Understanding Allergic Rhinitis and Non-Small Cell Cancer from Pathology to Treating Practice with Case Reports

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Abstract: Recently, COVID-19 has caused a pandemic and received substantial medical attention worldwide. Subsequently, we recognize the increasing public interest in not only antiviral treatments, but general respiratory health. Respiratory diseases can take place by endogenous as well as exogenous causes. Suffering from an unhealthy condition of the respiratory system, from annoying issues as seasonal allergic rhinitis, all the way to lethal lung cancer brings loads of burden to not only an individual, but also the whole society. Efficient care and treating practices thus require urgent improvement. Here we present a systematic study from case reports for the comprehensive understanding of therapeutic options progress focused not only the currently available, but also under development strategies for the summarised respiratory diseases based on the pathophysiology understanding. To be specific, currently available treatment options for these diseases, including pharmacological, immunogenic in according with oncogenic factors and relative treatments for NSCLC, whose efficacy and side effects are well-characterized. We also discuss and envision future treatment options that are underway of development, which may lead to advancements in both potency and reduced adverse effects. Applications of technologies should also be considered promptly by medical professionals.

1 INTRODUCTION

Cells in human bodies need oxygen to stay functional and alive, inhalation of oxygen from the atmosphere to the human body depends on the lungs and the function of the respiratory system. Oxygen first fills the alveoli and is delivered to each of the organs through blood vessels. The respiratory system has numerous functions in addition to gas exchange, and it is a crucial site where the interior of our body constantly 'communicates' to the extrinsic environment. People cough and sneeze to protect their airways from irritants that may cause diseases. Aerobic organisms have developed numerous defense mechanisms to protect the airway as they evolve. However, respiratory illness remains the leading cause of death and disability (Soriano 2020). This main global burden should be thoroughly studied to enhance the quality of human lives.

Upon understanding the significance of treating respiratory diseases, we realize that various types of respiratory diseases that affect different subsections of the respiratory tract have been investigated in the medical field. Our review will focus on respiratory diseases that are highly prevalent and have contributed heavily to the public health burden, such as Allergic rhinitis (AR), and Non-Small Cell Lung Cancer (NSCLC). We selected these diseases as references for analysis, as they differ in pathogenesis and treatment options, representing distinct categories within the broad scope of respiratory pathology. Until recently, potential therapeutic targets for all three diseases have been identified. Several treatment options for AR and NSCLC are widely implemented in clinical practices, while

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optimizations and novel drugs are still being explored.

In order to assist the public in the understanding of respiratory diseases, here we provide a systematic review of allergic rhinitis, COVID-19, and non-small cell lung cancer from bench to bedsides. We summarized the pathophysiology of each disease, as well as research leading to target identification and currently accepted treatment practices. Furthermore, we discussed the ongoing research suggesting potentially novel and more effective treatment approaches with emphasis on drug development. This paper is organized in three parts as each talks about one disease, with an ordered sequence from the upper to the lower respiratory tract.

2 ALLERGIC RHINITIS

Seasonal allergic rhinitis is caused by oversensitive immune response to certain allergens in the environment that are not generally considered harmful, which mainly affects the upper respiratory tract. The disease affects a large percentage of the general population, which leads to a number of complications that severely impacts patients' quality of life and leads to decreased productivity at the workplace (Lamb 2006). Although allergic rhinitis is not a particularly serious condition, treatments that relieve symptoms still constitute a medical need. The currently accepted therapeutic standards are antihistamines, intranasal corticosteroids and antileukotrienes, which target different mediators of the immune response pathway (Emeryk 2019). Recently, anticholinergic drugs have received attention for their anti- inflammatory properties, which are being repurposed as maintenance therapy for AR and have gained FDA approval. Some researchers have also proposed the activation of the anti-inflammatory cholinergic pathway as a potential therapeutic approach, which requires further pharmacological and clinical investigation (Yamada 2018).

