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Brief Communication

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The Illusion of Atrophy: Diagnostic Challenges in Liquid-Based Versus Conventional Cervical Cytology

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The evaluation of an atrophic cervicovaginal smear represents a classic and rigorous challenge in gynecological cytopathology. Hypoestrogenism induces an almost exclusive proliferation of parabasal cells, which are inherently characterized by an elevated nucleus-to-cytoplasm (N/C) ratio. With the widespread adoption of liquid-based cytology (LBC) over conventional cytology (CC), the morphological rules of the game have changed considerably. This transition has not only optimized cellular representation but has also transformed the criteria used to discriminate physiological atrophy from high-grade squamous intraepithelial lesions (HSIL) and invasive processes, which constitute the primary differential diagnoses in this scenario [1,2].

Comparative Morphology: Atrophy "Face-to-Face"

Cellular morphology, although static in a single snapshot, is dynamic when perceived by the human eye under the influence of critical pre-analytical variables, such as fixation methods and technical processing. Therefore, it is imperative to establish a comparative framework that serves as a bidirectional educational guide between both methodologies [3].

Feature	Conventional Cytology (CC)	Liquid-Based Cytology (LBC)
Cellular Clustering	Cohesive, large two-dimensional sheets or syncytial-like aggregates.	Predominantly isolated, dispersed cells, or small, rounded three-dimensional clusters [4].
Cell Size and Shape	Flattened cells due to mechanical smearing; well-defined cell borders.	Spheroidal cells ("rounded in suspension") with a smaller apparent diameter [3].
Nuclear Detail	Variable. Vulnerable to air-drying artifacts (false karyomegaly and chromatin pallor).	Excellent. Sharp chromatin, well-preserved nuclear membrane, and no distortion from air-drying [4,5].
Background	True "dirty background": cellular debris, abundant mucus, true tumor diathesis, and "blue blobs" (naked nuclei).	Clean background. Possible presence of pseudodiathesis (spherical condensation of proteins and debris) [5].

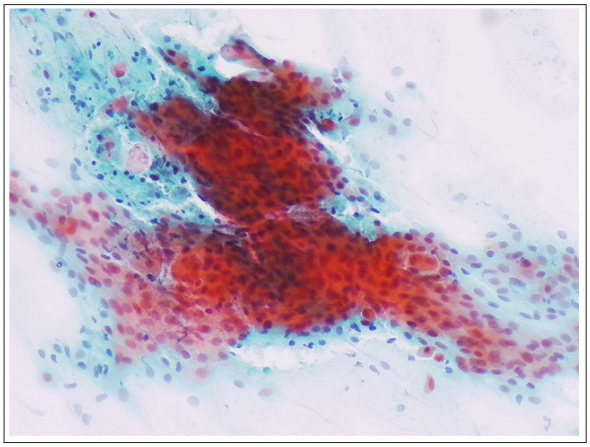

Figure 1: conventional cytology (cc). Large syncytial-like sheets of benign atrophic parabasal cells. While nuclei show some crowding and size variation, the cohesion of the sheet points to a benign process. Note the relatively clean background, which can be seen in some cases, contrasting with the inflammatory background seen later (papanicolaou stain).

Advantages and Diagnostic Challenges: A Critical Analysis

The excellent nuclear preservation of LBC minimizes false positives caused by air-drying (the "paradox of sharpness"). However, cellular dispersion and artificial rounding increase the risk of overdiagnosing HSIL due to three critical phenomena:

- **The Nucleus-to-Cytoplasm (N/C) Ratio Dilemma**

In CC, manual smearing spreads parabasal cells across the slide.

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Depending on the force applied, this action induces cytoplasmic expansion, which allows the screener to verify that—despite atrophic changes—a benign volumetric proportion between the nucleus and cytoplasm is maintained. Conversely, in LBC, cells are fixed in suspension and adopt a spheroidal shape. When deposited in a monolayer, the cytoplasm visually contracts around the nucleus. In a two-dimensional projection, this phenomenon artificially maximizes the N/C ratio, causing a benign atrophic parabasal cell to almost identically mimic an HSIL cell [3,6].

