

HPV-induced cervical glandular lesions can be overstated on Pap smear

Teresa Pusiol, Francesco Pisciole, Luca Roncati

It is well known the utility of human papilloma virus (HPV) testing in young women with atypical glandular cells (AGC) on Pap test. In fact, HPV testing may be useful in risk stratifying young women with AGC on Pap test, because they are at risk of having an HPV-positive cervical lesion [1]. It can happen to histologically observe occasional cases of HPV-positive glandular cervical dysplasia/metaplasia, labeled as adenocarcinoma on Pap smear. In these cases, the Pap smear reveals atypical cervical cells, characterized by increased size, irregular outline, nuclear hyperchromasia, prominent nucleoli, dense chromatin and inversion of the nucleus/cytoplasm ratio. These atypical cells can be sometimes arranged in a floral pseudo-glandular fashion (Figure 1A). For this reason, a cytological suspicion of adenocarcinoma can be formulated and the patient is submitted to cervical conization. However, the final histopathological examination shows only a glandular cervical dysplasia/metaplasia, characterized by pseudo-stratified and stratified lining epithelium, enlarged hyperchromatic nuclei with mild polymorphism and occasional apoptosis. Nucleoli are scantily noticeable, while mitotic figures or cribriform/ papillary formations are completely absent (Figure 1B and 1C). Moreover, the dysplastic/metaplastic glands can result immunoreactive for p16 protein (Figure 1D) and HPV DNA can be ascertained by molecular biology. Thanks to our experience, on pap smear it is not

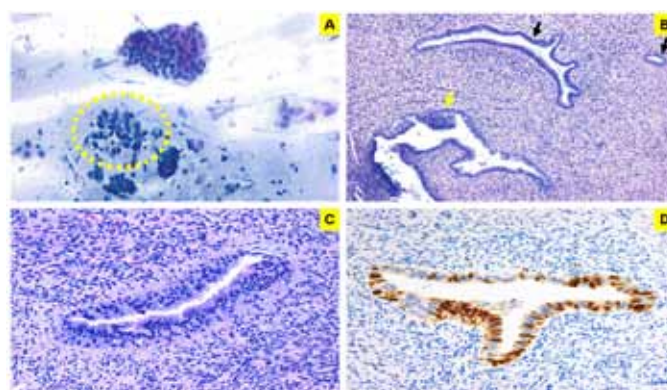


Figure 1: On Pap smear (A) the atypical glandular cells are arranged in a floral pseudo-glandular fashion (yellow circle) (Papanicolaou stain, x40), (B) On histopathological examination, a dysplastic/metaplastic gland (yellow arrow) is seen near to normal cervical glands, pointed out by black arrows (H&E stain, x10), (C) At higher magnification, the dysplastic/metaplastic gland shows pseudo-stratified and stratified lining epithelium, enlarged hyperchromatic nuclei and occasional apoptosis. No mitotic figures are observable, (D) The dysplastic/metaplastic glands can result immunoreactive for p16 (magnification, x20).

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possible to distinguish endocervical adenocarcinoma in situ from HPV-positive glandular dysplasia/metaplasia, which appears to be an its possible precursor. A well representative Pap smear can allow an early diagnosis of this insidious HPV-induced lesion, avoiding the under-treatment of a possible cancer precursor [2]. At the same time, the application of HPV testing in childbearing age women with AGC on Pap test can initially direct to a fertility-sparing treatment, with the awareness that behind these atypical cells there may be a non-invasive HPV-induced lesion.

Keywords: Atypical glandular cells (AGC), Human papilloma virus (HPV), Pap smear, Uterine cervix

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