Annales de pathologie (2012) 32, e8—e14

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REVIEW

Cytological screening of endocervical adenocarcinoma

Le dépistage cytologique de l'adénocarcinome du col

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Accepted for publication on 13 September 2012
Available online 22 November 2012

KEYWORDS
Cervical screening;
Adenocarcinoma;
Cytology;
Bethesda terminology

Summary Invasive endocervical adenocarcinoma represents on average 15% of cervical carcinomas and it is associated with the human papillomavirus infection high risk types 16 and 18 in most cases. Its detection has some special features compared to squamous cell carcinoma; glandular precancerous lesions are less known and only adenocarcinoma in situ is diagnosed by consensus among pathologists; adenocarcinoma in situ develops in the squamocolumnar junction by reserve cells but it is hard to be located by colposcopy in the endocervical canal or in the deep glandular recess. Sampling of endocervical cells requires brushes rather than an Ayre spatula. Cytological diagnosis of glandular cells abnormalities is based on the Bethesda System 2001 terminology which redefined endocervical cells abnormalities and also introduced the entity of adenocarcinoma in situ. This entity is characterized by specific morphological features, such as the radial arrangement of nuclei in the periphery, like ''at the end of the feathers of a bird's wing'' *(feathering of cells)*, images of nuclei palissading or rosette without tumoral diathesis. Glandular cells abnormalities are rare and represent less than 0.1% of all smears and less than 5% of abnormal smears. By improving the collection and the interpretation of abnormal endocervical cells, cytological screening should allow the diagnosis of in situ adenocarcinoma and detection of invasive adenocarcinoma at a very early stage. This will lead to a decrease in mortality from endocervical adenocarcinoma, especially in young women.
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MOTS CLÉS
Dépistage du cancer col ;
Adénocarcinome ;

Résumé L'adénocarcinome invasif du col utérin correspond en moyenne à 15 % des carcinomes du col utérin. Il est le plus souvent associé à une infection à papillomavirus humain de type 16 ou 18. Son dépistage présente des particularités par rapport au carcinome malpighien ; les lésions glandulaires précancéreuses sont moins bien connues et seul l'adénocarcinome in situ est diagnostiqué de manière consensuelle par les pathologistes ; l'adénocarcinome in situ se

DOI of original article: http://dx.doi.org/10.1016/j.annpat.2012.09.199.
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0242-6498/$ — see front matter © 2012 Elsevier Masson SAS. All rights reserved.
http://dx.doi.org/10.1016/j.annpat.2012.09.230

Cytologie ;
Terminologie
Bethesda 2001

développe autour de la jonction squamocylindrique à partir de cellules de réserve et peut être difficile à localiser en colposcopie dans le canal endocervical. Le prélèvement des cellules cylindriques nécessite une brosse plutôt que la spatule d'Ayre. Le diagnostic cytologique des cellules glandulaires se fait selon la terminologie Bethesda 2001 qui a redéfini le cadre des anomalies des cellules glandulaires et a introduit l'entité « adénocarcinome in situ ». Cette entité est caractérisée par des critères spécifiques, comme la disposition radiaire des noyaux en périphérie, donnant aux cellules un aspect ressemblant « à des plumes à l'extrémité d'une aile d'oiseau », des images de noyaux en palissade ou en rosette sans diathèse tumorale. Les anomalies des cellules glandulaires restent rares et correspondent à moins de 0,1 % de la totalité des frottis et moins de 5 % des frottis anormaux. En améliorant le prélèvement et l'interprétation des cellules cylindriques anormales, le dépistage cytologique devrait permettre le diagnostic d'adénocarcinome in situ et d'adénocarcinome invasif à un stade précoce. Une diminution de la mortalité par adénocarcinome du col, en particulier chez les femmes jeunes, devrait en résulter.
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Introduction

Endocervical adenocarcinoma's incidence remains stable or is slightly increasing in 2011, including those countries where a parallel decrease in squamous cancers' incidence is observed [1,2]. In some countries, like England or Australia, where there is a well-organized screening, invasive adenocarcinoma makes up almost one fourth of all invasive cervical cancers [3]. This increase has been particularly striking in women under 40 [1,4]. Over the last 20 years, invasive cervical adenocarcinoma's mortality has also increased in absolute and relative terms compared to squamous cell carcinoma [5]. Should we conclude that cytological screening is not suitable for detecting precancerous glandular lesions or invasive adenocarcinomas at a very early stage?

