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Collision Tumor-Breast Adenocarcinoma with Ovarian Carcinoma Metastasis

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Case Report

Keywords: Collision tumor, Tumor-to-tumor metastasis, Breast cancer, Ovarian cancer, Adenocarcinoma

Posted Date: May 26th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9442806/v1

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Additional Declarations: No competing interests reported.

Abstract

Collision tumors comprising two distinct neoplasms at the same site are exceedingly rare. We report the first documented case of a collision tumor between primary breast invasive ductal carcinoma and metastatic ovarian high-grade serous carcinoma in a 48-year-old woman. Diagnosis was established through immunohistochemical profiling (GATA-3 + breast component; WT-1+/PAX-8 + ovarian component) and next-generation sequencing revealing a somatic TP53 mutation. The patient received platinum-based chemotherapy, interval debulking surgery, and modified radical mastectomy. This case underscores the necessity of integrated pathological and genomic analysis for accurate diagnosis and individualized therapy in such rare scenarios.

Case Report

A 48-year-old para 2 gravida 2 woman presented with dyspnea at an external hospital, and imaging examination revealed right-sided pleural effusion. She underwent video-assisted thoracoscopic surgery (VATS) and right pleurectomy without prior thoracentesis for cytology, and postoperative pathological examination suggested a malignancy of gynecological origin. The patient was then referred to our hospital for further management, with an Eastern Cooperative Oncology Group (ECOG) performance status of 1. Physical examination found a 4 cm firm, ill-defined mass in the upper outer quadrant of the left breast and left adnexal thickening, with no ascites or other obvious abnormalities. Comprehensive imaging was performed: breast ultrasound showed a left breast mass (BI-RADS 4C) with ipsilateral axillary lymphadenopathy; abdominal and pelvic computed tomography (CT) revealed bilateral adnexal cystic-solid masses (right: 6.9×4.8 cm; left: 12.7×8.4 cm) and no ascites. Serum tumor markers were significantly elevated: CA-125 > 1000 U/mL, CA15-3 85 U/mL.

Percutaneous core needle biopsy of the left breast mass was performed, and histological examination revealed two distinct, non-intermingling adenocarcinoma components (Fig. 1a) with divergent IHC phenotypes (Table 1). Component A (primary breast tumor) was diagnosed as grade II IDC, with IHC results showing ER 5% (weak +), PR 50% (strong +), AR 10% (weak +), HER2 1+ (negative), and focal positivity for GATA-3 and mammaglobin. Component B (metastatic tumor) was consistent with HGSOC in morphology, with positive IHC staining for WT-1, PAX-8 and CA125, and negative for GATA-3. The final diagnosis was confirmed as: (1) Primary ER+/PR+/HER2- invasive ductal carcinoma of the left breast; (2) Bilateral ovarian HGSOC, FIGO stage IVB (with pleural metastasis); (3) Breast collision tumor composed of the above two tumor components.

Table 1

Comparative immunohistochemical profile of the two tumor components in the breast collision tumor.

Marker	Invasive Ductal Carcinoma (Component A)	High-Grade Serous Carcinoma (Component B)	Key Diagnostic Significance
Lineage-Specific Markers			
GATA-3	Focal +	-	Supports mammary origin
Mammaglobin	Focal +	-	Supports mammary origin
WT1	Focal +	Focal +	Supports Müllerian (ovarian) origin
PAX8	Focal +	Focal +	Supports Müllerian (ovarian) origin
CA125	Focal +	+	Consistent with serous carcinoma
Hormone Receptors			
ER	Weak + (5%)	NT	Luminal subtype (Breast)
PR	Strong + (50%)	NT	Luminal subtype (Breast)
AR	Weak + (10%)	NT	Potential therapeutic target in breast cancer
Other Relevant Markers			
HER2	1+(Negative)*	NT	HER2-negative (Breast)
P53	Focal +	+ (with TP53 mutation)	Characteristic of HGSOC
Ki-67	+ (70%)	+ (80%)	High proliferative index
Epithelial Markers			
CK7	+	Focal +	Adenocarcinoma
CK5/6	+	NT	Marker for basal-like breast cancer

