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AB0471 ELEVATED EXPRESSION OF PYRUVATE KINASE M2 IN GIANT CELL ARTERITIS

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Background: Giant Cell Arteritis (GCA) is an inflammatory disease of large and medium vessels. In GCA, expression of interleukin-6 (IL-6), a systemic marker of inflammation, is elevated and it has been shown that treatment with IL-6 receptor blockade (Tocilizumab) is beneficial for GCA patients.¹ To investigate the role of the IL-6 signaling pathway in GCA pathogenesis in more depth, we focused on the metabolic enzyme Pyruvate Kinase M2 (PKM2). PKM2 may exist as a tetramer, a dimer and/or a monomer in the cell. Tetrameric PKM2 acts as a glycolytic enzyme and catalyzes the last steps of glycolysis by converting phosphoenolpyruvate (PEP) to pyruvate and ATP. On the other hand, dimeric PKM2 translocates to the nucleus and mediates gene regulation via its non-canonical protein kinase activity. Dimeric PKM2 regulates hypoxia, IL-1 β expression and, phosphorylates signal transducer and activator of transcription 3 (STAT3) which functions downstream of the IL-6 signaling pathway.²

Objectives: To investigate the role of PKM2 in GCA diagnosis and pathogenesis.

Methods: Immunohistochemical staining for PKM2 was performed on inflamed (n=8) and non-inflamed (n=4) temporal artery biopsies (TAB) from GCA patients and on TAB from non-GCA (n=9) patients. To detect soluble, dimeric PKM2 in plasma commercially available dimeric PKM2 specific ELISA kit was used. To determine the modulation of dimeric PKM2 by treatment, samples of GCA patients at baseline (n=44), at 6 weeks (n=32) and at 1 year (n=31) after treatment were compared to samples from age- and sex-matched healthy controls (HC, n=45). As a positive control, samples from melanoma patients (n=8) were used. To investigate the role of dimeric PKM2 in the pathogenesis of GCA, we correlated PKM2 plasma levels with markers of inflammation (CRP, IL-6) and markers of angiogenesis (Angpt2, VEGF, YKL40). Statistical analysis included the Mann-Whitney U test for comparing different groups while the Wilcoxon rank test was used for paired samples. Correlations were assessed by Spearman's rank correlation coefficient.

Results: High expression of PKM2 was found in inflamed and non-inflamed TABs of GCA patients, while in non-GCA TABs PKM2 was sparsely expressed. Circulating levels of dimeric PKM2 were found elevated in melanoma and in GCA patients at baseline/active disease compared to those in healthy controls. Analysis of 6 weeks and 1 year follow up plasma samples showed that plasma levels of dimeric PKM2 significantly decreased upon treatment. Dimeric PKM2 weakly correlated with CRP at baseline ($r=0.399$, $p=0.048$) but not with angiogenesis markers.

Conclusion: Dimeric PKM2 plasma levels were found elevated in GCA patients at baseline. PKM2 plasma levels were down modulated by treatment. PKM2 plasma levels weakly correlated with inflammation marker CRP. The data suggest that PKM2 as a marker of glycolysis may have relevance in GCA at diagnosis and for monitoring disease activity. Future studies should aim to validate PKM2 in an independent cohort. Additional studies are needed to determine the molecular mechanism underlying the increase in elevated dimeric PKM2 levels and how this may contribute to IL-6 signaling.

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AB0472 INFECTIOUS PROFILE IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS: RETROSPECTIVE ANALYSIS IN A REFERRAL CENTRE

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Background: The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are rare multisystem autoimmune diseases of unknown cause, characterised by inflammatory cell infiltration causing necrosis of blood vessels. The treatment of AAV requires prolonged immunosuppressive therapy. Infections remain a major cause of morbidity and mortality.

Objectives: The aim of our study was to investigate the prevalence and characteristics of infection, and analyse the factors associated with infection in patients with AAV from Northern of Spain.

