

# Vaginal Metastasis from Colorectal Adenocarcinoma: Diagnosis in Cervicovaginal Cytology

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## **ABSTRACT**

Metastatic colorectal adenocarcinoma in the vagina is rare and there are few cases reported in the literature. This paper reports the case of a woman with an infiltrative mass in the vagina and a previous diagnosis of colorectal adenocarcinoma. The use of a liquid-based cervicovaginal cytology, together with CK20 and CDX2 immunostaining, allowed to confirm the neoplasia's colorectal origin. This case enhanced the importance of the clinical history as well as of the immunohistochemical staining in a diagnosis, since without them and only with the observation of the cellular characteristics, the diagnosis could be interpreted as endocervical or endometrial adenocarcinoma.

**Key-words:** colorectal adenocarcinoma, vaginal metastasis, liquid-based cytology, immunohistochemistry

## INTRODUCTION

The following case is about a 54 year-old woman in menopause, previously diagnosed with colorectal adenocarcinoma, who was submitted to a cervicovaginal cytology screening. The gynecological examination revealed an infiltrative mass in the vagina and, considering the clinical history of the patient, a suspicion for metastasis/direct invasion of the colorectal neoplasia arose. In addition to the cervicovaginal cytology, a biopsy of the infiltrative mass was performed.

In order to confirm the suspicion of metastatic lesion, an immunohistochemical study of the cervicovaginal cytology was performed to detect cytokeratin 20 (CK20) and caudal-related homeobox 2 (CDX2) biomarkers, and also on the tissue biopsy of the mass for detection of CK20, cytokeratin 7 (CK7) and CDX2 biomarkers.

## ANALYSIS AND DISCUSSION

### Cytological Findings

The cervicovaginal sample was treated according to the *ThinPrep® Hologic* instructions and stained by the *Papanicolaou* staining method. The same sample was considered satisfactory for evaluation, despite showing reduced cellularity and prominent tumor diathesis (**Fig. 1A**). Some three-dimensional clusters of atypical columnar cells were also observed, with increased nuclear-to-cytoplasmic ratio and hyperchromatic nuclei, with prominent nucleoli (**Fig. 1B, C, D**). The presence of cytoplasmic vacuolation should also be highlighted (**Fig. 1D**), as well as anisokaryosis and cytolysis.

The slide with the immunostaining for CK20 (**Fig. 1E**) presents an ambiguous reading, because not all cytoplasm are marked. On the other hand, in the slide with immunostaining for CDX2 (**Fig. 1F**), the nuclear staining was positive, despite the verification of

some cytoplasmic marking. Therefore, the results of the immunohistochemical study of the tumor cells were positive for CK20 and CDX2.

The diagnosis was interpreted as extrauterine adenocarcinoma, according to the *Bethesda*<sup>1</sup> system. Considering the morphological findings and the immunohistochemical study, it was possible to conclude that this was a metastasis arising from the previously diagnosed and treated colorectal neoplasia.

These findings were confirmed by the histological biopsy.

