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Sacituzumab Govitecan Combined with Anti-angiogenic Therapy and Radiotherapy in a BRCA1-Mutated Triple-Negative Breast Cancer Patient with Multiple Recurrences: A Case Report

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Introduction

Triple-negative breast cancer (TNBC), defined by the absence of estrogen receptor (ER^-), progesterone receptor (PR^-), and human epidermal growth factor receptor 2 ($HER2^-$) expression, accounts for 10%-15% of all breast cancers(1).It exhibits aggressive biological behavior characterized by high proliferative indices, genomic instability, and a paucity of targeted therapies(2). BRCA1-mutated TNBC may respond to PARP inhibitors and DNA-damaging agents(3).

However, a significant proportion of patients still experience disease progression, underscoring the urgent need for novel treatment strategies(4). This case report details a young female with BRCA1-mutated TNBC who presented with extensive systemic and brain metastases. The treatment strategy combining Sacituzumab Govitecan (SG), Anlotinib, and concurrent whole-brain radiotherapy (WBRT) provides unique insights into managing complex, relapsed TNBC.

Case Presentation

In March 2011, a 28-year-old female was diagnosed with left breast invasive ductal carcinoma ($ER^-/PR^-/HER2^-$, pT2N0M0). She underwent a left modified radical mastectomy, followed by 8 cycles of adjuvant chemotherapy (epirubicin + cyclophosphamide, followed by paclitaxel). In March 2017, a 2×2 cm invasive carcinoma (ER^-/PR^-/HER2 1+) was detected in her right breast. She received 6 cycles of neoadjuvant TAC chemotherapy (docetaxel + liposomal doxorubicin + cyclophosphamide), followed by a right nipple-areolar-sparing mastectomy, axillary dissection, and breast reconstruction on August 7, 2017. Adjuvant radiotherapy was subsequently administered.

Case Presentation

In December 2020, a right chest wall recurrence was found and treated with local extended resection in January 2021, followed by one year of oral capecitabine. In June 2023, she developed lung metastases and was found to have a germline BRCA1 mutation. She then enrolled in an investigator-initiated trial (IIT, NCT05085626) and received Fluzoparib plus Chidamide, achieving a partial response (PR) with a progression-free survival (PFS) of 14 months. In August 2024, the patient developed widespread metastases (involving the brain, lungs, soft tissues, liver, spleen, bone, and ileum). She declined brain surgery and was treated with Bevacizumab plus Trastuzumab Deruxtecan. After two cycles, symptoms of intracranial hypertension improved, and the disease was assessed as stable disease (SD). However, treatment was discontinued due to grade 3/4 nausea, vomiting, and fatigue. In December 2024, the original lesions (brain, lung, liver, ileum) progressed(figure.1), and new metastases were identified in the retroperitoneum, kidneys, left fourth metacarpal, and phalanges. Treatment with SG in combination with Anlotinib was initiated, accompanied by concurrent WBRT during the first cycle. After two cycles, the disease achieved a PR (figure.2). Grade 3 anemia occurred during treatment but was managed with supportive care. The PFS has exceeded 10 months to date, and the patient remains on continuous treatment.

Discussion

Preclinical studies have shown that SG delivers SN-38 to induce DNA damage in tumors with homologous recombination deficiency (HRD) (e.g., BRCA-mutated), which have impaired DNA repair capabilities. Anti-angiogenic agents are theorized to enhance the efficacy of SG by promoting VEGF-targeted vascular normalization and blocking survival signaling pathways(5). Additionally, SG has demonstrated the ability to penetrate intracranial tumors and exhibit promising activity against them. Combining SG with WBRT may synergistically induce DNA damage and enhance treatment efficacy(6). This patient's positive response to the combination regimen suggests a potential clinical benefit for metastatic TNBC, especially in cases with brain metastases. The occurrence of grade 3 anemia highlights the need for close toxicity monitoring.

Conclusions

This case report highlights the potential efficacy of SG combined with anti-angiogenic therapy and radiotherapy for treating BRCA1-mutated TNBC patients with multiple recurrences and brain metastases.

However, further studies are needed to confirm these findings and to optimize the use of these agents in this patient subset.

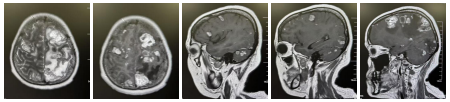


Figure 1: Before treatment with SG(540mg d1, d8) + anlotinib (10mg) combined with whole-brain radiotherapy

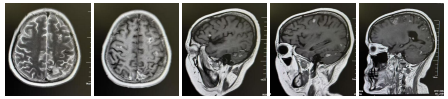


Figure 2: Partial response (PR) was achieved after 2 cycles of treatment

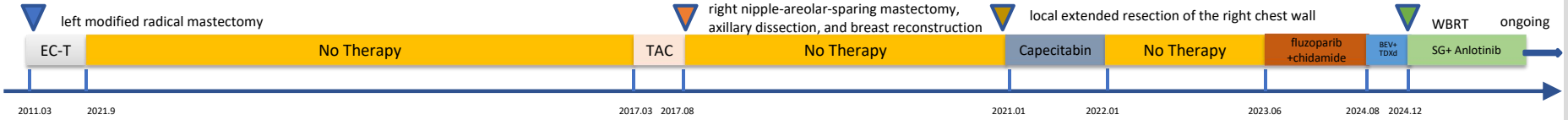


Figure 3: Timeline of the breast cancer patient's treatments

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