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Title: Increased numbers of alveolar mast cells with an altered phenotype are linked to peripheral airway remodelling in patients with allergic asthma

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Body: BACKGROUND: A significant proportion of asthmatics have symptoms despite treatment with inhaled corticosteroids. Recent studies have revealed an expansion of highly FcεRI-expressing alveolar mast cells (MCs) in asthma. The aims were to further phenotype alveolar MCs and explore their connection to peripheral tissue remodelling in different asthma cohorts. METHODS: Bronchial and transbronchial biopsies from controls, patients with rhinitis, mild and uncontrolled asthma were processed for immunohistochemical identification of MC subtypes and expression of pro-fibrotic markers. MC alteration in relation to tissue remodelling (density of collagen, versican, decorin and biglycan) in peripheral lung was studied. RESULTS: The alveolar parenchyma (AP) in uncontrolled asthmatics had increased densities of MC_{TC} (p=0.05) and MC_T (p=0.003). The expression of FcεRI on alveolar MCs was increased in mild (p=0.01) and uncontrolled (p<0.001) asthma compared to controls. The density of collagen (p=0.01) and decorin (p=0.03) was significantly increased in AP of uncontrolled asthmatics compared to controls. The number of alveolar MC_{TC} in the uncontrolled asthmatics was positively correlated to the density of collagen in the AP (rs=0.71, p=0.03). MCs in the AP of asthmatics expressed increased levels of pro-fibrotic markers. CONCLUSIONS: Our data show that the alveolar region in patients with asthma is infiltrated by activated MCs that correlate to increased alveolar matrix deposition. This may reflect an important involvement of MCs in the peripheral inflammation in asthma and underscores the need to target peripheral lung inflammation in this patient group.