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Review Article about Stages of Breast Cancer

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Annotation: Breast cancer stages are classified using Roman numerals ranging from 0 to IV, with stage 0 indicating cancer that is noninvasive or confined to the milk ducts. Higher numbers indicate more extensive cancer. By stage IV breast cancer, also called metastatic breast cancer, the cancer has spread to other parts of the body. The cancer staging system continues to evolve and become more complex as doctors improve cancer diagnosis and treatment.

Introduction:

The body consists of hundreds of millions of normal living cells that grow, divide and die regularly. During the first years of a person's life, normal cells divide very quickly to allow the person to grow. However, during puberty, most cells divide only to replace tired and old cells or to repair damage. Cancer forms in the body when some cells in one part of the body get out of control and begin to grow randomly. Cancer cells grow differently from normal cells. Instead of dying, they continue to grow and produce new abnormal cells. They can also invade other tissues, which is something that normal cells cannot do. Cancer cells transform normal cells in these tissues into cancer cells by programming them to grow and divide randomly and out of control. Cancer cells are often transferred to other areas of the body and begin to grow and form new tumors that replace normal tissue. This process is called metastasis. Metastasis occurs when cancer cells reach the bloodstream or lymphatic vessels. Cancer is named according to the organ in which it first began, not the organ to which it spread. For example, cancer that affects the breast and spreads from it to the liver is called breast cancer, not liver cancer. Cancer that began in the prostate and then spread to the bones is called prostate cancer, not bone cancer. Breast tissue is unique because of the complex hormonal effects and dramatic changes during various life events. Its hormone levels and metabolism are affected by environmental factors, and some chemicals and minerals used have the ability to inhibit endocrine functions and thus reduce the effects of some hormones, especially estrogen. 1-2 A

historical overview of the discovery of breast cancer: The first to know cancer was Hippocrates, who described it as a mass that grows and expands in the body. Over time, we have come to know that this tumor is either a benign tumor that does not cause harm, Benig tumor, or a malignant tumor that grows locally in its place and can spread to the rest of the body and will be (secondary tumors Malignant tumor). (Amin et al, 2017) 2_2 The breast anatomically: The breast varies in shape and size depending on age, genetics, menstruation, pregnancy, and the period after the menstrual cycle, as well as hormonal changes or taking birth control pills, as the female breast begins to swell during puberty, affected by the hormone's estrogen and progesterone. This swelling is accompanied by increased sensitivity with pain in the breast, and these symptoms quickly disappear. The breast consists of a group of glands, fatty tissues, and several parts under the skin, as it is derived from it, as well as from tissues located under the skin.

It consists of:

ϖ Glands that secrete milk and fat

ϖ Small tissues and muscles that connect the glands to each other

ϖ Ducts of the milk glands

ϖ Blood vessels, lymphatic vessels connected to the lymph nodes

ϖ Skin and nipple (Russell et al, 2000) The glands are more numerous during puberty and until menopause when the amount of fat increases and the density of the glands decreases. Some lymph nodes are located around the breast, some may be inside the breast, and some are inside the rib cage (Internal Mammary Chain Lymph Nodes), above the collarbone, but most of them are located under the armpit

(Supraclavicular Lymph Nodes) (Axillary Lymph Nodes). All of these glands receive lymph fluids and internal breast secretions and serve as the first line of defense against infections and tumors. The breast consists of 10-15 ducts that open into the nipple, and each duct drains into a separate system consisting of small ducts and lobes. (Assiri and Abdel, Wahab, 2003)