Key to Staining Terminology: +, Positive; Focal +, Heterogeneous or patchy positivity (not all tumor cells stain); Weak +, Low intensity staining; Strong +, High intensity staining; -,Negative; 1+.

abbreviations: ER, Estrogen Receptor; PR, Progesterone Receptor; AR, Androgen Receptor; HER2, Human Epidermal Growth Factor Receptor 2; NT, not tested; WT1, Wilms Tumor 1; CK7, Cytokeratin 7; CK5/6, Cytokeratin 5/6; CK20, Cytokeratin 20; TTF-1, Thyroid Transcription Factor-1; P53, Tumor Protein P53; P63, Tumor Protein P63.

*Note: HER2 1 + indicates incomplete, faint membrane staining in ≤ 10% of tumor cells, interpreted as negative according to ASCO/CAP guidelines.

Marker	Invasive Ductal Carcinoma (Component A)	High-Grade Serous Carcinoma (Component B)	Key Diagnostic Significance
P63	-	-	Excludes squamous differentiation
CK20	-	-	Excludes gastrointestinal origin
TTF-1	NT	-	Excludes lung origin
NapsinA	NT	-	Excludes lung adenocarcinoma
Key to Staining Terminology: +, Positive; Focal +, Heterogeneous or patchy positivity (not all tumor cells stain); Weak +, Low intensity staining; Strong +, High intensity staining; -,Negative; 1+.			
abbreviations: ER, Estrogen Receptor; PR, Progesterone Receptor; AR, Androgen Receptor; HER2, Human Epidermal Growth Factor Receptor 2; NT, not tested; WT1, Wilms Tumor 1; CK7, Cytokeratin 7; CK5/6, Cytokeratin 5/6; CK20, Cytokeratin 20; TTF-1, Thyroid Transcription Factor-1; P53, Tumor Protein P53; P63, Tumor Protein P63.			
*Note: HER2 1 + indicates incomplete, faint membrane staining in ≤ 10% of tumor cells, interpreted as negative according to ASCO/CAP guidelines.			

To explore the clonal relationship between the two tumors and screen potential therapeutic targets, NGS with a 520-gene panel was performed on ovarian carcinoma tissue. Molecular analysis identified a somatic TP53 p.R175H missense mutation (variant allele frequency, VAF: 3.93%) and an LRP1B p.Ser2383Ile missense mutation (VAF: 3.78%) of uncertain clinical significance. The ovarian tumor was homologous recombination proficient (HRD-negative, BRIDGE score = 0) with no pathogenic BRCA1/2 mutations detected, and exhibited low tumor mutational burden (TMB = 1.0 mut/Mb) and microsatellite stability (MSS). This molecular profile was consistent with the typical characteristics of HGSOC and ruled out a shared hereditary predisposition for the synchronous malignancies.

A multidisciplinary team (MDT) decided to prioritize systemic therapy for the more aggressive stage IVB ovarian HGSOC with higher tumor burden. The patient received two cycles of palliative chemotherapy with paclitaxel and carboplatin, and post-chemotherapy imaging according to RECIST 1.1 criteria showed a partial response of ovarian and pleural lesions. She underwent interval debulking surgery (IDS) in June 2024, with an intraoperative peritoneal carcinomatosis index (PCI) of 12; optimal cytoreduction (R0, no visible residual disease) was achieved. The surgical procedure included total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and pelvic/para-aortic lymph node dissection, and postoperative pathology confirmed bilateral ovarian HGSOC with lymph node metastases. After recovery from IDS, the patient completed a total of 6 cycles of adjuvant paclitaxel/carboplatin chemotherapy for ovarian cancer; no PARP inhibitor maintenance therapy was administered due to the HRD-negative status.

