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Background: Evidence supporting the classification of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) based on ANCA type is accumulating.¹
Objectives: To evaluate serum cytokine profiles in patients with AAV classified by ANCA specificity (proteinase 3 (PR3)-ANCA versus myeloperoxidase (MPO)-ANCA) or by clinical diagnosis (granulomatosis with polyangiitis (GPA) versus microscopic polyangiitis (MPA)) and clinical phenotypes.
Methods: An antibody array testing 30 soluble mediators, already shown to be implied in the pathogenesis of AAV, was performed in each patient with active AAV at inclusion in the Rituximab in ANCA-Associated Vasculitis (RAVE) trial, as previously described.^{2,3} By means of Wilcoxon signed rank test for univariate analyses, we analyzed the association of levels of these cytokines with ANCA specificity, clinical diagnosis, and distinct clinicopathologic phenotype categories derived from the BVAS/WG items recorded at the time of enrollment (capillaritis, granulomatous manifestations, renal involvement, and alveolar hemorrhage; new diagnosis and relapsing disease), as described.⁴
Results: All cytokines tested (see Figure 1 and legend for the complete list), except for RANTES, ACE, bFGF and VCAM-1, were significantly increased in the RAVE cohort when compared to healthy controls ($p<0.05$). Median Birmingham vasculitis activity score and steroid use at screening did not significantly differ between PR3-AAV and MPO-AAV, and between GPA and MPA. Within both ANCA specificities, levels of 9 mediators were significantly higher in PR3-AAV (IL-6, NGF, GM-CSF, IL-15, IL-18, IL-18Bb, sIL-2Ra, IL-8, TARC; $p<0.05$), compared to 5 different cytokines that were higher in MPO-AAV (sIL6R, NGAL, sICAM-1, VCAM-1, sTNFR II; $p<0.05$). In contrast, only 4 cytokines (GM-CSF, IL-15, IL-18, sIL-2Ra) were higher in GPA than MPA, and 1 (NGAL) was higher in MPA than GPA ($p<0.05$). The association of the majority of cytokines was stronger with ANCA specificity than with the clinical diagnosis (Figure 1). Similarly, the defined clinical phenotypes were also not separated by cytokine signatures as clearly as the ANCA specificity was (*data not shown*). Restricting the analysis to newly-diagnosed patients ($n=90$) showed the most significant cytokine profile differences associated with PR3-AAV (Figure 1).

Conclusions: Cytokine profiles separate patients more clearly by ANCA specificity than by clinical diagnosis, suggesting important differences in underlying pathophysiology and validating stratification of patients by ANCA specificity for treatment trials.
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FR10315 CLINICAL CHARACTERISTICS OF VASCULAR INVOLVEMENT IN BEHCET'S DISEASE

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Background: Behçet's disease (BD) is a multisystemic inflammatory disorder classified as vasculitis, which can affect all types of vessels. The prevalence of vascular involvement has been reported at rates ranging from 15 to 50%.
Objectives: In this study, we aimed to determine the characteristics of vascular involvement in patients with BD.

Methods: Six hundred and ninety-two patients with BD, who applied to the multidisciplinary BD polyclinic between 2006–2016, were retrospectively analyzed. The diagnosis of vascular involvement was made on clinical signs, by Doppler ultrasonography and/or angiography using computed tomographic or magnetic resonance techniques where appropriate.
Results: One hundred and seventy-six patients (25.4%) had vascular involvement. The mean age of patients with vascular involvement ($n=176$) and non-vascular involvement ($n=516$) was similar to 42.5 ± 12.3 and 42.2 ± 12.2 years, respectively, while male sex frequency was significantly higher in patients with vascular involvement (72% to 42%, $p<0.001$). Uveitis (45%) and erythema nodosum (EN) (47.7%) were significantly higher in patients with vascular involvement than those without vascular involvement (for Uveitis OR: 1.7, $p=0.003$ /for EN: OR: 2.5, $p<0.001$) (Table 1). Deep vein thrombosis was detected in 142 (80.7%) of the patients with vascular involvement and this was the most common type of vascular involvement (Table 2). Arterial involvement was detected in 52 (29.5%) of 176 patients with vascular involvement. Deep venous thrombosis alone was present in 125 (71%) patients, arterial involvement alone in 12 (6.8%) patients, arterial and venous involvement together detected in 40 (22.7%) patients. Arterial involvement was most commonly seen as pulmonary artery involvement in 45 (25.6%) patients [pulmonary artery thrombosis 35 (20%), aneurysm 10 (5.7%) and thrombosis + aneurysm 6 (3.4%) patients]. Twenty (11.3%) patients had other arterial involvement except pulmonary, 8 of them had thrombosis and 12 had aneurysm.

