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THE CANCER: TYPES, THE MECHANISM OF CANER GROWTH AND DIAGNOSIS: A REVIEW

Sarab Dalaf Khalaf*, Marwa M. Mahdi and Rafal Shakir Mahmood

Iraq.

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***Corresponding Author: Sarab Dalaf Khalaf**
Iraq.

ABSTRACT

Cancer is a medical term that includes a wide group of diseases that share one characteristic, which is the abnormal growth of cells that divide without control and out of control, where a change occurs in a cell that causes it to deviate from the system that controls the functioning of a healthy cell. Because these cells are abnormal and have hostile and destructive properties and have a tremendous ability to invade and control the body's tissues, cancer has become a serious and chronic disease that may affect all organs of the body. It is either a benign tumor covered with fibrous tissue and is non-spreadable and can be removed with surgery or treated with drugs. Or radiation, or it is a malignant tumor that has a tremendous ability to spread through the blood or lymphatic system. Cancer is a major medical problem and one of the leading causes of death around the world. Its classification varies according to the tissue from which it arises and the organs in which the disease develops. The type of tumor is determined by microscopic examinations performed on the tumor cells, and this is sometimes supported by blood. It is usually difficult to determine the causes of the disease, but we know the general causes of cancer. There are many risk factors that can cause this disease, such as obesity, lack of physical activity, smoking, environmental pollution, and others. Although this disease is considered fatal, recovery from it is constantly improving in most types thanks to advances in early detection methods and treatment options. Optimal treatment also includes the involvement of doctors and practitioners from other specialties such as pathology, radiology, targeted radiation to tumors, pain control, and supportive care. In addition to internal medicine, surgery, and oncology, prevention is the cornerstone of this disease. A radical change in lifestyle will preserve health.

KEYWORDS: Cancer, Tumor suppressor, carcinogens, Radiation Therapy, Apoptosis.

INTRODUCTION

Cancer is a disorder that results from genetic or epigenetic alterations in the somatic cells and has abnormal cell growth which may be spread to other body parts. They form a subset of neoplasm. The unregulated growth of cells in a group called neoplasm or tumor and they form a lump or mass and may be distributed diffusely.[1] Cancer is not a single disease, but a group of diseases caused by abnormal growth of cells that have the ability to spread and survive. An adult

human is made up of cells, and this number remains relatively constant. This is achieved through a tight balance between cell proliferation (replication) and cell death. The body can increase in size due to an increase in the size of cells, such as fat cells in obesity or muscle cells due to exercise (hypertrophy), but increases in the number of cells (hyperplasia) are rarely sustained if The process of cell birth exceeds the process of cell death, and this will result in new growth, or what is known in Greek as neoplasia, meaning tumor.[2] It is derived from the Latin this time Tumors and tumors (if they are "benign" or "new growth cells") are swellings. Tumors (if they are "benign" or "new growth cells") are tumor cells. The excessive proliferation of cells can be localized, or malignant if they invade surrounding structures. Malignant tumors are named because of their protrusions Diffuse, lobster-like cancers spread to nearby and distant organs through a process known as metastasis.[3]

Cancer includes a group of diseases that appear in the form of uncontrolled proliferation and division of cells and have the ability to spread, penetrate and destroy neighboring tissues. Cells are small structures from which the body's organs and tissues are composed. These cells work differently depending on their function, but they are renewed through division in a similar way. In order to replace dead cells, and in a normal situation, the division of normal cells is regular, as this process is subject to an internal system that controls, regulates and controls the division process, or it may eliminate cells that get out of control if it is impossible to correct the defect, in order to prevent them from multiplying and continuing, and in return This system fails in the case of cancer cells, which cause them to get out of control and continue to divide and multiply without stopping.[4]

Advanced scientific research so far indicates the relationship between cancer formation and hereditary genetic material, and this process is attributed to two groups of genes:

- Cancer suppressor genes, which are genes that protect us from cancer and return dividing cells to their normal path.
- Cancer genes, which are usually found in a "dormant" state. When these genes "wake up" in the cell as a result of several factors, including, for example: smoking, uncontrolled exposure to sunlight, radiation, carcinogenic substances, or the like, they turn a normal cell into a cancerous cell.[5,6] Cancer is a hereditary disease, but it is usually not inherited from parents. Normal cells develop into cancer cells by acquiring successive mutations in cancer-related genes. There are two main classes of cancer genes, pro-oncogenes and tumor suppressor genes. Oncogenes encode protein products that promote cell proliferation. These products are often growth factors and their receptors that act within signaling pathways to promote cell proliferation. A mutation in one of the precursor genes converts it to "oncogenes," a term first coined by George Todaro and Robert Hubner in 1969.[7]

