

## Case Report

# Coexistence of homologous-type cervical carcinosarcoma with endometrioid-type G1 endometrial cancer: a case report with an immunohistochemical study

Andrzej Semczuk<sup>1</sup>, Eva Colas<sup>2</sup>, Beata Walczyna<sup>3</sup>, Maciej Joźwik<sup>4</sup>, Andrzej Pyra<sup>5</sup>, Anna Semczuk-Sikora<sup>6</sup>, Tomasz Rechberger<sup>1</sup>

<sup>1</sup>I<sup>ND</sup> Department of Gynecology, Lublin Medical University, Lublin, Poland; <sup>2</sup>Research Unit of Biomedicine and Translational Oncology, Vall d'Hebron University Hospital, Barcelona, Spain; <sup>3</sup>Department of Clinical Pathology, Lublin Medical University, Lublin, Poland; <sup>4</sup>Department of Gynecology, Białystok Medical University, Białystok, Poland; <sup>5</sup>Obstetrics and Gynecology Chair, Municipal Hospital, Nowa Deba, Poland; <sup>6</sup>Department of Obstetrics and Pathology of Pregnancy, Lublin Medical University, Lublin, Poland

Received August 20, 2014; Accepted September 15, 2014; Epub September 15, 2014; Published October 1, 2014

**Abstract:** Coexistence of two or even more independent primary tumors derived from the female genital tract organs is a unique event. The most common combination is the coexistence of synchronous tumors in the ovary and endometrium. In the present case study, we described a coincidence of homologous-type cervical carcinosarcoma (CS) with endometrioid-type G1 uterine adenocarcinoma (EC) arising on the basis of hyperplastic endometrium. A panel of immunohistochemical markers was applied, either in both CS components or in endometrioid-type EC, to assess possible differences between both uterine malignancies. We also presented a short overview of the coexistence of cervical carcinosarcomas with other female genital tract malignancies.

**Keywords:** Cervical carcinosarcoma, endometrial cancer, endometrial hyperplasia, immunohistochemistry

### Introduction

Carcinosarcomas (CS) are extremely unique neoplasms, accounting below 1% of all the female genital tract malignancies worldwide [1]. They are composed of an intimate admixture of two malignant components, carcinomatous and sarcomatous. The carcinomatous element is generally of the endometrioid-type, whereas the sarcomatous one may be either homologous or heterologous [1, 2]. Four theories of their histogenesis have been proposed; in general, most cases represent metaplastic carcinomas, where the carcinomatous component is responsible for tumor invasiveness [3-5]. However, in vitro study by Gorai and co-investigators [6] suggested the combination theory of CS development, where the stem cells give rise both to carcinomatous and sarcomatous components.

Singh et al. [7] reported that only 1-2% of women with gynecological malignancies are simultaneously affected by two or even more, independent, primary tumors originated from the female genital tract organs. The most common combination is the coexistence of synchronous tumors in the ovary and endometrium [7-9]. The coexistence of cervical CSs with other female genital tract malignancies is uncommon; only a few case reports have been published worldwide up to now [10, 11].

In the present case study, we reported a coincidence of homologous-type cervical CS with endometrioid-type G1 uterine adenocarcinoma (EC) arising on the basis of hyperplastic endometrium. A panel of IHC markers was also applied, either in CS components or in endometrioid-type EC, to analyze possible differences between both uterine malignancies.

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**Table 1.** Summary of the immunostaining results in cervical CS and uterine adenocarcinoma

	Cervical CS		Uterine adenocarcinoma
	Carcinoma	Sarcoma	Carcinoma
ER	Negative	Negative	Negative
PgR	Negative	Negative	Positive
AR	Negative	Negative	Negative
p53	Negative	Negative	Positive, 90%
Vimentin	Positive	Positive	Positive
MyoD	Negative	Negative	Negative
Cytokeratin	Positive	Negative	Positive
CD10	Positive, weak	Negative	Negative
Calretinin	Negative	Negative	Negative
CD34	Positive, weak	Negative	Positive, weak