2.1 Pathology and Complication

Generally, allergic rhinitis (AR) is characterized by oversensitive IgE-mediated immune response to allergens and upper airway inflammation (Wheatley 2015). Symptoms include nasal itching, sneezing, watery rhinorrhea, and nasal obstruction (Min 2010). The disease is caused by immune sensitization to a large variety of inhaled allergens with either indoor or outdoor origins, including pollen, dust mites, pets, pests and mold (Wheatley 2015). From the pathophysiologic perspective, dendritic cells present characteristic peptide segments on the cell membrane to form histocompatibility complex (MHC) class I and II when exposed to allergens, which signal the transformation of naive CD4+ T cells to T-helper (Th2) cells. Allergen-specific Th2 cells secrete several Th2-type cytokines such as IL-3, IL-4, IL-5 and IL-13. Among these cytokines that are essential for inflammatory responses, IL-4 and IL-13 promote allergen-specific IgE production by B cells, which induces the proliferation of eosinophils, macrophages, and mast cells. Mast cells release several inflammatory mediators, including histamine and leukotrienes, which are responsible for increased nasal itching, vascular permeability, and mucus hypersecretion (Min 2010, Small 2018, Meltzer 1997). This stage of allergic response constitutes the early reaction (Min 2010). IL-3 and IL-5, on the other hand, promotes eosinophil proliferation and infiltration into the nasal mucosa, which secretes pro-inflammatory mediators, cationic proteins, and reactive oxygen species, directly contributing to increased mucus production and airway constriction (Antunes 2020). This process triggers the late reaction, exhibiting nasal congestion, smooth muscle hyperplasia and airway remodeling as chronic symptoms (Figure 1) (Min 2010).

Although mild to moderate allergic rhinitis rarely has serious complications, pharmacological therapy is recommended by physicians due to the disease's significant impacts on patients' quality of life and association with secondary inflammatory complications. AR contributes to unproductive time at school or work, sleep apnea, and reduced cognitive abilities, which results in indirect economic loss comparable to that of mental disorders and diabetes (Lamb 2006, Wheatley 2015). Clinical reviews have suggested an increased risk for several comorbidities if chronic AR is left untreated, including conjunctivitis, sinusitis, and otitis media with effusion (OTE) (Min 2010). Study results have proposed that inflammation involved in AR results in impaired ciliary function and sinus obstruction, which creates an anaerobic environment favorable for bacterial growth that eventually facilitates middle ear infection and chronic OTE (Bergeron 2005). Other complications of AR, such as nasal polyposis and adenoid hypertrophy, are suggested by clinical evidence, although their association with rhinitis has not been investigated thoroughly (Min 2010).

The association between allergic rhinitis and asthma is especially pronounced due to their similar

disease pathophysiology. Clinical data has confirmed that up to 40% of AR patients have concomitant asthma, and 94% of asthma patients have AR (Wheatley 2015). In AR patients without asthma, eosinophil infiltration, lymphocyte number, and increased IL-5 production in the bronchial mucosa have been observed after antigen challenge (Min 2010). It has been proposed that AR-induced airway hyperresponsiveness contributes to an increased risk of asthma through migration of IL-5 producing T cells to the bone marrow, which is associated with an increase in progenitors that can differentiate into eosinophils (Bergeron 2005). Eosinophils in the lower airway contribute to airway remodeling through the release of cytokines and reactive oxygen species (ROS), which stimulates mucus hyperproduction, eosinophil recruitment and damage to the bronchial mucosa (Kudo 2013). Kudo et al. also pointed out that cytokine and leukotriene production lead to proliferation of airway smooth muscle cells and deposition of extracellular matrix by myofibroblasts (Kudo 2013). The confirmed association between AR and allergic asthma becomes the basis for identifying biological targets that are involved in the pharmacological treatments of both diseases.

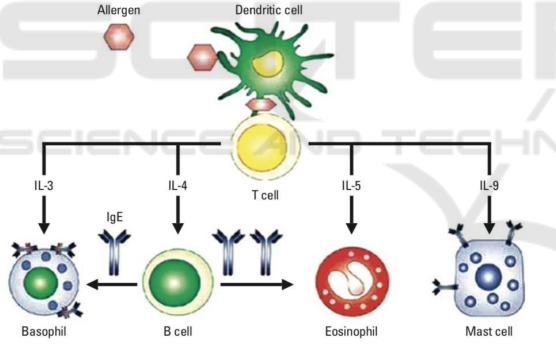

Figure 1: Pathogenesis of allergic rhinitis. Allergen binding activates the immune system's intracellular signaling pathway, releases inflammatory molecules and causes chemotaxis of immune cells to the upper respiratory tract tissue (Min 2010).