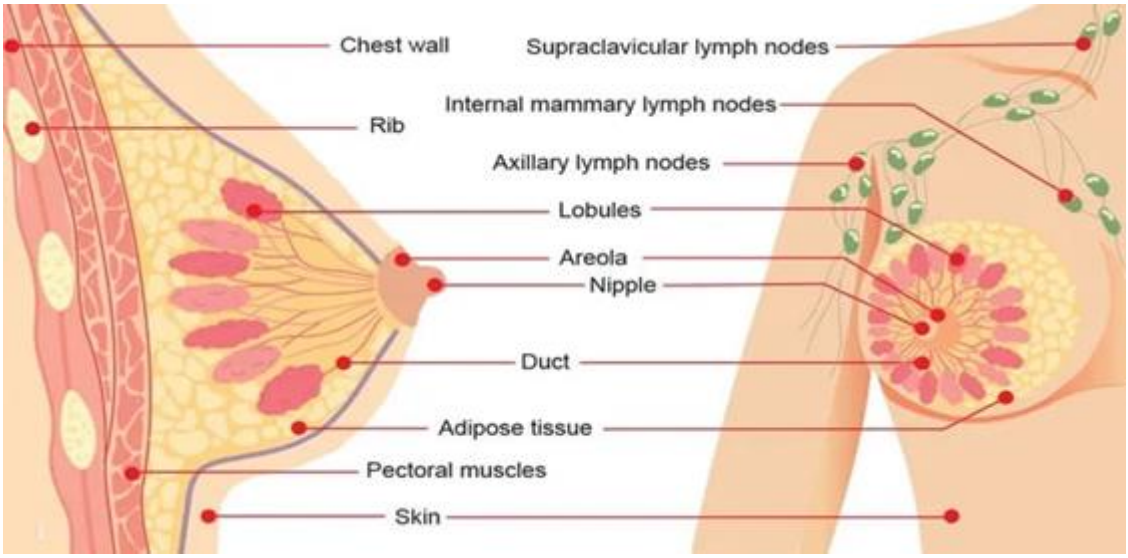

Figure (1) shows the anatomy of the breast (Assiri et al, 2003).

The breast Histologically:

The breast is formed during growth from the peripheral dermis that ends with semi-vesicular ends (Alveo vesicles (which are within a specialized thin connective tissue to form the breast lobules). The breast is under the control of several different hormones and the role of estrogen is central. Estrogen is responsible for developing the ductal system, while progesterone is necessary for lobular development (Etiology) (Jemal and Bray, 2011). 4_2 Breast cancer: It is an uncontrolled growth of

breast cells resulting from a defect in the DNA of the living cell that leads either to signals that encourage cell growth or to stop growth signals. The codes for this defect are translated through proteins that are present on the surface of the cell and are subject to proper monitoring by the body and the immune system. The transformed cell grows and multiplies irregularly and randomly and forms a tumor mass that invades its surroundings and can move into the blood and loses the mechanism of programmed death in multiple places in the body and may settle in some of them. We call it spreading. This mass works when its growth progresses by pressing on The surrounding tissues and their destruction, and the tumor can be benign and not dangerous to health, or malignant and has the potential to be dangerous to health. (Guyton and Hall, 2006) Benign tumors are not considered cancerous, as their cells appear close to the appearance of normal cells, and these cells do not invade nearby tissues or spread to other parts of the body. However, a benign tumor can turn into a malignant tumor in the event of a continuous and irreversible qualitative change in one or more of the characteristics of the tumor. As for malignant tumors, they are cancerous tumors, and if left untreated, they spread beyond the original tumor to other parts of the body and away from the affected organ (Kilian l 2003).

Figure (2): Breast cancer (Kilian, 2003)

Causes of breast cancer:

1. Family medical history: If first-degree relatives have breast cancer, the woman's risk of developing it increases by 1.5-2 times, and this risk increases if the infection is in both breasts.
2. Age: It is rare to develop breast cancer before the age of 25, but the risk of developing it increases in the age group of 44-50 years.
3. Age at puberty and menopause: Studies have shown that there is a decrease of approximately 20% in the risk of infection resulting from each year that puberty is delayed. (Henderson and others) indicated that women who experienced early puberty at the age of 12 years or younger with regular menstrual cycles had a four-fold increased risk of breast cancer compared to women who experienced puberty at the age of 13 years or older with irregular menstrual cycles. (Dixon and others) indicated that menopause after the age of 55 doubles the risk of infection compared to women who experienced menopause before the age of 45 years (Basma Sharif Haider Aziz Haider 2002).

4. Age at first pregnancy: Women who did not give birth before the age of 30 or gave birth to their first child after the age of 31 are more susceptible to breast cancer.
5. Breastfeeding: Breastfeeding, even for a short period of three months, helps protect against this disease even after menopause. It has become known that the role of breastfeeding in preventing breast swelling is greater when a woman breastfeeds her children for longer periods while she is young. Recent research has also confirmed that breastfeeding reduces the incidence of breast tumors at any age (Sarah Rosenthal, 2001).
6. Previous history of benign breast tumors
7. Dietary habits
8. Radiation
9. Birth control pills
10. Hormone replacement therapy after menopause
11. Certain breast changes
12. Race
13. Reproductive and menstrual health history

Breast cancer stages:

There are two main systems used to diagnose the stage of cancer:

The first uses information on the size of the tumor and is used in clinical diagnosis Cancer Staging Manual, and is called the American Joint Cancer Committee (AJCC)

The second, which is more common, is called the (Young JL et al, 2001) (SEER) system. Breast cancer goes through several stages until it reaches the advanced and dangerous stage, as shown in the table below:

Table (2-1) shows the stages of breast cancer development.

