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ADVANCED TREATMENT TECHNIQUES FOR NON-SMALL CELL LUNG CANCER – A REVIEW

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ABSTRACT

Lung cancer is the leading cause of cancer-related death not only in the United States, but worldwide. In North America, former smokers are more likely to develop lung cancer than current smokers. Nonetheless, a peak in lung cancer incidence is still expected in some countries, such as China, which has seen a dramatic increase in cigarette smoking rates over the last two decades. Approximately two-thirds of adult Chinese men smoke, accounting for one-third of all smokers globally. In the United States, non-small cell lung cancer accounts for 85% of all lung cancer cases. After a diagnosis of non-small cell lung cancer, accurate staging with computed tomography or positron emission tomography is critical for determining appropriate therapy. Surgical resection remains the most consistent and successful option for cure when it is feasible. However, nearly 70% of patients with lung cancer are diagnosed with locally advanced or metastatic disease. Chemotherapy is beneficial for patients with metastatic disease, and concurrent chemotherapy and radiation are recommended for stage III lung cancer. The introduction of new anticancer agents such as angiogenesis inhibitors, epidermal growth factor receptor inhibitors, and other anticancer agents is changing the present and future of this disease and will almost certainly increase the number of lung cancer survivors.

KEYWORDS: Adenocarcinoma, squamous cell carcinoma, bronchioalveolar cell carcinoma, Electrocautery and targeted therapy.

INTRODUCTION

Lung cancer is one of the most lethal cancers for both men and women. Its mortality rate exceeds that of the three most common cancers combined (colon, breast, and pancreatic). Over half of lung cancer patients die within a year of diagnosis, with a 5-year survival rate of around 17.8%. Small-cell lung carcinoma and non-small-cell lung carcinoma (NSCLC) are the two most common subtypes of lung cancer, accounting for 15% and 85% of all cases, respectively. Squamous-cell carcinoma, adenocarcinoma, and large-cell carcinoma are the three types of NSCLC.[1] Squamous-cell carcinoma accounts for 25-30% of all cases of lung cancer. It develops from squamous cells in the airway epithelial cells of the bronchial tubes in the centre of the lungs.

Adenocarcinoma is the most common type of lung cancer, accounting for roughly 40% of all cases. It develops from type II alveolar cells, which are small airway epithelial cells that secrete mucus and other substances. Adenocarcinoma is the most common type of lung cancer in both smokers and non-smokers of all ages. It is more common on the outskirts of the lung, which could be due to the addition of filters in cigarettes that prevent large particles from entering the lungs. This causes deeper inhalation of cigarette smoke, which leads to peripheral lesions. Adenocarcinoma grows more slowly than other types of lung cancer and is more likely to be detected before it spreads outside the lungs. 5-10% of lung cancers are large cell (undifferentiated) carcinomas. Because there is no evidence of squamous or glandular maturation in this type of carcinoma, it is frequently diagnosed by exclusion of other possibilities. Large cell carcinoma frequently begins in the central part of the lungs, spreading to nearby lymph nodes, the chest wall, and distant organs. Smoking is strongly linked to large cell carcinoma tumours.

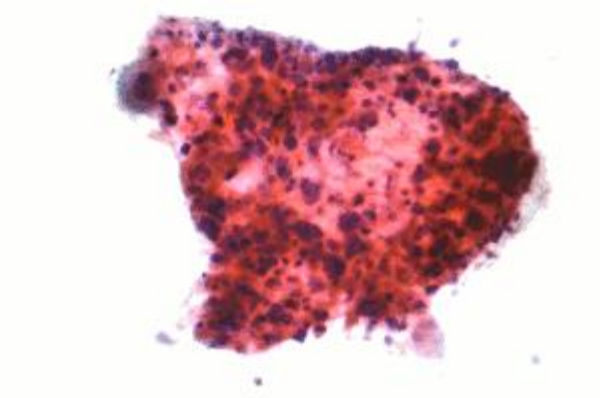

Figure 1: Non-Small-Cell Lung Carcinoma.

Etiology

The etiology of NSCLC can be further divided into avoidable and unavoidable risk factors. Inhaled tobacco use is the most well-known preventable risk factor for NSCLC. Other causes of lung cancer include alcohol use, environmental exposure to secondhand smoke, asbestos, radon, arsenic, chromium, and nickel, as well as ionizing radiation and polycyclic aromatic hydrocarbons. When used to treat other cancers, such as breast cancer and Hodgkin lymphoma, radiation therapy can also cause primary lung cancer. Patients with pulmonary fibrosis have a roughly sevenfold increased risk of developing lung cancer, which has been shown to be independent of tobacco use. The incidence of lung cancer in HIV patients has also been found to be higher than in the uninfected population, and this has been shown to be independent of smoking status or antiretroviral therapy use in the HIV population.[2]

Epidemiology

Tobacco use has been linked to the development of 90% of all lung cancers. Patients who currently smoke and have a 40 pack/year smoking history are twenty times more likely to develop lung cancer than nonsmokers. This risk may increase if additional environmental or lifestyle exposures, such as asbestos exposure, are combined with tobacco use. The invention of filter cigarettes in the 1960s is thought to have caused adenocarcinoma, but this has not been proven. Lung cancer is the leading cause of cancer death in men and the second leading cause in women worldwide. The incidence of lung cancer varies greatly between populations based on the prevalence of tobacco use in various countries. The prevalence of lung cancer is directly related to the rate of smoking in various populations.[3] For example, in the United States, the age-adjusted mortality rate.