2.2 Treatments

2.2.1 Current Treatment Options

Several types of pharmacological treatments available for allergic rhinitis include oral and intranasal antihistamines, antileukotrienes, decongestants, and intranasal corticosteroids. These drugs have well- characterized pharmacokinetic and pharmacodynamic profiles from clinical trials. Although each drug class targets a different step in the inflammatory response pathway, almost all are G protein-coupled receptor antagonists, demonstrating the selection of receptor proteins as excellent therapeutic targets.

Antihistamines target the H1 histamine receptors, which mainly mediate hypersensitive reactions and allergic responses (Devillier 2008). At the periphery level, antihistamines bind to H1 receptors and stabilize their inactive form, inhibiting allergic reactions induced by histamine binding (Devillier 2008). Synthesized by lipoxygenase from arachidonic acid, cysteinyl leukotriene (Cys-LT) is a class of lipid mediators that act as autocrine and paracrine factors in eosinophils, which promote the release of ROS, cationic proteins, and cytokines that directly contribute to inflammation (Miyata 2020, Kuehl Frederick 1980). Antileukotrienes inhibit the effects of Cys-LT as Cys-LT receptor type 1 antagonists, thereby reducing the level of cytokines and eosinophil chemotaxis to the site of inflammation (Miyata 2020, Wilson 2004). Note that dysfunction of arachidonic acid metabolism also appears in allergic asthma patients, which indicates a close association between rhinitis and asthma treatments (Miyata 2020). Corticosteroids are glucocorticoid receptor antagonists, which are observed to inhibit the production of multiple inflammatory mediators, including cytokines (IL-3, IL-5, granulocyte-macrophage stimulating factor) and arachidonic acid metabolites. Thus, corticosteroids suppress T-cell activation, eosinophil influx, cytokine release, mast cell count, and histamine content, relieving inflammatory symptoms effectively (Meltzer 1997). In summary, antihistamines and antileukotrienes target the final and intermediate steps, while corticosteroids have an observable effect on multiple steps of the inflammatory response pathway.

Among these treatment options, intranasal corticosteroids have been confirmed as the most effective by several meta-analyses of randomized, controlled clinical trials (Wilson 2004). Therefore, corticosteroids, sometimes in combination with antihistamines, are recommended by physicians as the frontline treatment that controls symptoms of moderate-to-severe allergic rhinitis (Wheatley 2015, Min 2010, Small 2018). Antihistamines and antileukotrienes are often prescribed as combined treatment to control mild persistent allergic rhinitis, but their potency is less than that of intranasal corticosteroids (Rodrigo 2006, Ciprandi 2004). We speculate that the enhanced potency of corticosteroids can be attributed to its effect on multiple steps of the inflammatory pathway, which

is yet to be confirmed by clinical evidence. Due to the seasonal or perennial nature of allergic rhinitis, regular administration of symptom-relieving pharmacological agents during peak season is usually relevant in the long term for patients with allergic rhinitis.

In rare cases, allergen immunotherapy may be applied to desensitize the immune response to certain allergens systematically (Durham 2016). Currently available methods include subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT), which are differentiated based on the routes of delivery (Durham 2016, Cox 2017). SCIT or SLIT requires at least 3 years of administration, can be costly overall, and can result in anaphylactic reaction 0.1% of SCIT injection visits (Cox 2017). Therefore, immunotherapy is recommended by physicians in limited cases only if pharmacological therapies are not well-tolerated or ineffective, which is relevant for only a small fraction of patients (Wheatley 2015).

2.2.2 Novel Targets in Cholinergic Immune System

Although corticosteroids are sufficiently potent and have been the standard allergic rhinitis treatment for years, recent reviews have discovered that systematic long-term administration of corticosteroids is associated with adverse effects on the cardiovascular, gastrointestinal, neuropsychiatric, endocrine, and immune systems (Yasir 2020, Kummer 2006). Therefore, an incentive was created to develop an alternative drug with comparable potency. Recently, cholinergic receptor antagonists, traditionally used as bronchodilators in the treatment of asthma and chronic obstructive pulmonary disease (COPD), have received attention for their anti-inflammatory properties. Although the use of anticholinergic drugs in allergic rhinitis treatment is uncommon, several preclinical and clinical studies have demonstrated their effectiveness in AR treatment with an improved safety profile (Pieper 2007, Wessler 2008, Li 2011).

