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NL Journal of Medical and Pharmaceutical Sciences

(ISSN: 3108-0502)

Volume 2 Issue 1 February 2026

Case Report

# Metachronous Double Primary Malignancy: Triple-Negative Carcinoma Breast Followed by Carcinosarcoma Uterus – A Rare Case Report

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doi: 10.71168/NMP.02.01.121

**Received Date:** November 13- 2025 **Publication Date:** January 08- 2026

**Abstract:** Double primary malignancies are uncommon occurrences, and their coexistence poses diagnostic and therapeutic challenges. While carcinoma breast and endometrial malignancy association is often linked to hormonal therapy (notably tamoxifen), the development of endometrial carcinoma in the absence of hormonal treatment is exceedingly rare. We report a case of a 32-year-old female with carcinoma breast (triple-negative subtype) successfully treated with multimodality therapy, who after a disease-free interval of seven years, developed a second primary malignancy—carcinosarcoma of the uterus. This case highlights the need for vigilance in long-term cancer survivors, even in the absence of endocrine therapy.

**Keywords:** Metachronous double primary malignancy, Triple-negative breast cancer, Uterine carcinosarcoma, Second primary malignancy, Long-term cancer survivor.

## Introduction

The occurrence of multiple primary malignancies in the same patient is an uncommon but well-recognized phenomenon, first described by Warren and Gates in 1932 [1]. Such malignancies are classified as synchronous when diagnosed within six months of each other and metachronous when separated by a longer interval. Among women, the combination of carcinoma breast and endometrial carcinoma is known, particularly associated with tamoxifen therapy [2]. However, double malignancy involving triple-negative breast carcinoma (TNBC) and uterine carcinosarcoma, without exposure to tamoxifen, is exceedingly rare [3]. We present a rare case of metachronous double malignancy involving TNBC followed by carcinosarcoma uterus, emphasizing that endometrial malignancy can occur independently of hormonal manipulation.

## Case Presentation

A 32-year-old premenopausal woman presented in 2017 with a 3 × 3 cm lump in the right upper outer quadrant of the breast and a single mobile right axillary lymph node measuring 2 × 1 cm. Core biopsy from the breast lesion revealed infiltrating ductal carcinoma, triple-negative subtype (ER-, PR-, HER2-). Staging workup showed T2N1M0 (Stage IIB) disease.

**Treatment for Carcinoma Breast**

- The patient received 3 cycles of neoadjuvant FEC chemotherapy (5-fluorouracil, epirubicin, cyclophosphamide).
- Followed by Modified Radical Mastectomy (MRM).
- Postoperatively, she received 3 additional cycles of FEC chemotherapy.
- This was followed by locoregional radiotherapy (40 Gy in 15 fractions) and ovarian ablation radiotherapy (15 Gy in 7 fractions).

The patient completed treatment uneventfully and remained on regular follow-up.

**Second Primary Malignancy**

In June 2024, seven years after initial diagnosis, she presented with bleeding per vagina. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH + BSO). Histopathological examination revealed carcinosarcoma of the uterus (malignant mixed Müllerian tumor). On IHC features favored carcinosarcoma of uterus with component of Endometroid Carcinoma and High-Grade Sarcoma, NOS.

**Adjuvant Management**

The patient received adjuvant concurrent chemoradiotherapy:

- External beam radiotherapy to the pelvis, 50 Gy in 25 fractions.
- Along with 6 cycles of paclitaxel and carboplatin chemotherapy.

She tolerated therapy well and was subsequently kept on close follow-up.

## Discussion

The incidence of double primary malignancies has increased in recent decades due to improved diagnostic techniques and longer survival after successful treatment of the first cancer. The occurrence of metachronous malignancies involving breast and uterine cancers is well-documented, most often attributed to the prolonged use of tamoxifen, which increases the risk of endometrial carcinoma two- to threefold due to its partial estrogen agonist effect.

However, the present case is distinctive because:

- The patient had triple-negative breast carcinoma, for which no hormonal therapy was used.
- The subsequent malignancy was a carcinosarcoma, a rare and aggressive uterine tumor of both epithelial and mesenchymal origin, rather than typical endometrioid adenocarcinoma [4].

This suggests that factors other than tamoxifen, such as genetic predisposition, therapy-related effects, or shared environmental/hormonal influences may play a role in the pathogenesis of second malignancies. Although radiation-induced sarcomas are recognized entities, the dose and site in this case make such causation unlikely. It is possible that underlying genomic instability contributed to the development of a second malignancy.

**Review of Literature**

Only a few similar cases have been reported. Most involved older, postmenopausal women and a clear history of tamoxifen exposur. The occurrence of carcinosarcoma uterus following TNBC in a young premenopausal woman is exceptionally rare.

## Conclusion

This case emphasizes that endometrial malignancy can occur independently of tamoxifen exposure in breast cancer survivors. Clinicians should maintain a high index of suspicion for any new symptoms, including abnormal uterine bleeding, even years after completion of primary therapy. Regular gynecologic evaluation should form a part of long-term surveillance in breast cancer survivors, regardless of hormone receptor status or adjuvant therapy received.

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**Citation:** Archana Singh.,et al. "Metachronous Double Primary Malignancy: Triple-Negative Carcinoma Breast Followed by Carcinosarcoma Uterus – A Rare Case Report". NL Journal of Medical and Pharmaceutical Sciences 2.1 (2026): 11-12.