Table 1. Clinical features in patients with and without vascular involvement

	With vascular involvement	Without vascular involvement	OR	95% CI	P value
n (%)	176 (25.4)	516 (74.6)			
Age (year)	42.5±12.3	42.2±12.2			0.762
Male n (%)	127 (72.2)	217 (42.1)	3.57	2.46–5.19	<0.001
Genital ulceration n (%)	123 (69.9)	392 (76.1)	0.728	0.498–1.065	0.101
Uveitis n (%)	79 (44.9)	166 (32.4)	1.698	1.196–2.409	0.003
Papulopustular erythema or acniform rash n (%)	101 (51.4)	186 (57.4)	1.274	0.886–1.832	0.190
EN n (%)	84 (47.7)	98 (27.1)	2.460	1.689–3.582	<0.001

Table 2. Venous involvement (%)

Deep vein thrombosis	142 (80.7)
Budd-Chiari syndrome	7 (4.0)
Inferior and superior vena cava syndrome	26 (14.7)
Iliac vein thrombosis	18 (10.2)
Safenus vein thrombosis	23 (13.1)
Femoral vein thrombosis	36 (20.5)
Popliteal vein thrombosis	43 (24.4)
Crural vein thrombosis	12 (6.8)
Cerebral sinus thrombosis	20 (12.2)

Conclusions: Vascular involvement in Behçet's disease is commonly seen in males. Deep vein thrombosis is the most common form of vascular involvement. Arterial involvement is important because of its higher risk of mortality (especially pulmonary artery aneurysm). The incidence of EN and uveitis is higher in patients with vascular involvement.
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FR10316 FACTORS ASSOCIATED WITH SURGICAL OUTCOMES OF SEVERE AORTIC REGURGITATION IN PATIENTS WITH BEHCET'S DISEASE

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Background: In rare cases, Behcet's disease (BD) can cause severe aortic regurgitation (AR) or aortic root destruction that might have lethal outcomes. Conventionally, simple aortic valve replacement (AVR) is performed for the management of severe AR in BD patients; however, the reoperation rate is as high as 78 to 100%, while mortality rate range from 20 to 47%. Recently, several series of case reports showed that compared to AVR, aortic root replacement (ARR) improved the surgical outcomes of AR in BD patients.
Objectives: To identify the factors associated with the long-term surgical outcomes of AR in BD patients.
Methods: We identified 23 patients who had been surgically treated for AR caused by aortic root involvement of BD from January 1996 through December 2013. We evaluated the occurrence of post-surgical adverse events, which were defined as follows: death, aortic valve/graft problem, infective endocarditis, cerebral infarction, and/or re-operation of aortic valve or root. Types of surgery were classified as simple aortic valve replacement (AVR), bioprosthesis aortic root replacement (bARR), and mechanical valved composite graft aortic root replacement (cARR). Clinical parameters including baseline characteristics, C-reactive protein (CRP), erythrocyte sedimentation rate, and medications were extracted from electronic medical records.
Results: Appropriate aortic valve or root surgery cases were 35 in total, with a mean follow up duration of 11 ± 5 years in 23 patients. Out of the 11 cases

that underwent AVR, post-surgical events were observed in 8 (73%) cases. Out of the 12 bARR cases (xenograft in 5 cases and homograft in 7 cases), 9 (75%) cases had post-surgical adverse events. Out of the 12 cARR cases, post-surgical adverse events occurred in 4 (33%) cases. Multivariable cox proportional hazards model indicated that levels of CRP at 1 month after discharge and age at operation were independent prognostic factors associated with event-free probability. Notably, performing cARR was the most significant factor that affected the surgical outcome (HR (95% CI) 0.147 (0.028 – 0.766), $p=0.023$).

Conclusions: In BD patients with severe AR, the occurrence rate of post-surgical adverse events was associated with the levels of CRP at 1 month after discharge, age at operation, and type of surgery. cARR may be a better surgical option in BD patients with aortic root involvement

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FRI0317 HUMORAL AND CELLULAR IMMUNITY TO VARICELLA-ZOSTER VIRUS IN GIANT CELL ARTERITIS PATIENTS: NO EVIDENCE OF VIRAL REACTIVATION AT ONSET OF DISEASE

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Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are strongly overlapping diseases that are thought to have a shared etiology [1]. The observation of varicella-zoster virus (VZV) antigen in temporal artery biopsies of GCA patients led to the hypothesis that VZV might be a trigger for the onset of the disease [2]. Herpes zoster occurs when the latently present VZV reactivates. It has been reported that patients with GCA do not appear to be at increased risk of herpes zoster compared with age and sex matched controls, even during treatment with high dose glucocorticoids [3]. Levels of VZV specific immunoglobulin G (VZV-IgG) are known to only slowly decline again after a reactivation [4]. We therefore hypothesized, in line with the proposed etiologic role, to find higher VZV-IgG levels in GCA and PMR patients at disease onset, compared to healthy controls. Furthermore, we expected to find no differences in cell-mediated immunity to the virus between patients and controls assuming that the incidence of herpes zoster is not increased in GCA.

