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Bronchial Remodeling – Once an Asthmatic Always an Asthmatic

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ABSTRACT

Just when the man was running triumphant of having conquered the communicable diseases, the non-communicable disease that was looking in the shadow. Very steadily they garnered enough attention from people. Bronchial asthma is one such disease with a mammoth prevalence of 300 million. Taking a significant toll on the patients concerning their progressively deteriorating quality of life.

Bronchial Asthma is a chronic disorder of conducting airways, usually caused by the immunological reaction which is marked by episodic bronco-constriction due to increased airway sensitivity to a varying of stimuli, inflammation of bronchial walls, and increased mucus secretion. Asthma is a type 1 hyperactivity reaction.

Extrinsic asthma also called atopic/allergic asthma constitutes >90% of the cases. here acute immediate response is brought about by the IgE-sensitized mast cell on the mucosal surface which results in the release of histamines, leukotriene, prostaglandins, PAF, and Chemotactic factors- ECF & NSF. The phase is dominated by bronchoconstriction, mucus hyper secretion, and accumulation of eosinophil and neutrophils. There is accompanying vasodilatation and increased vascular permeability in the pulmonary circulation. The late-phase response is brought about by the mobilization of leucocytes mostly basophiles, eosinophil, and neutrophils. Intrinsic asthma on the other hand is non-atopic or non-allergic and most often in association with nasal polyp, chronic bronchitis, or aspirin hypersensitivity.

Bronchial Asthma (BA) is a chronic disease notorious for relentless progression despite regular treatment. The chronicity of the disease results in some structural changes that occur in both small and large airways. This is called the Remodeling of airways.

Keywords: *Bronchial Asthma, Airway remodeling, Hypersensitivity, Allergens.*

INTRODUCTION

As Bronchial Asthma BA is a chronic inflammatory disease of the airways, it is characterized by an episodic breathlessness accompanied by wheeze, cough and chest tightness. Affecting mainly the young adults, it incapacitates the individuals in their most productive years of life. The disease has a wide spectrum of phenotype and hosts heterogeneous nature emanating a varying presentation in terms of disease frequency, severity, and prognosis. Being treated with sympathomimetic bronchodilators and inhaled corticosteroids successfully enough but that

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doesn't halt the disease progression. To add to trouble the adverse effects associated with the long-term use of these drugs can cause more menace than the disease itself [1].

Once an Asthmatic, always an Asthmatic.

BA is a chronic disease which does not show complete remission however is notorious for increasing in severity with time. One important factor contributing to this is **airway remodeling** in asthmatics [2].

Airway Remodeling [3]

These are the structural changes observed in the airways of asthmatics. They have been implicated in progressive airway hyper reactivity and their irreversible narrowing. These include

1) Sub epithelial fibrosis
2) Epithelial shedding
3) Hyperplasia of mucus glands and goblet cells
4) Hypertrophy of smooth muscle cells
5) Loss of integrity of cartilage
6) Angiogenesis.

A few studies suggest that the early institution of inhaled corticosteroid may reduce the severity of remodeling and preserve the lung function.

as the disease severity increases, there is a concurrent rise in the local secretion of growth factors that results in mucus gland hypertrophy, smooth muscle proliferation, angiogenesis, fibrosis, and Nerve proliferation. Airway remodeling condition the following[4]

1) Epithelial alteration
2) Sub epithelial fibrosis
3) Increased smooth muscle mass
4) Goblet cell and mucus gland hyperplasia
5) Angiogenesis
6) Loss of cartilage integrity

The single most important factor governing the process of remodeling is the elaboration of various inflammatory mediators.

TH2 cells play an important role in inflammation and the elaboration of inflammatory mediators. They secrete cytokine IL4, IL5, IL9, IL13. TGF B (beta), IL11, IL 17. All these mediator promoter remodeling infiltrating cells such as eosinophil, neutrophils and mast cells interact with the resident cells of airways such as fibroblast, smooth muscle cells, neuronal cells, epithelial cells *etc*. the combined interaction of these cells and the plethora of cytokines, enzymes, metabolites and growth factors, recall in the change that occur in the airways.

I4- stimulates IgE preclusion. Il5 active locally recruited eosinophil"s, IL13 stimulate mucus secretion from bronchial sub mucosal glands and promotes IgE production by B cells. Eosinophils play a major role in remodeling. They are responsible for the release of various

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enzymes reactive oxygen species cytokines and chromatins, cystinyl, leukotriene, eicosanoids. They help in the release of TGF B.