Definition	stage
Definition: Cancer cells remain within the breast ducts without invading normal breast tissue.	stage 0
The cancer is (2 cm) or less and is confined to the breast (without affecting the lymph nodes)	stage 1
There is no tumor in the breast, but cancer cells are found in the axillary lymph nodes (lymph nodes under the arm). Or the tumor is approximately 2 cm or less and has spread to the axillary lymph nodes. Or the tumor is larger than 2 cm but is not larger than 5 cm and has not spread to the axillary lymph nodes.	IIA
The tumor is larger than 2 cm but not larger than 5 cm and has spread to the axillary lymph nodes, or the tumor is larger than 5 cm and has not spread to the axillary lymph nodes.	IIB
There is no tumor in the breast, the cancer is in the axillary lymph nodes or the cancer can be in the lymph nodes near the sternum and the tumor is of any size, the cancer has spread to the axillary lymph nodes that are attached to each other) or to other structures, or the cancer is in the lymph nodes near the sternum.	IIIA
The tumor is of any size and spreads to the chest wall or breast skin or may spread to the lymph nodes that are clustered together or embedded in other structures. The cancer spreads to the lymph nodes near the breastbone.	IIIB
There may be no sign of breast cancer, or the tumor may be any size and may have spread to the breast wall or skin. Or the cancer may have spread to the lymph	IIIC

nodes either above or below the collarbone, or the cancer may have spread to the axillary lymph nodes or to the lymph nodes near the breastbone.	
Cancer spreads to other parts of the body.	IV

Types of breast tumors:

Breast tumors are divided into 3 main types:

First. Microbial infections of the mammary glands: These infections are among benign breast tumors and are accompanied by pain, redness, swelling, and sometimes heat. The number of white blood cells may increase. Microbial infection is treated with antibiotics such as penicillin or cephalosporin. However, if the infection develops into a cyst, the cyst must be removed using a syringe or a small incision made by a surgical specialist. (Hartmann, et al, 2005)

Second. Benign breast tumors

Benign breast tumors are divided according to the composition into:

1. Breast calcification

2. Fleshy or fibrous

3. Fluid cyst

4. Fluid cyst after pregnancy and breastfeeding

5. Fibrous cysts in the breast

6. Fleshy with fluid or blood secretions from the nipple

7. Swelling and redness in the nipple. (Collins, et al., 2007) Third. Malignant breast tumors: Malignant tumors usually grow locally and increase in size and are able to increase without the body controlling them. They are also able to bring food from the body and create their own blood vessels. They can move from their location into the blood and lymph fluid and spread to other parts of the body and become concentrated in them and cause additional symptoms. Malignant breast tumors are divided into several types:

1. Incipient cancer

2. Cancer of the glands and their ducts

3. Inflammatory breast cancer

4. Breast lymphoma (lymphoma in the breast) (Marcia, 2004)

8_2 Diagnosis: Diagnosis usually depends on many factors including stage, recurrence, age and health of the patient. The stage of breast cancer is the most important factor. The degree of breast cancer is evaluated by comparing cancer cells with normal breast cells. Diagnosis of breast cancer begins based on self-examination, clinical diagnosis with radiation, biopsy and taking a tissue sample (Salow, Hannan,2004)

Clinical diagnosis of breast cancer: The first symptom is usually a lump that is different from the rest of the breast tissue. Other symptoms include thickening of the breast tissue, changes in the shape and size of the breast or the shape of the nipples, skin wrinkling, nipple discharge, persistent pain in part of the breast or armpit, or swelling under the armpit. (Tazzite, Jouhadi, Saiss2013)

1. Radiography: It is an X-ray of the breast to detect breast cancer. Mammography plays a major role in detecting breast cancer early and helps reduce breast cancer deaths. It is worth noting that mammography can detect breast cancer 3 years before symptoms appear, and even before the tumor appears on the body (chouchane, Boussen, Sastry 2013)

2. Ultrasound imaging: Researchers in Zurich have developed a new ultrasound technique that helps distinguish between malignant and benign tumors in relation to breast cancer. Danilova,2006))

Figure (3) Ultrasound imaging (Danilova, 2006))

3. MRI: Breast MRI is used to diagnose breast cancer in cases where a definitive diagnosis cannot be made by mammography or breast ultrasound. Both breasts can be imaged at the same time using special breast coils. (2013, by Michael Dixon Family doctor books)

4. Biopsy: The best way to diagnose breast cancer is an invasive examination in which a sample of breast tissue is taken for close examination. A biopsy is often resorted to when previous examinations show the possibility of a problem in the breast, such as: discovering a solid mass during manual examination, or mammography without being able to reach an accurate diagnosis using non-invasive examination methods (2013, Michael Dixon)

