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Progression of Clinical Chronic Bronchitis Definable as Parenchymal Emphysematous Lesions

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Abstract: In chronic obstructive lung disease, an evolving dynamic mismatch of capillary bed perfusion with ventilation of airspaces appears possibly symptomatic of a central process of inflammatory injury to small airways early in childhood. Subsequent development of the chronic obstructive lung disease simply constitutes an endresult of multiple progressive lesions that determine an association between hypoxia and carbon dioxide retention on the one hand and a subsequent evolving consequence of repeated acute attacks of chronic bronchitis. A complex of acute infections in a patient suffering from chronic bronchitis adds to the progression of emphysematous changes and concurrent small airways disease characteristic of clinical disease that is definable as anatomic parenchymal lung disease.

Key words: Clinical chronic, lung disease

CHRONIC AIRWAYS OBSTRUCTION

Chronic obstructive lung disease denotes a progressive occlusion especially of the small airways arising as a result of extrinsic pressure together with accumulation of intraluminal mucus or mucopus. The airways would present a combined aggregation of mucus, mucopus and inflammatory cells that are associated with a tendency for bronchospasm and other allergic manifestations.

Chronic airways obstruction is reflected in a reduced forced expiratory volume in one second that evolves particularly in terms of the contributing role of the emphysematous changes to the airway occlusion. Small airway obstruction is a primary site of progression of changes that implicate an inflammatory role that promotes injury to the walls of the airways. Injury to airways would promote collapse particularly of the small airways due to a state of airtightness of the lungs.

Injury to the walls of small airways might indeed constitute an essential accompanying factor in the evolving airway obstruction in a manner that is only variably related to deposition of fibrous tissue in the walls. Indeed, one might speak of a range of subsequent events on itial stage of collapsible small airways further contributed by a state of increasing emphysematous change around terminal bronchioles[1].

The relationship of chronic bronchitis with emphysema in many patients with chronic obstructive lung disease bespeaks for a progression arising in terms of injury to the walls of the small airways. The increased number of goblet cells in the mucosa correlates with increased submucosal gland size in a manner relative to accompanying production of inflammatory cellular exudate and edema.

AGGREGATE PHENOMENA

One might speak of whole aggregate phenomena that demarcate regions of injury to airways that further extend to involve proximal major airways as well[2]. Elastic recoil is decreased in patients with emphysema and this phenomenon would reflect a constitutional upset in the development of ineffective expiration of air that converts the lungs to further emphysematous expansion. The formalization of the emphysematous state as an injury to the alveolar walls attests to a transformation of small airways obstruction to bronchiolar collapse in further promotion of injury to their walls.

Chronic bronchitis is particularly associated with chronic smoking[3] or an exposure to atmospheric pollution such as coal dust or industrial particulate matter[4].

Such particulate exposure would represent a progression that promotes injury based primarily on

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collapse of small airways. Indeed, one might speak of subsequent events such as bulla formation and fibrosis in the walls of bronchioles as evidence of a progression of the obstructive airways disease. It is in terms consistent with such injury that inflammation constitutes a representative pathway of aggregate injury to multiple tissue components of the lung parenchyma and of the airways.

A strict concept of aggregate tissue injury would constitute a fully representative progression of pathways that further compromise the lung tissue[5]. Indeed, strict consideration of the degree of airway patency contributed to by elastic recoil of lung tissue would constitute a primary consideration in the evolving injury as finally represented by a combined lesion of chronic bronchitis and emphysema. Such a combined lesion is complicated by a clinically defined state of chronic mucus production with an anatomic lesion of airway obstruction due to expansion of distal airways accompanied by destruction of alveolar septa.

ALVEOLAR SEPTA

The destroyed alveolar septa in emphysema would represent progression of lesions consistent with the continued injury particularly to the walls of the small airways. Such a picture would integrally combine injury to alveolar septal walls with injury of small airways in an aggregate lesion pattern of distribution in lungs affected by chronic obstructive lung disease. The chronicity in production of injury to both alveolar septa and walls of small airways represents a continuation of processes represented and manifested clinically by a reduced forced expiratory volume in one second. One might view the development of chronic obstructive lung disease as a formalization of various lesions that integrally progress in terms of injury to the walls of small airways in the first instance.