### *Clinical history and immunohistochemistry*

In December 2013, a 57-year-old woman (gravida 9, para 8) was admitted to the II<sup>nd</sup> Department of Gynecology, Lublin Medical University, Lublin, Poland, with the diagnosis of CS of the uterine cervix. Two weeks before, she was hospitalized at the Gynecologic and Obstetrics Unit of the Municipal Hospital in Radzyn Podlaski, Poland, with abnormal uterine bleeding. Histopathological assessment of the material collected thereafter revealed a uterine cervix CS. Gynecologic speculum examination showed a hypertrophic vaginal mucosa with enlarged and distended uterine cervix fulfilled with enlarged masses. The uterus was slightly enlarged whereas the endometrial thickness was within the normal range (5 mm). Both ovaries were of normal size. She had last menstruation 5 years ago, and there was no family history of female genital tract malignancies. Her past medical history consisted of one cesarean section. She was also suffered from chronic arterial hypertension; antihypertensive drugs were continually prescribed. She had not been exposed to exogenous hormones within the last 10 years. Last cervical smear, performed 4 years ago, was normal. The tumor markers of CA 125 and CA 19.9 were 320 U/ml and 22 U/ml, respectively. Total abdominal hysterectomy with bilateral salpingo-oophorectomy and surgical staging (pelvic and para-aortic lymph nodes dissection, appendectomy, omentectomy and peritoneal washings) were performed. Histopathological assessment of the post-operative material revealed a homologous-type (leiomyosarcoma) cervical CS, infil-

trating the endocervix with parametrial involvement and LVSI. In addition, complex endometrial hyperplasia with nuclear atypia coexisted with intramucosal, well-differentiated endometrioid-type EC has also been found out. There were no metastases, either to the lymph nodes, appendix or to the omentum. Peritoneal washings showed normal cells (lymphocytes, granulocytes, mesothelial cells and erythrocytes). The patient was staged IIB based on a new FIGO classification [12, 13]. The postoperative course was uneventful and the patient was discharged at day 9 and referred to the Oncology Hospital in Lublin, Poland. She underwent courses

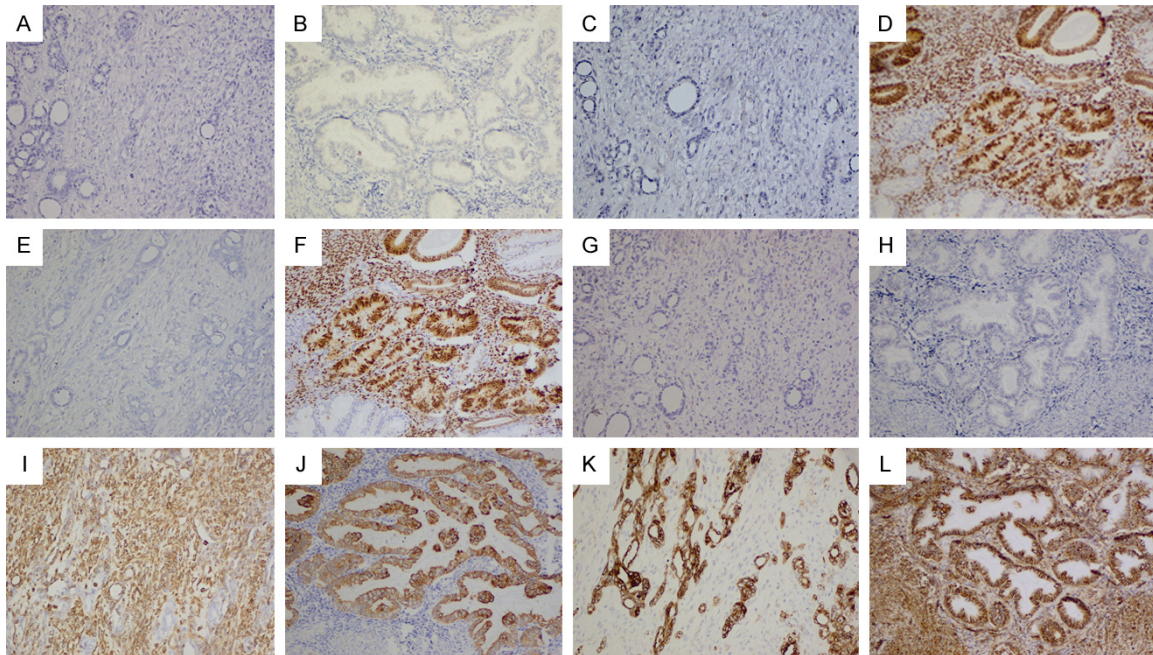
of chemotherapy (adriamicin and cyclophosphamide), and additional imaging studies (USG, PET). There was no evidence of recurrence 7 months after the surgery.

A panel of IHC markers has been applied in order to evaluate the staining patterns of both female genital tract malignancies. Immunohistochemical results are depicted at **Table 1**. In general, most of immunohistochemical markers showed similar staining pattern in both components of uterine CS and uterine adenocarcinoma, apart from p53, PgR, cytokeratin, CD10 and CD34 immunoreactivity. Examples of immunohistochemical staining are shown at **Figure 1**.

