

## Glandular Cell Atypia: Which Diagnosis?

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### **ABSTRACT**

Ovarian cancer has the highest mortality rate of all gynecological pathologies, as it is only diagnosed in an advanced stage, when first symptoms appear. This case-study describes a follow-up cytology performed after a total hysterectomy for an undifferentiated ovarian carcinoma. The cytological evaluation suggested an adenocarcinoma, while the histological diagnosis of the nodular lesion revealed a relapse of papillary serous ovarian carcinoma. Performing the histological examination, in this and other cases, is a fundamental piece for the confirmation of the cytological diagnosis, as well as for the differential diagnosis.

**Key-words:** gynecological cytology, *Surepath*®, follow-up, glandular cells, papillary serous ovarian carcinoma

## INTRODUCTION

Ovarian cancer is the most lethal gynecological cancer, as it is usually diagnosed in an advanced stage when the first symptoms arise - such as pressure or pain in the abdomen, pelvis, back or legs; a feeling of abdominal swelling and constant fatigue; nausea, indigestion, constipation or diarrhea<sup>1-4</sup>.

Epidemiological data shows that ovarian cancer develops mainly in women aged over 45 years, which constitute more than 80% of the cases. In what concerns to their histological group, epithelial, borderline or malignant are the most frequent types of tumors, representing 80-85% of the cases<sup>5</sup>. According to *Globocan's* data from 2012 concerning Portugal, ovarian cancer ranks ninth in the list of most prevalent oncological diseases in women and eighth in the mortality rate, with 616 new cases and 381 reported deaths<sup>6</sup>.

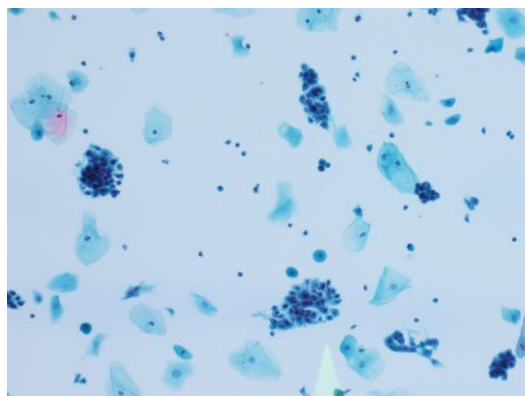
Besides the strong influence of a late diagnosis on the incidence of this type of cancer, which affects more than two hundred thousand women in the world every year, a major gap concerning the awareness of the female population still exists, which needs to be filled<sup>3,7</sup>.

## CLINICAL HISTORY

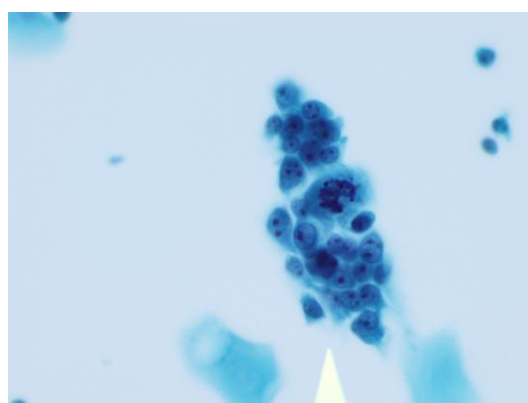
The present case relates to a liquid-based cytology (*Surepath®*) of the vaginal apex of a 47 year-old woman, with a clinical history of total hysterectomy made in 2008 in the sequence of an undifferentiated ovarian cancer. After follow-up cytologies made in 2011, 2012 and 2013, all with negative results, a new cytology of the vaginal apex was performed on January 2015, with a positive result for adenocarcinoma. On March 2015, a nodule taken from the vaginal apex revealed a relapse of a high-grade papillary serous ovarian carcinoma.

## CYTOLOGICAL FINDINGS

The cytological sample consisted of a smear with a clean background, where numerous three-dimensional clusters of cells are observed, often with a papillary conformation (**Fig. 1**) and with malignant characteristics, namely increased nuclear-to-cytoplasmic ratio, cyanophile and micro-vacuolated cytoplasm, enlarged, eccentric and slightly hyperchromatic nuclei, with an unequal distribution of chromatin and irregular nuclear contours (**Fig. 2**). Macronucleoli and mitotic figures can also be found (**Fig. 2**).



**Fig. 1** – General pattern of the cytology sample (*Surepath®*, *Papanicolaou* stain, Magnification: 10x).



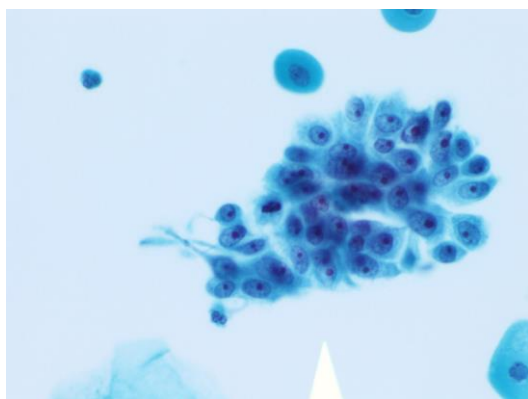
**Fig. 2** – Glandular cell group with malignant characteristics (*Surepath®*, *Papanicolaou* stain, Magnification: 40x).