Treatment / Management

Treatment is determined by the individual's functional status, comorbidities, tumor stage, and disease molecular characteristics. Patients with stage I, II, or III NSCLC are treated with the goal of curing them. This can include surgery, chemotherapy, radiation therapy (RT), or a combination of these treatments. Systemic therapy is recommended for patients with distant metastases and stage IV disease, or if symptoms recur after initial treatment. Lobectomy is widely accepted as a surgical approach for treating early-stage NSCLC. Patients who are surgical candidates with clinical stage I or II NSCLC are treated with resection followed by pathologic staging. Surveillance may be indicated based on pathologic staging if the patient is in pathologic stage IA. If the patient is diagnosed with pathologic stage IB or stage II/III, he or she may be given adjuvant chemotherapy.[4]

If the individual's tumor margins are found to be positive, they will need postoperative radiation therapy or resection, followed by adjuvant chemotherapy. If the patient is in clinical stage I or II and is deemed unsuitable for surgery, treatment would consist of stereotactic body radiation therapy (SBRT) or definitive RT. Clinical stage III would suggest a multidisciplinary approach to treatment[6], including consultation with medical oncology, radiation oncology, and thoracic surgery to determine the best combined approach to the disease process. Other mutations that can be found include ROS1, BRAF, RET, TRK, MET, and KRAS, and specific inhibitors for these should be included in the treatment plan. If a driver mutation is missing or unknown, the level of programmed cell death ligand 1 (PD-L1) expression should be measured, and if it is greater than 50%, pembrolizumab or atezolizumab may be used in the treatment plan. These can also be used as a single-agent treatment in the absence of chemotherapy. Finally, patients should be actively evaluated for clinical trial eligibility throughout the course of their disease.[5]

Differential Diagnosis

NSCLC is usually suspected when a pulmonary nodule is discovered on a chest radiograph after the patient presents with intrathoracic symptoms. The differential diagnosis can thus include the following based on the intrathoracic symptoms and potential chest radiograph findings.[6]

- Bronchogenic carcinoma (adenocarcinoma, squamous cell carcinoma, large cell carcinoma, small cell carcinoma) • Breast, head/neck, melanoma, colon, kidney, germ cell tumor, sarcoma metastatic disease.
- Carcinoid pulmonary.
- Lymphoma extra nodal.
- schwannoma or plasmacytoma.
- Non-cancerous neoplasms such as fibroma, neurofibroma, lipoma, hamartoma, leiomyoma, and angioma.
- Vascular abnormalities such as hematoma, pulmonary infarction, and arteriovenous malformation.
- A bronchodilator cyst.

ADVANCED TREATMENTS

i) Targeted Therapy

Targeted therapy is a type of cancer treatment that targets specific genes, proteins, or the tissue environment that

contribute to cancer growth and survival. This type of treatment inhibits cancer cell growth and spread while protecting healthy cells. NSCLC[7-8] targeted therapy includes.

- ❖ EGFR inhibitors
- ❖ Drugs targeting the EGFR exon 20 insertion
- ❖ ALK inhibitors
- ❖ Drugs targeting the *ROS1* fusion
- ❖ Drugs targeting *KRAS G12C* mutations
- ❖ Drugs targeting *NTRK* fusion
- ❖ Drugs targeting *BRAF* V600E mutations
- ❖ Drugs targeting *MET* exon 14 skipping
- ❖ Drugs targeting *RET* fusion

Targeted therapies can do different things to the cancer cells they target.

- ✓ Block or turn off signals that tell cancer cells to grow and divide
- ✓ Prevent the cells from living longer than normal
- ✓ Destroys cancer cells.

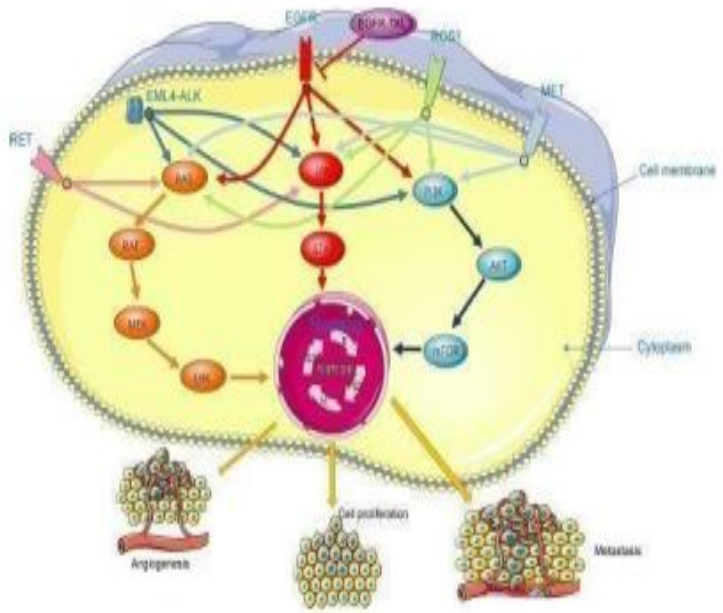

Figure 1: Mechanism of targeted Therapy.