Unregulated cell proliferation by itself does not lead to tumor formation; Because tumor suppressor genes counteract it by stimulating cell aging or death. This makes cancer a relatively rare possibility unless mutations appear in the same genes that make up the tumor suppressor system. So cancer arises when a mutation occurs that escapes normal controls and allows unregulated cells to survive and multiply. For more than a century, viral and bacterial infections have been established as risk factors for cancer. At least 15 percent of cancers are due to infectious agents, examples of which include the association of human papillomavirus with cervical cancer, gastroenteritis with stomach cancer, and the association of hepatitis B or C virus with liver cancer. Viral genes are sometimes inserted into the human genome where they are continuously expressed.[8]

Cancer can affect any organ or tissue that contains dividing cells and develops due to uncontrolled cell proliferation. A normal cell is subject to a set of complex molecular controls that limit inappropriate cell proliferation either by

undergoing cell cycle arrest or by inducing apoptosis. In cancer cells, these controls are disrupted, leading to unrestrained proliferation. To support this explosive growth, additional energy is needed; Cancer cells then reprogram their metabolic pathways to obtain this energy.[4] Because cancer cells are not normal cells, the body's immune system must recognize them as such and destroy them. However, cancer cells avoid destruction by adopting different strategies, and may even control the immune system to their own advantage. Cancer cells are also distinguished by their ability to grow new blood vessels, a process called neoangiogenesis. The stimulating factor for the formation of new blood vessels is oxygen deprivation or hypoxia, which arises in areas of metastasized tumor.[9]

Types of cancer

Caner can result from abnormal proliferation of any of the different kinds of cells in the body, so there are more than a hundred distinct types of cancer, which can vary substantially in their behavior and response to treatment. The most important issue in cancer pathology is the distinction between benign and malignant tumors.[4] Cancers are divided into various types that are:

a. Carcinomas: It starts in the tissue or the skin, which covers the glands and internal organ surface. It forms a solid tumor. Breast cancer, prostate cancer, colorectal cancer, lung cancer.
b. Sarcomas: It starts in the tissues which connect and support the body. It can be formed in nerves, tendons, joints, fat, blood vessels, bone, lymph vessels, muscles, or cartilage.
c. Leukemia's: Leukemia is a cancer of the blood. It begins when healthy blood cells grow uncontrollably and change. It is divided into 4 types, that are acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, and chronic lymphocytic leukemia.
d. Lymphomas: Lymphoma is cancer that begins in the lymphatic system and it is a network of glands and vessels that helps to fight with infection. Hodgkin lymphoma and Non Hodgkin lymphoma.
e. Central Nervous System Cancers: Cancer that starts in brain tissues and spinal cord called "brain and spinal cord tumors", and others primary CNS lymphomas, vestibular schwannomas, gliomas, pituitary adenomas, primitive neuro-ectodermal tumors, meningiomas, and vestibular schwannomas.
f. Multiple Myeloma: Multiple myelomas is cancer that begins in plasma cells, another type of immune cell. The myeloma cells which are plasma cells, are build up in bone marrow and make tumors in bones. It is called plasma cell myeloma and Kahler disease.
g. Melanoma: It starts in cells that become melanocytes. These cells are specialized cells that make melanin, i.e., the pigment that gives the color to the skin. Mainly melanomas develop on the skin, but it can also develop in other pigmented tissue like an eye.
h. Other Types of Tumors: **Germ Cell Tumors**: It is the type of tumor that starts in the cells which give rise to eggs or sperms. This can be occurring anywhere in the body and either malignant or benign.

