

## Primary endometrial endometrioid carcinoma with signet ring cells: why is this a special case?

### Carcinoma endometrióide endometrial primário com células em anel de sinete: porquê um caso especial?

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#### Abstract

A 76 years old woman presented to our emergency department because of post-menopausal bleeding in June 2019. Gynaecological ultrasound was performed detecting an heterogeneous endometrial thickness of 9,3 mm. An endometrial biopsy with Novak system was performed showing an endometrioid adenocarcinoma. A total hysterectomy with adnexectomy along with lymph node dissection and pelvic washing was performed for tumour staging. Anatomopathological and histological evaluation revealed a primary endometrial endometrioid adenocarcinoma with signet ring cells that was confirmed by immunohistochemical studies and imaging/endoscopic studies that excluded non-gynaecological tumour origin.

**Keywords:** Endometrial adenocarcinoma; Oncology; Signet ring cells.

#### INTRODUCTION

Signet ring cells are a common finding in endometrial metastatic adenocarcinoma with a non-genital primary tumour as the most probable diagnosis, namely, primary gastrointestinal or breast tumors.<sup>1</sup> However, despite being a rare condition, some cases of primary endometrial adenocarcinoma with signet ring cells have been reported in literature (Table I).<sup>1-6</sup> This is, to our knowledge, the 7th case reported.

When this finding is present, primary non-genital origin of the tumour has to be excluded by extensive staging studies. Immunohistochemical staining may be helpful in confirming or ruling out endometrial origin. In fact, positive staining to cytokeratin 7 (CK7), vimentin and estrogen receptor (RE) support this diagnosis (Figure 1).<sup>1,7</sup>

#### CASE REPORT

A 76 year-old woman, G4P3 (vaginal deliveries), presented to the emergency department of Centro Materno Infantil do Norte, in Oporto, complaining of post-

menopausal bleeding. She had no other complaints. She has the diagnosis of menopause since she was 50 years old and she did not take hormonal therapy. During evaluation, gynaecological examination showed to be normal and a vaginal ultrasound was done, revealing an endometrial thickness of 9,3 mm. An endometrial specimen was collected by endometrial biopsy performed with Novak system, whose anatomopathological examination was consistent with endometrial adenocarcinoma.

Radiologic and endoscopic evaluation did not showed any other tumour. The patient underwent abdominal total hysterectomy with bilateral adnexectomy. During the surgery, an extemporaneous anatomopathological evaluation showed more than 50% myometrium invasion justifying peri-aortic and peri-iliac lymph node dissection and peritoneal washing. The hysterectomy specimen consisted of uterus and cervix measuring 9x2,3 cm and weighting 70g, with attached bilateral adnexa. It was identified at the anterior surface of the endometrium a protruding plaque-like neoplasia measuring 3 cm in diameter that appeared to infiltrate the inner half of the myometrium wall in transverse section. Endocervix contained a pediculated polypoid mass of 1,5 cm and was not involved by the tumour. Adnexa were normal. Microscopic evaluation showed an endometrioid endometrial adenocarcinoma

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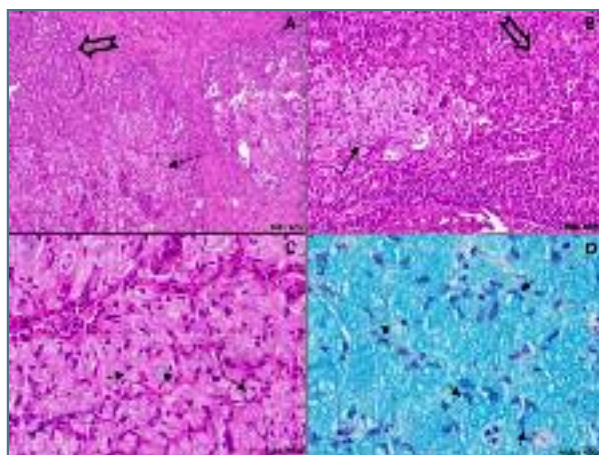
**TABLE I. ENDOMETRIAL ADENOCARCINOMA WITH SIGNET-RING CELLS: REVIEW OF THE LITERATURE.**

