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Surgical ovarian ablation for positive women with breast carcinoma in rural India

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Introduction

Breast cancer is cancer that develops from breast tissue. Signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, a newly inverted nipple, or a red or scaly patch of skin. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin.

Risk factors for developing breast cancer include being female, obesity, a lack of physical exercise, alcoholism, hormone replacement therapy during menopause, ionizing radiation, an early age at first menstruation, having children late in life or not at all, older age, having a prior history of breast cancer, and a family history of breast cancer. About 5–10% of cases are the result of a genetic predisposition inherited from a person's parents, including BRCA1 and BRCA2 among others. Breast cancer most commonly develops in cells from the lining of milk ducts and the lobules that supply these ducts with milk. Cancers developing from the ducts are known as ductal carcinomas, while those developing from lobules are known as lobular carcinomas. There are more than 18 other sub-types of breast cancer. Some, such as ductal carcinoma in situ, develop from pre-invasive lesions. The diagnosis of breast cancer is confirmed by taking a biopsy of the concerning tissue. Once the diagnosis is made, further tests are done to determine if the cancer has spread beyond the breast and which treatments are most likely to be effective.

The balance of benefits versus harms of breast cancer screening is controversial. A 2013 Cochrane review found that it was unclear if mammographic screening does more harm than good, in that a large proportion of women who test positive turn out not to have the disease. A 2009 review for the US Preventive Services Task Force found evidence of benefit in those 40 to 70 years of age, and the organization recommends screening every two years in women 50 to 74 years of age. The medications tamoxifen or raloxifene may be used in an effort to prevent breast cancer in those who are at high risk of developing it. Surgical removal of both breasts is another preventive measure in some high risk women. In those who have been diagnosed with cancer, a number of treatments may be used, including surgery, radiation therapy, chemotherapy, hormonal therapy, and targeted therapy. Types of surgery vary from breast-conserving surgery to mastectomy. Breast reconstruction may take place at the time of surgery or at a later date. In those in whom the cancer has spread to other parts of the body, treatments are mostly aimed at improving quality of life and comfort.

Outcomes for breast cancer vary depending on the cancer type, the extent of disease, and the person's age. The five-year survival rates in England and the United States are between 80 and 90%. In developing countries, five-year survival rates are lower. Worldwide, breast cancer is the leading type of cancer in women, accounting for 25% of all cases. In 2018 it resulted in 2 million new cases and 627,000 deaths. It is more common in developed countries and is more than 100 times more common in women than in men.

Pathophysiology

Breast cancer, like other cancers, occurs because of an interaction between an environmental (external) factor and a genetically susceptible host. Normal cells divide as many times as needed and stop. They attach to other cells and stay in place in tissues. Cells become cancerous when they lose their ability to stop dividing, to attach to other cells, to stay where they belong, and to die at the proper time.

Normal cells will self-destruct (programmed cell death) when they are no longer needed. Until then, cells are protected from programmed death by several protein clusters and pathways. One of the protective pathways is the PI3K/AKT pathway; another is the RAS/MEK/ERK pathway. Sometimes the genes along these protective pathways are mutated in a way that turns them permanently "on", rendering the cell incapable of self-destructing when it is no longer needed. This is one of the steps that causes cancer in combination with other mutations. Normally, the PTEN protein turns off the PI3K/AKT pathway when the cell is ready for programmed cell death. In some breast cancers, the gene for the PTEN protein is mutated, so the PI3K/AKT pathway is stuck in the "on" position, and the cancer cell does not self-destruct.

Mutations that can lead to breast cancer have been experimentally linked to estrogen exposure. Additionally, G-protein coupled estrogen receptors have been associated with various cancers of the female reproductive system including breast cancer.

Abnormal growth factor signaling in the interaction between stoma cells and epithelial cells can facilitate malignant cell growth. In breast adipose tissue, over expression of lepton leads to increased cell proliferation and cancer.

In the United States, 10 to 20 percent of women with breast cancer or ovarian cancer have a first- or second-degree relative with one of these diseases. Men with breast cancer have an even higher likelihood. The familial tendency to develop these cancers is called hereditary breast–ovarian cancer syndrome. The best known of these, the BRCA mutations, confer a lifetime risk of breast cancer of between 60 and 85 percent and a lifetime risk of ovarian cancer of between 15 and 40 percent. Some mutations associated with cancer, such as p53, BRCA1 and BRCA2, occur in mechanisms to correct errors in DNA. These mutations are either inherited or acquired after birth. Presumably, they allow further mutations, which allow uncontrolled division, lack of attachment, and metastasis to distant organs. However, there is strong evidence of residual risk variation that goes well beyond hereditary BRCA gene mutations between carrier families. This is caused by unobserved risk factors. This implicates environmental and other causes as triggers for breast cancers.

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