Given the persistent primary breast tumor with only partial response to platinum-based chemotherapy, local treatment was initiated in January 2025. The patient underwent left modified radical mastectomy with axillary lymph node dissection (sentinel lymph node biopsy was not performed due to pre-diagnosis clinically and radiologically suspicious axillary lymph nodes). Final breast pathology showed minimal residual invasive carcinoma (Miller-Payne Grade 2) with negative resection margins and no axillary lymph node metastasis (0/20). Adjuvant radiotherapy to the chest wall was not indicated, and adjuvant endocrine therapy with an aromatase inhibitor was initiated for the hormone receptor-positive breast cancer. Up to the time of writing, the patient is under regular follow-up with no evidence of disease progression.

This is the first reported case of a collision tumor between primary breast IDC and metastatic ovarian HGSOC, presenting unique diagnostic and therapeutic challenges for cross-system synchronous malignancies. The accurate diagnosis of collision tumors relies on multimodal pathological analysis, with genomic profiling also contributing to diagnostic precision to some extent. The 'triple verification' principle—encompassing distinct morphological features, divergent immunohistochemical (IHC) profiles, and molecular disparities—is essential for distinguishing collision tumors from other multicomponent neoplasms and avoiding misdiagnosis, such as metaplastic breast carcinoma[1–3]. For patients with known or suspected dual primary malignancies, a high index of suspicion for unusual metastatic patterns including tumor-to-tumor metastasis is required; in this case, the initial pleural effusion could easily lead to a misdiagnosis of primary pleural or lung malignancy, while the WT-1+/PAX-8 + IHC profile of pleural tissue correctly guided subsequent pelvic imaging and further diagnosis.

The therapeutic management of such complex synchronous collision tumors requires a staged, systemic-first paradigm, with clinical resources allocated to the more aggressive and higher-burden malignancy[5–6]. The short-course initial platinum-based chemotherapy in this case served a dual purpose: it not only assessed the platinum sensitivity of ovarian HGSOC but also evaluated the taxane responsiveness of the breast IDC, which mitigates the theoretical risk of "competitive release" (chemotherapy targeting one tumor component accelerates the progression of the other)[7]. The favorable systemic response enabled optimal IDS for ovarian cancer, and modified radical mastectomy was selected for breast cancer over breast-conserving surgery due to the challenges of margin assessment caused by the collision pathology. Postoperative adjuvant therapy was guided by molecular profiling: the TP53 p.R175H mutation in the ovarian component indicated a potential therapeutic vulnerability to DNA damage response inhibitors (e.g., WEE1 inhibitors) for future lines of therapy, while the MSS and low TMB phenotype ruled out the benefit of immune checkpoint inhibitors; standard aromatase inhibitor endocrine therapy was administered for the hormone receptor-positive breast IDC in accordance with clinical guidelines.

The absence of germline BRCA1/2 mutations and HRD proficiency in ovarian cancer supports that the collision tumor is a stochastic event rather than a hereditary predisposition. A noteworthy finding is the somatic TP53 p.R175H gain-of-function mutation in the ovarian component; mutant p53 has been reported to remodel the tumor microenvironment (TME) by secreting pro-tumorigenic cytokines and

chemokines, potentially creating a permissive niche for secondary tumor engraftment[8]. This raises a speculative hypothesis that the mutant p53-driven ovarian carcinoma may have actively modulated the local breast TME, facilitating its metastasis to the pre-existing breast tumor rather than normal breast parenchyma, which is supported by the specific "homing" of ovarian metastasis to the breast cancer site. Future research on cross-system tumor metastasis tropism should focus on spatial transcriptomic or proteomic analysis of the collision interface to validate the involvement of specific chemokine axes (e.g., CXCL12/CXCR4) and explore the unique TME characteristics of collision tumors[9].

In conclusion, this rare case confirms that integrated pathological, genomic and clinical analysis is indispensable for the diagnosis of cross-system collision tumors. A patient-centered, staged therapeutic strategy based on the aggressiveness and molecular features of each tumor component is the key to optimizing clinical outcomes for such complex malignancies.