- **Dispersion vs. Cohesion**

Atrophy in CC typically presents as cohesive sheets of parabasal cells (facilitating the recognition of benignity) (Fig1) or as a "cobblestone pattern" (Fig2-3), where individual parabasal cells fit together like flat mosaic tiles. This arrangement allows for the evaluation of degenerative nuclear changes associated with estrogen deficiency, such as karyolysis, karyopyknosis, and apoptosis (pseudoparakeratosis) (Fig4-5). The mechanical processing of LBC disrupts these intercellular junctions, releasing isolated parabasal cells. An observer unaccustomed to LBC may misinterpret these single cells with high N/C ratios as dyskeratotic elements or isolated malignant cells [2,4].

- **"Pseudodiathesis" in Liquid-Based Cytology**

In senile atrophic vaginitis, cell necrosis and inflammation can form dense aggregates of debris and mucus that precipitate into small, rounded clumps in LBC. This pseudodiathesis closely mimics the tumor diathesis of an invasive squamous cell carcinoma, especially when accompanied by degenerated naked nuclei (blue blobs) [7]. However, unlike true diathesis, pseudodiathesis in LBC lacks the diffuse, proteinaceous, and "ground-glass" background staining characteristic of CC [5,7].

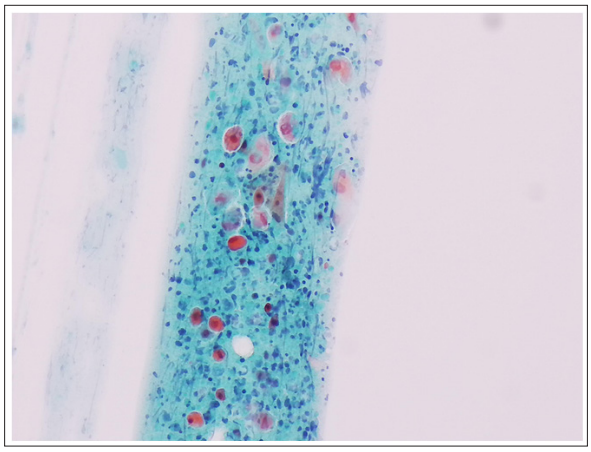

Figure 2: Conventional Cytology (CC). A cohesive sheet of benign, atrophic parabasal cells displays the classic "cobblestone pattern" (or calzada romana). Note how distinct cell borders distinguish individual cells within the mosaic-like flat sheet. The background shows moderate inflammation (Papanicolaou stain).

Final Reflection

Although liquid-based cytology offers indisputable technical quality—by eliminating obscuring factors such as blood, mucus, and inflammatory cells—it behaves as a double-edged sword in cases of severe atrophy. The loss of histological architecture (cohesiveness) and three-dimensional cellular shrinkage require cytopathologists to recalibrate their visual thresholds [4].

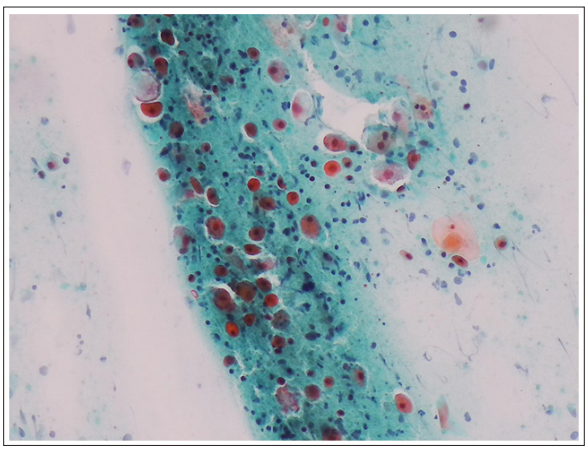

Figure 3: Conventional Cytology (CC). Focus on degenerative nuclear changes in atrophy. The background is denser with detritus. Parabasal cells show pronounced karyolysis (pale, disappearing nuclei), karyopyknosis (shrunken, dense nuclei), and a prominent orangeophilic cytoplasm (Papanicolaou stain).