Indeed, a redefinition of events that primarily initiate as lesions in the walls of terminal and respiratory bronchioles would then progress as obstructive lung disease in terms of the added contributing role of collapsed alveolar septa of emphysematous type.

COMPLEMENTARY PROGRESSION

Complementary progression of multiple lesions of primarily inflammatory type would constitute a diversification of origin in the development of an integral lesion that structurally disorganizes primarily the airways[6]. Secondary alveolar septal destruction and parenchymal expansion of the alveolar ducts, sacs and spaces would constitute a further developmental stage in pathologic transformation of the tissue injury.

A combined integral approach to the chronic bronchitic patient with emphysema would constitute a delineation of a single lesion primarily arising in the walls of small airways and in a manner constituted by a progression both distally to septal airspaces and proximally to major airways. One might recognize a representative array of secondary lesions in the evolution of such injury that is reflected in loss of elastic recoil and in post-expiratory expansion of the pulmonary airspaces[7].

ANTIPROTEASE ACTIVITY

Enzyme anti-protease activity constitutes a conceptual generalization of possible protective measure against the inflammatory cell activity of macrophages and neutrophils in particular, within the added context of allergic phenomena[8] as elicited by the eosinophil and of infection[9]. Dynamics of evolution of chronic obstructive airways disease represents a full array of differential distinguishing features that further redefine the subsequent course clinically and pathologically. One might further recognize primary, secondary and subsequent events that modify in turn even pathogenic expression of mechanistic pathways of obstructive versus destructive lesions primarily affecting bronchioles.

SELECTIVE INJURY

A selective injury to bronchioles appears distinct from the loss of elastin in the lung parenchyma of emphysematous patients. It appears that a disturbed ratio of proteases to protease inhibitor reflects only one aspect of a fundamental abnormality driven by an influx of macrophages and also neutrophils into the lungs[10]. The destruction in particular of the vascular capillary bed is conducive to development of right ventricular hypertrophy. In a sense, a whole array of hypoxic effects including secondary polycythemia combines with cor pulmonale to induce the component ventilatory failure that characterizes the history of most patients with chronic obstructive lung disease.

An essential aspect represents the constitutive inter-relationship between airway obstruction and lung parenchymal disease[11]. It would appear that emphysematous lung changes are strictly involved in the pathogenesis of an airway obstruction that evolves progressively, concurrent with persistent exposure to cigarette smoke and particulate pollution[12]. It would indeed be significant to consider the evolution of

emphysematous change as a critical feature in defining pathogenesis of an airway obstruction symptomatic of inflammatory bouts of chronic bronchitis.

DUAL COMPLEX DISORDER

Chronic bronchitis would represent a dual complex disorder consisting of both airway obstruction and involvement of the bronchiolar wall in terms of inflammation and excessive mucus production. It would appear significant to recognize a complex promotion of pathologic effects that induces parenchymal loss of elastin. Moderate to severe disease may not be a mere progression of mild chronic obstructive lung disease[13].

A central issue would apply to the sparing of some heavy cigarette smokers from the progressive effects of emphysema and chronic bronchitis[14]. A heterogeneous combination of effects would promote the initiation of parenchymatous emphysematous lesions that concurrently induce chronic bronchitis to evolve as an accompanying pathology[15]. One might recognize an integral complex disorder of chronic obstructive lung disease within the essential context of emphysematous parenchymal lesions. In this sense, perhaps, a relative effect of loss of elastin with dilation of alveolar ducts and sacs and alveolar spaces is symptomatic of disturbed ventilatory mechanics that strictly define chronic obstructive lung disease.

In defining such parenchymal disease as a strictly critical controlling factor in inducing chronic airways disease one might recognize the perpetuation of an initial lesion that primarily compromises the small airways, but that is secondarily reflected in inflammation evolving also in the more proximal airways[16].

