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Review Article

An Overview of Lungs Cancer

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ABSTRACT

In Taiwan mostly people are suffered from lung cancer for many years and on the basis of global cancer surveillance the data are limited based on lung cancer epidemiology. The lung cancer are caused by two factors such as predominant factors and nonpredominant factors in which the predominant factors include smoking of tobacco whereas the non- predominant factors include factors of life styles and infections of lungs. These diseases can be prevented by avoiding the smoking of tobacco, improving the life style, and also understanding the development of diseases and non-smoking strategies. The patient can also be prevented from serious cases in lung by early diagnosis and also getting proper treatment. In current scenario there are lots of treatment available for the treatment of lung cancers such as surgery, chemotherapy, immunotherapy, radiation therapy and some targeted therapy are available which are used in according to the stages of lung cancers. In furthers research's the pharmaceuticals scientist is involve in developing new therapies for the recognizing the biomarkers for the diagnoses the stages of cancer for understanding the stages and genetic alteration which are occur in the lung cancer and giving adequate treatment in time.

INTRODUCTION

The cancer is the disease in which the growth of cancer cell by unstoppable cell division the resulted cells have property that invaded the surrounding tissues which is metastasis or spread to other tissues or organs, if patient is not getting a proper treatment in time the patient may cause to

death. The cancer is called by a many names on the basis of cancer occur in body parts. So, the lungs cancer is due to uncontrolled cell division of cancer cell in the tissues of lungs which lead to occurrence of metastasis, infiltration and invasion of tissues of adjacent beside the lungs [1]. The lungs cancer is now become most serious and

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deadliest diseases in the world because people are affected in all the developed countries and developing countries [2]. On the basis of high mortality rate are the most dangerous cancer is the lung cancer which are mainly caused by the formation of tumor. The lung cancer is divided in two groups such as Non-Long Lung Cancer and Small Lung Cancer these two types of cancer are occur mostly which represent almost all the cancer while the other occur type of cancer are occur in rare cases [3]. According to the current scenario, in which the ICI which stands for Immunotherapy with checkpoints inhibitors are served as a new treatment of cancer in high stages of tumors, which now become well known for cancer treatment [4]. In a current scenario the lung cancer is observed rare in the well-established countries. [5].

Stages of Lung Cancer:

The lung cancer at the initial stage can be treated easily but many patient can live longer life at the advanced stage of lung cancer. In the staging of lung cancer; we can find out the location of cells of lung cancer, tumor size, location of spreading of lung cancer, in the staging of lung cancer finding out the treatment option of lung cancer for the patients [6]. General stages of lung cancer are-

1. **Stage 0 (In-situ):**

In this stage cancer found in the peak lining of bronchus and lung. It is not spread I different region of lungs or other body parts.

2. Stage I:

In this cancer is spread to lymph nodes and other body parts and not in metastasis.

3. Stage II:

In this stage, the cancer is found greater than stage I and they are spreaded to lymph node in lungs and one or more tumor are found in the lungs of similar lobe.

4. Stage III:

In this stage, the cancer is found greater than stage II. They spread into the structures and more than one tumor are found in the lungs of dissimilar lobe.

5. Stage IV:

In this stage the cancer spread to the other lungs and fluids are found to be around the lungs, hearts and other organs.

From stage I to stage IV are come in the NSCLC. In this type of lung cancer also having two types of stages such as; Pathological and clinical stage [7].

6. Limited stage SCLC:

It is found bounded to one lung and found in the lymph nodes of the chest.

7. Extensive stage of SCLC:

They found in the both lungs and lymph nodes of both lungs and spread to the different body parts [8].

TYPES OF LUNGS CANCER

There are mainly two types of types of lung cancer are-

1. Small Cell Lung Cancer (SCLC):

They occur due to heavy smoke. In lung cancer, there are about (15-20)% of people ae found to be suffered from SCLC. They are also come under the neuroendocrine tumors classes because tumor are found in lung of neuroendocrine cells.

2. Non-Small Cell Lung Cancer (NSCLC):

Generally, in many types of lung cancer, the NSCLC are come under the term of umbrella. There are about (80-85)% of people are found to be suffered from NSCLC. There are different types of lung cancer-

- a. Large cell carcinoma
- b. Adenocarcinoma
- c. Squamous Cancer cell

Large Cell Carcinoma:

In this type these cell is found to be enlarge size and under the microscopic view, round in shape.

Adenocarcinoma-

This is the one of the type of lung cancer that occur mostly. They initially occur in mucus and that makes the cell of glands lined of our airways.



