Universal Library of Medical and Health Sciences Case Report

ISSN: 3064-6545 | Volume 3, Issue 1

Open Access | PP: 16-19

DOI: https://doi.org/10.70315/uloap.ulmhs.2025.0301003

Discuss Possible Causes and Steps that should be Taken to Avoid False-Negative Cytology. A Case of Grade 3 Intraepithelial Neoplasia of the Cervix Associated with HPV

Kabulo Katshi Cedric[1,2]*, Shamba M Bokongo Didier[2], Tiago de Jesus Manjolo Chiambo[2], KapitaIzana Marie Jeanne[1]

[1]University of Lubumbashi, Department of Pathology, University of Lubumbashi Clinic.

[2]OCTAVIO Diagnostic Center.

INTRODUCTION

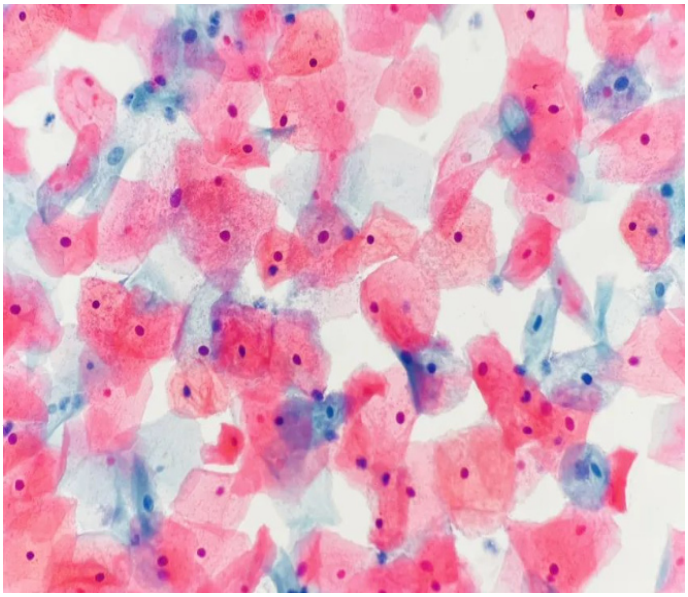
We recently encountered a case with TCT-negative cytology and extensive CIN3 on histological biopsy. We review the initial cytology and discuss possible causes and measures to avoid false-negative cytology leading to unfavourable results.

