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Case Report

A Case of Primary Bilateral Ovarian Cancer After Surgery for Primary Breast Cancer in A Fanconi Anemia Gene-Positive Patient

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Abstract

Breast cancer is the most common gynecological malignancy among Chinese women. Although the proportion of ovarian cancer recurrence in breast cancer patients after surgery shows a declining trend, compared with the general population, these patients still face a higher risk of recurrence, and their prognosis is much worse than that of patients with primary endometrial cancer or primary ovarian cancer. It is noteworthy that there is a time interval of more than 5 years between the onset of breast cancer and ovarian cancer in most patients. This suggests that breast cancer patients, especially those with high-risk factors for ovarian cancer, need regular ovarian cancer screening management after surgery. Patients with long-term survival should be more vigilant against the occurrence of ovarian cancer. Therefore, the task of reducing the recurrence of gynecological malignancies in breast cancer patients remains arduous and lengthy. At present, the specific mechanism of ovarian cancer recurrence in breast cancer patients is unclear, and we lack clear indicators to identify high-risk groups. This case study conducts an in-depth analysis of a patient with ovarian cancer recurrence after breast cancer. The patient, admitted to the Department of Gynecology of the Affiliated Hospital of Guizhou Medical University, tested positive for the Fanconi anemia gene. She had undergone surgery for primary breast cancer, subsequently developed ovarian cancer, and received surgery and chemotherapy again. Unfortunately, she still experienced recurrence. By analyzing this case, we aim to provide a solid basis for the systematic management of high-risk groups.

Keywords: ovarian cancer; breast cancer; fanconi anemia; gene; tumor recurrence

Introduction

Breast cancer is the most common gynecological malignant tumor in Chinese women. According to relevant surveys, although the proportion of postoperative recurrence of ovarian cancer in breast cancer patients shows a downward trend, they still face a higher risk of recurrence compared with the general population, and the prognosis is far worse than that of patients with primary endometrial cancer or primary ovarian cancer. It is worth noting that most patients have a time interval of more than 5 years between the onset of breast cancer and ovarian cancer. This suggests that patients with breast cancer, especially those with high risk factors for ovarian cancer, need regular ovarian cancer screening and management after surgery.

For patients who achieve long-term survival, more attention should be paid to the occurrence of ovarian cancer. Therefore, the task of reducing recurrent gynecologic malignancies in patients with breast cancer remains arduous and protracted.

At present, the specific mechanism of ovarian cancer recurrence in breast cancer patients remains unclear, and there is a lack of clear indicators to identify high-risk groups, which brings great challenges to the prevention and treatment of this kind of tumor recurrence. Fanconi anemia (FA) is a rare genetic disorder, and its related gene mutations are closely related to DNA damage repair defects and increased tumor susceptibility. Studies have shown that FA gene mutation carriers have a significantly higher risk of breast cancer and ovarian cancer, but the specific relationship between FANCM gene, one of the FA genes, and these two cancers is still not fully understood. Based on the above background, this study aims to conduct an in-depth analysis of a patient with primary bilateral ovarian cancer after primary breast cancer surgery and FANCM gene positivity. By exploring the potential relationship between FANCM gene and the occurrence and development of breast cancer and ovarian cancer, as well as the role of FANCM gene in tumor recurrence, it provides a basis for the systematic management of high-risk groups and contributes to the formulation of more effective prevention and treatment strategies.

Case reports :

