A case of triple negative breast cancer in Lynch Syndrome

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Background

Although there are numerous inherited syndromes that predispose individuals to developing breast cancer, it is inconclusive whether Lynch syndrome (LS) increases the risk of breast cancer. We present a case of a triple-negative breast cancer in a woman with Lynch Syndrome.

Case Presentation

Our patient is a 73-year-old woman with a past medical history of Lynch syndrome (MSH2 deletion), endometrial cancer status-post TAH/BSO, rectal cancer status-post abdominal perineal resection and end ileostomy, and colon cancer status-post right hemicolectomy with appendectomy and chemotherapy with 5-fluorouracil and leucovorin. A 2.7 cm mass was found in her right breast during a screening mammogram.

MRI showed a 3.7 cm right breast mass. CT of the chest, abdomen, and pelvis showed no lymphadenopathy or evidence of metastatic disease. Biopsy of the right breast mass indicated **grade 3 invasive ductal carcinoma with ER 10%, PR 2%, HER2 1+**.

Treatment

She began neoadjuvant chemoimmunotherapy based on the KEYNOTE-522 trial. Chemoimmunotherapy was discontinued after five cycles due to intolerable side effects, including neuropathy, rash, and musculoskeletal pain.

She then underwent a bilateral mastectomy with sentinel lymph node biopsy, which revealed residual invasive ductal carcinoma measuring 6 mm without lymph node involvement, consistent with stage ypT1b pN0. Pembrolizumab was resumed.

Adjuvant treatment with dose-reduced Capecitabine, was initiated following the CREATE-X trial. This was stopped after 5 cycles due to palmar-plantar erythrodysesthesia, diarrhea and pulmonary embolism.

Timeline

- Screening mammography: 2.7 cm mass in the right breast at 12:00
- MRI: 3.7 cm right breast mass and an asymmetric right axillary lymph node
- Breast mass biopsy: Grade 3 Invasive ductal carcinoma ER 10% PR 2% HER2 1+
- KEYNOTE-522 Neoadjuvant pembrolizumab, paclitaxel, carboplatin, doxorubicin, cyclophosphamide
- KEYNOTE-522 stopped after cycle 5 due to peripheral neuropathy, rash, musculoskeletal pain
- Bilateral mastectomy with sentinel lymph node biopsy: 6 mm residual invasive ductal carcinoma, ypT1 pN0
- CREATE-X: Adjuvant capecitabine in addition to pembrolizumab
- CREATE-X stopped after 5 cycles due to palmar-plantar-erythrodysesthesia, diarrhea, pulmonary embolism

Discussion

Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, is an inherited condition caused by germline mutations in a series of DNA mismatch repair genes, including MLH1, MSH2, MSH6, and PMS2.

LS is well known to increase the risk of multiple cancers, such as **colorectal, endometrial, ovarian, and stomach** cancers. **Breast cancer has not been considered a part of the LS spectrum.**

Despite several studies, a clear link between LS and breast cancer has not been established. A few studies have also looked at the possible association between pathogenic variants of LS and breast cancer risks; however, the data have not been consistent.

A cohort study by Sheehan et al. found a significantly higher prevalence of breast cancer in women with PMS2 mutations compared to other genetic alterations, while a study by Scott et al. reported overrepresentation of breast cancer in MLH1 mutations compared to MSH2 mutations.

Currently, LS screening guidelines recommend general population-based screening for breast cancer.

Immunotherapy with PD-1 blockade has demonstrated profound results with mismatch repair-deficient colorectal cancer as well as other cancers such as endometrial, gastric, pancreatic, ovarian, and cholangiocarcinoma, but whether this translates to breast cancer is unknown.

In this case, the patient with triple-negative breast cancer and LS received five cycles of neoadjuvant chemoimmunotherapy, and her mass decreased from 3.7 cm before treatment to 6 mm pathologically. There are no treatment recommendations specific to LS patients with breast cancer.

Larger prospective studies are warranted to establish a potential need for intensified breast cancer screening in patients with LS, as well as to study outcomes of breast cancer in LS patients.

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