

Breast metastases from uterine cancer – literature review

**Nicolae Bacalbasa^{1,2}, Irina Balescu³, Claudia Stoica^{4,5}, Cristina Martac⁶, Valentin Varlas^{1,7},
Andrei Voichitoiu^{1,8}, Lucian Pop^{1,8}, Sorin Petrea⁹, Mihaela Vilcu^{9,10}, Iulian Brezean^{9,10}**

¹Department of Obstetrics and Gynecology, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

²Department of Visceral Surgery, Center of Excellence in Translational Medicine, Fundeni Clinical Institute, Bucharest, Romania

³Department of Visceral Surgery, Ponderas Academic Hospital, Bucharest, Romania

⁴Department of Anatomy, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

⁵Department of Surgery, Ilfov County Emergency Hospital, Bucharest, Romania

⁶Department of Anesthesiology, Fundeni Clinical Institute, Bucharest, Romania

⁷Department of Obstetrics and Gynecology, Filantropia Clinical Hospital, Bucharest, Romania

⁸Department of Obstetrics and Gynecology, “Alessandrescu-Rusescu” National Institute of Mother and Child Care, Bucharest, Romania

⁹Department of Surgery, “Dr. I. Cantacuzino” Clinical Hospital, Bucharest, Romania

¹⁰Department of Surgery, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

ABSTRACT

Uterine cancer represents a common gynecological malignancy affecting women worldwide which can lead to the apparition of distant metastases through different patterns of spread such as direct contiguity, peritoneal, lymphatic or hematogenous route. When it comes to the hematogenous pattern of spread, the most commonly encountered viscera in which metastatic lesions can be found are represented by liver and lung. Meanwhile, breast metastases from uterine cancer represents a very scarce event, only few cases being reported so far. The aim of the current study is to review the case reports published so far on this issue.

Keywords: uterine cancer, breast metastases, therapy, survival

INTRODUCTION

Uterine cancer is usually diagnosed in early stages of the disease due to the fact that in most cases it induces the apparition of abnormal vaginal bleeding which worries the patients and determines them to self address to the gynecologist [1]. Therefore, a significant number of cases will be diagnosed in early stages and will benefit from radical surgery with curative intent. However, a certain percent will develop distant metastases via different patterns of spread such as hematogenous, lymphatic or peritoneal route, conducting in this way to the apparition of disseminated lesions [2,3]. Moreover, certain histopathological subtypes such as uterine sarcomas present a very poor biology, characterized through a high capacity of spread, metastatic disease being encountered from the initial diagnostic [4,5]. In the mean-

time, breast represents one of the most improbable sites of developing metastatic lesions with uterine origin. Meanwhile it is estimated that less than 7% of all breast tumors represent in fact metastatic lesions, the most commonly cited malignancies responsible for the development of metastatic lesions at this level being represented by lung and stomach [6].

MECHANISMS OF DEVELOPMENT OF BREAST METASTASES FROM UTERINE PRIMARIES

As mentioned before, the most commonly incriminated pattern of spread is represented by the hematogenous route, which also explains why in certain cases other parenchymatous lesions such as splenic metastases have been also reported in association with breast metastases; however, other

Corresponding author:

Nicolae Bacalbasa

E-mail: nicolae_bacalbasa@yahoo.ro

Article History:

Received: 18 April 2022

Accepted: 30 April 2022

TABLE 1. The most relevant cases of breast metastases from uterine cancer

Author, year	Age	Location and histopathological type of the initial tumor	Stage at initial diagnostic	Initial therapeutic strategy	Time to diagnostic of the breast metastasis	Therapeutic strategy at the time of breast lesion diagnostic	Survival
Aitelhaj, 2014 [10]	55	Uterine cervix, squamous cell carcinoma	IIB	Chemoradiotherapy with 46 grays on the pelvis with cisplatin (40 mg/m ²) followed by high-dose-rate intracavitary brachytherapy	8 months	Excisional biopsy followed by a chemotherapy regimen based on paclitaxel 175 mg/m ² and cisplatin 50 mg/m ² every three weeks,	Died three months later
Sabatier, 2012 [13]	74	Uterine cervix, squamous cell carcinoma	IV	Fluorouracil- and platinum-based chemotherapy followed by adiation therapy (45 Gy in 15 fractions)	26 months	Platinum-based chemotherapy (weekly paclitaxel and carboplatin)	Died of disease 3 months after diagnostic of the breast metastasis
Kelly, 1991 [7]	32	Uterine cervix, adenosquamous carcinoma	IB	Radical hysterectomy, pelvic and para-aortic lymph node dissection followed by external beam radiation therapy	2 months	Cyclophosphamide, methotrexate, 5 fluorouracil, external beam radiation therapy	Died after the diagnostic of the breast metastasis
Ward, 1988 [14]	48	Uterine cervix adenocarcinoma	IIB		3 months		Died 1 month after the diagnostic of metastatic disease
Gonzalez, 2016 [15]	35	Uterine cervix, squamous cell carcinoma	IIIB	-	9 months	biopsy	Died 2 months after the diagnostic of metastatic disease
Mangla, 2017 [16]	50	Uterine cervix, squamous cell carcinoma	IVB	External beam radiation therapy (45 Gy delivered over 22 fractions) to the pelvis and concurrent chemotherapy with weekly Cisplatin (40 mg/m ²) followed by temic therapy with Carboplatin (AUC 5) and Paclitaxel (175 mg/m ²)	Synchronous breast metastase	biopsy	Alteration of the general status after the first cycle of carboplatin and paclitaxel, declined any further treatment, lost from follow up
Saywon, 2021 [17]	27	Uterine cervix, Squamous cell cervical cancer	IIB	weekly dose of cisplatin was given intravenously at 40 mg/m ² for five cycles. External beam pelvic radiation - at 2 Gy per fraction with a total of 50 Gy given for 5 to 6 weeks. Pelvic boost of high dose external beam radiotherapy - 3 weeks later after completion of the initial radiotherapy	6 months	5 cycles of cyclophosphamide, doxorubicin and 5 fluoro Uracil, progression of the disease	Not reported

pathways of spread such as the lymphatic one has been also proposed [7-10].

