Prevalence of preclinical AA-amyloidosis in CF patients with chronic P. aeruginosa infection

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Objectives: AA-amyloidosis is a known complication of diseases associated with chronic inflammation and often leads to renal insufficiency. Several case reports of CF patients with AA-amyloidosis have been published but no systematic studies have been performed. Therefore, aim of our study was to determine the prevalence of preclinical AA-amyloidosis in CF patients with chronic P. aeruginosa infection.

Methods: 80 patients older than 14 years chronically infected with P. aeruginosa were included. A fine needle subcutaneous fat aspiration was stained with Congo red and examined in bright light, in polarized light and in fluorescent light. If amyloid was detected, classification was performed by immunohistochemistry and/or amino acid sequencing.

Results: All biopsies were performed without complications and were suitable for examination. Amyloid could be detected in three out of the 80 biopsies. One of these patients suffered from renal insufficiency due to AA-amyloidosis as detected also by renal biopsy. The extracted amyloid fibril protein of another patient was of insulin origin resulting from s.c. insulin treatment of diabetes mellitus for six years. The biopsy of the third patient showed small amounts of amyloid in the first but not in the second biopsy (amyloid-subtype not classified) without presenting clinical signs for AA-amyloidosis indicating one case of preclinical amyloidosis.

Conclusion: In our study, we could only detect one patient with preclinical amyloidosis. AA-amyloidosis should not be confused with the locally insulin-induced amyloid in fatty tissue in insulin-treated diabetes mellitus.

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Increased susceptibility to allergic airway inflammation in a murine model of cystic fibrosis lung disease

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Increased airway Na+ absorption is a characteristic abnormality of cystic fibrosis (CF) airways and causes CF-like lung disease in [βENaC-Tg (Tg)] mice. Recent studies demonstrated that juvenile [βENaC-Tg mice also exhibit spontaneous allergic airway inflammation. We hypothesized that airway surface hydration in [βENaC-Tg mice causes increased susceptibility for allergic airway inflammation due to reduced pulmonary clearance of inhaled allergens. To test this hypothesis, we induced allergic airway inflammation by repeated intratracheal instillations of Aspergillus fumigatus extract (Af), i.e. natural aeroallergen, and compared total and differential cell counts in bronchoalveolar lavage, pulmonary IL-13 expression, and airway morphology in [βENaC-Tg mice with wild-type littermates. We demonstrate that elevation of airway eosinophils and pulmonary IL-13 caused by intrapulmonary exposure to Af are significantly increased in [βENaC-Tg mice compared to wild-type controls. Further, we show that genetic deletion of Stat6 critical for Th-2 signaling protects [βENaC-Tg mice from airway eosinophilia, elevated IL-13, goblet cell metaplasia and airway mucus obstruction. Our studies demonstrate that airway surface dehydration, characteristic of CF airways, plays a critical role in the pathogenesis of Stat6-dependent allergic airway inflammation. These findings are consistent with a high incidence of allergic bronchopulmonary aspergillosis (ABPA) and confounding allergic airway inflammation in CF patients.

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