The discovery of anticholinergic drugs as a new treatment option started with an understanding of the cholinergic signaling pathway of immune cells. Traditional views have limited the function of acetylcholine to the autonomic nervous system, yet literature has demonstrated solid evidence on the role of a non-neuronal cholinergic system that regulates immune function (Verbout 2012). Experimental results revealed that acetylcholine is secreted by immune cells and acts as an autocrine and paracrine factor for airway epithelial and inflammatory cells (Kistemaker 2012). In the cholinergic signaling pathway for the inflammatory response, acetylcholine can be secreted into human blood, which is transported by organic cation transporters to the site of infection and signals chemotaxis of immune cells. Acetylcholine is detected by muscarinic cholinergic receptors, which stimulates increased release of cytokines and chemotactic factors that initiate inflammatory response. Experiments with human cell lines and mouse models indicated an effect on lymphocyte proliferation and cytokine production when known muscarinic receptor agonists, such as carbanol and Oxo-M, were applied to stimulate acetylcholine secretion (Verbout 2012). Collectively, laboratory evidence supports that muscarinic receptor in this system are viable drug targets for the attenuation of an immune response.

Indeed, further research confirmed the expression of muscarinic receptors (mChA) in human lymphocytes and characterized the effect of several muscarinic antagonists, validating M3-subtype mChA as the target for a novel immunosuppressant drug. Experimental evidence suggested the expression of all five subtypes of muscarinic receptors (M1-M5) in both mouse and human lymphocytes, including T cells, B cells, natural killer cells, and macrophages, through radioligand binding and RT-PCR (Verbout 2012). Furthermore, studies regarding human airway epithelial cells confirmed the role of the cholinergic system in airway remodeling that leads to bronchoconstriction and mucus production, which was effectively alleviated by anticholinergic drugs (Kistemaker 2012, Wang 2019). However, it was also discovered that there was variance by individual in the levels of subtype mChA expressed: unlike M1 and M2, M3-M5 receptors are reliably expressed in all subjects, with M3 being the most abundant (Tayebati 2002). Therefore, although concerns were raised regarding the specificity of mChA antagonists as drugs, it was logical to explore M3 receptor antagonists as potential drug molecules for respiratory system inflammation (Jiang 2011). In fact, several M3 receptor antagonist drugs of the quaternary ammonium bromide class, such as tiotropium and ipratropium, have been approved by the FDA as intranasal sprays that relieve the symptoms of severe allergic rhinitis (Albertson 2017).

Tiotropium was approved by the FDA in 2004 as a bronchodilator in maintenance therapy for COPD, and severe asthma when used in conjunction with

corticosteroids (Albertson 2017). Research has demonstrated that tiotropium bromide blocks the M3 receptor and regulates apoptosis of immune and airway epithelial cells, thus inhibiting eosinophil infiltration and alleviating bronchoconstriction (Pieper 2007). Recently, bencycloquidium bromide (BCQB) was approved and became available on the Chinese market. While tiotropium bromide is designated for COPD or asthma treatment and BCQB for allergic rhinitis, their mechanisms of action are quite similar. Both drugs possess a quaternary ammonium ion in a six-membered, bridged ring, a benzene group, and a bromide ion, indicating similar pharmacokinetic properties and binding mechanism. To minimize toxicity, these mChA receptor antagonist drugs were designed as charged molecules in dosage forms to prevent the crossing of biological membranes (Albertson 2017). This similar structure is observed in several short-acting and long-acting muscarinic receptor antagonists that were approved by the FDA as maintenance therapies in COPD and acute asthma.

The recent development of mChA receptor antagonist drugs has recognized acetylcholine as a pro- inflammatory signaling molecule, where drugs were designed to inhibit the chemotactic and proliferative effects of acetylcholine. However, some researchers have raised opposing views, suggesting that ACh released by the central nervous system might confer anti-inflammatory protective effects through a distinct neuroimmune pathway (Grando 2015, Borovikova 2000). Experimental evidence has proved that low levels of ACh can inhibit histamine release, as well as activate α-7 nicotinic receptors that cause local anti-inflammatory effects (Grando 2015). ACh released by the efferent vagus nerve also reduces the level of tumor necrosis factor (TNF), a pro-inflammatory cytokine, and promotes the production of anti-inflammatory cytokines (Borovikova 2000). Antunes et al. also discovered that neostigmine, an acetylcholinesterase inhibitor, can reduce eosinophil influx and increase antioxidant defense by increasing the level of ACh in a BALB/c mice model (Antunes 2020). Collectively, these studies provide solid evidence for a cholinergic anti-inflammatory pathway (CAP), which is worth further investigation for the future discovery of viable drug targets.

