Cancer: A Silent Killer

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Abstract: Cancer is the most prevalent life threatening disease worldwide. The burden of cancer in society is growing day by day. It is due to uncontrolled growth and spread of abnormal cells which can be cured if diagnosed in early stage of life. The disease is caused by many external factors and some internal factors. Different types of cancer are present based on the tissues and organs affected. Various screening tests and a number of treatments such as chemotherapy, gene therapy, radiation therapy, immunotherapy, surgery etc. are now available for the detection of cancer. Apart from these, the treatments with medicinal herbs also provide a feasible alternative against cancer.

Keywords: Cancer, oncogenes, carcinoma, colorectal cancer, histone deacetylases

Cancer is a major healthcare threat worldwide. Every year the incidence of cancer will continue to rise. In India about 11 lakh new cancer patients are diagnosed every year. There are more than two hundred different types of cancer that affects human beings. The symptoms shown by each type of cancer is different and their required treatment also differs. Cancer is not a single disease but a group of diseases characterized by uncontrolled growth and spread of abnormal cells. The causes of cancer are diverse and complex. External factors like tobacco use, chemicals, radiations and infectious organisms and internal factors such as inherited mutations, random mutations, hormones and immune conditions contribute to cancer. The current lifestyle including lack of physical activity, obesity, dietary factors and environmental pollutants increase the risk of cancer (Mathur et al., 2015). Cancer can be detected by the symptoms like pain, skin changes, unusual bleeding, fatigue, lump formation etc. There are mainly two types of cancers, namely benign and malignant. Malignant tumor has the ability to invade the parts of the body and has a property known as metastasis. Benign tumor is a mass of cells which cannot invade to the parts of the body and are not cancerous (Ferlay et al., 2008).

According to GLOBOCAN data, there were an estimated 18.1 million new cases of cancer and 9.6 million deaths from cancer worldwide in 2018 (Ferlay et al., 2012). The most frequently diagnosed cancers are breast, colorectal, prostate and lung cancer. In this, the highest percentages of cancer types present in men are prostate, lung, bronchus, colon, rectum and urinary bladder cancer. In women, the most commonly found cancers are breast,

lung, bronchus, colon, rectum, uterine corpus and thyroid (http://refhub.elsevier.com). In case of children, blood cancer and cancers related to the brain and lymph nodes are more common. Cancer incidence worldwide is higher in men than in women. The global burden of cancer is increasing day by day (Moscow et al., 2011).The lack of effective prevention and awareness leads to the development of cancer.

1. Diversity in cancer

More than 100 types of cancers are diagnosed till date. Cancers are named according to the tissues or organs affected. There are different types of cancer that begins in specific types of cells. Carcinoma, sarcoma, leukemia, lymphoma, multiple myeloma, melanoma, carcinomas and brain and spinal cord tumors are some among them.

