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REVIEW

What should not be reported as atypia in urine cytology

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The term “atypia,” although not well characterized, is widely used in diagnostic surgical and cytopathology. Because there are no guidelines regarding when to use this term, in the majority of cases, it is used as a “wastebasket.” This definitely applies to urine cytology, where the reported rate of atypia ranges from 1.9% to 23%. This review lists a number of cytomorphologic findings in urine cytology that are associated with known and specific causes. Urine specimens in which the morphologic changes can be attributed to particular etiologic factors should no longer be classified as “atypical.” These include urine specimens showing reactive umbrella cells or seminal vesicle cells, reactive changes due to stones, cytologic changes characteristic of infectious processes or therapy effect, instrumented urines with pseudopapillary clusters, and urinary diversion specimens.

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We all recognize that any disease process is defined by a spectrum of characteristic features on which a diagnosis is made. Diagnoses are usually obvious at both ends of this continuous spectrum: when most or all characteristic features for a specific disease are either present or absent, a precise diagnosis can be either made or excluded. However, in between, when the diagnostic features or the morphologic characteristics of a disease are not clearly defined, or not all of the diagnostic features are present, our diagnostic abilities may be limited.¹⁻³ The presence of this “gray zone” has been recognized in practically all pathological classifications.³⁻⁵ Therefore, the term “atypia” has been used widely in both surgical pathology and cytopathology whenever there is a diagnostic uncertainty. A number of classifications include entities with the description of “uncertain clinical significance” or “low malignant potential.”⁶ In some classifications, atypia has been specifically defined. For example, in the Bethesda Reporting System for Cervical Cytology, the atypical squamous cells of undetermined significance, or ASC-US, category includes cells with nuclear enlargement of 2× to 3× the size of intermediate cells.⁷ Similarly, the atypical category is defined in the Bethesda classification for thyroid cytopathology⁸ and in the recently proposed Papanicolaou Society of Cytopathology guidelines for pancreatobiliary cytology.⁹ Despite multiple attempts to evaluate at least the significance of the atypical category in breast fine-needle aspirations,^{4,10-15} no agreed-on definitions of atypia are available in breast cytology or in the remaining areas of cytopathology. Therefore, the term atypia is being used widely and, in many instances, is being used as a wastebasket for any cases that are not clearly negative but do not have clear-cut evidence of malignancy. This is particularly true for urine cytology, in which the reported rate of atypia varies from 1.9% to over 23.2%.¹⁶ This wide variation of the percentage of cases interpreted as atypical reflects the lack of a widely accepted definition of what should be reported as atypical in urinary tract cytology, despite a number of attempts to standardize atypia as a diagnostic category in urine cytology. Therefore, there is an obvious need to standardize our reporting scheme in urinary cytology and to try to define what the diagnostic circumstances are that allow us to use this indeterminate category.

The word atypia comes from the Greek language and is a combination of *a* + *typos*, meaning without type or a condition of being irregular or nonstandard. The recently formed Paris Group that is currently working on a reporting system for urinary cytology will attempt to define and categorize atypia in urine specimens. For such a diagnostic category of atypia to be clinically useful, it is important to

narrow it down as much as possible, to include only cases in which the observed cytologic changes cannot be attributed to a specific cause. Therefore, cases in which we recognize a particular morphologic alteration in urothelial cells and can determine its non-neoplastic etiology should be classified as negative for malignancy and not as atypical. In this review, we will illustrate these circumstances.

Superficial (umbrella) cells

Superficial cells, or umbrella cells, form the single top layer of the urothelium. These cells are commonly seen, particularly in instrumented urine specimens. They usually occur singly, but sometimes are seen still attached to much smaller, intermediate types of urothelial cells. Umbrella cells are large, have characteristic scalloped edges and abundant cytoplasm. They are often multinucleated, binucleated, or may contain a single large nucleus. The nuclei are centrally located, are round to oval, and have a smooth nuclear membrane. The nuclear/cytoplasmic (N/C) ratio is characteristically low. The chromatin is fine, and occasionally prominent chromocenters are present (Fig. 1). Although sometimes umbrella cells can appear very “atypical,” they are recognized as benign/reactive by their low N/C ratio, characteristic scalloped edges, and smooth nuclear membrane. Even the most atypical umbrella cells do not

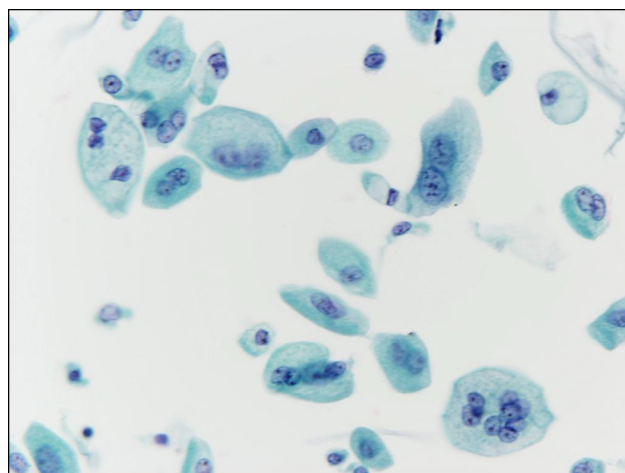


Figure 1 Bladder washing showing numerous superficial (umbrella) cells. Notice a great variation in size of cells and nuclei, as well as variation in number of nuclei. However, the nuclear/cytoplasmic ratios are low and nuclei are uniform and have smooth nuclear membranes.

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