

Endocervical Adenocarcinoma in Young Women: Case Report

Sousa R¹ †, Soares S¹ * †, Figueiredo A CT (IAC), EFCS(Gyn)², Agapito P CFIAC, EFCS(Gyn)²,
Fernandes G MD², Castro L MD²

¹ School of Allied Health Technologies – Polytechnic Institute of Porto (ESTSP-IPP), Portugal

² Centro Hospitalar e Universitário de Coimbra (CHUC-HUC), E.P.E., Portugal

† These authors have contributed equally to this work

Received: March 2016/ Published: April 2016

***Corresponding author:**

Sílvia Soares

silvaisabelsilvasoares@gmail.com

ABSTRACT

The incidence of endocervical adenocarcinoma is increasing, especially in women aged between 20 and 30 years. According to recent studies, this increasing incidence might be due to persistent HPV infections associated with endogenous and exogenous risk factors. Sometimes, the treatment of this type of cancer may require a total hysterectomy, with consequent infertility and psychological trauma.

This paper aims to draw attention to the development of adenocarcinoma in young women and, in addition, to reflect on the factors that may be associated with the appearance of this pathology and the causes related to its late diagnosis, in order to avoid radical therapeutic actions. To this end, a clinical case is reported, regarding a screening cytology of a 30 year-old woman, with a cytological diagnosis of atypical glandular cells not otherwise specified (AGC, NOS), who was later sent to the Cervical Pathology Unit of the reference hospital. The second cytology allowed to diagnose endocervical adenocarcinoma, later confirmed histologically.

Key-words: gynaecological cytology, endocervical adenocarcinoma, young women, incidence.

INTRODUCTION

The endocervical adenocarcinoma is a malignant neoplasia arising from the mucus-secreting glandular cells of the endocervix. This condition is ten times less frequent than squamous-cell carcinoma; however, the most recent literature indicates an increase of three to four times in its incidence over the last few years^{1,2}.

The reasons behind this escalation are unclear¹. Can this growing incidence be due to an increasingly earlier diagnosis, as a result of the implementation of screening programmes? Or is there a real upsurge? What situations may hinder an early detection of adenocarcinoma? Why does it appear in young women?

CLINICAL HISTORY

A 30 year-old woman, with a red area in the uterine cervix, was submitted to a conventional cervical cytology in the context of a screening programme conducted on January, 2015. The diagnosis was atypical glandular cells, not otherwise specified (AGC, NOS).

The patient was referred to the Cervical Pathology Unit of the *Centro Hospitalar e Universitário de Coimbra*, E.P.E. (CHUC-HUC), on April 2015, where a liquid-based cytology of the cervix was performed, with a diagnosis of endocervical adenocarcinoma (SOE). The detection and genotyping of the Human Papilloma Virus (HPV) was then performed, using the Cobas® test, and the result was positive for HPV type 18.

CYTOLOGICAL FINDINGS

The conventional cytology screening was obscured with blood; however, it was possible to acknowledge the presence of syncytial groups and clusters of glandular cells, with nuclear and cytoplasmic characteristics that could not be appropriately assessed (**Fig.1A**). Still, the cytology under study presented some

more individualized groups, with an increased nuclear-to-cytoplasmic ratio, hyperchromasia and moderate anisokaryosis, with some cellular and nuclear overlapping (**Fig.1B**). Additionally, in a cluster of glandular cells it was also possible to observe pseudostratification (**Fig.1C**).