Methods: Retrospective, descriptive study of patients with AAV followed in a specific Systemic Autoimmune Diseases and Thrombosis Unit from January 2000 to December 2019. Demographic, laboratory, microbiology, treatment and clinical data were collected from the medical records. AAV was diagnosed according to the definitions of the Chapel Hill nomenclature and designated as granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), microscopic polyangiitis (MPA) or pauci-immune necrotizing and/or crescentic glomerulonephritis without systemic vasculitis (renal-limited vasculitis, RLV). Disease activity of AAV was evaluated by Birmingham Vasculitis Activity score (BVAS). The infection episode was considered on the basis of clinical, laboratory, microbiology, radiology information, and response to therapy. Different episodes of infection in one patient were independently reflected. Data were analysed using SPSS 25.0

Results: Thirty-six patients of which 20 (55.6%) were males. Median follow-up was 42 months. The mean age at the diagnosis was 61.14 ± 17.49 years and mean BVAS was 18.81 ± 5.96 . 15 patients were diagnosed of GPA, 13 of MPA, 5 of EGPA and 3 of RLV. 72.2% MPO, 11.1% PR3. Lung involvement occurred in 75% of patients, upper airways was detected in 41.7%, skin involvement in 16.7%. Nervous system affection occurred in 33.3%. 30 patients (83.3%) had renal affection with a mean of 1.93 ± 1.66 gr/dl of Proteinuria and 2.9 ± 2.17 mg/dl of creatinine. We detected hypocomplementemia in 27.8% of patients (C3 in 19.4% and C4 in 16.7%). Regarding induction treatments, all patients received corticoids at high doses, 21 (58.3%) Cyclophosphamide, 3 (20%) Rituximab and 2 (13.3%) patients, Azathioprine. When we analyse infections, we detected 15 patients (41.66%) who presented any infection after the diagnosis of AAV, with a total of 71 episodes of infection. The most frequent were bacterial infections (29 episodes), specifically gram negative pathogens. The most frequent location was the respiratory (56.3%) followed by urinary (22.5%) and Skin (8.5%). Also opportunistic infections were described: 3 patients with *Aspergillus fumigatus* and one patient with *Cryptococcus neoformans*. 41 of these episodes needed hospitalisation with a median stay of 11 days. 6 episodes warranted intensive care unit (ICU) admission. Infection related mortality was 2.82%. We made latent tuberculosis screening and *Pneumocystis* prophylaxis in all our patients. No cases of Tuberculosis or *Pneumocystis* were recorded. Factors associated with increased risk of hospitalisation with statistical significance in univariate study were MPA, Hypocomplementemia and increased BVAS. But in the logistical regression study, only the value of the BVAS maintained statistical significance. The only factor associated with elevated risk of ICU admission was IgG deficit in the multivariate analysis. Neither immunosuppressive therapy nor age was associated with increased risk of infection in our study.

Conclusion: More than 50% of the episodes of infection needed hospitalisation in patients with AAV. Risk factors for hospitalisation and ICU admission were BVAS and IgG deficit respectively. Bacterial infections were the most frequent but fungal infections were the most severe.

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AB0473 "HALO SIGN" IN ULTRASOUND OF TEMPORAL, FACIAL AND AXILLARY ARTERIES: ASSOCIATIONS WITH CLINICAL SYMPTOMATOLOGY AND LABORATORY FINDINGS

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Background: Giant cell arteritis (GCA) has two subtypes, the cranial form ("cranial GCA") and the large-vessel form ("LV-GCA"). GCA can present with "cranial" symptoms (headache, visual symptoms, jaw claudication, scalp tenderness), constitutional symptoms (fever, fatigue), limb claudication and symptoms of polymyalgia rheumatica (PMR) and usually causes increased inflammation markers, anemia and thrombocytosis. Ultrasound (US) of the temporal and axillary arteries