A 54-year-old female patient was admitted to the Affiliated Hospital of Guizhou Medical University for surgical treatment of breast cancer in 2007. Postoperative chemotherapy was given for 6 courses and regular follow-up was performed. In 2017, he was hospitalized in Guizhou Provincial Cancer Hospital for tumor cytoreductive surgery due to stage IIIA ovarian cancer. The postoperative pathological examination results were as follows: 1. The left adnexal malignant tumor with necrosis tended to be of epithelial origin. 2. A large number of tumors were involved in the tissues of the "greater omentum", and multiple tumor emboli were found in the interstitial vessels. Immunohistochemistry: combined with HE tissue and immunohistochemical markers, the results supported that it was ovarian high-grade serous adenocarcinoma. Tumor CK +, WT - 1 +, CK7 +, P16 +, P53 +, Ki67 + 80%, ER + 10%, PR -, GATA - 3 -, GCDFP - 15 -, CEA, CDX - 2 -, CA125, part CD56 +, Vim, BRCA1 +, BRCA2 +. After surgery, 6 courses of TP regimen chemotherapy were given. In 2018, the blood CA125 was 1262U/ml and HE4 was 142.2pmol/L, and the results of PET/CT examination were as follows: [1]. Postoperative ovarian cancer: cystic lesion with solid nodule in the left adnexal region, local metabolism increased, and metastasis was considered. [2] Local peritoneal thickening, multiple soft tissue density nodules in the abdominal cavity, pelvic cavity, right iliac vessels and liver membrane, peritoneal metastasis was considered; [3]. Perihepatic and lower abdominal effusion with increased metabolism, considered malignant ascites; [4] After right breast cancer operation: no signs of abnormal high metabolism recurrence were found; [5]. The metabolism of bilateral thyroid lobes is generally increased. Hashimoto's thyroiditis is considered, and relevant laboratory tests are recommended. [6]. Slight thickening of the right local pleura, calcification of the left lateral lobe of the liver cell membrane, and degeneration of L4 vertebral body. Considering the recurrence of ovarian cancer, she was hospitalized again and treated with TP regimen chemotherapy. Admission diagnosis: 1. Recurrence of bilateral ovarian serous high-grade adenocarcinoma stage IIIA after postoperative chemotherapy; 2. After postoperative chemotherapy for right breast cancer; 3. Hashimoto's thyroiditis. The patient was asked about the history of cervical cancer in her first degree relatives. After discussion, the patient was considered to be platinumsensitive, so TP (paclitaxel: 140mg/m2 IV infusion, cisplatin: 70mg/m2 intraperitoneal perfusion) chemotherapy regimen was given, and 8 cycles of chemotherapy were completed. With informed consent, the patient's venous blood was collected for tumor susceptibility gene sequencing, and the results showed: FANCM (+) (c.4733A > G). After 8 cycles of TP regimen chemotherapy, CA125 did not decrease significantly, considering the poor effect of chemotherapy, combined with the characteristics of FANCM gene, the chemotherapy regimen was changed to "paclitaxel + carboplatin + bevacizumab" chemotherapy for 6 cycles. The patient's CA125 decreased slightly, and then oral niraparib treatment was given, CA125 maintained about 20U/ml. In January 2020 and December 2022, the patient relapsed again and was treated with "paclitaxel + carboplatin + bevacizumab" chemotherapy. The last recurrence was delayed in treatment due to the COVID-19 infection period. The patient died of multiple organ failure in September 2023.

Discussion

The FANCM gene, located on the long arm of chromosome 14 (14q21.3), is an important part of the Fanconi anemia pathway. The FANCM protein encoded by this gene is a DNA helicase, which plays a key role [1] in DNA damage repair and genome stability maintenance. At present, 22 FA genes are known, among which FANCA, FANCC and FANCG are the most common mutated genes. Due to the defect in DNA repair ability, FA patients are highly sensitive to DNA cross-linking agents, and are prone to chromosome breakage and genomic instability, which lead to tumorigenesis. Studies have shown that the risk of cancer in FA patients is 500-700 times [2] higher than that in the general population. In addition to hematological malignancies such as acute myeloid leukemia, FA patients are also prone to solid tumors such as squamous cell carcinoma of the head and neck, esophageal cancer, breast cancer, and ovarian cancer. It is worth noting that although carriers of FA gene mutations (i.e., relatives of FA patients) do not show typical FA symptoms, they also have a higher susceptibility to tumors, especially breast and ovarian [3,4] cancers.

Surgical treatment is one of the important means of ovarian cancer treatment.

