P79
Predicting relapse in granulomatosis with polyangiitis: The role of biomarkers

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Introduction.– Granulomatosis with polyangiitis (GPA) is a small vessel vasculitis which can cause a severe systemic disease. The use of biomarkers to predict disease relapse was explored.

Methods.– Thirty patients with GPA who had experienced at least one relapse, with a total of 55 individual relapse events necessitating potent immunosuppression, and a control group of 11 patients with GPA who had not experienced a relapse were selected. The level of anti-neutrophil cytoplasmic antibodies (cANCA), proteinase 3 (PR3), white cell count (WCC), neutrophil count, lymphocyte count, monocyte count, C-reactive protein (CRP) and creatinine were assessed for any association with relapse. A total of 13,288 tests were analysed, including 1438cANCA results. The clinical yield was calculated for each marker. Remission values were compared between the cohorts. Changes from remission values in the six months prior to relapse were analysed.

Results.– Clinical yields were higher with a greater increase from remission values: a neutrophil count and cANCA titre of more than twice the average remission values were associated with relapse within six months in 67 and 32% of cases, respectively, whereas, this was 26 and 19% for a less than two-fold increase. Remission values for most of the biomarkers were higher in the relapse group, for example average WCC was 7.6 (± 2.0) for the relapse group and 6.3 (± 1.7) for the controls.

Conclusion.– A number of the biomarkers showed promise for use in predicting a relapse. None were sufficiently correlated to the relapse events to warrant use as a sole predictor of relapse. They may be of use when trying to evaluate the risk: reward ratio of commencing cytotoxic therapy.

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P80
Circulating gamma delta T cells are significantly reduced in granulomatosis with polyangiitis

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Introduction.– Granulomatosis with polyangiitis (GPA) is a systemic autoimmune disease affecting small blood vessels leading to tissue damage. The pathogenesis of the disease is unclear and the specific contribution of lymphocytes remains to be clarified. In this study extensive phenotyping of lymphocyte subsets was undertaken and this included investigation of γδ T cells, an innate-like T lymphocyte population.

Methods.– Multicolour flow cytometry was used to phenotype lymphocytes of GPA patients (n = 33) and healthy controls (n = 14). Lymphocyte subsets analysed included γδ T cell cytotoxic and T helper cells, B cells, γδ T cells (including the major γδ T cell subset Vγ9Vδ2), natural killer cells and invariant natural killer T cells. All patients were cANCA positive at time of diagnosis and the study group included those with both limited and systemic disease.

Results.– No significant changes were found in the majority of the cell populations studied. However, a significant decrease in the γδ T cell population was noted in GPA patients, both in frequency (P = 0.0117) and absolute number (P = 0.0031, Mann–Whitney test). This was independent of disease activity and disease phenotype. A significant decrease was also observed in the Vγ9Vδ2 subset (P = 0.0014). A non-significant decrease in invariant natural killer cells was also found. CD4+ CD8+ double positive T cells were increased in GPA subjects.

Conclusion.– Reduced numbers of circulating γδ T cells, noted here in GPA, have been reported in other chronic inflammatory diseases. This may reflect migration of this cell type to the inflammatory lesion.

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P81
Proteinase 3 reactive T cells in patients with granulomatosis with polyangiitis

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Introduction.– Granulomatosis with polyangiitis (GPA) is a systemic autoimmune disease affecting small blood vessels leading to tissue damage. In many patients GPA is characterised by cytoplasmic antineutrophil antibodies (cANCA), which target the enzyme proteinase 3 (PR3). The role of these autoantibodies in disease pathogenesis is unknown and their presence suggests that PR3-specific helper T cells are also involved.

Methods.– T cell reactivity to PR3 was investigated in patients with GPA (n = 18) and healthy control subjects (n = 11). All GPA patients were cANCA positive at time of diagnosis. PBMCs were isolated from peripheral blood and cultured with PR3 (Enzo Bioscience) for six days. T cell proliferation was measured by 3H thymidine incorporation and a stimulation index of two was considered significant.

Results.– T cells from 8 of the 18 GPA patients but none of the controls responded to PR3 in culture. The mean stimulation index of responders was 3.28 (range 2.2 to 4.9) and four were cANCA positive at the time of study.