Table 1: Risk factors related to lung cancer (Darby 2005)..

Risk factors	*Relative risk*	*Risk factors*	*Relative risk*
Tobacco use or exposure		**Comorbidities**	
Current smoking	20	Human Immunodeficiency virus infection	2 to 11
Former smoking	9	Chronic obstructive pulmonary disease	2 to 3.1
Secondhand smoke exposure	1.3	Tuberculosis	—
Environmental exposures		**Other**	
Asbestos	3	History of chest radiotherapy	5.9
Radon	3	Family history of lung cancer	2
Other exposures	—	History of chemotherapy	4.2
Air pollution		Older age	—
Arsenic			
Beryllium			
Beta-carotene ingestion			
Chromium			
Nickel			
Soot			

3 LUNG CANCER AND NON-SMALL CELL LUNG CANCER

Non-small cell lung cancer (NSCLC), accounting for 80% to 85% in lung cancer cases, has four main subtypes which are adenocarcinoma, squamous cell carcinoma and large cell carcinoma (Liu 2019).

Though these subtypes start from different lung cells, they are all classified as NSCLC because of the similar treatment and prognosis (Ettinger 2017). Different from small-cell lung cancer (SCLC), NSCLC tends to grow and spread slower, which is more likely to be found before spread. For instance, according to detect mutations in epidermal growth factor receptor (EGFR), recent trials have suggested that instead of chemotherapy, initial therapy with tyrosine kinase inhibitors (TKIs) may be the best choice for treating NSCLC (da Cunha Santos 2011). In addition, the use of immune checkpoint inhibitors (ICIs) has been successfully applied in clinical cancer treatments (Fan 2017). ICIs targeting programmed cell death protein 1 (PD-1) and programmed cell death protein ligand 1 (PD-L1) display apparent benefits for the treatment of advanced NSCLC (Xia 2019). We also introduce other treating options of lung cancer such as chemotherapy and radiation together with their perspectives.

3.1 Epidemiology

There are two types of lung cancer, micro-cell lung cancer, and non-small cell lung cancer (NSCLC) with the latter accounts for 85% of all lung cancer. NSCLC tends to be the toxic infection in both genders (Siegel 2019). Its mortality rate is rather high when compared with three other most common occurred cancer types (ie. colon, breast and pancreas cancer). The life-threatening risk of NSCLC is more obvious as more than a quarter of patients have died within 12 months of diagnosis. Besides, the five-year survival rate is only 17.8% (Kenfield 2008).

Among NSCLC, lamellate cell carcinoma accounts for 30%. It originates from the first generation of lamellate cells in the airway epithelial cells of the lungs. This subdivision is strongly associated with smoking (Noguchi 1995). About 40% of tumorigenesis happening in the lung is in the form of adenocarcinoma. Secretory epithelial is consisted of type II alveolar cells, where are full of mucus and other nutrients (Gavelli 2000). Morbidity of adenocarcinoma is the highest among all the cancer types happened in lung, but unlike lamellate cell carcinoma, smoking has no obvious effect on its morbidity (Stellman 1997), so as the age factors. Results have shown that the use of filters to prevent smoke from entering the lung had failed but caused deeper penetration into the lung (Xu 2014). In this scenario, the smoke becomes carcinogen, and adenocarcinoma appears. Compared with other forms of lung cancer, adenocarcinoma grows slowly and is more likely to be early detected before metastasis. Large cell cancer accounts for only 5-10% of lung cancer. There is no obvious symptom of this type of cancer or tumor growth and as a result it is usually diagnosed by chance. Bigger cells carcinomas usually start at the center of the lung and occasionally causing lymph swellings and limbs frigi (Whitrow 2003).