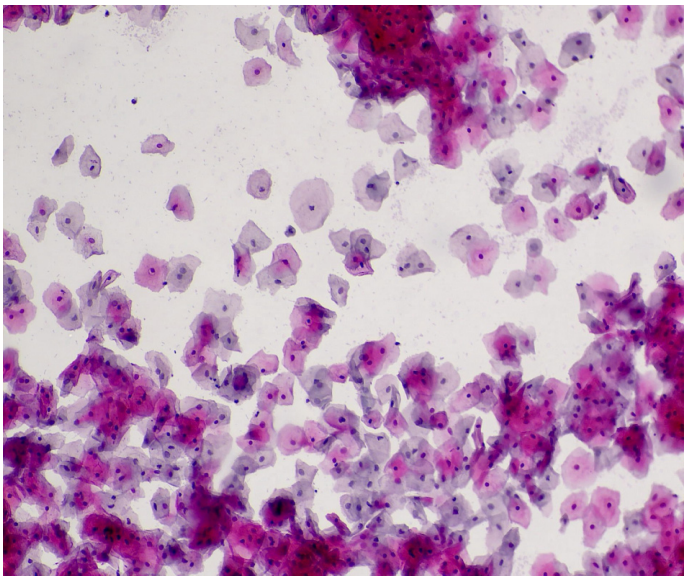
Clinical Background

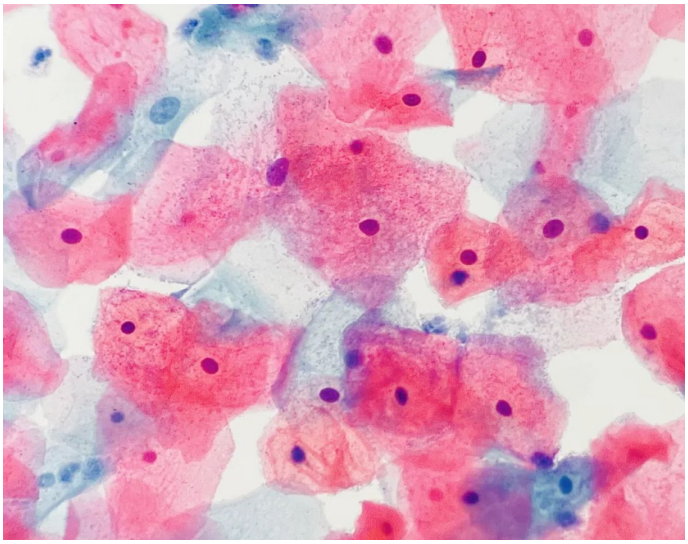
The patient, a 36-year-old woman, presented to the clinic with brown discharge before and after menstruation and underwent a full range of HPV testing and liquid-based thin-layer cytology in the outpatient clinic.

Cervical Cytology

Liquid cervical samples were sent for examination, preparation of the membrane and staining by pasteurisation as follows: of interest







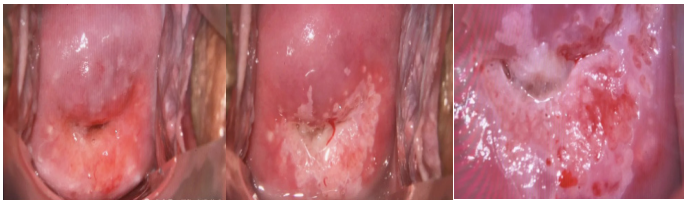
More indicator cells are visible.

Citation: Kabulo Katshi Cedric, Shamba Bokongo Didier, KapitaIzana Marie Jeanne, "Discuss Possible Causes and Steps that should be Taken to Avoid False-Negative Cytology. A Case of Grade 3 Intraepithelial Neoplasia of the Cervix Associated with HPV", Universal Library of Medical and Health Sciences, 2025; 3(1): 16-19. DOI: https://doi.org/10.70315/uloap.ulmhs.2025.0301003.

Interpretation of liquid cervical cytology: Specimen quality: Satisfactory sample interpretation: No intraepithelial lesions or malignancy (NILM). Altered flora suggesting bacterial vaginosis.

Colposcopy

Although the TST was negative, the patient was clinically examined by colposcopy after 2 months because she was HPV16 positive:

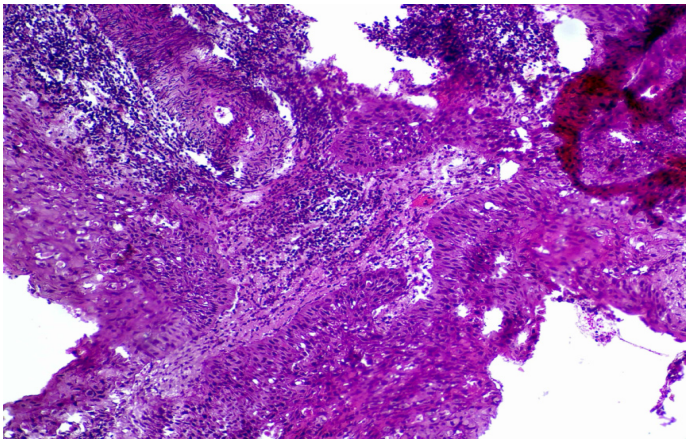


Colposcopic images: normal vulva, no vaginal wall abnormalities, heavy columnar epithelial ectasia in the lower lip of the cervix, thick white epithelium on the vinegar-white test, faint discoloration in 3 minutes, scattered white rings in the gland mouths. The iodine test is not coloured. Colposcopic evaluation impression: squamocolumnar junction partially visible: type 2 transformation zones: satisfactory colposcopic results.