Abbreviations

BI-RADS
Breast Imaging Reporting and Data System
BRCA1/2
Breast Cancer Gene 1/2
CT
Computed Tomography
CXCL12
C-X-C Motif Chemokine Ligand 12
CXCR4
C-X-C Chemokine Receptor Type 4
FIGO
International Federation of Gynecology and Obstetrics
HRD
Homologous Recombination Deficiency
HGSOC
High-Grade Serous Ovarian Carcinoma
IHC
Immunohistochemistry
IDC
Invasive Ductal Carcinoma
LRP1B
Low-Density Lipoprotein Receptor-Related Protein 1B
NGS
Next-Generation Sequencing
RECIST
Response Evaluation Criteria in Solid Tumors

TP53
Tumor Protein P53
TMB
Tumor Mutational Burden
TMB-H
Tumor Mutational Burden-High
VAF
Variant Allele Frequency
VATS
video-assisted thoracoscopic surgery.

Declarations

Author Contributions

Shujie Song: case review, writing – original draft. **Xianshu Kong:** investigation, writing – original draft, writing – review and editing. **Lin Wu:** investigation. **Ying Liu:** resources. **Shaojia Wang:** case review. **Wenlin Chen:** case review. **Nianqiu Liu:** resources. **Zhonghua Liu:** supervision. **Fanghui Mu:**investigation. **Zhen Li:** conceptualization, funding acquisition, investigation, supervision, writing – review and editing.

Funding

This research was funded by First-Class Discipline Team of Kunming Medical University, grant number 2024XKTDYS08; Biomedical Projects of Yunnan Key Science and Technology Program, grant number 202302AA310046; National Natural Science Foundation of China, grant number 82060481; National Natural Science Foundation of China, grant number 82260542; Kunming Medical University Breast Cancer Metastasis and Drug Resistance Basic Research Innovation Team, grant number K1322137; Training Program for Medical Reserve Talents of Yunnan Provincial Health Commission, grant number H-2024048; Yunnan Province Higher Education Collaborative Innovation Center for Research on Breast Cancer Drug Resistance Mechanisms and Transformation Application, grant number K1322147; Yunnan Talent Development and Recruitment Support Plan, the Scientific Research Fund of Yunnan Provincial Department of Education, grant number 2024Y547; Qingfeng Program of the Qingyan Research Fund, Beijing Huakang Public Welfare Foundation.

Data availability

The data of this case are available from the authors upon reasonable request.

Ethics approval and consent to participate

The implementation process of this research conforms to the principles of the Helsinki Declaration. The study involving human participants were reviewed and approved by the Clinical Research Ethics Committee of The Third Affiliated Hospital of Kunming Medical University, Peking University Cancer

Hospital Yunnan, (KYLX2025-188). This patient signed a written informed consent form after receiving a complete study description.

Consent for publication

We have successfully obtained all the necessary approvals and consents required for conducting this research and publishing this manuscript. Informed consent to publish the clinical data, radiographic images and pathological findings was obtained from the individual participant.