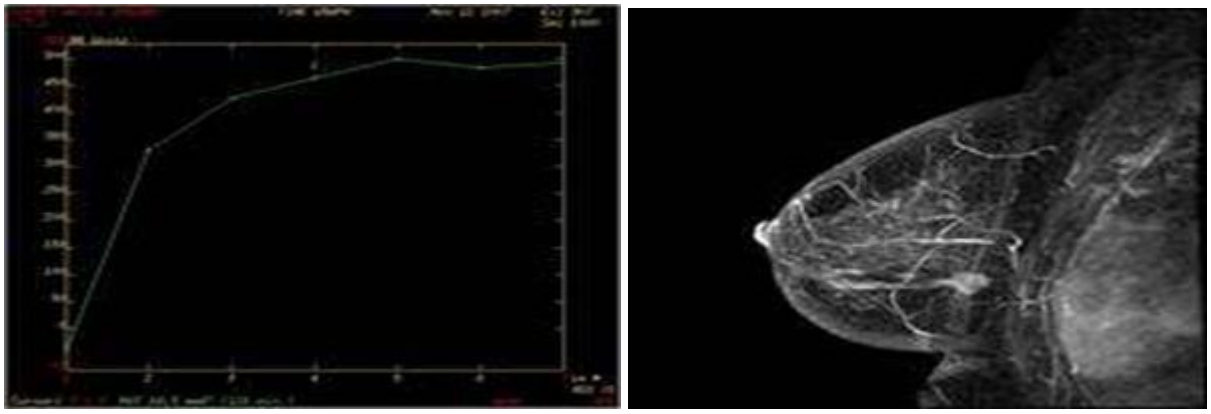

Figure (4) MRI (Salow and Hannan, 2004)

Breast cancer treatment:

Breast cancer treatment depends on many factors including the stage of cancer and the patient's age. Breast cancer is usually treated with surgery and may be followed by chemotherapy, radiation therapy, or both. Hormone-receptor cancers are often treated with hormone therapy.

1. Radiation therapy: Radiation therapy for breast cancer uses high-energy X-rays, protons, or other particles to kill cancer cells. Rapidly growing cells, such as cancer cells, are more susceptible to the effects of radiation therapy than normal cells (Kay and Glorioso, 2001)

2. Chemotherapy: Chemotherapy for breast cancer uses drugs that target and destroy breast cancer cells. These drugs are usually injected into a vein with a needle or taken orally as tablets. Chemotherapy for breast cancer is often used in addition to other treatments such as surgery,

radiation therapy, or hormone therapy. Chemotherapy can be used to increase the chances of recovery, reduce the risk of cancer recurrence, relieve symptoms caused by cancer, or help people with cancer live longer and with a better quality of life (Zhao and Ramaswamy 2014).

3. Targeted therapy: Targeted breast cancer therapy uses drugs that may inhibit the growth of breast cancer cells in specific ways. For example, in patients with HER2-expressing cancer, a monoclonal antibody known as Trastuzumab is used to block the activity of the protein in breast cancer cells. In advanced cases, Trastuzumab can be used in combination with chemotherapy to delay cancer and improve patient survival (Chen et al, 2001).

4. Gene therapy: It is a new therapeutic approach for cancer and can be defined as the delivery of genes to cancer cells in the body that have a direct or indirect therapeutic effect in the person. The delivery of therapeutic genes involves the use of vectors that can specifically target cancer tissues or cells. To achieve the optimal therapeutic effect, the vector must meet certain conditions such as high efficiency of transfer and the vector must specifically target cancer cells, including metastatic cells. For optimal gene expression, it must be. Gene vectors can be classified as viral vectors and non-viral vectors. There are a number of vectors used, including viral vectors. Higher transmission efficiency compared to non-viral vectors (Thomson and Heyworth, 2014)

Prevention:

Advances in breast cancer prevention research have led to new and innovative opportunities to modify breast cancer risk, potentially reducing incidence and mortality, according to a study by researchers from the Mayo Clinic Cancer Center published in the Clinical Oncology Practice Journal. It is wise for a health care provider to be aware of the benefits of assessing individual breast cancer risk, and to provide counseling and implement strategies to reduce the risk of the disease. She adds that for many years, breast cancer prevention research has focused primarily on the use of antiestrogen medications to reduce the incidence of hormone-sensitive and higher-risk breast cancers, but it is important to re-examine and implement other risk-reduction strategies for prevention (Middle East Journal 2021

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