Conclusion.– These results demonstrate the presence of PR3 reactive T cells in patients with GPA. The role of these cells in disease pathogenesis is unknown. Additional studies focused on HLA-restriction, cytokine analysis and generation of cell lines are underway. PR3-specific T cells are a potential therapeutic target in patient management.

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Large vessel vasculitis

P82
Vitamin D level is decreased in patients with Takayasu’s arteritis

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Introduction.– Takayasu’s arteritis (TAK) is a chronic, inflammatory vasculitis of the aorta and its major branches. Vitamin D (Vit D) is increasingly implicated in the pathogenesis of autoimmune diseases. The immune-regulatory role of Vit D affects both the innate and adaptive immune systems, contributing to the immune-tolerance of
Presence of fibromyalgia and fatigue is not increased in patients with Takayasu’s arteritis

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Introduction.— To our knowledge, no data is reported about the frequency of Fibromyalgia Syndrome (FM) in TAK. We aimed to investigate the frequency of FM in TAK, according to the 2010 ACR Preliminary Diagnostic Criteria for FM. The correlation between ACR-1990 and 2010 FM criteria and the effect of patient-reported outcomes (PROs) such as Health Assessment Questionnaire (HAQ), Multidimensional Assessment of Fatigue Scale (MAF), Short-Form 36-item survey (SF-36), hospital anxiety-depression scales (HADS) on FM were also analyzed.

Methods.— We studied 51 patients with TAK (F/M: 47/4, mean age: 42.3 years), 50 (F/M: 35/15, mean age: 40.89 years) healthy controls (F/M: 35/15) with HAQ. All patients were examined for FM tender points by two observers (kappa: 0.648), asked to complete new ACR 2010 FM questionnaire for FM, SF-36, MAF and HADS were used to assess quality of life together with HAQ.

Results.— Six (11.7%) patients with TAK, 5 HC (10%) met the ACR-2010 FM criteria, whereas only 3 (5.8%) TAK patients and no controls (0%) met the 1990 Criteria. No significant differences regarding the FM frequency were present according to both FM criteria between TAK and HC. No differences were also observed for the 2 subscales of 2010 criteria, the Widespread Pain Index (WPI) and Symptom Severity scale (SSS) scale among the groups. Fourteen patients (33.3%) were clinically active. FM presence was also similar between active and inactive patients (P = 0.188). Results of the PROs in TAK and controls were given in Table I. WPI correlate significantly with MAF (r = 0.623, P < 0.001), HAQ (r = 0.477, P < 0.001), anxiety (r = 0.458, P < 0.001), depression (r = 0.378, P < 0.001). SSS correlate significantly with MAF (r = 0.775, P < 0.001), HAQ (r = 0.437, P < 0.001), anxiety (r = 0.557, P < 0.001), depression (r = 0.438, P < 0.001).

Discussion.— The frequency of FM and other PROs are similar to general population in TAK. The correlation between new FM criteria subscales and PROs suggest that PROs are affected with FM presence in minority of patients with FM and TAK.

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Impaired endothelial function in patients with Takayasu’s arteritis

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Introduction.— Takayasu’s arteritis (TAK) is a chronic, inflammatory, large-vessel vasculitis. In the present study, we aimed to evaluate vascular endothelial function in patients with TAK compared to systemic lupus erythematosus (SLE), another inflammatory, autoimmune disorder.

Methods.— We studied 33 patients with TAK, 18 patients with SLE and 20, age and sex-matched healthy controls. Brachial artery Doppler ultrasonography (USG) and bilateral carotid artery intima-media thickness (CIMT) measurements were performed.

Results.— Basal diameter and nitrate-induced dilatation (NID) values of the brachial artery were similar between the three groups. However, flow-mediated dilatation (FMD) was markedly reduced in patients with TAK (Table I). Carotid artery intima-media thickness (CIMT) was also significantly increased in TAK group, compared to the controls (0.11 ± 0.03 vs. 0.07 ± 0.009 cm, respectively, P = 0.0001). Presence of hypertension had no association with FMD and CIMT measurements. In the SLE group, a marked impairment in FMD % was obtained (8.85 ± 2.8, P = 0.0001). Percentage NID and CIMT measurements was observed to be similar between the patients with SLE and the healthy controls (P = 0.60 and P = 0.05, respectively).