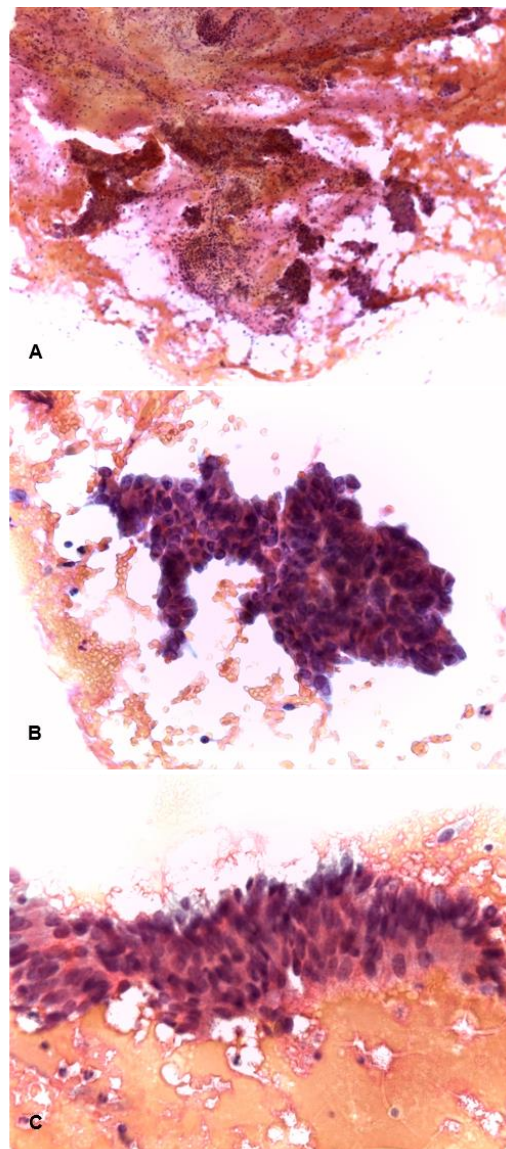


Fig.1 - Conventional cytology – Atypical glandular cells, not otherwise specified (AGC, SOE). **A** – Blood-obscured sample, with presence of syncytial groups and clusters of glandular cells, with no evinced cytoplasmic and nucleic details. Magnification: 100x. **B** – In more individualized groups, it was possible to observe an increased nuclear-to-cytoplasmic ratio, nuclear hyperchromasia and moderate anisokaryosis, with cellular and nuclear overlapping. Magnification: 400x. **C** – Pseudostratification. Magnification: 400x. *Papanicolaou* stain.

In the assessment of the liquid-based cytology, it was possible to notice the presence of superficial and intermediate squamous cells, as well as syncytial groups of endocervical glandular cells (**Fig.2A**). In what concerns to the glandular cells, the examiners observed cellular groups with pseudostratification, loss of honeycomb architecture and “*feathering*”. The cells exhibited a loss of polarity, increased nuclear-to-cytoplasmic ratio, nuclear hyperchromasia and presence of nucleoli. In addition, a background with tumour diathesis was also evident. (**Fig.2 B and C**).

The patient underwent two complementary cytological examinations: the HPV testing and genotyping, with a positive result for HPV18; and a dual-immunocytochemical staining technique (CINtec®), addressed to the cytoplasmic protein p16 and to the nuclear protein ki67 - presenting a positive dual stain result (**Fig. 3**) which, according to the literature, means that the HPV is already integrated in the host cell's DNA^{3,4}. The diagnosis of endocervical adenocarcinoma was confirmed histologically. (**Fig.4**).

DISCUSSION AND CONCLUSION

In this clinical case, two cervicovaginal cytologies were performed: the first one of screening (conventional cytology), with a diagnosis of atypical glandular cells not otherwise specified (AGC, NOS), and a second one, a liquid-based cytology, with a diagnosis of endocervical adenocarcinoma (NOS).

The cytomorphological characteristics of the two samples revealed some parameters that support the diagnosis of endocervical adenocarcinoma.

According to the literature review, some of the characteristics observed in the preparation obtained from the liquid-based cytology, namely the presence of “*feathering*”, three-dimensional clusters, pseudostratification,

nuclear atypia with a noticeable increased nuclear-to-cytoplasmic ratio, loss of cell polarity and tumour diathesis point to an endocervical adenocarcinoma.²

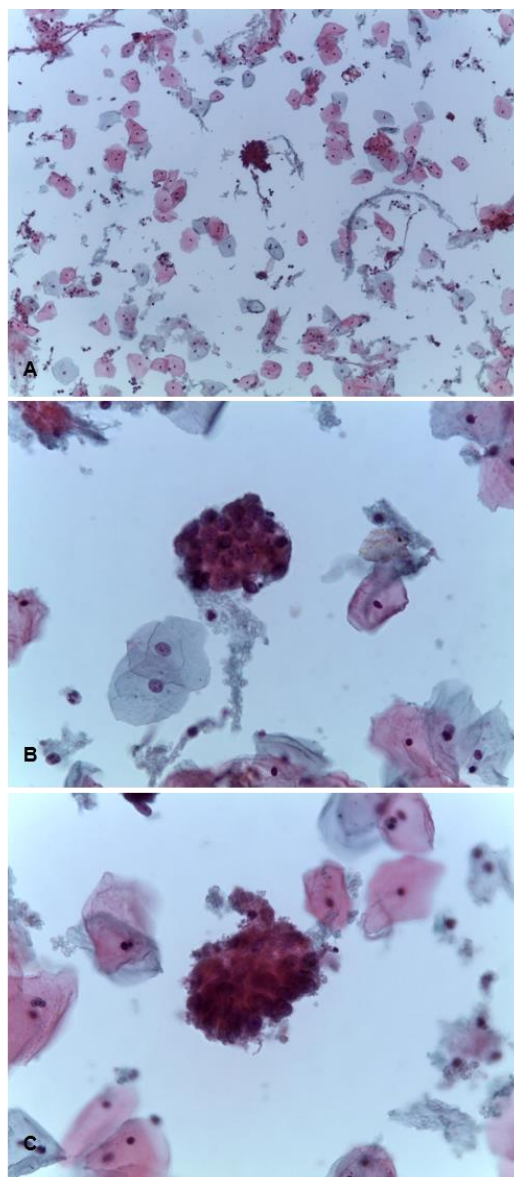


Fig. 2 – Liquid-based cytology - Endocervical adenocarcinoma (SOE). **A** – Superficial and intermediate squamous cells and syncytial groups of endocervical glandular cells. Magnification: 100x. **B and C** – Clusters of glandular cells with pseudostratification, loss of honeycomb architecture, “*feathering*”, loss of nuclear polarity, increased nuclear-to-cytoplasmic ratio, presence of nucleoli. Background with tumour diathesis. Magnification: 400x. *Papanicolaou* stain.