### **Discussion**

Synchronous appearance of two histologically independent tumors within the female genital tract is a unique event [7, 14, 15]. For gynecological pathologists as well as gynecological oncologists, it is of utmost important to "...recognize these combinations of tumors to avoid their misinterpretation as a combination of primary and metastatic tumors because of widely different management and prognostic implications" [7]. In the present study, synchronous primary homologous-type CS of the uterine cervix with uterine corpus adenocarcinoma has been reported. The first one composed of two unrelated malignant components, whereas the second one was consisted of atypical complex endometrial hyperplasia coexisting with well-differentiated G1 endometrioid-type uterine adenocarcinoma (**Figure 1**). On reviewing the literature (Pubmed®), we did not find out the

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**Figure 1.** Immunohistochemical staining of selected proteins in cervical CS and endometrioid-type EC-ER (A and B), PgR (C and D), p53 (E and F), AR (G and H), vimentin (I and J) and cytokeratin (K and L) (Original magnification  $\times 200$ ).

coexistence of uterine cervix CS with endometrioid-type EC, although rare cases encountered the simultaneous occurrence of cervical/uterine CSs with other female genital tract malignancies [10, 11, 16-18]. For example, a 63-year-old woman affected by primary synchronous uterine CS and serous carcinoma of bilateral fallopian tubes was presented by Jain and Puri [11]. Two cases of collision of the endometrioid EC and stromal sarcoma of the uterus were previously published [16]. Interestingly, Japanese researchers described a case of hepatoid carcinoma of the uterus that was in collision with a uterine CS [17]. Even three pathologically different components of uterine malignancies (CS, uterine papillary serous carcinoma and endometrioid-type EC) were reported and a detailed review of the literature has also been presented [18].

D'Angelo and Prat [4] suggested "...frequent association of carcinosarcomas with otherwise typical endometrial adenocarcinomas within the same hysterectomy specimen...". In general, uterine CSs revealed more aggressive behavior compared even with high-risk epithelial ECs [19, 20]. They probably represent a distinct biologic entity and should not be incorporated in the studies of ECs [20]. cDNA microar-

ray analysis of 29 uterine CSs and 66 endometrioid-type ECs displayed a distinct gene expression pattern in various histological subtypes of malignancies, reporting that "...greater expression of *IGF2* and lower expression of *MUC1*, *SCGB2A1*, *HOXB6* and *TFF3* was observed in mixed mullerian tumor specimens when compared with endometrioid carcinomas" [21]. Based on microarray analysis, endometrioid-type ECs, uterine papillary serous and uterine CSs may develop in part *via* alternate genetic pathways [21].

Immunohistochemical evaluation of various protein markers play a role not only as a differential diagnostic tool but also as a matter of scientific investigation [18, 22-25]. The use of a panel of specific antibodies is generally recommended in routine gynecologic pathology [24, 25]. For example, application of IHC shares a new light in the differentiation diagnosis between simultaneously occurring independent carcinomas of endometrium and ovary *versus* cases of EC with ovarian metastases [26]. Results of different proteins immunoreactivity (ER, PgR, p53, cytokeratin, vimentin and MyoDs1) displayed various staining patterns in three histologically different collision neoplasms of the uterus [18]. Although similar

staining patterns of uterine CSs support a monoclonal origin of this case study, a significant different IHC results were observed between sarcomatous CS component and EC [18]. Differences of IHC between carcinomatous and sarcomatous elements of uterine CS has previously been published [23]. Currently, differences between cervical CS and type I EC in spite of IHC markers (particularly of PgR and p53) may suggest both tumors develop independently and share different genetic/immunologic alterations. It will be of utmost import for our future study to evaluate p53-pathway alterations, in both elements of uterine CS as well as in endometrioid-type EC, at the IHC and genetic levels.

#### Acknowledgements

The authors would like to acknowledge Mrs Mariola Bigas and Mrs Marian Nowak for their excellent immunostaining analysis and to Mr Robert Klepacz for high-quality photographs. This study was supported by a grant from the Lublin Medical University, Lublin, Poland (Dz. St. 326/14 to A.S.).

#### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Andrzej Semczuk, II<sup>nd</sup> Department of Gynecology, Lublin Medical University, 8 Jaczewski Street, Lublin 20-954, Poland. Tel: +48 81 7244268; Fax: +48 81 7244849; E-mail: andrzej.semczuk@am.lublin.pl

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