Neuroendocrine Tumors: Neuroendocrine tumors form from cells that release hormones into the blood in response to a signal from the nervous system. It forms from those cells which release hormones in blood in response to signal from the nervous system. These tumors, which can create higher-than-normal amounts of hormones, will cause many various symptoms. It may be either benign or malignant.[4,10]

Cell cycle and cancer

Loss of control of the cell cycle is usually a critical step in cancer development. Cells become abnormal and processes regulating normal cell division are disrupted. Cancer cells are caught in an unregulated cell cycle. Most cancers aren't a result of a single event or factor. A number of factors are required for a normal cell to evolve into a cancerous cell and these factors include both environment and heredity. There are four main types of genetic change seen in cancer:

1- Spontaneous mutagenesis;
2- Environmentally-induced mutagenesis (causative agents include chemicals, radiations and viruses);
3- Environmentally-induced mutagenesis, but with genetic predisposition; and 4- change due to hereditary factors.[11,12]

The cell cycle and cancer

Genes involved in cell cycle control are important among those subject to the genetic alterations that give rise to cancer.[13] However, the proliferation of cancer cells requires that the cells retain functional cell cycle processes. The cell cycle alterations seen in cancer are mainly confined to two major sets of regulators: those involved in the negative control of cell cycle progression (inactivation of which leads to accelerated and unchecked cell proliferation) and those involved in coupling the maintenance of genome integrity to the cell cycle (inactivation of which results in cells having gene alterations that progressively accumulate during carcinogenesis). Most of the genes corresponding to these two categories fall within the group of tumour suppressors, and many of them are also direct participants in DNA repair processes.[14]

Impact of X inactivation on cancer genetics

In addressing how alterations of X-linked genes might contribute to cancer, the genetic hallmarks of cancer should be emphasized. Like other diseases, cancer can be initiated by a single genetic event occurring either in somatic cells or in germ cells, leading to sporadic cancers or hereditary cancers, respectively. However, unlike most other diseases, cancer usually begins as a clonal growth, reflecting a selective advantage brought about by genetic alterations that occur in a single cell. Because of X-chromosome unisomy (genetic unisomy in males and functional unisomy in females), the common genetic events that cause cancer — oncogene activation and tumour-suppressor inactivation — are expected to produce different results when they affect genes that are carried on the X chromosome to those produced when they affect autosomal genes.[15]

X-chromosome inactivation represents an epigenetics paradigm and a powerful model system of facultative heterochromatin formation triggered by a non-coding RNA, Xist, during development. Once established, the inactive state of the Xi is highly stable in somatic cells, thanks to a combination of chromatin proteins, DNA methylation and nuclear organisation. However, sporadic reactivation of X-linked genes has been reported during ageing and in transformed cells and disappearance of the Barr body is frequently observed in cancer cells. In this review we summarise current knowledge on the epigenetic changes that accompany X inactivation and discuss the extent to which the inactive X chromosome may be epigenetically or genetically perturbed in breast cancer.[16]

The mechanism of caner growth

The ability of cancer cells to spread inside the body is what make cancers one of the most devastating and dreaded diseases worldwide. This spreading - known as metastasis - starts with a few cancer cells breaking free from the primary tumor site, after which they can migrate around the body via the blood stream and infiltrate distant secondary

tissue locations. However, not all cancer cells spread alike. Where, and to what extent they spread is distinct for each cancer type and is determined by multiple factors. For instance, breast cancer cells spread to multiple locations including bones, lungs, brain, and liver, while prostate cancers usually spread only to bones. Similarly, the time-scales of cancer reoccurrence at a secondary location can vary dramatically. Breast cancers are known to recur years or sometimes decades after their first detection, whereas lung cancers spread within months of their first occurrence.[17] Mechanisms of tumour development: The phenotypic changes which a cell undergoes in the process of malignant transformation is a reflection of the sequential acquisition of genetic alterations. This multi-step process is not an abrupt transition from normal to malignant growth, but may take place over 20 years or more. The mutation of critical genes, including suppressor genes, oncogenes and genes involved in DNA repair, leads to genetic instability and progressive loss of differentiation. Tumours enlarge because cancer cells lack the ability to balance cell division by cell death (apoptosis) and by forming their own vascular system (angiogenesis). The transformed cells lose their ability to interact with each other and exhibit uncontrolled growth, invade neighbouring tissues and eventually spread through the blood stream or the lymphatic system to distant organs.[18]