Case	Authors	Age	Diagnosis	Treatment	Stage	Follow-up
1	Mooney et al., 1997 (2)	65	Signet ring cells	Hysterectomy, bilateral salpingo-oophorectomy and pelvic and para-aortic lymph node dissection. Partial O. abdominal, pelvic washing	NS	Free of disease 6 months after surgery
2	Chebin et al., 2010 (3)	51	Primary signet ring cells	Hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection. Abdominal, pelvic washing.	FIGO stage IVB	Death of metastatic disease 6 months after surgery
3	Boyd et al., 2010 (4)	46	Primary mucinous adenocarcinoma of the endometrium with signet-ring cells arising in adenomyosis	Subtotal hysterectomy.	NS	NS
4	Boyd et al., 2010 (4)	59	Primary endometrioid adenocarcinoma of the endometrium with signet-ring cells	Hysterectomy	NS	NS
5	Pusiol, 2014 (5)	53	HPV11 Positive Endometrioid Carcinoma of the Endometrium with Signet-Ring Cells	Hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection.	FIGO stage IB	Free of disease 22 months after surgery
6	Akkalp et al., 2015 (1)	77	Primary endometrioid adenocarcinoma of the endometrium with signet-ring cells	Radical hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection.	FIGO stage IA	Free of disease 14 months after surgery
<b>Present case</b>	–	76	Primary endometrioid adenocarcinoma of the endometrium with signet ring cells	Hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection. Abdominal, pelvic washing.	FIGO stage IIIa	Free of disease 6 months after surgery

with signet ring cells and positive immunohistochemical staining for CK7, ER (focally), PAX-8 and vimentin. No endometrial hyperplasia was detected. An Alcian Blue staining highlighted the signet ring cells containing mucin (Figure 2). Pelvic wash was negative for malignant cells. Two of the 25 dissected lymph nodes showed metastasis. Final staging was consistent with a FIGO 3c1 stage and additional chemotherapy (carboplatin and paclitaxel) and radiotherapy were proposed. The patient underwent 3 cycles of chemotherapy and was doing well until the writing of this report. No recurrences have been reported.

## DISCUSSION

Endometrium is rarely affected by metastasis of non-gynaecological malignancies. The first case of endometrial metastasis was reported in 1878 by Legg et al.<sup>1,2</sup> Since then more cases have been exposed and they most frequently arise from breast or gastrointestinal tract (namely, colon or stomach). Histological characteristics consistent with an endometrial metastasis are absence of premalignant lesions, high degree of myometrium infiltration, sparing of benign endometrial areas and the presence of signet ring cells. Although,



**FIGURE 1.** (A, B & C): Endometrioid adenocarcinoma with cribriform pattern (large arrow) and areas showing cells containing mucin (slim arrow) with signet ring cells (short arrows); (D): Alcian Blue staining highlighting intracellular mucin in signet ring cells (short arrows).

subsequently some cases of signet ring cells in endometrial malignancy were found with no other primary tumours detected. The first case of endometrial primary adenocarcinoma was reported by Mooney et al in 1997.<sup>2</sup> Primary endometrial adenocarcinoma with signet ring cells is, in fact, a rare entity.

We believe our case is in line with the diagnosis of a primary endometrial endometrioid adenocarcinoma with mucin-containing signet ring cells and this hypothesis is based on the following facts: first, additional imaging and endoscopic studies did not find any other tumour or metastasis; second, classic endometrioid carcinoma coexists with signet ring cells pattern; third, immunohistochemical pattern was similar between signet ring cells and endometrioid carcinoma. This diagnosis is one of exclusion and when this histological pattern is detected, breast imaging and endoscopic examination of stomach and colon are of paramount importance to rule out these primary, most frequent tumours.

#### ACKNOWLEDGMENT

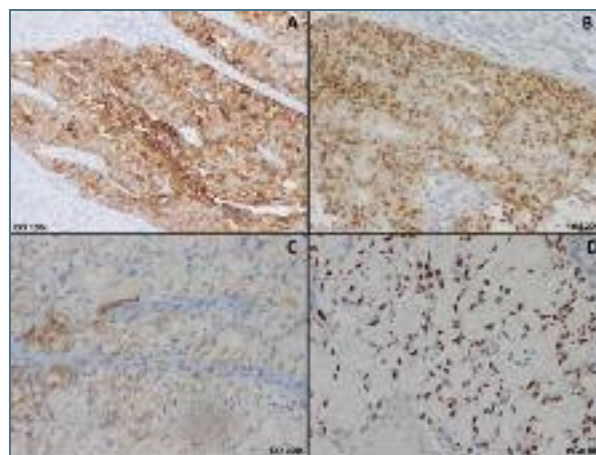
Informed consent was obtained after exposing our publication objective to the patient.

#### AUTHORS DISCLOSURE

The authors do not have any conflict of interest to declare.

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**FIGURE 2.** (A & B): Endometrioid adenocarcinoma with cribriform pattern, showing immunohistochemical positive staining for CK7 (cytoplasm) and Pax8 (nuclear); (C & D): Endometrioid adenocarcinoma with signet ring cells showing immunohistochemical positive staining for CK7 (cytoplasm periphery) and for Pax8 (nuclear).

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