

Recent Studies & Advances in Breast Cancer

Chapter 4

An Introduction to Breast Cancer

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Abstract

Cells are the basic unit of organisms. Cells grow and divide to form daughter cells as our body grows. Usually, old cells die and are replaced by new ones. Cancer begins when cells start to grow uncontrollably due to some genetic changes and form a mass of cells, called a tumor. A tumor can be malignant (cancerous) or benign. Breast cancer is one of the most common cancers in world after lung cancer. It is more common in women than men. In the year 2018, 2,088,849 new cases were reported (for both sexes). Breast cancer is detected by mammograms, sometimes even before it has spread to other parts of the body.

1. Introduction

Breast cancer is the abnormal growth of cells in the lobes or ducts of the breast. . Lobules are milk producing glands . Ducts bring the milk to the nipples from the glands. Uncontrolled cells often invade other healthy breast tissues and travel to lymph nodes under the arms (axillary lymph nodes) and these lymph nodes act as the primary pathway that helps the cancer cells move to other parts of the body. There is a direct link between prognosis and number of

lymph nodes involved with metastatic disease [1]. Patients with axillary lymph node micro-metastasis have less survival rates than patients dependent on age or tumor size [2].

2. Causes of Breast Cancer

Breast cancer is caused due to mutation in DNA. What causes these mutations is still not clear. Most breast cancers are diagnosed in women above age 50 but there is a risk factor of women aged 40 -49 too [3]. It is highest for women in their 70. Having close blood relatives with breast cancer also indicates chances of developing the disease. A women's breast cancer risk is double if she has a mom, sister, or daughter with breast cancer and gets triple is she has two or more first degree relatives with breast cancer [4]. Around 10% of all the breast cancers are said to be inherited, due to the defects in either one or two genes. Main genes involved with these mutations are BRCA1 and BRCA2 genes. Defective genes don't cause breast cancer always but there is always a greater risk [5]. Women with bigger size breast usually are at a higher risk of nodal metastasis and detection in heavy breasts is also difficult because of more tissue mass [6]. White women are at slightly greater risk than Asian, Hispanic and African American women to develop breast cancer. Risk of development of aggressive breast cancer is higher in African American that too at a younger age and both African American and Hispanic women are more likely to die from the breast cancer than other races women [7]. A long time exposure to the hormones like estrogen also increases the risk of breast cancer as this hormone is said to be a proliferative factor. Women with early menstrual period (starting before age 12) and late menopause (after age 55) are at greater risk than other women [8]. Women who are obese or gains weight after menopause are more likely to develop breast cancer. This may be due to the fact that fat cells release estrogen after menopause [9]. Studies suggest women who drinks 2 or more beverages a day have a higher risk of getting breast cancer as breasts are more susceptible to the carcinogenic effects of alcohol [10]. Drug diethylstilbestrol (now banned) was used to prevent miscarriages decades ago. Women who were given this drug face a slightly increased risk of breast cancer, as do their daughters [11].

3. Breast Cancer Symptoms

Breast cancer symptoms may vary from person to person. Often, there are no warning signs of breast cancer. Even if there is a lump it could be so small to be detected. Therefore, routine mammography is always recommended to check the possible early symptoms. Some of the symptoms of breast cancer include: new lump in the breast, armpit or collarbone with or without pain which could be a sign that breast cancer has spread. ; Retraction, Scar, Secretion or discharge from nipple which may be clear or bloody, Mole [12]. Other symptoms may include change in breast size or shape, dimpling, peeling or redness; red, thick or scaly nipple (Paget's disease) [13].

4. Breast Cancer Screening and Diagnostics

A screening mammogram (a type of breast X-Ray) can be used to identify cancer even before the onset of symptoms. Breast MRI can also be used for the women at higher risk. Apart from this, breast self-examination (BSE) can also be used as a screening process [14]. Diagnostic methods of breast cancer involve, a diagnostic mammogram, which includes more X-Rays than a screening mammogram. A breast MRI and ultrasound can be used to gather further information. One sure way to confirm cancer is to do biopsy. PET/ computed tomography can also be used for clear results [15].

5. Types of Breast Cancer

Non-invasive breast cancer, is confined to a particular place and do not invade. The most common form is ductal carcinoma in situ (DCIS) which accounts for 90% of non invasive breast cancers and starts in the cells lining the milk ducts of breasts [16]. The less common form is lobular carcinoma in situ (LCIS) also called as lobular neoplasia, starts in the milk-producing lobules and is considered as a marker for increased breast cancer risk. Technically, it is not a breast cancer but rather a collection of abnormal cells. People with LCIS are more likely to develop breast cancer in future [17].

Invasive breast cancers as the name suggests, invade the surrounding fatty tissues and connective tissues of the breast. Invasive ductal carcinoma (IDC) accounts for 80% of invasive breast cancers and usually starts in milk ducts and spreads to other parts of body as well. Invasive Lobular Carcinoma (ILC), a type of invasive metastatic cancer, accounts for about 10% of invasive breast cancers which starts in the milk producing glands (Lobules) and metastasize to other part of the body. It is more difficult to detect ILC than IDC by mammography and thus, is detected in later stages [18]. Metaplastic breast cancer is a rare, invasive breast cancer that begins in a milk duct and forms large tumors. It is difficult to diagnose because of mixture of cells that looks different than typical cancer cells of breast.

Inflammatory breast cancer (IBC) is aggressive type of breast cancer and is rare. It poses more threat to colored women than others [19]. Most of the times it might not show up on a mammogram. IBC usually strikes five years earlier than other type of breast cancers. Its symptoms include swelling up of breast, burning sensation in breast area, redness, heaviness, tenderness and hard skin [20].