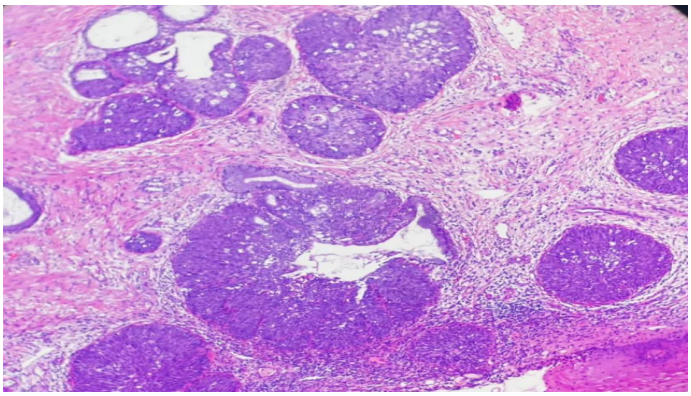
Further management advice:

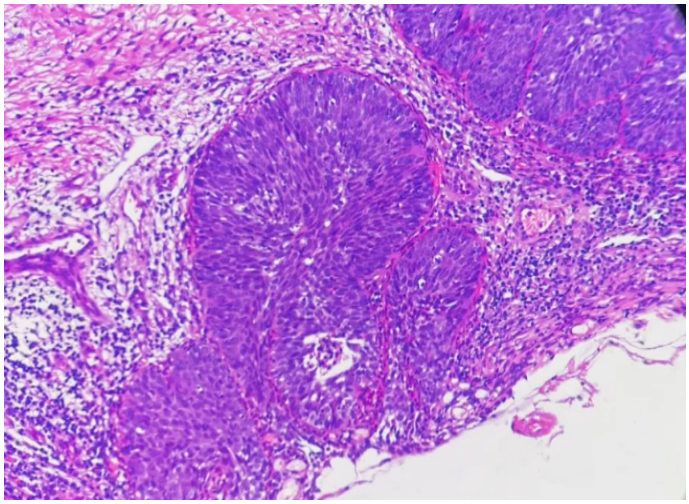
1. 11-point and 6-point cervical tissue biopsy.

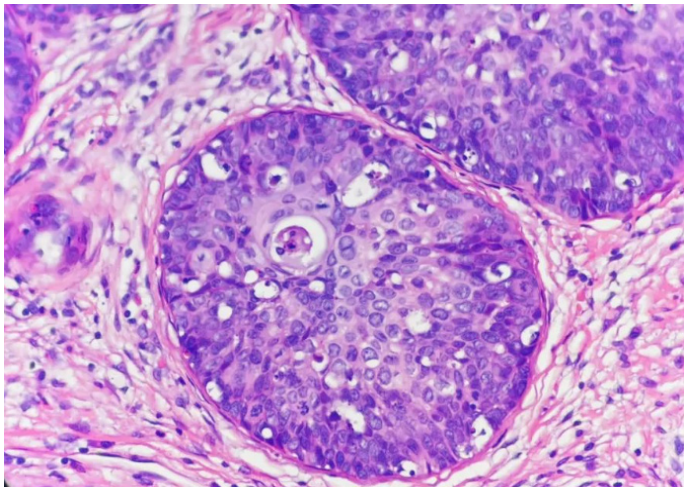
Cervical Biopsy



Cervical biopsies were taken at two time points (6 and 11). At the time of biopsy, CIN-III with affected glands was detected at point 6.



