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Preneoplasia and Atypical Adenomatous Hyperplasia (AAH) in Peripheral lung Parenchyma

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Adenomatous hyperplasia of the peripheral lung has been suggested to be a preneoplastic lesion leading to peripherally localized lung carcinomas. The paucity of data about cellular and vascular characteristics of this lesion in comparison to normal lung prompted this investigation.
Given the assumed significance of the hyperplasia for carcinoma development, we carried out a retrospective analysis to evaluate the expression and binding capacities of a panel of immuno/glycohistochemical markers with emphasis on endogenous lectins. In detail, the markers were selected to offer an insight into the relationship of AAH to changes in immune factors with relevance of p53-dependent growth regulation (macrophage migration inhibitory factor (MIF), interleukin-2 (IL-2)), in the expression of endogenous lectins with relevance for growth control and cell adhesion/migration (galectin-1 (Gal-1), galectin-3 (Gal-3), galectin-7 (Gal-7) and their biotinylated antibodies, heparin-binding lectin (HBL)), in the arrangement of vascularization (CD34), in proliferation (Ki-67 (MIB-1)) and in expression of apoptosis-associated proteins (BCL-2). We also measured the structural arrangements of alveolar lining cells in relation to expression/intensity of binding capacities of applied substances in search for a detailed evaluation of AAH in comparison to normal lung parenchyma.

Statistically significantly increased levels of expression of anti-apoptotic BCL-2, macrophage migration inhibitory factor (MIF) capable to suppress p53 activities, heparin-binding lectin, interleukin-2, galectin-1 and of binding capacities for the endogenous lectins galectins-1, -3 and -7 were determined. In addition, alveolar-lining cells, which express these markers, formed spatial clusters, which harbor different levels of structural entropy. AAH displayed an increased level of vascularization characterized by regular size and increased number of newly formed vessels.

Chronic obstructive pulmonary disease (COPD) was the most common additional disease observed in this study, though there was no statistical significant correlation between COPD and the development of preneoplastic lesions in human lung. The analysis of the clinical data

revealed an association of the development of preneoplastic lesions of human lung with exposure to external noxes, notably asbestos and cigarette smoking. A strong dose-response effect of asbestos exposure as well as a synergistic and multiplicative effect of smoking has been shown to increase the risk of AAH lesions. Development of preneoplastic lesions differed not significantly with age, sex and familial history.

Thus, this study highlights the clinicopathological characteristics of AAH lesions, showing them to be significantly associated with adenocarcinoma and multiple primary carcinoma of the lung and suggesting common factors in the histogenesis of preneoplastic lesions of human lung and preceding malignancy.