Carcinoma: Carcinoma is the most common type of cancer formed by epithelial cells. Adenocarcinoma forms in the glandular tissue, which lines certain internal organs and makes and releases substances in the body such as mucus, digestive juices and other fluids. Cancers in breast, prostate and colon are adenocarcinomas. Cancer that begins in the lowest layer of epidermis is called basal cell carcinoma. Squamous cell carcinoma forms in squamous cells, which lines the organs such as stomach, intestine, lungs, bladder and kidneys. Some cancers of the bladder, ureters and kidneys are transitional cell carcinomas which form in transitional epithelium. Different types of cancer includes bladder cancer, breast cancer, cervical cancer, colorectal cancer, gynecologic cancer, head and neck cancer, kidney cancer, liver cancer, lung cancer, ovarian cancer, prostate cancer, skin cancer, thyroid cancer, uterine cancer, vaginal and vulvar cancers, lymphoma, mesothelioma and myeloma. ***Sarcoma:*** It is a type of cancer which forms in bones and soft tissues like cartilage, muscle, fat, fibrous tissue, blood vessels and lymph vessels. More than 70 types of sarcoma are found. The most common types of sarcoma are angiosarcoma, Kaposi's sarcoma, dermafibrosarcoma protuberans, epitheloid sarcoma etc.. ***Leukemia:*** It is the cancer of blood forming tissues including bone marrow. In leukemia patients, the bone marrow produces abnormal functionless white blood cells. There are four common type of leukemia like acute lymphocytic leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia and chronic myelogenous leukemia. ***Lymphoma:*** The cancer forms in lymphatic system and begins in T or B cells. The main subtypes of lymphoma include Hodgkin lymphoma and Non-Hodgkin lymphoma. ***Melanoma:*** It begins in cells that become melanocytes which produces melanin. This is most dangerous type of skin cancer. ***Multiple myeloma:*** In this condition, the plasma cells in bone marrow become cancerous and spreading to other parts. These abnormal plasma cells are called myeloma cells that can damage the kidneys, bones, immune system and red blood cell count. ***Brain and spinal cord tumors:*** Main reason of the cancer is the DNA changes inside the cell. Growth of abnormal cells in brain causes brain tumor and also cancer in the body can spread to the brain. A spinal cord tumor develops within spinal cord, also called intradural tumor. Intramedullary tumors and extramedullary tumors are the main types of intradural tumors (https://www.cdc.gov; https://www.cancer.org).

The most common cancers reported in 2020 are breast (2.26 million cases), lung (2.21 million cases), colon and rectum (1.93 million cases), prostate (1.41 million cases), skin (1.20 million cases) and stomach cancer (1.09 million cases) (https://www.who.int/news-room/fact-sheets/detail/cancer).

1.1. Breast cancer

The second most common cancer found in females is breast cancer. It is also found in men too. It accounts for about 22% of all female cancers and 15% of cancer related death among females (Edward et al., 2003; Stewart, 2004). The most breast lumps are benign not malignant. The spreading of breast cancer occurs when the cancer cells get in to the blood or lymph system. These cancer cells

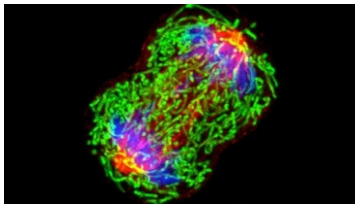

Fig.1. A dividing breast cancer cell (Credit: National Cancer Institute / Univ. of Pittsburgh Cancer Institute)

are carried to other parts of the body (https://www.cancer.org). Statistically each year breast cancer is about 30% of all new female cancer. It mainly affects middle aged and older women. The incidence of breast cancer is increasing rapidly in developing countries. Breast cancer is caused by changes in many different genes. Intraductal epithelial cells account for the majority of breast cancer (Russo et al., 2001). Weight gain and obesity increase are the risk of breast cancer. High penetrance of breast cancer is caused by the mutations in genes like BRCA1, BRCA2, p53, PTEN and ATM.

1.2. Lung cancer

Lung cancer is a common cause of cancer deaths worldwide. It is the most often diagnosed cancer with an incident rate of 22.5 per 100,000 persons-years worldwide in 2018. The chance of lung cancer is higher in males than females. Tobacco smoking, earlier lung diseases, exposure to carcinogens and air pollutants, and any family history of malignancy are the typical risk factors of lung cancer. Generally the survival of lung cancer patient is low.

1.3. Liver cancer

In liver cancer, the malignant cells form in the tissues of the liver. The main types of adult primary liver cancer include hepatocellular carcinoma and bile duct cancer. In this, hepatocellular carcinoma is high risky pathological types of liver cancer. Both adults and children are prone to primary liver cancer. Abdominal pain, weight loss, ascites and hypertension are common symptoms of liver cancer. It is most commonly found in males with liver disease caused by alcohol consumption, hepatitis or hemochromatosis. The best treatment choice for liver cancer is chemotherapy because of its capability to completely kill the cancerous cells.

