



## Case Report

## Reactive and Reparative Changes Mimicking Dysplasia: A Gynecologic Cytopathology Case Report

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### Abstract

**Background:** Reactive and reparative endocervical changes may closely resemble dysplasia or glandular neoplasia, creating potential diagnostic challenges. Cervical cytology is a key component of cervical cancer screening. **Methods:** A 42-year-old woman undergoing a routine cervical cancer screening is the subject of our descriptive gynecologic cytopathology case. Cytomorphological results were interpreted in relation to clinical data after a traditional Papanicolaou smear was examined. Since this is a single case report, no statistical analysis was done. Reactive squamous and endocervical cells with smooth nuclear contours, finely granular chromatin, mild nuclear enlargement, and occasionally prominent nucleoli were seen in the Pap smear. Mucus and inflammation were visible in the background. Preserved nuclear polarity, the lack of coarse chromatin or aberrant mitotic activity, and benign clinical findings supported a reactive and restorative process despite early concerns about glandular atypia. Malignancy or intraepithelial lesions were not found in the final diagnosis. **Conclusions:** In cervical cytology, reactive and reparative atypia may resemble dysplastic or neoplastic alterations. To prevent overdiagnosis and needless interventions, careful cytomorphological evaluation in conjunction with clinicopathological correlation is crucial.

**Keywords:** Cervical cytology; Endocervical glandular atypia; Reactive changes; Repair Endocervical; Pap smear.

### Introduction

Cervical cytology continues to be the mainstay of early detection and prevention of cervical cancer globally, offering a reliable way to detect malignant and precancerous lesions prior to clinical progression. The presence of endocervical cells, a crucial indicator of sampling from the transformation zone, is closely associated with the quality of Pap smear samples [1]. Nonetheless, a diagnostic challenge in gynecological cytopathology remains the interpretation of endocervical glandular and reactive changes.

In routine cytology, endocervical glandular atypia is relatively rare. Even when it is found, a significant percentage of subsequent histological follow-up specimens do not confirm malignant or premalignant disease. The substantial overlap in cytomorphological characteristics between reactive or reparative endocervical alterations and actual premalignant glandular lesions is a major contributing factor to this diagnostic uncertainty [2]. Recent developments in image analysis and artificial intelligence have improved the accuracy and reproducibility of cervical lesion detection, helping cytologists avoid such diagnostic pitfalls [3].

In routine screening practice, such as the adjustment of atypical squamous cells, especially ASC-US that usually indicate reactive or inflammatory changes instead of real dysplasia, will come additional difficulties. It is important to know the cytomorphologic spectrum of ASC-US so that it can be distinguished from higher-grade lesions, which requires appropriate management [4]. This complexity is compounded by the presence of inflammatory conditions (eg, cervicitis and vaginitis), which may modify cellular morphology, hide diagnostic detail, and mimic atypical glandular or squamous abnormalities. Such morphologic similarity can lead to interpretive pitfalls, particularly when reactive endocervical changes show nuclear enlargement, hyperchromasia, or irregular chromatin distribution that resembles neoplasia [5,6].

As precision cytopathology gains importance, case-based documentation of these difficulties is important to heighten awareness among cytologists and pathologists. We report a case of longstanding reactive and reparative endocervical cellular changes that closely mimicked neoplastic changes, where we emphasize cytomorphologic features must always be correlated with clinical context and follow-up

investigations in order to avoid overdiagnosis and unnecessary intervention.

## Case Presentation

### 1. Patient Information

A 42-year-old married female, gravida 3 para 3 presented for routine cervical cancer screening. She had intermittent mild chronic vaginal discharge, but denied pelvic pain, fever or abnormal bleeding. Her menstrual cycles are regular, and she does not take hormonal contraception. Patient's past medical history is unremarkable except for no previous abnormal Pap smears and there are no known sexually transmitted infections. Her pelvic examination revealed a reddened cervix with everted endocervical mucosa compatible with ectropion and many small translucent Nabothian follicles. The examination did not reveal suspicious lesions or ulcerations.