These features were not so evident in the screening cytology, due to some limitations associated with the conventional cytology, namely the abundant presence of blood.

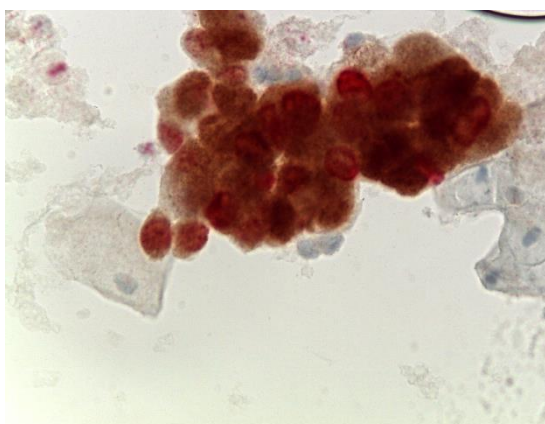


Fig. 3 – Double immunostaining of ki67 (red) and p16 (brown) proteins, using CINtec®. Magnification: 400x.

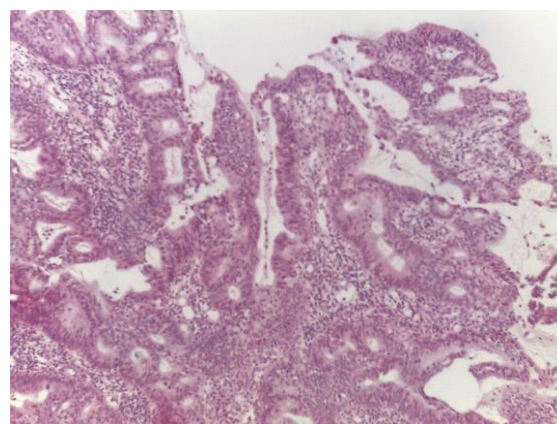


Fig. 4 – Biopsy of the uterine cervix. Well differentiated endometrioid adenocarcinoma of the endocervix. Haematoxylin e Eosin stain. Magnification: 100x.

However, despite being different, the cytological result did not condition the therapeutic behaviour of the patient².

The diagnosis of endocervical adenocarcinoma by gynaecological screening is harder to accomplish in comparison to the diagnosis of squamous-cell carcinoma. This is mainly due to the peculiar characteristics of the glandular endocervical epithelium, namely its location, which hinders the access by the cervixbrush, and the cellular monomorphic pattern, making more difficult to diagnose adenocarcinoma precursor lesions^{1,2}.

The appearance of adenocarcinoma in young women is rather uncommon; yet, according to the most recent literature, the incidence of endocervical adenocarcinoma is increasing (unlike the epidermoid carcinoma), mainly in women aged between 20 and 30 years. The use of oral contraceptives has been pointed as one of the factors contributing to the development of adenocarcinoma *in situ* and invasive⁵. However, infection by HPV, multiple sexual partners, sexual relationships before the age of 16 and multiparity have been referred to as the main risk factors for the occurrence of these glandular lesions in young women^{5,6}.

In the age group of 20-30, infections by some types of HPV, particularly HPV18, are described as an etiological factor for glandular lesions⁷⁻⁹, as it happens in this clinical case.

The infection by HPV 18 is said to be responsible for the development of precursor lesions of pathologies of the glandular epithelium, being a factor for a worst prognosis for these lesions in comparison to squamous-cell lesions (usually more associated with HPV16)⁶. In the age group above 50 years, glandular lesions of the endometrium are the most common, and their etiology is not related to HPV infection^{10,11}, but with an increase in the estrogen levels caused, for instance, by post-menopause obesity¹¹.

The non-implementation of screening programmes and the low adherence to the same by women constitute risk factors for the appearance of endocervical adenocarcinomas^{12,13}. The persistence of HPV infection, if not early detected, might be the trigger for the development of adenocarcinoma. The treatment of this neoplasia is highly aggressive and often a total hysterectomy proves to be necessary which, in women of such a young and fertile age, will prevent a future pregnancy. Therefore, we reinforce the need to conduct sexual education programmes and raise awareness on screenings among adolescents as preventive measures for these infections and, consequently, for the development of cancer.

A positive immunoreactivity for the ki67 and p16 proteins through dual-

immunocytochemical staining was observed in the cells with malignant morphology. This means that the HPV's DNA is integrated in the host cells, promoting the replication and proliferation of virions, with consequent evolution to a malignant transformation of the epithelium^{3,4}.

Summing up, cytological screenings enable the early detection of endocervical glandular lesions and, together with HPV genotyping and other complementary examinations, allow the treatment of pre-neoplastic and neoplastic lesions, in time and at an early stage.

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