CASES REPORTED SO FAR OF UTERINE CANCER BREAST METASTASES

The first cases diagnosed with breast metastases from cervical cancer were reported in 1947 in an autopsy study while the first case diagnosed in a living patient was made in 1948 [11,12]. Since then, isolated cases have been reported so far.

An important issue which should be taken in discussion when it comes to the subject of breast metastases from cervical cancer is related to the differential diagnosis between metastatic disease and primary carcinoma of the breast. Most often metastatic disease acts like an inflammatory mass, attention being needed in order to differentiate it from primary inflammatory breast cancer; meanwhile permeation nodules can be also found at clinical examination, orientating therefore the diagnostic to a metastatic condition [13]. As expected, metastatic contamination of the breast occurs via hematogenous spread, leading to the apparition of multiple breast nodules; interestingly, they are usually found at the level of the upper outer quadrants [19]. When

it comes to the imagistic studies which can be used in order to establish the differential diagnostic between metastatic and primary lesions, metastases usually exhibit benign features; therefore, metastatic lesions have well defined shapes and posterior acoustic enhancement [18]. In order to establish the final diagnostic, biopsy and immunohistochemistry is needed.

As for the efficacy of treatment in such cases, it is extremely reduced, irrespective of the type of therapy. As it can be observed from the table below, the overall survival of patients diagnosed with breast metastases from uterine primaries are limited to a few months, the presence of these metastases being usually the sign of diffuse neoplastic impregnation.

CONCLUSIONS

Breast metastases from uterine primaries represent a very scarce eventuality, few cases being reported in literature so far. Therefore, a standard therapeutic protocol guide could not be established, different therapeutic strategies being proposed so far. However the reported results are extremely poor, the overall survival being usually of only few months since the moment of breast metastases diagnostic.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

- Sung H, Ferlay J, Siegel RL et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021;71(3):209-49.
- Jones ER, O'Flynn H, Njoku K, Crosbie EJ. Detecting endometrial cancer. *Obstet Gynaecol.* 2021;23:103-112.
- Menzies R, Wallace S, Ennis M et al. Significance of abnormal sonographic findings in postmenopausal women with and without bleeding. *J Obstet Gynaecol Can.* 2011;33(9):944-51.
- Tortorella L, Restaino S, Zannoni GF et al. Substantial lymph-vascular space invasion (LVSI) as predictor of distant relapse and poor prognosis in low-risk early-stage endometrial cancer. *J Gynecol Oncol.* 2021;32(2):e11.
- Hayashi T, Sano K, Ichimura T et al. Characteristics of Leiomyosarcoma: Induction of Hematogenous Metastasis by Isolated Uterine Mesenchymal Tumor Stem-like Cells. *Anticancer Res.* 2020;40(3):1255-1265.
- Oksüzoglu B, Abalı H, Güler N et al. Metastasis to the breast from nonmammarian solid neoplasms: a report of five cases. *Med Oncol.* 2003;20(3):295-300.
- Kelly JL 3rd, Shakir AK, Williams SL, Christopherson WA: Cervical cancer-metastatic to the breast: a rare presentation of tumor dissemination. *Gynecol Oncol.* 1991;43(3):291-294.
- Hamy A, Letessier E, Gaschignard N et al. Métastases spléniques, à propos de quatre cas. *J Chir.* 1993;130(11):467-469.
- Kumar L, Pokharel YH, Dawar R, Thulkar S. Cervical cancer metastatic to the breast: a case report and review of the literature. *Clin Oncol.* 1999;11(6):414-416.
- Aitelhaj M, Khoyaali SL, Boukir A et al. Breast and splenic metastases of squamous cell carcinoma from the uterine cervix: a case report. *Journal of Medical Case Reports.* 2014;8:359.
- DeAlvarez RR. The causes of death in cancer of the cervix uteri. *Am J Obstet Gynecol.* 1947;54(1):91-96.
- Speert H, Greeley AV. Cervical cancer with metastasis to breast. *Am J Obstet Gynecol.* 1948;55(5):894-896.
- Sabatier R, Roussin C, Riviere JP et al. Breast metastasis of a squamous cell carcinoma of the uterine cervix mimicking inflammatory breast cancer. *Case Reports in Oncology.* 2012;5(2): 464-470.
- Ward R, Conner G, Delprado W, Dalley D. Metastatic adenocarcinoma of the cervix presenting as an inflammatory breast lesion. *Gynecol Oncol.* 1989;35(3):399-405.
- Gonzalez V, Petersen L, Ghai R et al. Recurrent cervical cancer presenting as inflammatory breast cancer. *Am Surg.* 2016;82(9): 275-277.
- Mangla A, Agarwal N, Saei Hamedani F et al. Metastasis of cervical cancer to breast: a case report and review of literature. *Gynecol Oncol Rep.* 2017;21:48-52.
- Saywon DM, Mulamira P. Cervical squamous cell carcinoma metastasis to the breast – A case report from Uganda Cancer Institute. *Gynecologic Oncology Reports.* 2021; 38:100892.
- Feder JM, de Paredes ES, Hogge JP, Wilken JJ. Unusual breast lesions: radiologic-pathologic correlation. *Radiographics.* 1999;19:S11-S26.
- Younathan CM, Steinbach BG, DeBose CD. Metastatic cervical carcinoma to the breast. *Gynecol Oncol.* 1992;45:211-213.