Competing interests

The authors declare no competing interests

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Figures

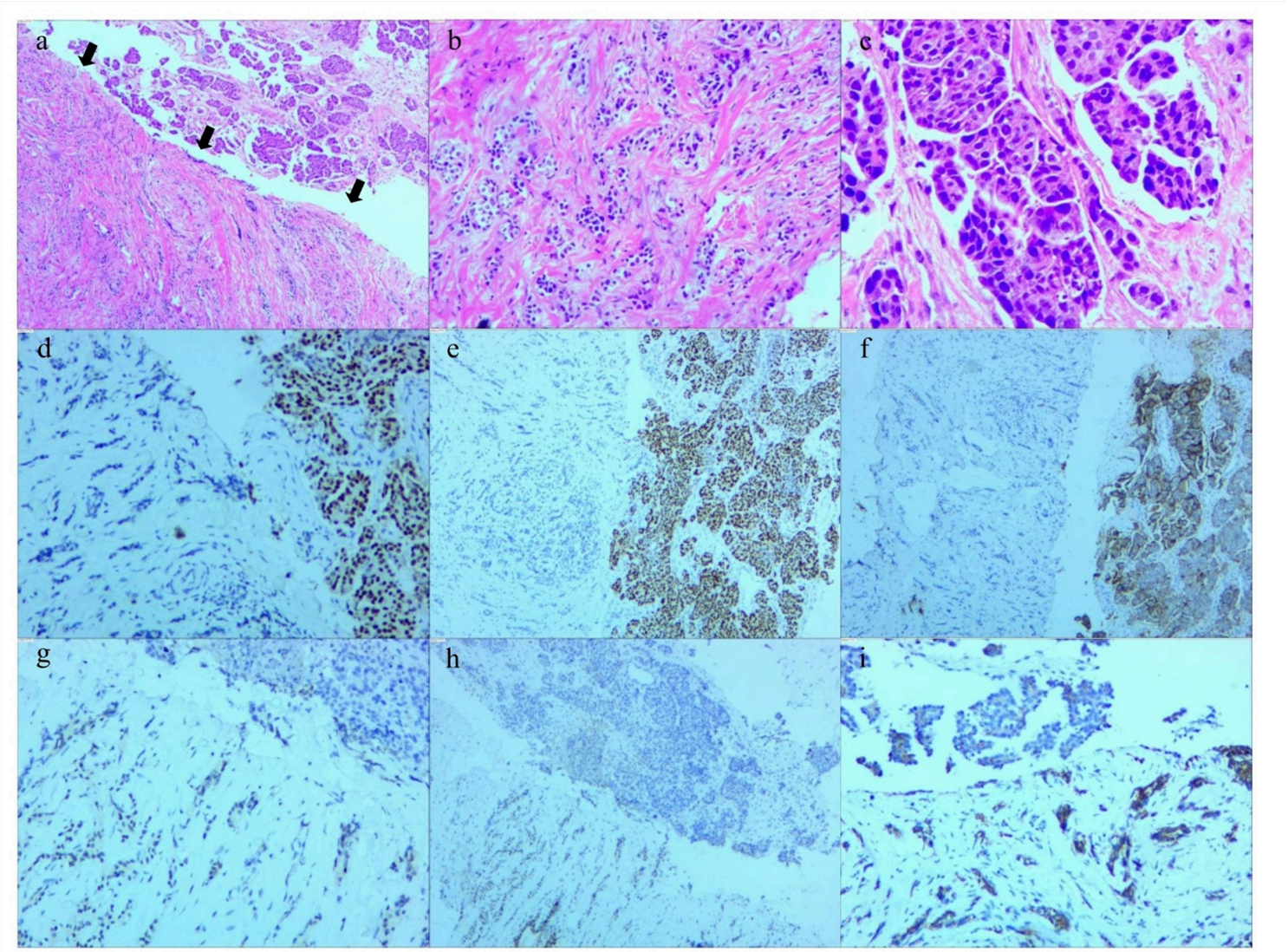


Figure 1

Histopathological and immunohistochemical features of the breast collision tumor.

(a) Low-power H&E (×100): Two distinct, non-intermingling tumor components with a clear interface (arrow) in the same breast mass. (b) High-power H&E (×400) of Component A (breast IDC): Tumor cells in nests/cords with moderate pleomorphism. (c) High-power H&E (×400) of Component B (metastatic ovarian HGSOC): Marked cellular atypia with papillary/solid patterns. (d) WT-1 IHC: Strong nuclear positivity in Component B (ovarian origin). (e) PAX8 IHC: Strong nuclear positivity in Component B (Müllerian lineage). (f) CA125 IHC: Cytoplasmic/membranous positivity in Component B (serous carcinoma). (g) GATA-3 IHC: Focal nuclear positivity in Component A (mammary origin). (h) Mammaglobin IHC: Focal cytoplasmic positivity in Component A (mammary differentiation). (i) E-Cadherin IHC: Membranous positivity in both components (epithelial nature).

Abbreviations: H&E, hematoxylin and eosin; IDC, invasive ductal carcinoma; HGSOC, high-grade serous carcinoma; WT-1, Wilms tumor 1; PAX8, paired box gene 8; CA125, cancer antigen 125; GATA-3, GATA binding protein 3.