimately associated with the practice of diagnostic cytopathology and is so ingrained into the cytologist's vocabulary that he or she hardly stops to think about its meaning. Surprisingly, unlike the term *dysplasia*, which has been the subject of many publications and editorials regarding its semantics,[4-9] the author is not aware of a single publication addressing the meaning, origins, and evolution of the term *atypia* and its use in diagnostic cytopathology. A better understanding of this term is, however, important for its appropriate diagnostic use, because otherwise, confronted with a term that has a vague, ambiguous, or unintelligible definition, we tend to make up our own definitions, according to the "Humpty-Dumpty principle" ("When I use a word," Humpty Dumpty said, in rather a scornful tone, "it means just what I choose it to mean – neither more nor less"[10]).

In daily practice, we tend to use *atypia/atypical* in 2 main contexts, with different ramifications. The first is as a descriptor of something unusual, but not necessarily "bad" (dysplastic or malignant), when we encounter cases in which the cells or their arrangement look unusual, that is, they do not conform to our expectations of cytologic normalcy because they differ from our referential mental images[11] of normalcy formed during our training and modified through experience. Whereas *atypia/atypical* as a descriptor of "unusual" cytologic findings is used liberally among cytology professionals, its use in this general descriptive sense in diagnostic reports is probably best minimized, because of the potential for misinterpretation by clinicians. The second main context of the use of *atypia/atypical* is as a diagnostic category such as "atypical (squamous/glandular) cells" or "atypia," usually with the explicit disclaimer "of undetermined significance," in both gynecologic cytopathology ("atypical squamous/glandular cells of undetermined significance")[12] and nongynecologic cytopathology, as in "atypia of undetermined significance" and "follicular lesion of undetermined significance"[13] used in thyroid fine-needle aspirates. In this second context, we use "atypia/atypical" as a diagnosis of exclusion and do not only mean that the cells differ from our expectation of normalcy, but that we have also excluded any known benign (reactive) cellular and neoplastic or preneoplastic changes and patterns.

In their seminal article regarding communication between the pathologists and their clinical colleagues, Powsner et al[14] stated: "Just as medical language may be hard for lay people to understand, medical specialists may use language that is obscure to practitioners outside their specialty. Among specialists, the language of diagnostic anatomic pathologists is arguably furthest from daily medical discourse." *Atypical* is certainly one of the diagnostic words used by pathologists that is most "obscure" to clinicians and can therefore hardly fulfill the main purpose of a medical diagnostic term, which is to convey information that is useful in the identification, treatment, prevention, or prediction of disease. What information do we convey when we are diagnosing a cytologic specimen as "atypia/atypical"? Unless used in a standardized reporting system[15] with clear clinical and management implications, "atypia" as diagnostic term has little diagnostic meaning. Moreover, *atypia* may be used by different pathologists or different laboratories to describe or diagnose different cytologic findings, which may have different clinical connotations.[16]

The clinical consequence of the use or overuse of *atypia* or of other expressions of uncertainty by pathologists is that clinicians may misunderstand the pathologist's report[14,17-20] or interpret such pathology reports, which are perceived as "foggy," "hedging," or "waffling," to match their own clinical impression,[15] or they may altogether ignore the pathologist's diagnosis of "atypia." Another consequence is that it may increase the clinicians' diagnostic uncertainty, leading to excessive testing, greater expenditure of resources, increased costs, increased patient anxiety, decreased patient satisfaction, and