TGF B is a potent profibrotic and anti-inflammatory cytokine, it has a stimulatory effect on the fibroblast which helps in the synthesis and secretion of type I & type 2 collagen fibroneclin, vitronectin, tenascin and various proteoglycans TGF B decrease the production of enzymes that degrade extracellular matrix and promote the synthesis of inhibitors of the enzymes the result favors fibrosis.

Epithelial Alteration [5]

The respiratory epithelium is a psudostratification ciliated columnar type with the presence of a few goblet cells, integrity of the epithelium is of utmost importance for optimal functioning. A breach in the epithelium results in the occurrence of higher properly of the allergen insult thereby promoting more inflammation and aggravating the process of increased epithelial damage hence directly co-relates with the progressive airway hyper reactivity changes occurring due to remodeling including the shedding of cilia and functional goblet hyperplasia resulting in increased mucus secretion there is an overexpression of epithelial growth factors receptor and up regulation of release of growth factor. Reticular basement membrane thickening is also seen on asthmatic airways.

Sub Epithelial Fibrosis [6]

Sub epithelial fibrosis occurs in the lamia reticular i.e. just below the basement membrane.The inflammatory mediatory mainly TGF B results in the increased reposition of extracellular membrane protein including collagen I III V; fibroneclin, tenascin, luminine , and biglycan there is concurrent recruitment of neutrophils, macrophages which along with interstitial cells elaborate protease and anti-protease. The level of these enzymes favors a profibrotic balance promoting fibrosis also there is an imbalance between the production and degradation of extracellular matrix. The entire process results in sub-epithelial fibrosis which contributes to the increase in the airway thickness seen in Asthmatics.

Increase Smooth Muscle Cell Mass [7]

Normally airway contains a minimal amount of smooth muscle cells that regulate broncho construction and bronchodilation in asthmatics however due to remodeling there is an increase in the smooth muscle mass as a result of both hyperplasia and hypertrophy. Smooth muscle cells are secretory in function they are capable of releasing proinflammatory cytokines, chemokines, and extracellular matrix proteins. Smooth muscles have proliferation capacity as evidenced by their hypertrophy and hyperplasia they can even migrate to the sub-epithelial area smooth muscle hypertrophy and hyperplasia are directly proportional to the clinical severity of the disease with The increasing smooth muscle cell mass the capacity of bronchodilatation is compromised accompanied with ready and effective bronchoconstriction which triggered.

Angiogenesis [8]

Angiogenesis refers to the formation of new blood vessels or simply an increase in the size of the airway wall vessels. This results in increased airway edema and pronounced chest congestion. The increased vascularity is due to the over-expression of vascular endothelial growth factor VEGF along with fibroblast growth factor is considered relevant to angiogenesis.

Angiogenesis results in airway edema and hence a significant reduction in airway caliber. Also, it further deteriorates the situation by delivering more and more inflammatory and remodeling mediators into the airway wall.

Goblet Cell and Mucus Gland Hyperplasia [9]

Goblet cell and mucus gland hyperplasia occur in response to ongoing chronic inflammation and elaboration of various inflammatory mediators. There are two factors that result in increased sputum production. They also contribute to an increase in the thickness of the airway wall resulting in their narrowing.

Loss of Cartilage Integrity [10]

The airway contains hyaline cartilage that provides caliber to the airways and also keeps bronchoconstriction under check. It determines the stiffness and integrity of the airway wall. However, in an activated airway, a decrease in cartilaginous volume and an increase in cartilage proteoglycan degradation are seen. This result is reduced cartilage integrity which paves the way for powerful bronchoconstriction which is amplified by increased smooth muscle mass.

CONCLUSION

The components of airway remodeling viz sub epithelial fibrosis increase in smooth muscle mass, mucus gland hyperplasia, and angiogenesis result in further narrowing of the airway coupled with enhanced bronchoconstriction. They occur over line and are a measure of the duration and severity of the illness. It is a phenomenon from which there is no escape. However, a few studies claim that as the remodeling changes are mainly due to ongoing inflammation early use of inhaled corticosteroids can not only halt the process of remodeling but also reverse it. The final result is however inconclusive further research into asthmatic individuals with a prime focus on remodeling and methods to control it could be of great benefit to improve the quality of the life of an individual.

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