27th ECCMID Vienna, Austria 22 – 25 April 2017

The congress of ESCMID

Session: OS185 Immunity and immunogenetics of infections in immunocompromised hosts

Category: 10a. Host genetics: infection susceptibility & immunodeficiency

25 April 2017, 11:54 - 12:04
OS0901

Innate and adaptive immune defects in chronic pulmonary aspergillosis

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Background: Chronic pulmonary aspergillosis (CPA) is a progressive debilitating infection that affects immunocompetent or subtly immunocompromised individuals usually with underlying structural lung disease. The aim of this study was to evaluate the expression of T-cell, B-cell and natural killer cell biomarkers and immunologic homeostasis in correlation with underlying conditions and severity of disease in a large population of CPA patients.

Material/methods: We retrospectively evaluated 144 patients with the diagnosis of CPA at the National Aspergillosis Centre, Manchester, UK. Patients with complete medical and radiological records, total and differential white cell counts and a complete panel of CD3, CD4, CD8, CD19 and CD56 lymphocyte subsets were included in this study.

Results: Eighty-five (59%) patients were male with a median age of 60 (22-84) years. Eighty-four (58%) patients had lymphocytopenia. CD3, CD4, CD8, CD19, and lymphocytes were significantly correlated (Spearman's rho (p) ranged from 0.42 to 0.92, all p <0.001). Six (4%) patients had lymphopenia in the entire five CD variables. There were 62 (43%) patients with low

CD56 and 62 (43%) patients with low CD19. Ten (7%) patients had isolated CD19 lymphopenia, 18 (13%) had isolated CD56 lymphopenia, and 15 (10%) had combined CD19 and CD56 lymphopenia only. Forty-eight (33%) patients had low CD3 and 46 (32%) had low CD8 counts. Twenty-five (17%) patients had low CD4, 15 (10%) of whom had severe CD4 lymphopenia (absolute CD4 counts <200/μl). None of the 144 patients had isolated CD3 and/or CD4 lymphopenia. Sixty-eight (47%) patients had CD4:CD8 ratio above 1.9. Multivariable logistic regression showed statistically significant independent associations between: Low CD19 and pulmonary sarcoidosis (OR, 5.53; 95% CI, 1.43-21.33; p=0.013), and emphysema (OR, 4.58; 95% CI; 1.36-15.38; p=0.014). Low CD56 and bronchiectasis (OR, 0.27; 95% CI, 0.10-0.77; p=0.014). Low CD3 and multicavitary CPA disease (OR, 2.95; 95% CI, 1.30-6.72; p=0.010), and pulmonary sarcoidosis (OR, 4.94; 95% CI, 1.39-17.57; p=0.014).

Conclusions: Several subtle immune defects are found in chronic pulmonary aspergillosis. A low CD3 count may be a risk factor for more extensive disease. Patients with sarcoidosis may be at risk of CPA due to persistent effects of immunosuppressive therapy on the immune system. This study is, to the best of our knowledge, the first of its kind to elucidate evidence of considerable immune defects, affecting both the innate and adaptive pathway, in a large population of patients with chronic pulmonary aspergillosis.