Squamous Cancer Cell- In this type of lung cancer occur in the cells that are flat in shape and cover the surface of our airways [9].

CAUSES OF LUNG CANCER

In the year 2015, about 1.8 million people diagnosed individually in lung diseases and there are approx. 1.6 million people died due to lung cancer. Mostly males are died due to lung cancer as comparison to females.

The general cause is-

- 1. Smoking of cigarettes
- 2. On contact with second hand smoke
- 3. On inhalation to radon gases
- 4. Family history
- 5. On smoking carcinogenic and asbestos products.

Smoking of cigarettes-

On each day and per year of cigarettes smoking cause lung cancer and on quitting smoke at any age can reduce the risk from lung cancer.

On contact with second hand smoke-

If you not smoking cigarettes there will be risk of lung cancer when you are contact with second hand smoke [10].

Family history-

The lung cancer is also found in the family histories on the basis of genes that transfer from one generation to another. The family history has also been found for the main cause of lung cancer [11].

Radon-

Degradation of radon in water, rock and soil produce radon which is spread in air then that infected air is unsafe for our health that can cause lung cancer [12]. On smoking carcinogenic and asbestos products- In industries and research place on inhalation to other substance and asbestos can cause lung cancer. If you are smoking that are also become the major factor to cause lung cancer [13].

Symptoms of Lung Cancer:

- 1. Loss of appetite.
- 2. Insomnia

- 3. Coughing
- 4. Fatigue [14]

On study examined in giving chemotherapy-

- 5. Nausea
- 6. Vomiting
- 7. Hair loss
- 8. Anorexia
- 9. Pain
- 10. Dysnea [15]

PATHOPHYSIOLOGY OF LUNG CANCER

On giving to overview of lung cancer there are a lot of reason that become a major responsible for the cause of Lung cancer are-

- 1. Carcinogens
- 2. Pollutants of environment
- 3. Genetic mutation

Carcinogens:

These are the major factors that cause lung cancer which cause mutation of normal cell by rapid cell division that become responsible for the formation of tumor which cause lung cancer because these carcinogens reached in the tissues of lungs and it also found that there are difference in gender in lung cancer and on doing more studies it is found that there some role play of estrogen in the carcinogenesis of lungs by the conduction of proliferation of cells [16].

Pollutants of environment:

Important pollutant is smoking of cigarettes, radon that cause lung cancer. Other pollutants are the gases such as Nitrogen oxides, Sulphur oxides and some microbes etc. [17].

Genetic Mutation-

There are several genes that become common in Lung cancer-

- 1. KRAS
- 2. TP53
- 3. EGFR
- 1. TP53-

When the TP53 gene become abnormal and then they become a larger factor for the cause of Tumorigenesis of lung cancer. They are mostly



found in smoker patients as comparisons to nonsmokers [18].

2. KRAS-

This mutated gene is mostly found in heavy smokers, in adenocarcinoma and small cell carcinoma.

3. EGFR-

This mutated gene is found in non-smoker patients. They are also seen in small cell carcinoma and adenocarcinoma [19].

MOLECULAR CHANGES

In the current scenario, that our information are more rapidly increases because cells of lung cancer are changes somatically during the duration of pathogenesis [20]. In the alteration of molecules of NSCLC firstly is that the loss of genome, which is the chromosome region that is 3p and 9p and remove of the arms of chromosomes on 5p and cause of the mutation of K-ras and p53 [21]. In the alteration of molecules of lung cancer that is the loss in the region of chromosomes which are 3p and 9p are known to be the initial event [22]. In the alteration of cells of lung cancer which shows the genetic changes and difference in expression of genes which are shown by SqCC and ADC [23]. In lung cancer also cause because of large number of changes due to large number of variation of mostly tumors [24]. The molecular biology of Lung cancer are easily to be understand by Nextgeneration Technology and they give several methods to recognize the whole gene of cancer which are mutated. In the lung cancer their genome are in the complex form and they are being observed in the study of exome sequences in big scale in 31 NSCLC in which there are 727 gene which are mutated are recognized and not found in the report of COSMIC [25]. Genomics studies has confirmed earlier modification in lung cancer such as BRAF, EGFR and KRAS and also founded rare but recurrent mutation in lung cancer [26], involve mutations in JAK2, ERBB4 [27], RET [28], fibroblast growth factor receptor1(FGFR1) [29]

and discoid domain receptor 2 (DDR2) [30]. The desirable targets for pulmonary SqCC are not discovered. The lung SqCC are analysed by the TCGA research network and recognize the desired therapeutic agent in mostly pulmonary SqCC in researching. The alteration in oncogenic pathways in pulmonary SqCC involves the RTK pathways(26%), PI(3) pathways(47%), the RAS pathway(24%) [31]. The Small Cell Lung Carcinoma is the dangerous type of lung cancer and no targeted therapies are developed. In recent studies of Small Cell Lung Carcinoma are founded that there are some genetic changes involve such as TP73 Δ ex2/3 and RLF-MYCL1 fusion [32].