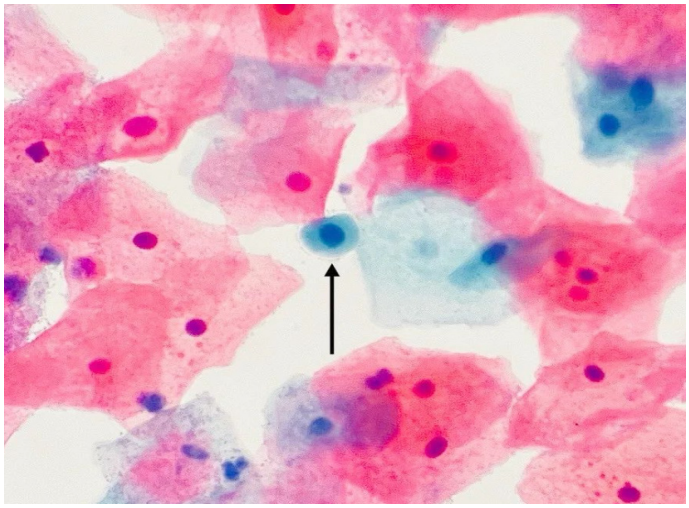




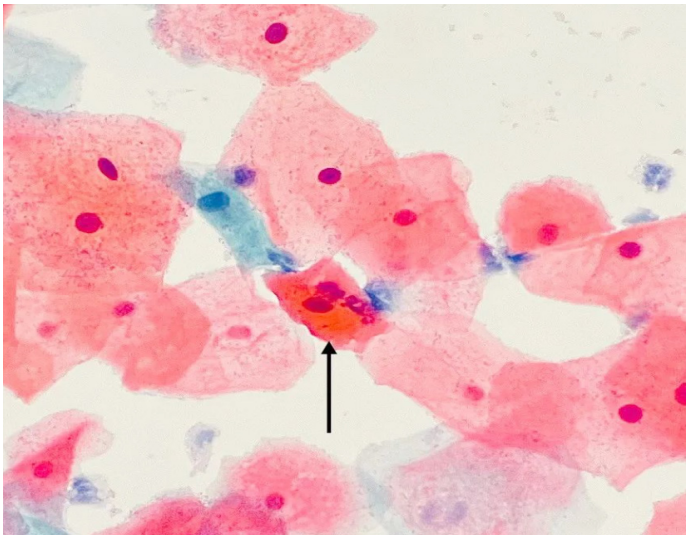
Subsequently, a cervical conization was performed and postoperative pathological findings showed the cervix to be at points 1-12, with CIN-III with involved glands detected at points 1-11.

Cervical Cytology

Initial liquid-based cervical cytology examination:



This smear examination revealed few components of the migratory zone, with only a few squamous cells (black arrows) and no ductal cervical gland cells. There are fewer than 10 component cells in the migratory zone.



Re-examination and careful reading of the smear failed to detect heterogeneous cells, individual keratosis pilaris cells or other indicator cells.

The TST was re-examined by two physicians and the sample was interpreted as follows: Sample quality: satisfactory (insufficient migratory zone component) Sample interpretation: no intraepithelial lesion or malignancy (NILM). Altered flora, suggestive of bacterial vaginosis.

DISCUSSION

2.1 Confusion and examination The patient's cervix was found to have extensive CIN3 after conization, whereas the preoperative TCT was negative. Why would a false-negative cytological result be obtained for such an extensive high-grade lesion? In line with quality control management recommendations [1], we reviewed the preoperative TST. The examination was performed by the original TST diagnostician and another cytology specialist. On review, the number of squamous epithelial cells in the TST sample met satisfactory criteria, and the negative reading (NILM) of the original TST was correct.

2.2 Concerning the migratory zone: cytology and colposcopy It should be noted, however, that examination of the TCT revealed that the migratory zone component of the smear did not meet the TBS recommendation of at least 10 cells, with only a few individual squamous cells and no cervical ductal adenohypoplasmic cells. In accordance with the requirements of the TBS report, the absence of migratory zone composition does not alter the satisfactory evaluation of the sample, but must be mentioned in the report [2]. Because of the extreme contrast between the negative cytology and the extensive histology of CIN3 in this case, we initially hypothesized that this was due to a displacement of the migration zone that did not allow adequate exposure, to an elevated location of the cervical lesion or to a deeper location of the lesion relatively close to the internal os of the cervical canal, which led the gynaecologist not to take cytological samples to reach the site of the lesion, and the paucity of migration zone components in the TCT smear seemed to support this conjecture. It has been suggested that a negative cervical cytology devoid of migration zone components presents an increased risk of false negatives [2]. More indicator cells are visible.