Such a complex setting for airways obstruction is particularly significant as a correlate system of involvement in the loss of vascularity of the lung parenchyma in most patients with emphysema. Parenchymal destruction would represent an emphysematous redefinition of onset mechanics that progress also as chronic bronchitis in many patients with chronic obstructive lung disease.

ANATOMIC LINK

The difficulty in recognizing an anatomic link basis between repeated clinical bouts of chronic bronchitis and parenchymal loss of vascular bed perfusion in emphysematous lung tissue would reflect disturbed dynamics in evolution of obstructive features in ventilatory/perfusion mismatch. One might recognize the loss of perfusion of lung parenchyma as indicative not only of elastase activity but also of disruption of vascular wall integrity.

An interactivity relative to destruction of multiple capillary beds in emphysematous lungs is indicative of the perpetuation of chronic inflammatory activity extending along small and also more proximal airways in patients who invariably smoke heavily. The hypoxic microenvironment that induces intense vasoconstriction in lung parenchyma in patients suffering from chronic obstructive lung disease would evolve particularly with the onset and progression of retention of carbon dioxide in patients with accompanying significant chronic bronchitis. One might recognize a complex inter-relationship between hypoxia and carbon dioxide retention symptomatic of the precipitation of respiratory failure. The onset of bouts of respiratory failure indicates a poor prognosis for many patients within a period of only a few years of onset.

PROGRESSION

The protease inhibitor status in individual patients indicates a discriminatory influence determining progression rather than simply initiation of lung and airway pathology in many patients presenting with a significant emphysema or chronic obstructive lung disease[17]. The sparing of a significant number of heavy cigarette smokers from the effects of chronic obstructive lung disease may in part lie with effective relative activity of protease inhibitor in such patients.

In addition, there might evolve a preservation of capillary bed integrity that critically safeguards against the onset of hypoxic vasoconstriction in lung parenchyma.

In terms of such definition, it would be significant to better redefine emphysematous lung pathology in terms of a hypoxia that progresses in terms of a secondary retention of carbon dioxide. Indeed, loss of capillary beds in lung parenchyma constitutes an integral reflection of the onset and progression of a disturbance in dynamics of airflow due to accompanying emphysematous anatomic changes. An associated destruction of alveolar septa is symptomatic of a progression in airway obstruction that initially progresses as hypoxia and subsequently includes significant carbon dioxide retention in many patients with chronic obstructive lung disease.

INFLAMMATION

A concept of inflammation with subsequent repair in the pathogenesis of emphysematous parenchymal change is suggestive of destruction of alveolar septa in the

absence however of significant fibrosis. Such a concept might indicate a pathogenetic link to secondary bacterial infections considered important in the repeated relapses of chronic bronchitis in many patients with chronic obstructive lung disease.

One might speak of ongoing dynamics relative to failed resolution of inflammation in both the lung parenchyma and in airways, particularly the terminal and respiratory bronchioles[18]. In such terms, the onset and progression of inflammation would concurrently evolve with the relative impaired action of protease inhibitor in many heavy cigarette smokers.

In such terms, perhaps, it would be significant to recognize the evolution of small airways disease in terms especially of parenchymally derived depletion of capillary beds. Hypoxia and secondary polycythemia in a patient with right ventricular hypertrophy or cor pulmonale would evolve in terms of a susceptibility to airways disease in its own right, particularly precipitated by anatomic mechanics of the parenchymal emphysematous changes.

A concept that is strictly clinically defining in terms of chronic bronchitis contrasts with an anatomic characterization of the emphysematous lung features. In terms of such a dually contrasting approach to an integrally evolving chronic obstructive lung disease entity there would arise a simple redefinition of dynamics of hypoxic injury to alveolar lining cells and a particular susceptibility to airway inflammation and infection[19].

In terms both inclusive with regard to onset of the airways obstruction and also conducive to further repeated attacks of chronic bronchitis one might recognize a progressive course centered on the small airways pathology in further increasing both proximal airways disease and parenchymal lung destruction[20]. Oxidative stress and vascular endothelial growth factor pathway appear implicated[21].