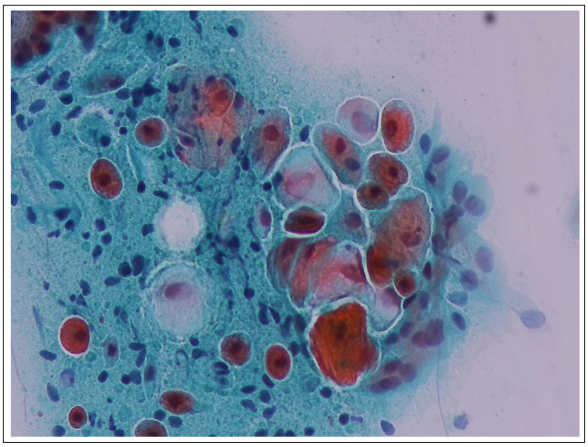

Figure 4: Conventional Cytology (CC). A large sheet of atrophic parabasal cells showing signs of severe degeneration and necrosis within a very messy, dense background. Multiple cells show severe orangeophilia (orange-red cytoplasm). This image depicts the "dirty background" challenge, where abundant cellular debris must be differentiated from tumor diathesis (Papanicolaou stain).

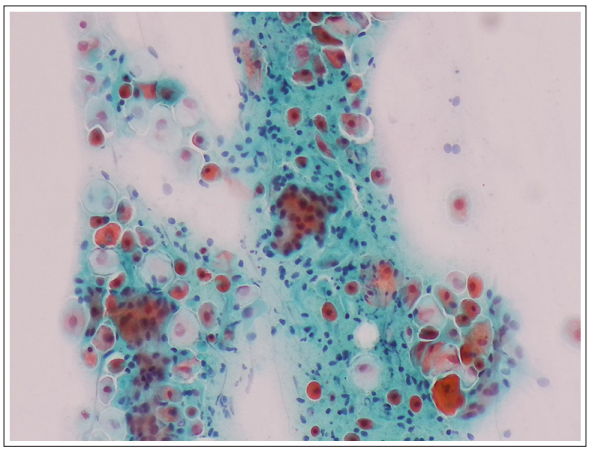

Figure 5: Conventional Cytology (CC). Overview of severe atrophy and inflammation. This large field demonstrates the typical conventional smear appearance with a mixed inflammatory exudate and dense sheets of parabasal cells, some with orangeophilia and other showing degenerative changes in a busy, non-monolayered background (Papanicolaou stain).

To prevent unnecessary overdiagnosis and the subsequent cascade of colposcopies and interventions in postmenopausal women, it is imperative to rely on the excellent nuclear membrane definition provided by LBC (which remains smooth and regular in atrophy, unlike the angulated and irregular contours of HSIL). When persistent morphological doubt remains, recommending a local estrogen maturation test before rendering a definitive diagnosis of atypia continues to be the most prudent and cost-effective clinical approach [1,8].

References

1. Nayar R, Wilbur DC, editors. The Bethesda System for Reporting Cervical Cytology: Definitions, Criteria, and Clarifying Images. 3rd ed. Cham: Springer; 2015.
2. Nance KV. Evolution of cytology in the liquid-based era: Challenges and opportunities in gynecologic cytology. Diagnostic Cytopathology. 2008. 36: 873-879.
3. Bishop JW. Comparison of the ThinPrep Pap Test and the conventional Papanicolaou smear in a gynecology clinic setting. Visual and morphological differences. Acta Cytologica. 2002. 46: 795-802.
4. Clark SB, Dawson AE. Liquid-based cytology of atrophic smears: A challenge in everyday practice. Cancer Cytopathology. 2004. 102: 83-88.
5. Kovatich AJ, Henderson RA. The "clean background" of liquid-based cytology: Pitfalls in the evaluation of atrophic vaginitis and tumor diathesis. Diagnostic Cytopathology. 2011. 39: 411-417.
6. Deshou H, Changhua W, Qiyu J, Chunjie L, Lihua L. Evaluating the diagnostic accuracy of liquid-based cytology in postmenopausal women with atrophic changes. Journal of Lower Genital Tract Disease. 2016. 20: 234-238.
7. Atla BL, Prasad U, Sri L, Kumar KP. Comparison of conventional Papanicolaou smears and liquid-based cytology: Detailing the background and cellular features. Journal of Cytology. 2019. 36: 151-156.
8. Wright TC, Massad LS, Dunton CJ, Spitzer M, et al. 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. American Journal of Obstetrics and Gynecology. 2007. 197: 346-355.