

Bericht der Arbeitsgemeinschaft Zytopathologie der Deutschen Gesellschaft für Pathologie

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Bei der Sitzung der AG Zytopathologie am 1. Juni 2023 im Rahmen der 106. Jahrestagung der Deutschen Gesellschaft für Pathologie (DGP) in Leipzig wurden in diesem Jahr 2 Fortbildungsvorträge zum Thema „Gynäkologische Zytopathologie“ gehalten, da die Zytologie im Rahmen der seit Anfang 2020 geänderten Zervixkarzinomvorsorge nach wie vor einen wichtigen Stellenwert hat. Der erste Vortrag beschäftigte sich mit den plattenepithelialen Läsionen der Cervix uteri, der zweite mit den glandulären Veränderungen.

Gynaecological cytology as an essential component in the prevention of cervical carcinoma. Squamous and glandular changes: squamous lesions

Squamous cell carcinomas account for about 85% of cervical cancers. Most squamous cell carcinomas are associated with high-risk HPV infection; only a small proportion of these carcinomas are not. HPV-independent carcinomas are said to have a worse prognosis than HPV-associated squamous cell carcinomas. Severe squamous epithelial dysplasia/carcinoma in situ (CIN 3; HSIL (WHO)) is the precursor lesion of squamous cell carcinoma and therefore the target lesion in the cervical cancer screening systems established in many countries.

Until a few years ago, cytological examination of a PAP smear was the only method to identify such a lesion. In the meantime, however, DNA or RNA testing for high-risk HPV viruses has taken over

this role in several countries. In Germany, this test is used together with cytology (co-testing) for the group of women over the age of 35. For women younger than 35 years of age, an annual cytological examination is still performed. In the event of an abnormal finding, this finding is checked with an HPV test in women between 29 and 34 years of age. Since 1 July 2014, the basis for the classification of cytological findings has been the Munich Nomenclature III. This is a morphological classification whose groups have a different risk of higher-grade dysplasia (CIN 3; HSIL), either at the time of diagnosis, cumulatively in the further clinical course, or at subsequent screenings. Detailed knowledge of the morphological characteristics of each group is therefore essential. Diagnostic difficulties are more likely to occur in the low-grade groups of findings. Diagnostic support could be provided by additive tests with the biomarker p16/Ki-67, which shows double staining for both markers in the case of a transforming HPV infection. This marker is also very useful in HPV-positive, cytologically negative cases, which may react positively, although no abnormalities can yet be detected by conventional morphology. Furthermore, this marker can be used in the differential diagnosis of various reactive changes in the cervix uteri. In the meantime, with the help of digital cytology and artificial intelligence, the automated evaluation of p16/Ki-67-stained slides has also been achieved. This new technique removes the remaining subjective component of cervical cancer screening and delivers consistent quality for providers and



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patients. Switching from PAP smears to automated evaluation of the double-stained specimens significantly reduces the number of colposcopies and achieves excellent performance even in a simulated, fully vaccinated population. Since it is a cloud-based implementation, this approach is globally accessible.

Digital cytology, together with artificial intelligence, also offers new approaches for conventionally stained PAP smears. Compared to conventional morphology, this new method shows increased sensitivity without loss of specificity. This means that lesions requiring treatment are detected earlier without increasing the number of colposcopies.

Dietmar Schmidt

Gynaecological cytology as an essential component in the prevention of cervical carcinoma. Squamous and glandular changes: glandular lesions

Adenocarcinomas constitute about 25 % of all cervical cancer. With its heterogeneity and about 15 % of non-HPV associated subtypes, this tumour represents a substantial challenge in the prevention and the diagnosis of cervical carcinomas. Furthermore, it is often necessary to distinguish between true HPV-negative cervical cancer and false HPV-negative cases or an incorrect classification of non-cervical cancer. The aim of this study is a documentation of the importance of cytological examination of glandular cells in the context of already established HPV tests and the continuing increase of additive techniques. The following conclusions are based on a review of literature data and our own expertise. The most benign glandular changes do not require any additional examinations. But advanced knowledge of the same issue is essential for the correct diagnosis of adenocarcinoma in situ (AIS) of the uterine cervix. The most common HPV-associated AIS of usual type shows characteristic cytological criteria and can be additionally substantiated by p16/Ki67 positivity. The cytological diagnosis of invasive HPV-associated adenocarcinoma is also possible, but support with some immunohistochemical methods is occasionally necessary.

The cytological diagnosis of HPV-negative AIS is difficult because the typical cellular changes are usually much less pronounced or even missing. However, the cytological identification of HPV-negative adenocarcinoma and its precursors, with often very subtle glandular changes in a PAP smear, is currently the only option for an early detection of this aggressive and therapy resistant neoplasia. This assumes an awareness of these lesions and a familiarity with their cytomorphological features, which in the meantime have been well described. The definitive differentiation between an HPV-negative adenocarcinoma of the uterine cervix and a non-cervical cancer is oftentimes not possible without the support of additional methods, especially immunohistochemical methods and additional molecular techniques. Currently, in the age of immunohistochemical and molecular methods, which are inaccessible to some, the cytological examination of glandular cells is an important indicator for setting the correct prophylactic and diagnostic paths.

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Einhaltung ethischer Richtlinien

Interessenkonflikt. D. Schmidt und I. Baltisser geben an, dass kein Interessenkonflikt besteht.

Für diesen Beitrag wurden von den Autor/-innen keine Studien an Menschen oder Tieren durchgeführt. Für die aufgeführten Studien gelten die jeweils dort angegebenen ethischen Richtlinien.

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