Interpretation of liquid cervical cytology: Specimen quality: Satisfactory sample interpretation: No intraepithelial lesions or malignancy (NILM). Altered flora suggesting bacterial vaginosis.

2.3 Colposcopy Although the TST was negative, the patient was clinically examined by colposcopy after 2 months because she was HPV16 positive The cervical migration zone: As there was a two-month interval between the initial liquid-based cervical cell sampling and the colposcopy, and as the state of the cervical migration zone varies according to a number of factors (e.g. hormones), it is also not possible to know with certainty its state at the time of the initial cytological sampling. The patient's TST suggests bacterial vaginosis (BV), and patients with BV often have heavier, grey-white, homogeneous and dilute vaginal secretions. Gynaecologists need to swab excessive vaginal secretions during cervical cytology, and unregulated sampling can lead to false negative cytology results due to insufficient sampling of diseased cells. In addition, TCT in our department is a semi-automated procedure where the technician manually aspirates the sample from the preservative fluid and places it in the sample tray for membrane preparation by the machine. If the specimen is not properly shocked and mixed, uneven aspiration of the specimen may also increase the risk of false negative results. In addition, sample titration can also be the cause of a rare cytological-histological discrepancy. However, we did not see HSIL in any of the 20 samples before or after this patient's TCT number, and only one case of ASC-US with very few heterogeneous cells was in fourth place after it.

2.4 How to avoid or minimize false-negative results and their negative consequences Although this case had a false-negative cytological result, fortunately, after active management by the gynecologist and a series of investigations including colposcopy and biopsy at a later stage, this patient's diagnosis was finally clarified and she was given regular treatment accordingly. This confirms the importance and necessity of combining cervical cancer screening with direct referral for colposcopy evaluation of HPV16/18 positive patients [4]. Furthermore, according to relevant studies, there is a positive correlation between BV and precancerous cervical lesions, with BV-positive patients showing a higher incidence of high-grade cervical intraepithelial neoplastic and cervical cancer than BV-negative patients [5]. Cytologists should therefore be reminded to take extra care when examining the films of BV patients to avoid false-negative results due to misdiagnosis or omission. At the same time, we suggest that all BV patients should be linked to HPV testing results and followed up after treatment.

CONCLUSION

False-negative cytology results do occur and the analysis of the cytology-histology correlation is very important. Avoiding or reducing the incidence of false-negative cytology and its negative consequences requires the combined efforts of clinicians, technicians, and pathologists.

REFERENCES

1. Davey DD, Austin RM, Birdsong G, Zaleski S. The impact of the Clinical Laboratory Improvement Amendments of 1988 on cytopathology practice : a 25th anniversary review. J Am Soc Cytopathol. 2014, 3(4):188-198.
2. Nayar R, Wilbur DC, traduit par Samuel Chen et revu par Yu S. Meng. Système de rapport Bethesda pour la cytologie cervicale-définitions, vertèbres étiquetées et annotations [M]. Beijing:Science Press,2018:1-288.
3. Mills, SE, ed. Practical histology for pathologists (4e éd.) [M]. Beijing: Science Publishing House,2017:1-1277.
4. Comité professionnel de la prévention et du contrôle des tumeurs de la Société chinoise de médecine préventive, Comité professionnel de la colposcopie et de la pathologie cervicale de la branche des obstétriciens et gynécologues de l'Association chinoise des médecins, et branche de la colposcopie et de la pathologie cervicale utérine de l'Association chinoise des sciences eugéniques, et al. Chinese expert consensus on human papillomavirus nucleic acid testing for cervical cancer screening (2022) [J].ChineseMedicalJournal , 2023, 103(16) : 1184-1195
5. Liu Zhengnan, J. Review. Relations entre les micro-organismes vaginaux, l'infection cervicale par le VPH et les lésions cervicales [J]. Journal of PracticalObstetrics and Gynaecology, 2022, 38(1) : 33-36.