For patients with early ovarian cancer, surgical removal of the tumor and the affected organs can achieve the goal of cure. For ovarian cancer patients with FANCM gene mutations, the choice and scope of surgical treatment should be individualized according to the specific conditions of patients. Chemotherapy is one of the important treatments for ovarian cancer. For patients with advanced or recurrent ovarian cancer, chemotherapy can prolong survival and improve quality of life. For ovarian cancer patients with FANCM gene mutations, the choice and dose of chemotherapy drugs may need to be adjusted [3] individually according to the specific conditions of the patients. Because FANCM gene is involved in DNA damage response and repair processes, its mutation may lead to increased or decreased [5] sensitivity of cells to chemotherapeutic drugs. With the in-depth study of the molecular mechanism of ovarian cancer, more and more targeted therapeutic drugs have been developed. For ovarian cancer patients with FANCM gene mutation, targeted therapy drugs can be considered. For example, PARP inhibitors, a class of targeted therapeutic drugs targeting DNA repair defects, have shown good efficacy in the treatment of ovarian cancer.

In recent years, the relationship between FA gene mutations and breast cancer and ovarian cancer has received extensive attention. Studies have shown that the FA/BRCA pathway plays a key role [6] in DNA damage repair and genome stability maintenance. Mutations in the FA gene can lead to defects in homologous recombination repair and increase susceptibility to breast and ovarian cancer. In particular, mutations in the FANCA, FANCC and FANCD1/BRCA2 genes are closely associated [7] with the development of breast and ovarian cancer. In terms of clinical management, tumor screening and prevention strategies for FA gene mutation carriers are research hotspots. For FA patients and mutation carriers, annual breast self- examination and clinical breast examination are recommended starting at age 18 years, and annual breast MRI screening [8] starting at age 25 years. For ovarian cancer screening, although there is no uniform standard, annual pelvic ultrasound and CA125 testing are recommended starting at age 30 to 35 years. In addition, preventive surgery (e.g., bilateral mastectomy and bilateral salpingo-oophorectomy) and chemoprevention (e.g., tamoxifen) may also be considered. Patients with positive FANCM gene have an increased [2, 9] risk of breast cancer and ovarian cancer, but the specific relationship between FANCM gene and these two cancers is still not fully understood. With the in-depth study of FANCM gene function, the continuous development of genetic testing technology and the reduction of cost, we

will be able to evaluate the relationship between FANCM gene and breast and ovarian cancer more comprehensively in the future, and develop more effective prevention and treatment methods. In terms of treatment, traditional treatment methods such as surgery, chemotherapy, and radiotherapy are mainly used, as well as new treatment methods such as targeted therapy and immunotherapy [10]. In the future, with the development of individualized treatment and the strengthening of multidisciplinary collaboration, we will be able to formulate more accurate treatment plans for each patient, improve the treatment effect and quality of life.

Conclusions

This study presents a case of a patient who developed recurrent ovarian cancer 10 years following breast cancer surgery, with genetic testing confirming a positive FANCM gene mutation. By integrating the patient's clinical course and genetic findings, this paper explores the potential association between the FANCM gene and the pathogenesis of breast and ovarian cancers, as well as the role of the FANCM gene in tumor development and progression.

Notably, while existing literature on the direct correlation between FANCM gene mutations and ovarian cancer remains limited, the critical function of the FANCM gene in DNA damage repair—along with its established involvement in breast cancer pathogenesis—leads to a reasonable hypothesis: FANCM gene mutations may also contribute to the initiation and progression of ovarian cancer. This speculation is rooted in the gene's pivotal role in maintaining genomic stability, where its dysfunction could potentially promote tumorigenesis through impaired DNA repair mechanisms [11].

Finally, further research is urgently needed to elucidate the precise molecular mechanisms by which the FANCM gene influences ovarian cancer development. Additionally, the development and clinical application of targeted therapeutic agents specifically directed against FANCM gene-related pathways represent promising avenues for advancing personalized cancer treatment. Such efforts hold the potential to not only deepen our understanding of the genetic basis of gynecological malignancies but also to foster the creation of more effective preventive and therapeutic strategies for high-risk populations.

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