1.4. Leukemia

The cancer focuses in blood forming cells. It may be acute or chronic. The risk factors of leukemia include genetic history, environmental factors and exposure to radiations. Fever, fatigue, weight loss, body pain and bleeding are some of the symptoms of leukemia (Amanda et al., 2014). Generally

the prevalence of leukemia is higher in males and white. Incidence will also increase with the age (NCI, 2014).

1.5. Colorectal cancer

The cancer begins in the last part of digestive tract colon or rectum. It is reported as the second leading cause of cancer death in US.

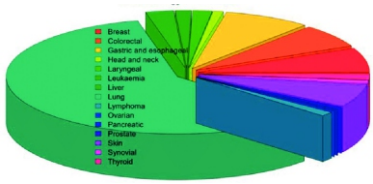

Fig.2. Different types of cancer that analyzed in humans

CRC is the third most diagnosed type of cancer worldwide. In the prevalence rate males rank third and females rank second (Sung et al., 2020, Duan et al., 2022). It is more related to environmental factors, diet and lifestyle. The cancer risk increases with age and considered as a multifactorial disease. Carcinogenic factors initiate the epithelial cells of colorectal mucosa to undergo hyperplasia and adenomas which will eventually transforms in to carcinomas (Bu et al., 2018).

1.6. Prostate cancer

Cancer origins in prostate gland, a part of male reproductive system. Prostate cancer causes blood in urine and semen, painful ejaculation and erectile dysfunction. Almost all prostate cancers are recognized to be adenocarcinomas. There are other types of cancers that can start in prostate including small cell carcinomas, neuroendocrine tumors, transitional cell carcinomas and sarcomas.

2. Cancer causing agents

Cancer is a disease caused when cells divide uncontrollably and spread in to surrounding tissues. It is a genetic disease caused by changes to genes that control the way our normal cells function. Normal cells only grow when they receive the appropriate signals, but cancer cells ignore those signals that tell cells to stop dividing. The changes in the DNA cause cancer and it transforms the genes involved in the normal cell growth to become oncogenes. A normal cell contains genes which help to control cell growth and cell division. Those genes are known as proto oncogenes. The mutated proto oncogene becomes an oncogene (https://www.cancer.org). Oncogenes cause uncontrolled cell growth. Tumor suppressor genes present in normal cells prevents cancer by stopping the cell growth. In cancer cells, the DNA changes inactivate the tumor suppressor genes that lead to uncontrollable cell growth. Three main types of genes are affected by the genetic changes of cancer namely proto oncogenes, tumor suppressor genes and DNA repair genes. The process by which cancer cells spread to other parts of the body is called metastasis. In metastatic cancer, cancer cells divide and move away from their originally formed position and spreads to other parts of body to form new tumors.

The risk of developing certain cancer depends on the changes in certain inherited genes. For example, if any mutations happen in tumor suppressor genes like BRCA genes (BRCA1 and BRCA2) it will lose its ability to suppress abnormal cell growth. Thus it will increase the risk of cancer (https://www.cancer.

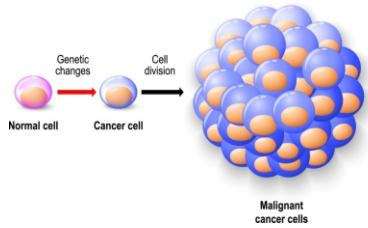

Fig.3. The formation of cancer cells from a normal cell

org). The causes of cancer are too many and some are preventable. Smoking, heavy alcohol consumption, obesity, poor nutrition, lack of exercise, unhealthy diet and lifestyle contribute to the cancer risk.

The causes of cancer include the person's genetic factors and also environmental factors. The external agents of cancer include physical carcinogens (UV and ionizing radiation), chemical carcinogens (tobacco smoke, alcohol, asbestos etc.) and biological carcinogens (infections from virus, bacteria or parasites) (https://www.who.int/news-room/fact-sheets/detail/cancer). Cancer mortality can be decreased by the early detection and effective treatment. Early diagnosis can avoid the delays in care given to the patient. Screening test like HPV test for cervical cancer and mammography screening for breast cancer helps in cancer diagnosis. The treatments include chemotherapy, radiation therapy, gene therapy and immunotherapy.