DIAGNOSIS

1. Sputum Cytology:

This method is used for the screening of squamous lung cancer which are formed in the mid-early and located centrally [33]. They are also used for the evaluating procedure for the analysis of benign and malignant diseases of lungs but this method is not very successful for the screen of lung cancer [34]. In the year of 1970s, many screening trials and sputum cytology was done in this National Cancer Institute which giving the funds to Cooperative Early Lung Cancer Detection Program for the establish the scheme for the proper evaluation of sputum cytology monitoring program and chest radiograph for reduce lung cancer in male person whose are using the tobacco [35]. In current scenario chest radiography and sputum cytology are not performed for the screening of lung cancer which are formed in the mid-early [36].

2. Autofluoresence Bronchoscopy:

It is the other important method for spotting of the premature lung cancer, carcinoma in-situ etc. Their main important objective is to detect the pre-invasive neoplastic lesions to eliminate them before they become the cancer in invasive form [37].

3. Lung Tissues Biopsies:



The Biopsy methods is the most widely used method for the detection of lung cancer in the tissues of lungs. By the used of histopathological procedures it confirms the types of lung cancer. On biopsy that is crucial in reporting in early diagnosis of lung cancer and do not required another biopsy which are more difficult and procedures in perform. There are some procedures used in the detection of lung cancer such as-

- 1. Endobronchial ultrasonography
- 2. Mediastinoscopy
- 3. Thorascopy
- 4. Surgical approaches
- 5. Thoracentesis
- 6. Fiberoptic Bronchoscopy
- 7. Image-guided trans-thoracic needle aspiration These above procedures are very costly and require large samples [38].

4. Metabolomics:

They are the data which contain the information of the amount of metabolites which are present in the body that are having the abilities to show the characteristics of diseases which are in the different stages. In a current scenario on observing the uses of metabolomics on prediction of the growth of tumor which are found in several fluids such as urine, sweat, sputum and bloods which are shown in report in properly [39]. In the analysis of serum in the studies of metabolomics which are recognized in variation in the levels of aspartate and pyruvate metabolites which served as the distinguished factors between the people suffering from cancer and the people are found in state of good health [40]. On evaluating the sputum for making distinguishes the patients suffering from lung cancer from the people are found in the state of good health, it is found that cardiolipin, cystic acid, hexanal and hydroxyprocaine acid is significant with the ranging of AUC 0.81-1.0 [41]. In the analysis of sweat, trisaccharide carbide MG(22:2), tetra hexoses, azelaic acid and Tri hexoses showing sensitivity and specificity is

found below 80% and 79% accurately 20% [42]. Finally in predicting the hypothesis of the level of SSAT-1 that are found in increase amount in the lung cancer confirming that the enzyme is reason for causing the metabolism of polyamine [43].

TREATMENT OF LUNG CANCER

1. Radiation Therapy:

The radiation therapy is also known for giving effective treatment of NSCLC types lung cancers in several ways. They are now become a first treatment of unresectable local cancer and this therapy are also given along Chemotherapy [44]. These therapy are used as adjunctive therapy which control the stage 3 of NSCLC type lung cancer and their main objective is to enhance local control. They have application in the treatment of metastatic and advanced lung cancer. These treatment are used for the breast cancer and deliver external – beam treatment. In this scenario there are some new modified methods are arises which give better profile of toxicity and also increase dose by preventing the tissues from unwanted radiations [45].

2. Chemotherapy:

The treatment used earlier the chemotherapy is the median overall survival for pulmonary cancer was about 2 to 4 months with supportive care [46]. In this the drugs which comes under the category of chemotherapy such as Doxorubicin, Methotrexate are used for the treatment of pulmonary cancer in 1970 clinical report were inadequate [47]. When the platinum and new generative drugs come under the categories of chemotherapy such as Gemcitabine, Vinorelbine and Taxanes in 1980 and 1990 then the better results obtain from the pulmonary cancer patients. In 1995, Non-Small Lung Cancer Cooperative Group perform landmark analysis that give the result that the Platinum based chemotherapy enhance OS as compare to earlier supportive care (In 1 year OS rate of 15% vs 5%) [48].

