only expressed intracellularly. Co-staining of IgA with pPTKs showed that IgA+ PCs in both subsets are responsible for enhanced PTK phosphorylation independently of CD19 expression.

Conclusions: CD19+ and CD19- BM PC express kinases involved in BCR signaling and respond by enhanced phosphorylation of PTKs upon BCR stimulation with IgA-expressing cells being exclusively responsible for this increase. Further functional consequences of IgA expression in BM PC and autoimmune remain to be delineated.

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Background: Mammalian target of rapamycin complex 1 (mTORC1) drives the proinflammatory expansion of T helper (Th) type 1, TH17 cells and controls fibroblast proliferation, typical features of large vessel vasculitis (LVV) pathogenesis. Molecular pathways involved in arterial lesions of LVV are unknown.

Objectives: To analyse mTOR pathway activation in LVV (giant cell arteritis and Takayasu arteritis).

Methods: We evaluate pathway activation in the mTORC1 and the nature of cell proliferation in blood and vessels of patients with LVV compared non-inflammatory aorta by using double immunostaining, western blot and flow cytometry. Finally, using flow cytometry, we study the effect of rapamycin on T cells homeostasis in LVV compared to HD.

Results: Proliferation of both endothelial cells and vascular smooth-muscle cells was shown in vascular lesions in LVV. The vascular endothelium of proliferating aorta vessels from patients with LVV showed indications of activation of the mTORC1 pathway in endothelial cells (S6RP phosphorylation) compared to non-inflammatory aorta (45% vs. 48 versus 10.4% [9.7;14.9] positive S6RP endothelial cells and antibodies to be involved in the disease course.

Conclusions: Our results suggest that the mTORC1 pathway is involved in the vascular lesions of LVV. Targeting mTORC1 pathway may represent a new therapeutic option in patients with LVV.

Disclosure of Interest: None declared


AB0027 SCREENING FOR ANTIBODY REACTIVITY IN EARLY AXIAL SPONDYLOARTHRITIS IDENTIFIES NOVEL ANTIGENIC TARGETS

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Background: Diagnosis of axial spondyloarthritis (axSpA) is challenging since clinical manifestations, such as inflammatory back pain, peripheral arthritis, enthesitis and inflammatory bowel disease, often overlap with other disorders. Despite the use of the genetic marker Human Leukocyte Antigen (HLA)-B27 in axSpA patients, an appropriate serological test is still lacking. Although antibodies are not considered to be a hallmark of axSpA, emerging evidence suggests plasma cells and antibodies to be involved in the disease course.

Objectives: Our aim is to screen for antibodies reactive against antigenic targets in plasma of early axSpA patients which may potentially result in novel antibody biomarkers to improve axSpA diagnosis and can enhance the assessment of disease activity, prognosis and therapy response.

Methods: We applied Seattle Antigen Selection (SAS), un biased and high-throughput antibody profiling procedure based on cDNA phage display. First, a cDNA phage display library was constructed from synovial hip tissue from 3 axSpA patients and screened for antibody reactivity in pooled plasma of early axSpA patients (n=10). By performing SAS, we identified antibodies in the axSpA plasma pool that were reactive against 104 different antigenic targets. These targets correspond to both known proteins and novel linear peptides. In a first validation, antibody reactivity against each of these 104 SAS-identified targets was determined in pooled plasma of additional early axSpA patients (n=50) and healthy controls (HC, n=30). Antigenic targets that showed highest reactivity in axSpA plasma pools were further validated in individual plasma samples of early axSpA patients (n=71) and HC (n=73) using phage enzyme-linked immunosorbent assay (ELISA).

Results: Increased antibody reactivity against 7 targets was found in pooled plasma of additional early axSpA patients. Further validation of these 7 antigenic targets in individual plasma samples revealed antibody reactivity in 39% of the early axSpA patients (28/71) compared with 21% of the HC (15/73). By forming a biomarker panel with 4 of these targets, specificity could be improved to 88% (9/73 HC) with only a slightly decrease in sensitivity (34%, 24/71).

Conclusions: We identified autoantibody reactivity to novel antigenic targets in early AS patients. In order to establish the true biomarker potential, antibody reactivity against our identified novel antigenic targets will be further validated in an independent cohort of axSpA patients, rheumatic controls and low back pain controls. Identification of antibody reactivity against novel antibody targets in early axSpA patients can contribute to novel biomarkers for an enhanced diagnosis and might provide more insight into the underlying disease pathology, resulting in novel treatment strategies and eventually improve disease outcome in axSpA patients.

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