3. Mechanism behind cancer

Gene mutations have a pivot role in the abnormal cell proliferation. The generation of oncogenes and genetic disorders are caused by the DNA changes. This leads to deletion, point mutation, amplification and chromosomal translocation. An unusual protein is formed by the mutation of p53 gene. This will trigger the molecular process related to p53. It is reported that p53 abnormality leads to the formation of cancer cells (https://doi.org/10.1016/j.jcrpr.2017.07.001). Hypomethylation activates the ectopic expression of oncogenes. This is found in MASPN as a tumor suppressor gene in breast and prostate cancer. Another example for hypo methylation includes L1 from the LINE family which contributes for breast, lung and bladder cancer. Deacetylation by Histone deacetylases (HDACs) is involved in the formation of different tumors. The expression of HDAC can be controlled by microRNA. The suppression of HDAC-1 expression can be regulated by miR-449a during prostate cancer. Many cancers like colon cancer, lung and leukemia involve the deletion of HAT genes and trigger in histone acetylation

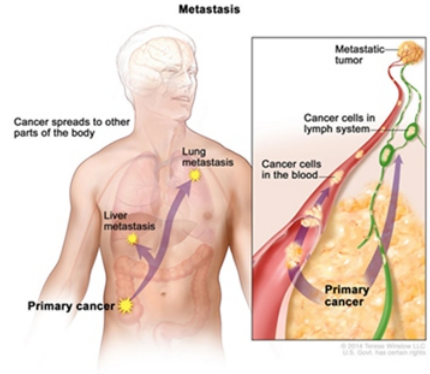

Fig.4. The process of spreading of cancer cells (metastasis) (Credit: © Terese Winslow)

(Noonan et al., 2021). The studies also show that the exposure to asbestos, pesticides, benzene and chlorinated hydrocarbons may increase the risk of pancreatic cancer (Antwi et al., 2015).

4. Cancer prevention by plant derived compounds

The increasing incidence of cancer worldwide calls for alternative treatment solution. Herbal medicines are one of such alternative against cancer. Anticancer plants which contain the plant sources of anticancer agents can be used for the treatment of cancer. This type of herbal medicine is safe, non toxic and easily available. Many anticancer medicinal plants, *Phaleria macrocarpa* (Mahkota dewa) and *Fagonia indica* (Dhamasa) have been used traditionally for the anticancer properties of their active ingredients. In cancer cells, apoptosis can be induced by the metabolites extracted from plant material. Gallic acid extracted from *P. macrocarpa* has role in inducing apoptosis in lung and colon cancer. Gallic acid which act as a natural antioxidant is also extracted from grapes, strawberries, bananas, green tea and vegetables. In addition to gallic acid, *Vinca* alkaloids, podophyllotoxin and camptothecin obtained from various plants are used for the treatment of cancer (Khan et al., 2019). The researchers have tested anticancer activity of many plants and proved that many of such plants and plant based compounds can be used effectively against one or more types of cancers. Thus more researches should be carried out to find out the mechanism of anticancer actions of many explored and unexplored plants.

5. Outlook

The risk of cancer can be reduced by maintaining a healthy lifestyle, avoiding the exposure to known carcinogens and taking medicines. As per the data of World Health Organization, between 30-50 % of all cancer cases are preventable. Tobacco smoke is one of the major causes of many severe cancer types. Avoiding the use of tobacco and alcohol will decrease the risk of cancer. Cancer causing infections like hepatitis and human papilloma virus can be prevent by taking vaccines. Many cancer screening tests and treatment methods are now available. Apart from that future research works may focus on alternative methods like use of anticancer plants along with other treatments in order to achieve effective cancer therapy.

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