### Histological Findings

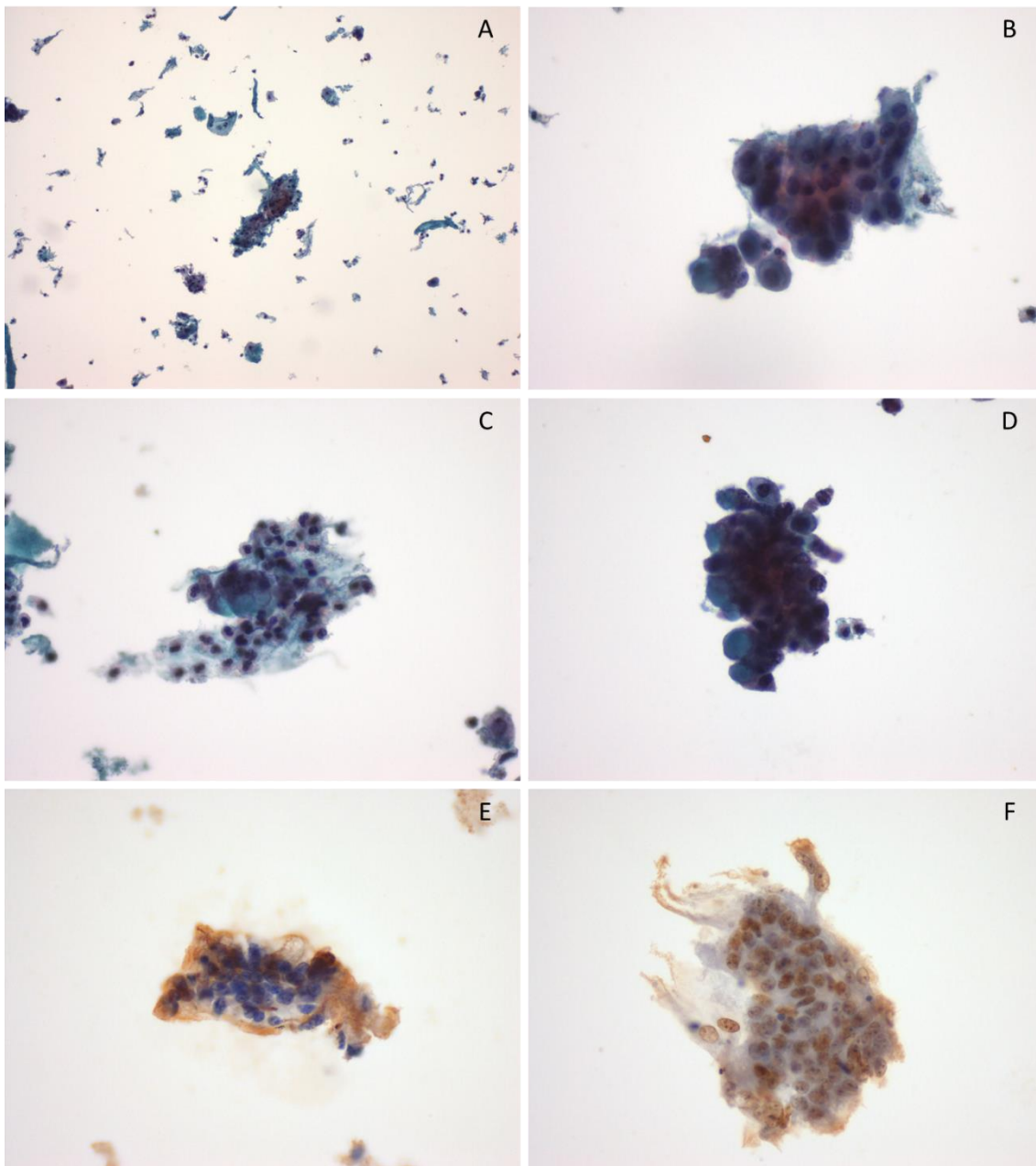
The observation of the histological preparation stained with hematoxylin and eosin (HE) and obtained from the tissue of the biopsy embedded in paraffin revealed a neoplasia with a papillary architecture invading the vaginal tissue – metastasis from colorectal adenocarcinoma (**Fig. 2A**).

The immunohistochemical study confirmed the suspicion of a metastatic colorectal adenocarcinoma, consistent with the patient's clinical history, since the immunostaining was positive for the CK20 (multifocal) (**Fig. 2B**) and CDX2 (**Fig. 2C**), and negative for the CK7 (**Fig. 2D**).

## CONCLUSION

Primary malignant neoplasms of the vagina are uncommon, being vaginal metastasis the main sources of malignancy. The majority of the metastasis arise from the uterine cervix, endometrium or ovary. Metastasis can also occur from more distant areas, such as the pancreas, breast and colon<sup>2</sup>.