Objectives: To investigate humoral and cellular immunity to VZV in GCA and PMR patients and compare these to results in age- and sex matched healthy controls.

Methods: Antibody responses to VZV glycoprotein were measured in serum samples of 35 GCA patients and 26 PMR patients at baseline (before glucocorticoid treatment) and during follow up, and in 58 healthy controls by an enzyme-linked immunosorbent assay (ELISA). Cell-mediated immunity to VZV was determined by performing interferon- γ (IFN γ) enzyme-linked immunosorbent spot (ELISpot) and intracellular cytokine flow cytometry measurements in 11 GCA patients and 15 PMR patients, and in 26 age and sex matched healthy controls.

Results: Similar levels of VZV-IgG were found in GCA and PMR patients at baseline, and healthy controls. The number of VZV specific IFN γ spot-forming cells was significantly lower in GCA patients than in healthy controls ($p=0.029$), but not different in PMR patients compared to healthy controls.

Conclusions: Since antibody levels at baseline were not different in GCA and PMR patients compared to healthy controls it seems unlikely that VZV has an important role in the aetiology of GCA or PMR. The finding of a decreased cell-mediated immunity in GCA patients, especially after treatment with high dose corticosteroids may indicate an increased risk of developing herpes zoster.

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FRI0318 QUALITY OF LIFE IN PATIENTS WITH BEHCET'S DISEASE

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Background: Behcet's disease (BD) is a chronic and multisystemic inflammatory disorder affecting the skin, mucosa, joints, eyes, arteries, veins and the nervous and gastrointestinal systems. The symptoms may be separated by long or short intervals, occur simultaneously or in sequence, and exhibit a pattern of exacerbation and remission. The disease itself or the impact of the symptoms affect patients physically, mentally and socially with a negative effect in the quality of life (QoL).

Objectives: To determine the health status and quality of life in patients with BD followed in a rheumatology unit and to identify associated demographic and disease-related parameters influencing them.

Methods: Cross-sectional study of 44 BD patients and 39 healthy controls matched for age and sex. All subjects completed the Health Assessment Questionnaire (HAQ) to assess impairment in daily activities due to illness, Short Form-36 (SF-36) and EuroQol Visual Analogic Scale (EQ-VAS) to assess health related quality of life (HRQL). The disease characteristics, including disease duration and clinical involvements were collected. The Birmingham Vasculitis Activity Score (BVAS) was applied for the evaluation of current disease activity among BD patients. P value <0.05 was defined as statistically significant.

Results: Among 44 patients, 35 (79.5%) were female, with a mean age of 40.07 years and mean disease duration of 5.93 years. BD patients had significantly higher HAQ score ($p=0.009$) and lower levels of SF-36 ($p<0.001$) than the healthy controls. The predominant contributors to this low SF-36 were general health, vitality and role-emotional domains. In comparison with healthy controls, patients with inactive disease (BVAS=0) also had a higher HAQ, but without significant differences ($p=0.53$). The total SF-36 score also showed lower levels in patients with inactive disease ($p=0.04$), but when compared the different components, only half of them maintained significant differences, namely role-physical ($p=0.03$), general health ($p<0.001$), vitality ($p<0.001$) and social functioning ($p=0.05$). The controls showed a higher EQ-VAS, with a mean of 88.44 comparing to 68.36 in all BD patients ($p<0.001$) and 74.12 in the subgroup with inactive disease ($p=0.003$). SF-36 score was negatively correlated with HAQ ($r=-.553$, $p<0.001$) and positively correlated with EQ-VAS ($r=.388$, $p<0.001$). Longer disease duration correlated with lower levels of only some SF-36 domains, namely physical functioning ($r=-.436$, $p=0.003$), role-physical ($r=-.533$, $p<0.001$) and role-emotional ($r=-.465$, $p=0.001$). There was no correlation between disease activity and disease duration ($p=0.678$) or different scores evaluating QoL ($p=0.876$). The gender was not associated with statistical differences when compared clinical involvements, disease duration, current disease activity, HAQ, EQ-VAS or SF-36 scores. The heterogeneous nature of the disease expression did not allow the study of the association with the levels of health status and QoL.

Conclusions: Our findings showed lower levels of QoL and global health status in BD compared to healthy controls, mainly in active disease, accordingly with previous studies. The disease itself could be a determinant of disability.

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