Gene Changes within Cells (Mutations): When a cell is dividing mainly, a mutation occurs in this step but also by the chemical changes which are coming from outside like tobacco smoke, and it is happening by chance. Mutation means the gene is copied twice, damaged or lost. The meaning of mutation is that the cells are not growing by its instructions, and grow unnecessarily. Mutation of genes may mean that a cell stops producing proteins that require cell division and may produce too many proteins by which the cell division occurs rapidly and form lump or tumor, the tumor is made up of millions of cancer cells.[19]

The role of cell death in tumour growth Apoptosis, or lack of it, may be critical to tumorigenesis. BCL2, a gene mediating resistance to apoptotic stimuli, was discovered at the chromosomal.[18] The term apoptosis refers to a type of cell death that occurs both physiologically and in response to external stimuli, including X-rays and anticancer drugs. Apoptotic cell death is characterized by distinctive morphological changes different from those occurring during necrosis, which follows ischaemic injury or toxic damage. Apoptosis is regulated by several distinct signalling pathways. Dysregulation of apoptosis may result in disordered cell growth and thereby contribute to carcinogenesis. Selective induction of apoptosis in tumour cells is among current strategies for the development of novel cancer therapies. Apoptosis and necrosis are distinguished by characteristic morphological changes.[20]

APOPTOSIS: Shrinking/ rounding up, fragmentation of cell and nucleus Condensation and fragmentation of chromatin Engulfing by neighbouring cell as ‘apoptoticbody’ NECROSIS Organelle disruption and breakdown, cell swelling Membrane blebbing, residual ‘ghost’ cell 114 Mechanisms of tumour development translocation in low grade B cell nonHodgkin lymphoma. It thus became apparent that neoplastic cell expansion could be attributable to decreased cell death rather than rapid proliferation. Defects in apoptosis allow neoplastic cells to survive beyond senescence, thereby providing protection from hypoxia and oxidative stress as the tumour mass expands. Growth of tumours, specifically in response to chemical carcinogens, has been correlated with altered rates of apoptosis in affected tissues as cell populations with altered proliferative activity emerge. Paradoxically, growth of some cancers, specifically including breast, has been positively correlated with increasing apoptosis.[21]

Diagnosis: Diagnosis of cancer is carried by doctors by taking screening tests of patients. For example, colonoscopy, mammography, and a pap test. Other tests are also performed before screening tests to check the abnormalities in the

body. For example, CT scan, MRI scan, X-rays and ultrasound. In that area which is not clearly visualized like some lymph nodes or inside bones, radionuclide test is performed for this purpose.

Person with cancer who have no symptom then they diagnosed during tests of other condition or issues, and if any person has symptoms of cancer doctor will perform various tests.[21,22]

Lab Tests: Lab test include urine, blood and other body fluids to measures the substances which are responsible for the cancer in our body, like low and high levels of the substance which can cause cancer. Tumor markers are produced by the cancer cells and other cells in response to cancer. Lab tests are not the accurate result for cancer diagnosis, so doctor needs to clarify these tests by performing other cancer tests also.

Imaging Tests: In this test, the picture of the area inside the body are created which help to see the tumor present or not. It involves tests like:

