events in 2 (testicular abscess and worsening renal failure) and refractory disease in 2.

Conclusion: The results of this study suggest that TNF-alpha blockers and TCZ may achieve higher rates of remission and GC-sparing in relapsing and/or refractory PAN than other biologics. Our data warrant further study to confirm or not these findings.

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SAT0222 COOPERATION OF T FOLLICULAR HELPER CELLS AND B CELLS IN TERTIARY LYMPHOID STRUCTURES IN TAKAYASU ARTERITIS

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Background: Takayasu's arteritis (TA) and giant cell arteritis (GCA), the two most common types of large vessel vasculitis (LVV), are characterized by an arterial inflammatory granulomatous infiltrate mainly located in the media and the adventitia. However, distinct histological features of the immune response are poorly known.

Objectives: To investigate distinct pathological mechanisms of the immune response in patients with GCA and TA.

Methods: We performed comparative immunohistochemistry analysis of aorta of GCA and TA patients. We performed microarray gene analysis of purified CD4+ T cells of TA and GCA patients. Reverse transcriptase PCR, flow cytometry analysis and cell culture were used to investigate T and B cells subpopulations in 54 patients with TA, 52 with GCA and 60 controls.

Results: We found higher proportion of tertiary lymphoid structures composed of CXCR5+, CD4+, PD-1+ and CD-20+ cells in inflammatory aortic lesions in TA as compared to GCA. We demonstrated increased proportion of aortic B cells in TA.

We next evaluated differentiation of circulating CD4+ T cells in both diseases. Among sixty-seven genes differentially expressed in CD4+ T cells of TA compared to GCA patients, we identified a specific "T follicular helper" (Tfh) signature in TA patients. We also found a specific Tfh 17 signature in TA patients. Flow cytometry analysis confirmed increased circulating Tfh, defined as CXCR5+ CD4+ T cells, in TA patients as compared to GCA and healthy donors (HD) [median of 15.4 (10;30.8)% versus 5.3 (1.4; 12.2)% and 9.7 (5.6; 12.5)% (p<0.0001 and p=0.0001)] in TA, GCA and HD, respectively. Among Tfh subpopulations, Tfh-17, CXCR5+ CCR6+ CXCR3- CD4+, cells were specifically increased in TA. Functionally, CXCR5+ CD4+ T cells of TA patients helped B cells to differentiate into memory cells, to proliferate and to secrete type G immunoglobulins.

We sequenced the TCR repertoire α/β in CD3+CD4+CXCR5- and CD3+CD4+CXCR5+ cells, in aortic and blood samples from 2 patients. In both patients, we identified oligoclonal profile of TCR repertoire only for aortic CXCR5+ cells, suggesting antigenic selection of CXCR5+ CD4+ T cells.

Conclusion: We provide evidence of the presence of tertiary lymphoid structures composed of Tfh and B cells in TA aorta. We identified a specific Tfh signature in circulating CD4+ T cells that distinguishes TA and GCA patients. The key cooperation of Tfh and B cells in TA and the oligoclonal repertoire of CXCR5+ CD4+ T cells strongly suggest the role of antigenic trigger.

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SAT0223 FACTORS ASSOCIATED WITH DAMAGE PROGRESSION IN BEHÇET'S SYNDROME UVEITIS

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Background: Uveitis in Behçet's syndrome (BS) follows a recurrent disease course with inflammatory exacerbations causing damage in the uvea, retina and optic nerve even with treatment. Frequent attacks and posterior involvement are considered as predictors of poor visual outcome.

Objectives: The aim of this study is to delineate the predictors of damage in more detail using a standard screening method among a group of BS patients with long term regular follow-up.

Methods: Patients with uveitis who were registered in our multidisciplinary BS clinic between 1990 and 2008 were screened. Among these, 50 patients who were followed for at least 10 years, who were regularly seen in our clinic at least once in every 4 months, who did not have > Grade 2 damage at baseline, and who represented different levels of damage severity during the last visit (between Grade 0 and 5) were selected. The damage severity was graded according to a validated damage grading instrument (5=worst) specifically developed for BS uveitis (Ozyazgan et al. in preparation). One patient was later excluded because it was realized that he did not fulfill these criteria. A standard form was used for retrieving data on demographics, baseline and final visual acuities, number and localization (anterior/posterior/panuveitis) of attacks during follow-up, presence of retinal infiltration, retinal hemorrhage and hypopyon uveitis. Candidate factors for damage progression were compared between patients who had a progression in damage score and those who did not.

Results: 98 eyes of 49 patients (M:F 35:14, mean age at baseline 27±8 years, mean follow-up duration 20.9±5.5 years, mean number of visits 76.5±35.2) were evaluated. The mean visual acuity was 0.02±0.08 at baseline and 0.47±0.52 at the final visit. The mean number of attacks was 13.2±9.4. Damage grades at baseline were Grade 0 in 79, Grade 1 in 16 and Grade 2 in 3 eyes. Damage grades at final visit were Grade 0 in 15, Grade 1 in 21, Grade 2 in 32, Grade 3 in 12, Grade 4 in 10 and Grade 5 in 8 eyes. There was damage progression in 81/98 eyes at the final visit. Isolated anterior uveitis attacks were not associated with progression of damage (2.5±2.9 vs 2.8±5.5, p=0.7). Parameters that were significantly more frequent among patients with damage progression were: number of attacks (14.5±10.8 vs 23.3±12.3; p=0.008), number of posterior attacks (0.4±1.2 vs 6.5±4.9, p<0.001), number of panuveitis attacks (0.8±1.3 vs 6.6±5.0, p<0.001), number of attacks with severe vitreous opacity preventing examination of the retina (0 vs 3.2±3.8, p<0.001), retinal infiltration (0.2±0.4 vs 1.4±1.9, p<0.001) and retinal hemorrhages in the arcuate region (0.1±0.2 vs 0.7±1.4, p<0.001), and the number of hypopyon attacks (0.2±1.0 vs 0.9±1.3, p=0.019)

Conclusion: This study confirmed that the anterior uveitis attacks are not associated with progressive damage in BS, whereas posterior and panuveitis attacks, attacks causing severe vitreous opacity, retinal infiltrates and hemorrhage in the arcuate region and hypopyon attacks are important predictors of damage. Patients showing these features should be treated more aggressively.

REFERENCE

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