Mucus hypersecretion appears a pivotal aspect in progression of repeated episodes of chronic bronchitis beyond simple redefinition of onset of the airways disease. It would prove significant to consider modes of potentiation of events that in multiple ways promote inflammatory reactivity in bronchioles and even more distally[22]. It is perhaps the absence of septal fibrosis in states of centrilobular and paraseptal emphysema that contributes to the evolving consequences of a disease that depends pathogenically largely on extensive loss of regional capillary beds. The dissociation of capillary bed perfusion and ventilation with mismatching of airflow in the alveolar spaces in relation to unventilated lung regions might imply a progression derived largely from consequences of such hypoxia and carbon dioxide retention[23].

EVOLVING INJURY

In terms borne out by evolving consequences of injury to lung parenchyma and of small airways inflammation that extends both proximally in the airways and also distally in the lung parenchyma, there would develop a full array of features determined almost exclusively by dynamics of progression of inflammatory reactivity[24]. The repeated bouts of chronic bronchitis predispose to and also enhance progression of injury to airways in terms largely conducive to eventual mismatch between ventilation and capillary bed perfusion of the lungs.

The diffusion distance between the capillary and the alveolar space appears intimately reflective of an essential abnormality largely independent of fibrosis of alveolar septa or interstitium. Decreased levels of vascualar endothelial growth factor are related to impaired airflow and alveolar injury in patients with emphysema[25]. One might recognize an inflammatory reactivity that both predetermines patient susceptibility to parenchymal lung injury and to consequential progression as repeated bouts of chronic bronchitis.

SECONDARY INFECTIONS

Secondary infections in chronic bronchitic patients constitutes another aspect in the development of susceptibility patterns in patients who otherwise chronically suffer from a progressive mismatch between capillary perfusion of unaerated alveoli and the nonperfusion of aerated alveoli[26].

A central operative index of nonaeration appears however only another aspect of consequences of a lung lesion that progresses as alveolar septal collapse[27]. In spite of the confluence of alveolar spaces, disruption of alveolar septa would constitute a variability of involvement dependent on a number of complex pathways. Decreased serum C4 complement correlates with degree of emphysema in chronic bronchitic patients[28]. In this regard, airways obstruction and alveolar septal destruction are conducive to the precipitation of acute attacks of bronchitis. However, the full impact of an accumulative series of acute bronchitis attacks would appear indicative of a propensity for repeated injury to the bronchial and bronchiolar wall in terms related to dynamics of hypoxia and carbon dioxide retention.

AIRFLOW LIMITATION

Airflow limitation appears particularly induced by narrowing of airways less than 2 mm in diameter.

Early childhood infection in association particularly with heavy cigarette smoking and exposure to atmospheric pollution later in life appear critically determinant in the production of a mucous gland hyperplasia and goblet cell metaplasia accompanied by inflammation. Infections are particularly predisposed to in these patients in a manner promoting chronicity of the bronchitic inflammation. Impaired mucociliary clearance and mucous plugging appear conducive to refractory forms of chronic bronchitis attacks of acute infection.

EARLY CHILDHOOD INFECTION

Early childhood exposure to irritants or infection in the development of subsequent chronic airways obstruction disease would be indicative of a variety of injuries extending anatomically from large to small airways disease to nonfibrotic disruption of the alveolar septa. The role of inflammation in such a complex of injuries appears centrally operative in provoking a progression of subsequent obstruction of airways to ongoing parenchymal emphysematous change in its own right as by apoptosis[29]. The role of obstruction of small airways in inducing distension of alveolar spaces during the expiratory phase may be centrally implicated in the development of ongoing attacks of inflammation centered on distal airways[30].

.Acute attacks of chronic bronchitis represent a complex interaction of the macrophage infiltrate admixed with a significant component of neutrophils in engendering enzymatic digestion of elastin in vascular walls, bronchiolar walls and in alveolar septa.

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