### 2. Cytotechnical Assay

Standard Pap smear (two slides, from the endocervix and ectocervix) was obtained. Papanicolaou stain (Hematoxylin, OG-6 and EA65) was done for smear

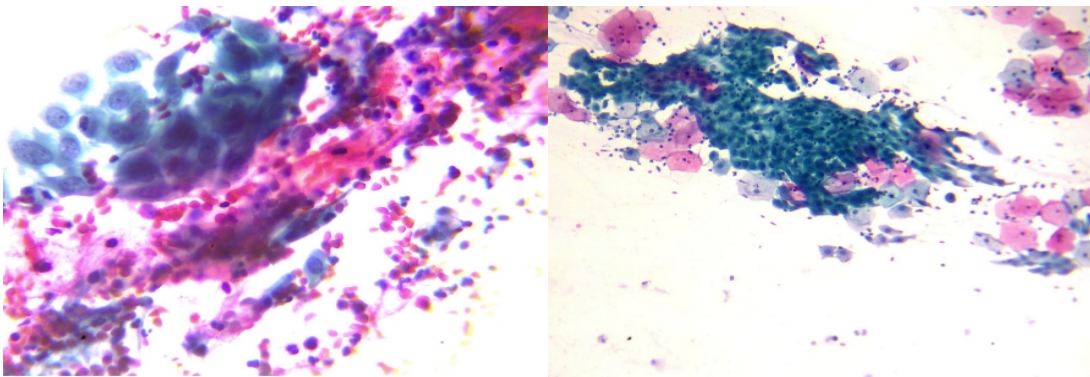
preparation, which was acceptable for evaluation. The transformation zone was adequately represented, and the test conducted was a Pap test only.

### 3. Adequacy Description

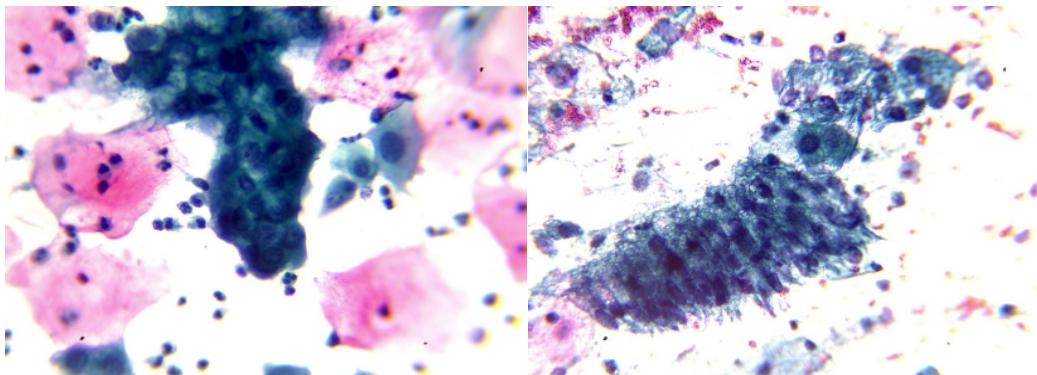
Slides showed thin and evenly spread smears with good cellularity and clear representation of transformation zone.

### 4. Cytomorphological Findings

Microscopic examination showed superficial and intermediate squamous epithelial cells with scattered parabasal cells. Reactive and reparative changes were seen including cohesive streaming, mild nuclear enlargement, pale finely granular chromatin, smooth nuclear contours with prominent nucleoli in some cases **Figure 1**. Sufficiently cytoplasm and homogeneous staining. There were endocervical and metaplastic cells which showed reactive changes but no dysplasia with technical feathering in **Figure 2**. Background revealed mixed inflammatory cells and sparse mucus; no significant microorganisms were identified.



**Figure 1:** Cervical cytology smear demonstrating reparative endocervical cells characterized by nuclear enlargement and prominent nucleoli (Pap stain)





**Figure 2:** Representative photomicrograph demonstrating endocervical cells in a Pap smear exhibiting reactive changes that mimics adenocarcinoma in situ. The cells appear in crowded clusters with enlarged hyperchromatic nuclei and increased nuclear-to-cytoplasmic ratio, features that may raise suspicion for glandular neoplasia in cervical cytology.

### 5. Final Cytological Diagnosis

No intraepithelial lesion or malignancy (NILM). These reactive and reparative cellular changes are characteristic of chronic cervicitis or a post-procedural/reactive process

### 6. Interpretation and Significance

These results suggest chronic cervicitis consistent with cervical ectropion and Nabothian follicles. Satisfactory sampling of the transformation zone was not achieved, reinforcing the need to differentiate between reactive nuclear enlargement or prominent nucleoli from dysplastic changes to prevent over diagnosis.

### 8 Ethics Approval and Consent to Participate

This study was conducted in accordance with institutional ethical standards. Ethical approval was obtained from the Ethics Committee Libyan International University. Written informed consent was obtained from the patient for the procedure and for publication of anonymized clinical data and images.