Table1 summarized the commonly reported risk factors of lung cancer. One of the major factors that cause the lung cancer is smoking. Increasing number of cigarettes and daily consumption is highly related with morbidity of lung cancer (Straif 2009). Non-smokers, however, still have potential risk of developing lung cancer with risk ratio ranging from 1.14 to 5.20 according to meta-analysis and general evaluation. The underlying reason is that they live with smokers (Stayner2008). According to the American Surgeon General, living with smokers can increase the risk of non-smoking lung cancer by 20-30% (Hecht 1999). Radon, a natural cancer-causing agent, is one of the leading causes of lung cancer, with an estimated 21,000 deaths from lung cancer in the United States (Darby 2005). Although Radon has been in contact with miners sometimes, there is growing concern that Radon's exposure to natural gas from uranium deposits are increasing. A series of randomized controlled trials from North America, Europe, and China have shown a 2.7-fold increase in the risk of lung cancer-related lung cancer per liter (PC).

3.2 Treating Options

Asbestos is used in industry or manufacturing in conjunction with an improvement in mesothelioma and lung cancer. The link between asbestos fiber levels has been found to be a strong indicator of lung cancer mortality (Wang 2014). As a result, the US government has implemented steps to decrease the use of asbestos in marketable and organizational programs. Additional experimental risk factors associated with lung cancer comprise the use of arsenic solvents, disclosure to beryllium and beryllium oxide; Ingredients include, nickel alloys, chromium alloys and chloroses ester (Hung 2008). The disease is more common for the individuals in the growing periods with effective strategies.

3.2.1 Visual Aided Operation

Patients in stages I, II and III of NSCLCs could have surgery to remove the tumor if it is feasible for the tumor as well as the patients. Medical imaging

detection and biopsies help surgeons to distinguish the originality of tumorigenesis and identify the patients' condition in the tumor progression. Video-enable surgery is now available in clinical practice and is popular among surgeons. During the surgery, a tiny camera wrapped in a box is placed in the body of the patient. Since a large piece of paper does not need to be cut, a sphere is removed through a piece of paper [90]. The operation criteria are created on the basis of achieving a scope that is associated with a general aim of preventing cancer.

3.2.2 Chemotherapy

Approximately 40% of patients have been diagnosed in stage IV in recent cases. The goal of treating these patients is to save their lives and reduce the incidence of disease-related complications. For the fourth level NCC, which is Cytotoxic Combination Chemotherapy, is the first line of treatment that can affect histology, age and related conditions (PS). According to the American Society of Clinical Oncology, patients with 0 or 1 PM are treated with platinum (cislatine or carbofolatin), pastazal, gemetitabine, doxtaxil, vinorelbine, erythromycin or modified. The results of four large randomized controlled trials have been applied to study platinum or carboplatin. The results of one of these studies have shown that the effects of one unit are larger than the other. The median overall recovery for these patients was approximately 8-10 months. The specific combination depends on the type and frequency of toxic effects and must be determined individually. However, patients with adonacarcinoma may benefit from permethrin. Cysteine is slightly more effective than platinum but has been proved to induce more side effects. Data from 2 PPS patients have shown that they only need one drug, which is not usually platinum. For chemotherapy, serious events should motivate agents to change. In addition, if cancer occurs, therapy should be discontinued when the disease resolves after four treatment cycles, but the treatment does not reduce the tumor. 3PS patients do not routinely use cytotoxic chemotherapy because the risk of adverse events greatly worsens their quality of life. More supportive care is generally recommended for these patients (Hung 2008).

3.2.3 Radiotherapy

Radiotherapy uses the most powerful poles to damage DNA in cancer cells. This helps to control or eliminate tumors in the body. Patients with NCCL who have had chest surgery and are not eligible for surgery may benefit from radiotherapy. Radiotherapy may be part of pain relief to improve the quality of life for patients who do not respond to surgery or chemotherapy. There are no nearby lymph nodes for the first NCs with small nodes in the lungs. Patients are treated with a procedure called SBRT. This method uses advanced coordination systems to accurately identify the tumor and ensure the correct placement of the tracking device. This allows for stronger and more focused radiation therapy (Sher 2008). For NCN, compared with the effectiveness of radiotherapy with photons, protons, and carbon ions, SBRT presented a 2-year overall life expectancy, low cost, and high patient comfort in meta-analysis. In the next stage study, environmental controls were significantly higher in patients who did not receive treatment at SBRT Level 1 NSCC in 70 untreated patients receiving SBR (Hwang 2003). However, with NCC, a non-pharmaceutical NC, patients conducted a three-pronged multidisciplinary study of SBRT toxicity and efficacy. Of the 55 patients evaluated, SBRT patients had a 55.8% survival rate in three years. In these studies, SBRT has been found to provide surgical treatment for day-to-day disease- related illnesses to environmental control and results among certain scope of patients.