The Randomized trial is become interpreted through analysis by comparison of Cisplatin and Carboplatin and it is reported that Cisplatin doublets were improved performance than Carboplatin therapy and they are not show more toxicities [49]. Recently in 2006, the monoclonal antibody which is Bevacizumab are granted against the Vascular Endothelial Growth Factor and they can be use along with the Carboplatin and Paclitaxel which become the important treatment of Non-squamous NSCLC [50].

3. Stereo static Body Radiotherapy:

The Stereo static body radiotherapy are the therapy which provide therapeutic invasive treatment against NSCLC types lung cancer [51]. This therapy provides more doses of radiation directly to the tumor regions without causing any side effects [52]. In a current scenario, the stereo statics body radiotherapy are now rapidly used in the treatment of Carcinoma in-situ. They are used along with other modified techniques like EGFR-Inhibitors and immunotherapy for treating the patient suffering from Oligometastatic cancer [53]. In a complicated case record, there are many studies are carried out along with the use of Stereo static body radiotherapy in serious cases. On studying the Eichkorn et al and Wang et al we can Stereostatic body radiotherapy assess the techniques in patients which are serious conditions in NSCLC. In a stage 3 of pulmonary cancer this therapy are used along with the immunotherapy to increase the response of immune [54].

4. Targeted Drug Therapy:

In lung cancer, the cancer cells have altered gene, proteins, which are different from the normal tissues. They are spread very rapidly to other tissues of organs so in the targeted therapies, therapeutics drugs are given and these drugs are acted targeted directly to the tumors without causing any side effects. These drugs are taken in the serious case of lung cancer.

There are several drugs that are use in the pulmonary lung cancer are FDA approved. In this personalized cancer treatment are given to the patient because it is the most rapidly use treatment in lung cancer by confirming situation of targeted genes and protein are confirm by the standard test. In this therapy inhibitors of EGFR, RAS-MAPK, RET, MET, BRAF, NTRK, PD1etc are used in the targeted therapy for the treatment of lung cancer [55].

5. Immunotherapy:

The cause of lung cancer not only due to the alteration in genes, proteins and molecular properties of cancer cell but they also interaction of carcinomic tumor with the immune system in the body [56]. The therapeutics methods that are given to the patients which are suffered from lung cancer is basically based on the vaccines which are slowly become therapeutic due to less activated immune system in first encounter in the body [57]. This method basically based on the sequence of ligands and receptors which stimulating or inhibiting the response of immune system [58].

6. Radiofrequency or Micro ablation:

They firstly established for therapy of liver cancer then further they are used in treatment of lung that treatment called Percutaneous Radiofrequency ablation which are made by Dupuy et al in 2000 [59]. They are used for the patients which are with the tumors found in lung tissues which are in premature state and peripherally located [60]. They are well known for giving the adequate therapy for primary and secondary lung cancer [61]. Recently Radiofrequency Ablation are used for the detection of NSCLC type of lung cancer in the stage of Ia where the size of tumor are found about not more than 3cm [62]. They cause the thermal ablative method which are responsible for the cause of tisues death by the process of Coaglative necrosis [63].

The Radiofrequency show their effect in the specific regions by removing the tumor which detected in the lungs of animal VX2 tumor models which shows the achievement in the sequence steps of Radiofrequency ablation [64].

CONCLUSIONS

Lung cancer is most rapidly occur diseases that cause death related diseases in all over the world. According to worldwide survey it is observed that these diseases are observed in the peoples who are smoking cigarettes and those who also use second cigarettes also. There are the ways to prevent from lung cancer is maintain our health and weight of our body by doing exercises and yoga in a early morning daily, consuming heathy foods like fruits and vegetables. It is observed that mostly stage 3 of NLCSC type lung cancer are caused. They can be cured by using several surgical methods such as RATS and VATS methods are used along with Immunotherapy are given also. In these recent scenario, the health professionals used the Targeted therapies along with the Immunotherapy which give the improved results in the treatment of patients suffering from pulmonary cancer. In chemotherapies there are several drugs are given for the treatment of lung cancer such as erlotinib and gefitinib (EGFR inhibitors), everolimus (mTOR inhibitors), entrectinib (ROS1 inhibitors) are now most rapidly used for the treatment of lung cancer. It is important to understand the risk factor of lung cancer and molecular alteration and mutation of genes caused by Lung cancer.

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