Ct Scan: This scan is used to create 3-dimension images of your organs from different angles by Xray machines which are linked to the computer. Usually, before the scanning, you may have to take a dye or other contrast material which helps to make the picture easier to identify certain areas of body. In the donut-shaped scanner machine the picture taken by moving around the body. MRI: This scan is also used to take the picture of the body organs by taking pictures in slices and create detailed image. Radio waves and powerful magnet are used to take the slices. This scan shows the exact difference between unhealthy and healthy tissues. As in CT scan, before MRI scans also you have to take a dye for further scan. It is a round chamber machine in which the body is pushed and it makes rhythmic beats and loud thumping noise. Nuclear Scan: It is also called a radionuclide scan because radioactive material is used to take the picture of body organs. As a CT and MRI scan, the person needs to receive a small amount of radioactive material in the injection form known as a tracer. It collects in the bones by flowing through blood. In this scanner measure the radioactivity and create pictures of organs or bones on film or on the screen of the computer. It includes 2 scans named as: Pet and bone scan. **Bone Scan**: It is used to checking for damage to bones or abnormal areas. Before the scan person has to take the small radioactive material in his/her vein, it travels through the blood and collects in an abnormal area in the bones. A special scanner pictured the material where it collects, and these areas are called hot spots. **Pet Scan:** In this scan, the radioactive glucose material is used for the 3-D picture of body organs because cancer cells consume more glucose than healthy cells. **Ultrasound:** In ultrasound, high energy sound waves are used for the echo of tissues because these waves, people cannot hear. The computer uses these echoes to create a picture of body organs where a device called transducer slowly moves on the skin and the picture is called a sonogram. **X-rays**: In X-ray scan, x-rays are used in low doses of radiation to create a picture of body organs and you have to stay still withholding the breath for 1-2 seconds when the beam is directing on the body part. **Biopsy:** Biopsy is the test in which the doctor removes a sample of tissue from the patient's body for diagnosing cancer. Then a pathologist does further test and looks tissue in the microscope and described all details in the pathology report. Sedative and anesthesia are given to patients before biopsy for relaxation. The biopsy sample is obtained in various ways: i. **With Needle**: Needle is used to withdraw fluid or tissue from the body. This method is used for spinal taps, bone marrow aspirations, prostate, and liver and breast biopsies. ii. **With Endoscopy**: In this method, the endoscope which is a thin and lighted tube, goes inside from natural body openings, such as anus or mouth to examine the areas inside the body. If the doctor sees any abnormal tissue during an examination, then he removes the abnormal tissue with normal tissues. For example, Colonoscopy, bronchoscopy. **iii. With Surgery:** Through surgery, the area of abnormal cells is removed. It may be excisional, in

which the surgeon removes the entire area of abnormal cells with some normal cells and incisional, in which a small part of an abnormal area is removed.[22,23]

Diagnosis: After tests and reports if anyone having cancer then the doctor will figure out the stage of cancer for the best treatment. Side Effects of Cancer Treatments: The treatment of cancer can affect also to the normal cells, tissue, and organs. Side effects are the effects of treatment which are shown with therapeutic effect. Common side effects are shown below:

Anemia, Appetite loss, Bruising and bleeding (thrombocytopenia), Constipation, Delirium, Diarrhea, Edema, Fatigue, Fertility issue in boys and men, Fertility issue in girl and women, Flu-like symptoms, Hair loss (Alopecia), Infection and Neutropenia, Lymphedema, Memory or concentration problems, Mouth and throat problems, Nausea and vomiting, Nerve problems (Peripheral Neuropathy), Organ related inflammation and immunotherapy, Pain, Sexual health issue in both men and women, Skin and nail changes, Sleep problems, Urinary and bladder problems.[24]

Types of Cancer Treatments: There are various types of cancer treatments, which depend upon the cancer type and how to advance it is. Some patients have only one cancer treatment but mainly have a combination of treatments like surgery with radiation therapy. The various types of treatments are: Surgery: To prevent or reduce the disease's spread and remove cancer from the body, surgeon may remove lymph nodes.[25]

Radiation Therapy: In this therapy high doses of radiation are used to treat cancer by shrinking tumors and to kill cancer cells.

Chemotherapy: In this therapy, chemicals are used to treat cancer by killing cancer cells and also by shrink tumors but have severe side effects.

Immunotherapy: In this therapy, the immune system is boost by medication or other treatments. Example, adoptive cell and checkpoint inhibitors treatment.

Targeted Therapy: In this therapy, changes in a cancer cell that help them divide, spread and grow by targeting and immune system also boost. Example, monoclonal antibodies and small-molecule drugs.

Hormone Therapy: In this therapy, hormones are used to treat cancer, such as prostate and breast by stop and slow growth.

Stem Cell Transplants: In this therapy, the stem cells restore in cancer patients, which are destroyed by very high doses of radiation or chemotherapy.

Precision Medicine: It is the newer approach, in which the best treatment for a patient is determined by genetic testing.

Surgery: To prevent or reduce the disease's spread and remove cancer from the body, the surgeon may remove lymph nodes. Small thin knives called scalpels are used by the surgeons and other sharp tools also used to cut through muscle, skin and sometimes bones during surgery. These cuts are painful after surgery before surgery anesthesia is given to the patient to relieve from pain . Surgeries are used for the solid tumor, which is the local treatment because it contained in one area. Surgery is not used for metastatic cancer or leukemia i.e., blood cancer. The patient needs good nutrition before and after the surgery if he/she is underweight and weak.[26,27]

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