3.2.4 Targeting Specific Biomarkers

It helps to improve patient survival by targeting appropriate molecular targets in private drug tumors in the NSCLC. Besides, biomarker tests often regard the quicker and effective way of occupying various instances needed to maximize the achievement of the epidermal role. There are agents that have been successfully targeted in epidermal development factor receptor (EGFR) mutations and in the restoration of anaphylactic lymphoma kinase (ALK). Through genetic testing, ROS1 and RET gene mutations, MT amplification, and other molecular changes in B-RAF, HER2, and K-RAS genes may be targeted for future treatments.

3.2.5 Activating Epidermal Growth Factor Receptor (EGFR) Gene

When EGFR is activated, it is a cellular tyrosine kinase receptor that can activate pathways associated with cell growth and proliferation. This gene carries to a larger extent the distribution of the factors that determine the mutation rate of the receptor factor. In cancer, EGFR mutations continuously trigger uncontrolled cell division. EGFR gene mutation: 10–15% of lung cancer adenocarcinoma of European

Table 2: Clinical and disease features of patients with EGFR gene (Muscat 1997).

Characteristics	Mutation arm (N = 50)	Wild-type arm (N = 50)	P value
Age, y			0.419
Mean	57.3	59.1	
Standard deviation	11.6	10.5	
Sex, No. (%)			0.016
Male	18(36.0)	30(60.0)	
Female	32(64.0)	20(40.0)	
Smoking history, No. (%)			0.043
Smoker	16(32.0)	26(52.0)	
Never smoker	34(68.0)	24(48.0)	
Histologic type, No. (%)			0.131
ADC	49(98.0)	44(88.0)	
SCC	1(2.0)	4(8.0)	
Others	0(0)	2(4.0)	
Disease stage, No. (%)			0.603
IB	8(16.0)	10(20.0)	
IV	42(84.0)	40(80.0)	
EGFR-TKI treatment, No. (%)			ND
No	3(6.0)	26(52.0)	
Yes	47(94.0)	24(48.0)	
First-line	29(58.0)	5(10.0)	
Second-line	15(30.0)	13(26.0)	
Third-line or greater	3(6.0)	6(12.0)	

and Asian origin, especially in non-smokers and in women. Although these behaviors are common, mutation testing is important for patients using targeted tyrosine kinase inhibitor therapy (Muscat 1997). The risk of exposure to EGFR tyrosine kinase inhibitors is usually these models encode the EGFR kinase domain segment. Approximately 90% of these mutations are due to 19 abrasions and a mutation of L858R point 21, which corresponds to a 70% response rate for patients receiving erlotinib or gefitinib treatment.

4 CONCLUSIONS

This paper presents the pathophysiology, current and prospective treating options for allergic rhinitis (AR) and non-small cell lung cancer (NSCLC), which represents certain types of respiratory diseases and affects distinct regions in the respiratory tract. Allergic rhinitis is characterized by oversensitive inflammatory response to an environmental factor while NSCLC is caused by genetic mutation in the lung tissue. Medical treatments are available for AR, from which many target G-protein coupled receptors and inhibit cell signaling events in the pathogenesis pathways. With the improved understanding of pathophysiology, we may find a better option for treating NSCLC instead of current treatment options such as operation, chemotherapy, and radiotherapy to reduce adverse events and improve quality of life for patients. To enhance the potency and minimize side effects of treatments, ongoing medical research on allergic rhinitis and NSCLC have identified novel therapeutic targets. New drugs differ in action mechanism as well as novel targets have been developed and identified. For allergic rhinitis, the acetylcholine-mediated cholinergic immune system has been explored for its role in generating inflammatory response, and several drugs (tiotropium, ipratropium, bencycloquidium bromide) targeting muscarinic receptors have been developed to inhibit the pro- inflammatory effect of acetylcholine. Future treatments for NSCLC may emphasize on finding a kinase inhibitor which functions by blocking a key enzyme or activating EGFR gene. Recent studies found targeting specific biomarkers and activating EGFR have been known as future treatment options of NSCLC. However, these treatment options may need more future research to address drug resistance therefore improve the outcomes in NSCLC patients.

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