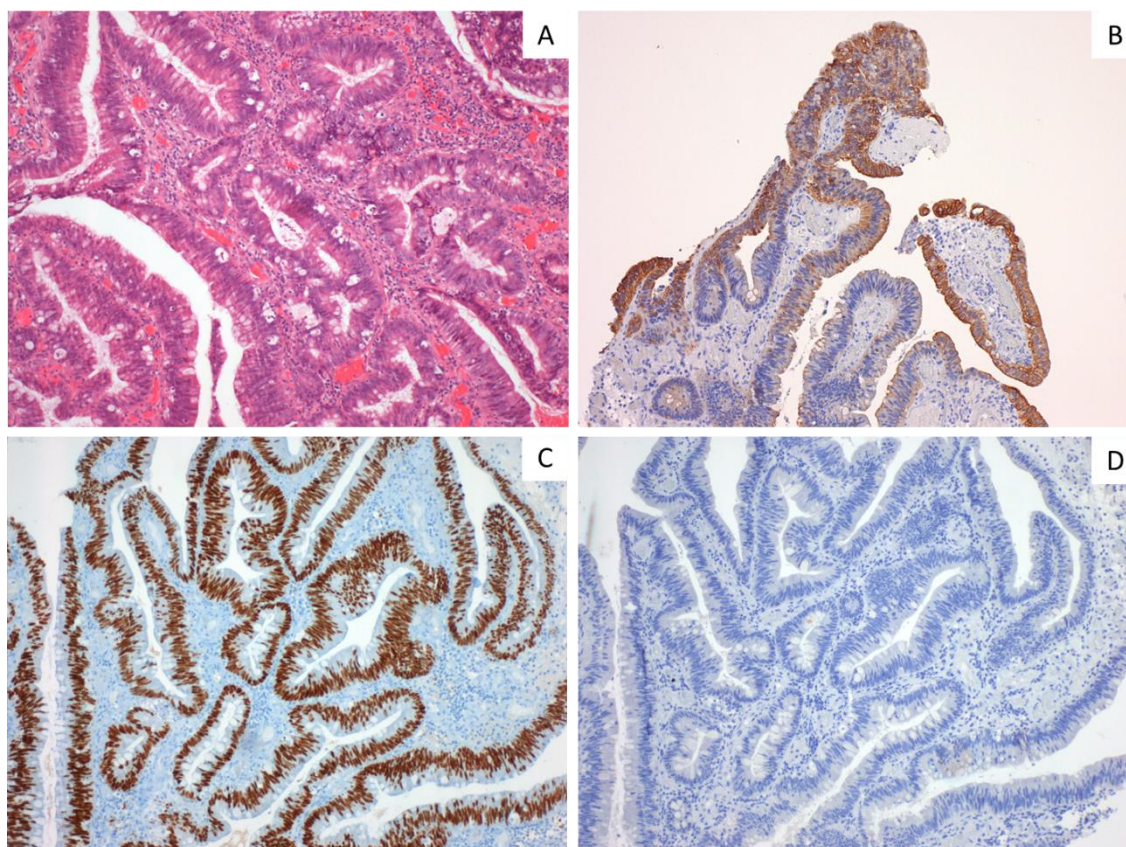
The involvement of the vagina in colorectal cancer occurs more often by continuous and direct invasion of the primary tumor<sup>3</sup>.



**Fig.1** – Cervicovaginal cytology. **A:** Tumor diathesis (*ThinPrep*®, Papanicolaou stain, 10X) **B, C e D:** Cluster of atypical columnar cells (*ThinPrep*®, Papanicolaou stain, 40X) **E:** Cluster of atypical columnar cells (*ThinPrep*®, CK20, 40X) **F:** Cluster of atypical columnar cells (*ThinPrep*®, CDX2, 40X).

Because vaginal metastasis arising from colorectal adenocarcinomas are so rare, these lesions prove to be a diagnostic and therapeutic challenge. A standardized treatment is not yet available, therefore, prognosis among these patients are generally dismal<sup>4</sup>.

The origin of vaginal metastasis can be defined based on morphological findings and on immunohistochemistry. Determining the origin of the metastasis is extremely important at a clinical and therapeutic level<sup>2,5</sup>.



**Fig. 2** – Histology of the infiltrative mass, with HE staining and immunohistochemical markers. **A:** Malign glandular neoplasia (HE, 10X) **B:** Multifocal staining for CK20 (CK20, 10X) **C:** Positive staining for CDX2 (CDX2, 10X) **D:** Negative staining for CK7 (CK7, 10X)

The liquid-based cytology indicated the presence of a glandular neoplasia, which makes differential diagnosis with endocervical adenocarcinoma, endometrial adenocarcinoma and extrauterine adenocarcinoma. However, the clinical history of the patient and her gynaecological examination led to a main diagnostic hypothesis of vaginal invasion by the previously identified colorectal adenocarcinoma. In order to confirm this suspicion, an immunohistochemical study was performed, with CK7, CK20 and CDX2.

The expression pattern of the CK7-/CK20+ is typical of colorectal carcinomas. Occasionally, colorectal carcinomas can show a significant variation in the CK7 expression, and CK20 expression can be seen in a wide variety of non-colorectal carcinomas, such as urothelial, gastric and pancreatic-biliary tract carcinomas<sup>5</sup>.

Thus, there is a great interest in developing new markers to obtain a differential diagnosis of colorectal cancer, and the CDX2 seems to be one of those markers<sup>5</sup>.

In conclusion, determining the primary site of the neoplasia is crucial, both at clinical and therapeutic levels. The correlation between the clinicopathological findings and the immunohistochemical staining helps to define the lesion's primary site and, consequently, to prescribe an adequate treatment.

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