### Discussion

Endocervical glandular changes in cervical cytology are one of the most difficult aspects of gynecological pathology to interpret. While the Pap smear is an invaluable screening test, its diagnostic capabilities have limitations such that reactive and reparative processes can masquerade as atypical glandular or neoplastic processes. Inflammatory or reparative processes are a common source of false-positive diagnoses of atypical endocervical cells (AEC)1,2A recurrent theme in the literature. Pulkkinen et al. [12] found that many of the smears initially categorized as atypical were ultimately shown to represent benign processes, including chronic inflammation, squamous or tubal metaplasia, and microglandular manifestations, demonstrating that cytomorphologic overlap is misleading if not correlated with clinical follow-up and parameters seen on histology [2].

Similarly, Nasu et al. histology revealed that some cytologic features initially considered atypical could instead represent a normal reactive change of the glandular epithelium rather than precancerous lesions or adenocarcinoma [8]. Lack of notable mitotic activity. Three-dimensional crowding or coarse chromatin, therefore, substantiates a benign interpretation and highlights the need for corroboration of cytological impressions with histopathologic confirmation. McCluggage further elaborated, warning that benign glandular processes such as tubal metaplasia, microglandular hyperplasia, and inflammation can closely

mimic neoplastic lesions. His review emphasizes utility of adjunctive testing, like HPV DNA assays and immunohistochemical stains (p16, MUC6), to help reconcile difficult cases and avoid unwarranted excision. [9]. Lee et al also warned that cytologic diagnoses of atypical endocervical cells have a high risk of overinterpretation, as mild nuclear enlargement or prominent nucleoli can be reactive and not signify adenocarcinoma[10]. Conversely, Wilbur identified diagnostic features favoring adenocarcinoma in situ or invasive endocervical adenocarcinoma, including prominent nuclear hyperchromasia with coarse chromatin, glandular crowding with 3-dimensional papillary architecture, and increased mitotic or apoptotic activity [11]. The absence of these features, especially in conjunction with a setting of inflammation, makes reactive or reparative interpretation more likely.

Nuclear enlargement with smooth contours, pale granular chromatin and occasional collateral nucleoli were characterized as cytological findings in the present case associated to clinical evidence of ectropion and nabothian cysts. This is consistent with Kamal's description of "atlas" like characteristics of benign reactive processes that are often streaming, cytoplasmic vacuolization and inflammatory backgrounds that can mimic dysplasia but respond to targeted clinical management [12]. Goff's earlier work also acknowledged that a considerable fraction of both background and glandular atypia in Pap smears was reactive, reinforcing benignity in this case [13]. Scott et al. Atypical reactive proliferations of the endocervical epithelium were specifically noted, especially in association with endometrial sampling or cancer [13.14]. Although such lesions are sometimes described as potentially alarming due to features such as nuclear stratification or micropapillary processes, these findings are usually explainable based on the clinical context. Our patient had none of these associations, supporting a diagnosis of benign reparative change. Similarly, Ghorab et al showed that cases of reactive glandular atypia associated with polyps or inflammation did not evolve into adenocarcinoma at follow-up, supporting conservative management when HPV is negative and cytologic atypia does not persist [15].

The importance of clinical context is further underscored by Lesack et al [7], who showed that glandular atypia after radiation therapy may be very similar to precancerous changes but is in fact reactive. Despite its lack of radiation



history, the principle remains the same: cytological interpretation needs to be contextualized with patient history to prevent misclassification. Calof and Cooper, on squamous intraepithelial lesions (SIL), supported this eclectic approach emphasizing quality control methods, incorporation of HPV testing and close clinicopathological correlation as protection against over diagnosis [16].

### Conclusion

Reactive and reparative endocervical changes that persist may show cytomorphologic characteristics that resemble neoplastic or premalignant gland lesions and this may pose a significant diagnostic challenge in routine cervical cytology. This case serves reminds to consider the broad spectrum of benign reactive changes, including nuclear enlargement, prominent nucleoli and streaming patterns in

chronic cervicitis, ectropion or Nabothian cysts context. Proper discrimination of reactive and neoplastic processes (especially in borderline cases) requires meticulous cytomorphologic assessment with clinical correlation, as well as ancillary tests when needed (HPV DNA assays or immunohistochemistry). Reactive changes may be overinterpreted, incurring undue stress, invasive procedures and overtreatment or they might not be identified in a timely fashion allowing substantial pathology to develop. Thus, correlation with clinicopathology remains key for balanced interpretation. Documenting these types of cases is important to create awareness among cytologists and pathologists, which would improve diagnostic accuracy and also help strengthen evidence-based conservative management policies and timely follow up of the patients.

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