## DISCUSSION AND CONCLUSION

The cytological characteristics led to a diagnosis of adenocarcinoma. Despite the suggestive clinical information and cytological pattern, it was not possible to guarantee that this was a case of extrauterine adenocarcinoma based solely on the cytology.

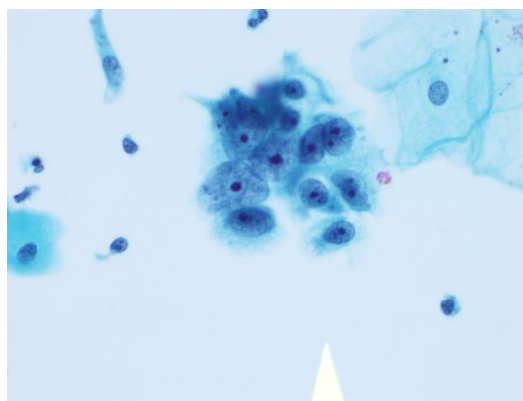
As **Fig. 3** shows, it is possible to observe cytological characteristics of both endocervical and endometrial adenocarcinomas<sup>8</sup>.

According to the literature, the existence of three-dimensional clusters of cells, increase in the nuclear-cytoplasmic ratio, anisokaryosis, the presence of prominent nucleoli and an irregular chromatin distribution can be observed in cases of both endocervical and endometrial adenocarcinoma<sup>8</sup>.



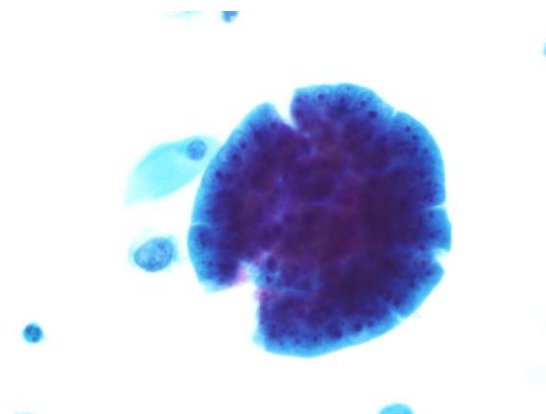
**Fig. 3** – Glandular cell group with cytological characteristics suggestive of adenocarcinoma (Surepath®, Papanicolaou stain, Magnification: 40x).

In **Fig. 4** it is possible to notice the presence of microvacuolation, which is a characteristic of endocervical adenocarcinoma. However, this finding is not sufficient, by itself, to attribute a cytological diagnosis of endocervical adenocarcinoma. On the other hand, despite the existence of some cytological features suggestive of endometrial adenocarcinoma, such as papillary configuration, scant and cyanophile cytoplasm, as can be seen in **Fig. 5**, it is not possible to attribute a final diagnosis of endometrial adenocarcinoma<sup>8</sup>.



**Fig. 4** – Glandular cell group with cytological characteristics suggestive of adenocarcinoma (Surepath®, Papanicolaou stain, Magnification: 40x).

The presence of a clean background (**Fig. 2, 3, 4 and 5**), the presence of clusters (**Fig. 5**), as well as nuclear pleomorphism (**Fig. 4**), are all characteristics that suggest a possible extrauterine carcinoma, as reported by the literature<sup>8</sup>.



**Fig. 5** – Glandular cell group with cytological characteristics suggestive of adenocarcinoma (Surepath®, Papanicolaou stain, Magnification: 20x).

Since the characteristics observed in the cytology were not sufficient to draw a conclusive diagnosis, the cytology was complemented by a histological examination of a nodule taken from the vaginal apex. The histological diagnosis of the nodular lesion was reported as relapse of papillary serous ovarian carcinoma.

## CONCLUSION

This clinical case allows to reinforce what has been stated in the literature, i.e., ovarian cancer is one of the most aggressive pathologies of the female gynecological tract, and approximately 60-85% of the cases are susceptible for relapse after completing therapy<sup>9</sup>. As this type of pathologies can be detected with a non-invasive and low-cost method (the *Papanicolaou* test), it becomes important to raise awareness among women so they perform routine gynecological screenings in order to prevent the different types of gynecological cancer and as a way of doing the follow-up of a previously treated pathology, enabling the early detection of relapses.

On the other hand, this case proves that, sometimes, cytology is not sufficient to obtain a precise diagnosis, being necessary to resort to other techniques in order to ensure that the patient receives the best possible treatment.

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