Precancerous lesions of the endocervical cylindrical epithelium

Adenocarcinoma in situ is the only histological recognized entity by consensus as a preinvasive lesion of the cervix [6] (Fig. 1). The adenocarcinoma in situ is sometimes referred to as high-grade intraepithelial glandular lesion or dysplasia. Progression from adenocarcinoma in situ to invasive adenocarcinoma is estimated to last between 5 and 13 years [7,8]. The adenocarcinoma in situ arises at the squamocolumnar junction after persistent infection with high-risk human papillomavirus (HPV) infection, types 16 and 18 being the most common [9]. Persistent HPV16 and 18 infections are usually associated with cervical squamous intraepithelial neoplasia (CIN 2—3) starting at the junction because these viruses have a higher affinity with keratinocytes and they can more easily reach the basal layers of the squamous epithelium where the viral cycle starts. HPV can also infect at the same time or, more rarely, separately reserve cells around the squamocolumnar junction which may differentiate towards glandular columnar cells [10]. The infection usually remains latent and in case of persistence it may allow the expression of viral oncogenes E6 and E7 in the columnar epithelium causing a transforming infection. Immunohistochemical expression of p16 is an indirect way of highlighting the transforming infection in the endocervical columnar epithelium [11]. Morphologically, the transforming infection results in adenocarcinoma in situ,

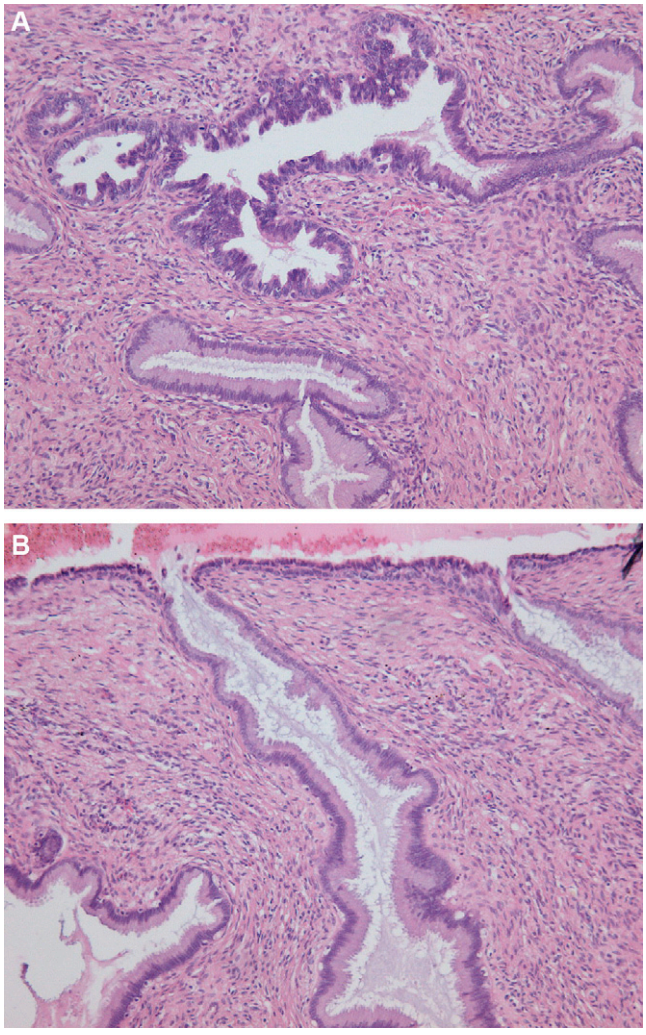

Figure 1. Adenocarcinoma in situ on a biopsy. A. The abnormal epithelium affects only a part of the endocervical glands. B. The abnormal epithelium reaches the surface of endocervical glandular structures which can be reached by a brush.
Adénocarcinome in situ sur une biopsie. A. L'épithélium cylindrique anormal n'intéresse qu'une partie des glandes endocervicales. B. L'épithélium cylindrique anormal atteint la surface des récessus endocervicaux. Une brosse peut donc prélever les cellules glandulaires anormales.

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