PROTEASES-ANTIPROTEASES IMBALANCE IN COMORBIDITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND CHRONIC PANCREATITIS

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Background: COPD is a major worldwide problem with marked underdiagnosis prevalence. COPD often coexists with other diseases (comorbidities) that may have a significant impact on prognosis. Despite cigarette smoke has been identified as a major cause of COPD, it is not clear why clinical COPD develops in only a minority – in 15% of smokers. Genetic predisposition comes to mind as a possible explanation for this phenomenon. Alpha-1-antitrypsin (A1AT) deficiency is one of the most common inherited disorders which characterized by a low serum level of A1AT, which predisposes individuals to early-onset pulmonary disease. However A1AT deficiency is still an under-recognized condition. A1AT deficiency results in an imbalance between circulating proteases and protease inhibitor which is thought to play role in the development of oxidative stress, systemic inflammation and tissue injury. It is well-known that an imbalance between proteases and antiproteases is the central factor of pathogenesis of pancreatitis. It seems reasonable to postulate a role for A1AT in prevention protease-induced damage of pancreas in COPD patients. **Aim:** To determine the role of A1AT serum levels and genotypes for the course of comorbidity of COPD and CP. **Methods:** 21 patients with the comorbidity of COPD and CP (1st group) had been studied compared with a group of 89 patients with COPD (2nd group). There were 27 (24,54%) women and 83 (75,46%) men, aged 26-91 (average 54,7±2,1 years). Among the patients of 1st group there were 14 smokers (66,67%), average number of packs/years amounted to 34,6±3,2. Tobacco consumption in subjects of 2nd group was more than those of 1st group - 65 smokers (73,03%) and 39,8±3,6 packs/years, respectively. Serum concentrations of A1AT, C-RP and amylase were measured; DNA was extracted from peripheral blood (using Dry Blood Spots), genotyping of S and Z deficiency alleles' was performed by polymerase chain reaction method; spirometry, X-ray, CT, sputum analysis, USG, coprology were also performed. **Results:** In 1st group mild stage of COPD was diagnosed in 2 patients (9,52%), moderate in 9 (42,86%) while severe in 7 subjects (33,33%) and very severe in 3 (14,28%). In 2nd group these data are 18 (20,22%), 39 (43,82%), 28 (31,46%) and 4 (4,49%), respectively. Two patients (9,52%) of 1st group were heterozygous for an A1AT deficiency allele (1 for S allele and 1 for Z allele). In 2nd group the genotype Non-S,Non-Z was significantly more prevalent – in 87 patients (97,75%, $p < 0,01$), while the genotype Non-S, Z was revealed in 2 subjects (2,25%). In respect to A1AT serum concentrations in 1st group there were one patient (4,76%) with low A1AT concentration (below 80 mg/dL), three (14,28%)- with intermediate (80-100 mg/dL) and 17 (80,95%) with normal levels. In 2nd group in majority of subjects (97,75%) A1AT was within normal limits, one (1,12%) had intermediate and one (1,12%) low level. **Conclusions:** Comorbidities occur frequently in COPD patients, and should be actively looked for and treated appropriately if present. Our study suggests a moderating, but not predominant, role of A1AT variants in the course of COPD combined with CP.