Paget disease of the breast is rare and effects nipple as well as areola surrounding it. Nipple/areola usually becomes hard, red and scaly. Bloody or yellow discharge can also be seen. Two or more tumors are found in same breast under Paget disease [21].

Angiosarcoma of the breast is rare and grows very quickly in the inner lining of blood

vessels. It is generally related to the prior radiation treatment of breast [22].

6. Stages of Breast Cancer

Breast cancer or any type of cancer of any body part is assigned a stage after diagnostic process based on biopsy and other findings from blood samples and imaging scans. Allotment of stage is important to design a treatment map for patient. Breast cancer stages reflect the size of tumor, whether it is invasive or *in situ* and has reached the lymph nodes or metastatic and has spread to other parts of the body. The stage of breast cancer is based on the factors – size of the tumor within the breast, number of affected lymph nodes, signs which indicate the metastasis of cancer cells. If cancer cells have invaded other body parts or metastasized, evidence may be found in liver, lungs, brain or bones [23]. TNM system is the most common staging system used in the breast cancer. There are 5 stages of breast cancer- stage 0 followed by stages 1 to 4 (Table 1). Roman numerals are used to write the stages like I, II, III and IV. A higher level cancer indicates a more advanced stage in which cancer cells have spread to other regions also [24].

A brief description of breast cancer stages is given in the following Table 1.

Table 1: (source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3255438/>)

Stage	Description
In situ carcinoma	
0	The tumor is confined, usually to a milk duct or milk-producing gland, and has not invaded surrounding breast tissue.
Localized and regional invasive cancer	
I	The tumor is less than 3/4 inch (2 centimeters) in diameter and has not spread beyond the breast .
IIA	The tumor is larger than 3/4 inch but smaller than 2 inches in diameter, and it has spread to one to three lymph nodes in the armpit, microscopic amounts have spread to lymph nodes near the breastbone on the same side as the tumor, or both or The tumor is larger than 2 inches in diameter but has not spread beyond the breast.
IIIA	The tumor is larger than 3/4 inch but smaller than 2 inches in diameter, and it has spread to one to three lymph nodes in the armpit, microscopic amounts have spread to lymph nodes near the breastbone on the same side as the tumor, or both or The tumor is larger than 2 inches in diameter but has not spread beyond the breast.
IV	The tumor can be any size plus at least one of the following: It has spread to 10 or more lymph nodes in the armpit. It has spread to lymph nodes under or above the collar bone. It has spread to lymph nodes in the armpit and has enlarged at least one lymph node near the breastbone on the same side as the tumor. It has spread to four or more lymph nodes in the armpit, and microscopic amounts have spread to lymph nodes near the breastbone on the same side as the tumor.
Metastatic cancer	
IV	The tumor regardless of size has spread to distant organs or tissues. such as the lungs or bones. or to lymph nodes distant from the breast .

7. Breast Cancer Treatment

Depending upon the stage and type of breast cancer/tumor lumpectomy (removal of lump only) or mastectomy (removal of entire breast) is done. Lumpectomy is performed under breast-conserving surgery (BCS). In this only the tumor and the surrounding area is removed. On the other hand under Quadrantectomy, one fourth of the breast is removed. BCS with radiation therapy is useful for low grade breast cancer and is most preferred as it gives the same level of survival chances as mastectomy [25]. Before any radiation therapy or surgery, chemotherapy (treatment that uses drugs) is performed to shrink the size of tumor. This type of treatment is called as neo-adjuvant therapy [26]. Some cancer cells are hormone receptor positive (2 out of 3) and have receptor proteins that attach to the hormones estrogen (ER Positive) or progesterone (PR Positive). For such cancer cells, levels of estrogen/progesterone help in growth and metastasis. Hormone therapy is given to such patients in whom drugs are given so that estrogen/progesterone receptors should be blocked. Some of the drugs used are- Tamoxifen, Toremifene and Fulvestrant [27]. Targeted therapy is also used now days to treat cancer cells without harming normal cells. In this, drugs or other substances are given to patients to identify and target/attack specific cancer cells without harming normal cells. Some of the targeted therapies used in breast cancer treatment are- monoclonal antibodies, tyrosine kinase inhibitors, cycline-dependent kinase inhibitors, mammalian target of rapamycin (m-TOR) inhibitors and PARP inhibitors [28]. Treatment of breast cancer also causes side effects like, inflammation of the lung, arm lymphedema, heart failure, blood clots, second cancer like and leukemia [28].

8. Future Aspects

8.1. Apoptosis Chip

The use of micro-technologies for cell biology applications receives great attention specifically for cancer. Lab-on a chip technology is a promising approach to see/check the response of therapy. Now a promising ‘Apoptosis Chip’ which is made up of the polymer poly (dimethylsiloxane) (PDMS) has many advantages over existing conventional essays for checking the drug sensitivity and measure cell death [29].

8.2. Cancer Stem Cells Research

Cells in the tumor growth with the potential to initiate tumor are cancer stem cells. Normal stem cells are capable of self-renewal, divide and differentiate and have strict control on stem cell number. As compared to the normal stem cells, cancer stem cells have no control over their division and number [30]. Research on cancer stem cells revealed the link of deficiency of Vitamin D and increased breast cancer risk. Also, there is a need of exploring this side of cancer cells and develop suitable targets for cancer stem cells so as to stop these cells

from division and hence, the prognosis of cancer [30].

9. References

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