Epidermal growth factor receptor (EGFR) inhibitors: About 10% to 15% of all lung cancers are EGFR-positive. Researchers have found that drugs that block specific EGFR mutations may be effective for stopping or slowing the growth of lung cancer when the cancer cells have that EGFR specific mutation. The following EGFR inhibitors are approved by the FDA. Afatinib, Erlotinib and Gefitinib are used for the treatment.

Drugs targeting the EGFR exon 20 insertion: Some people have a specific change to the EGFR gene in the exon 20. Amivantamab is used for the treatment.

Anaplastic lymphoma kinase (ALK) inhibitors. ALK is a protein that is a part of the cell growth process. When present, this helps cancer cells grow. Ceritinib and Crizotinib are used for the treatment.

Drugs targeting ROS1 fusion: rearrangement can cause problems with cell growth and cell differentiation. Drugs targeting KRAS G12C mutations: The KRAS G12C is one of the most common genetic mutations found in people with NSCLC. Adagrasib and Sotorasib are used for the treatment.

Drugs targeting NTRK fusion: This type of genetic change is found in a range of cancers and causes cancer cell growth.

Drugs targeting BRAF V600E mutations: The BRAF gene makes a protein that is involved in cell growth and can cause cancer cells to grow and spread. BRAF mutations have been found in 4% of NSCLC cases. Metastatic NSCLC with BRAF V600E mutations can be targeted with the following drugs: combination of dabrafenib and trametinib and combination of ecorafenib and binimetinib are used for the treatment.

Drugs targeting MET exon 14 skipping: MET exon 14 skipping is a genetic mutation found in over 3% of NSCLC cases. Capmatinib and Tepotinib are used.

Drugs targeting RET fusion: Up to 2% of all NSCLC cases are RET fusionpositive. Selpercatinib.

Figure 2: Targeted Therapy changes for NSCLC patients.

ii) Electrocautery[9-12]

Electro cautery is a procedure that uses heat from an electric current to destroy cancer cells. It's a treatment for some people with non-small-cell lung cancer (NSCLC). You might get electro cautery if your cancer is very small and it hasn't spread. Or it may be done to ease symptoms if the cancer is blocking one of your airways and causing breathing problems. It can sometimes be used during segmentectomy surgery to help the surgeon divide up the parts of your lung to remove. Stage 0 NSCLC means the cancer is only in the lining of your airways or in your air sacs (alveoli). Another name for stage 0 is carcinoma in situ. The cancer hasn't spread deeper into your lungs or to other parts of your body.

Electro cautery is one of a group of treatments called end bronchial therapies. Other end bronchial therapies include photodynamic (light) therapy, cry therapy (cold therapy), and laser therapy. The electric current, light, cold, or laser is passed through a tube called a bronchoscope into your lung. Brachytherapy is a type of radiation treatment that places Radioactive material into the body.

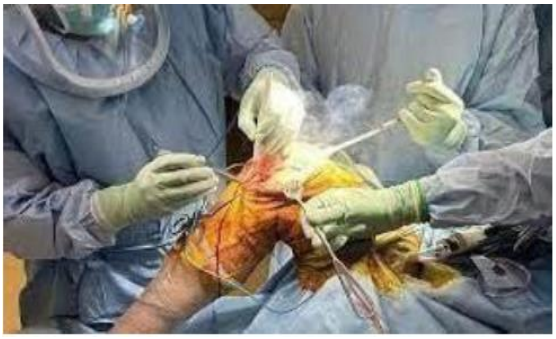

Figure 3: Treatment of Eectro Cautery for NSCLC.

CONCLUSION

Significant progress has been made in the reduction of occupational health hazards associated with lung cancer, particularly smoking, as well as in the prevention of a variety of disorders. Targeted therapy and immunotherapy have made significant contributions to lung cancer management in recent decades. Treatments for NSCLC are individualised and can target specific mutations with greater precision, with the goal of extending progression-free survival. To increase testing success rates, improved communication among specialists involved in lung cancer diagnosis and patient care, as well as the establishment of local molecular testing protocols, are required. Furthermore, the real challenge will be incorporating these agents into the management of patients with earlier stage disease in the hope of significantly improving cure rates for the devastating illness known as lung cancer.

The key to the future success of theragnostic and truly personalized oncological management will be to ensure appropriate patient selection using predictive biomarkers to optimize limited resources and minimize harm. Our knowledge translation intervention improved knowledge and awareness regarding molecular testing, as well as its importance in lung cancer and relevance to improving patient outcomes.

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