Methods: Patients with IgAV from January 1, 1997, through December 31, 2016 were retrospectively identified. Clinical characteristics, laboratory parameters and outcomes were abstracted from direct medical chart review. Proteinuria was classified as non-nephrotic (≥0.2 g/d, ≤3.5 g/d) or nephrotic (>3.5 g/d). Microscopic hematuria was defined as ≥5 RBCs/hpf or ≥2+ on dipstick. Disease activity at each follow-up visit was categorized as complete response (normalization of all baseline abnormalities due to IgAV), partial response, non-response (lack of improvement of any abnormalities) or relapse (development of clinical signs of IgAV after a symptom-free period of at least one month). Prevalence of disease activity and competing risks were estimated using multi-state models.

Results: A total of 243 IgAV patients were identified (97% Caucasian, 58% male). 174 patients were adults (>21 years) and 69 were <21 years. Compared to patients <21 years, adults at baseline had more frequent ulcerative skin lesions (11% vs. 1%; p=0.02) and nephrotic-range proteinuria (22% vs. 3%; p=0.007) but less commonly had abdominal pain (34% vs. 61%; p<0.001), ischemic gastrointestinal involvement (10% vs. 20%; p=0.04) and arthralgias (38% vs. 61%; p<0.001). Frequency of microscopic hematuria was similar between groups (47%). Oral corticosteroids were the most common initial treatment used (80%).

Dialysis was required in 13 patients (8 adults) and renal transplant was performed in 4 cases (1 adult). Of 137 patients with hematuria during the study, 72% had complete resolution by 1 year after onset, compared to 50% of 179 patients with proteinuria. The prevalence of disease activity state at each follow-up time point is shown in figure 1. During 389 person-years of follow-up, 29 deaths were observed. The main causes of death were cancer, cardiovascular disease, infection and vasculitis. Five year survival rates (95% CI) for patients aged <21, 21-50, and 51+ years were 100%, 94% (87, 100) and 40% (26, 63), respectively (p<0.001). Standardized mortality ratio for patients aged 21-50 years at diagnosis was 5.62 (0.68, 20.3) and 7.60 (5.0, 11.1) for those 51 or older.

Conclusion: IgAV in adults is associated with more severe skin/kidney involvement and poorer renal outcome. Among adults with IgAV, patients aged 51 years or older at diagnosis have significantly higher mortality.

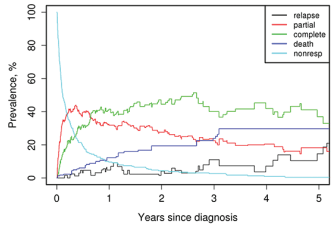

Figure 1. Prevalence of IgA vasculitis disease state at each study time point during follow-up
At 1 year after diagnosis, 42% (95% CI: 30-51%) of patients were in complete response, 32% (95% CI: 24-39%) in partial response, 10% (95% CI: 6-13%) in non-response, 5% (95% CI: 0-10%) in relapse and 12% (95% CI: 5-19%) were deceased.

Abstract THU0322 – Figure 1

REFERENCES:

[1] Audemard-Verger A, Terrier B, Dechartres A, et al. Characteristics and Management of IgA Vasculitis (Henoch-Schonlein) in Adults: Data From 260 Patients Included in a French Multicenter Retrospective Survey. Arthritis & rheumatology (Hoboken, N.J.). 2017;69:1862-1870.

[2] Pillebout E, Thervet E, Hill G, Alberti C, Vanhille P, Nochy D. Henoch-Schonlein Purpura in adults: outcome and prognostic factors. Journal of the American Society of Nephrology : JASN. 2002;13:1271-1278.

[3] Westman K, Flossmann O, Gregorini G. The long-term outcomes of systemic vasculitis. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2015;30 Suppl 1:i60-66.

[4] Shrestha S, Sumingan N, Tan J, Alhous H, McWilliam L, Ballardie F. Henoch Schonlein purpura with nephritis in adults: adverse prognostic indicators in a UK population. QJM : monthly journal of the Association of Physicians. 2006;99:253-265.

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THU0323

THE MANAGEMENT OF BIOPSY NEGATIVE GIANT CELL ARTERITIS BY AUSTRALIAN RHEUMATOLOGISTS

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Background: The diagnosis of Giant Cell Arteritis (GCA) by Rheumatologists is based on a typical history of headache, jaw claudication and visual disturbance, examination findings such as scalp tenderness and abnormal temporal arteries, and confirmed by temporal artery biopsy (TAB) (1). Temporal artery biopsy is the gold standard for GCA diagnosis (2, 3). However clinicians may diagnose biopsy-negative GCA if there is a high enough pre-test probability for this condition, even if the biopsy is negative. There are few guidelines to assist clinicians with management of biopsy-negative GCA.

Objectives: The primary aim of this research project was to determine if there were differences in the management of patients with biopsy-positive versus biopsy-negative GCA with respect to duration of corticosteroid (CS) use, relapse rates, and use of steroid-sparing agents over a 12-month follow-up period in an Australian cohort. We also sought to determine if there were differences in patient characteristics, examination findings and investigation results between the two groups.

Methods: All patients who underwent a temporal artery biopsy during 2013-2016 for suspected GCA at three geographic sites (Prince of Wales Hospital, Royal Prince Alfred Hospital and Mid-North Coast Arthritis Clinic, Coffs Harbour) had their files reviewed for clinical presentation, examination findings, investigation results, and management over the 12-months following presentation. Comparison was made between biopsy-positive and biopsy-negative patients.

Results: One hundred and forty-two patient files were reviewed. One hundred and one patients were excluded. Of those remaining, 23 were biopsy-positive and 18 were biopsy-negative GCA. Biopsy-negative patients were younger at presentation compared to biopsy-positive GCA patients (69.3 years vs 76.1 years, p = 0.01). There was no difference in the frequency of headache, jaw claudication, polymyalgia rheumatica symptoms or visual disturbance between the two groups of patients. There was also no difference in ESR, CRP, platelet count, total WCC, ALP or Hb level. However, there was a trend towards higher ALP levels in biopsy-positive patients (p = 0.058). The length of temporal artery biopsy was similar between biopsy-positive and biopsy-negative patients (19.4mm vs 19.7mm, p = 0.902). Fewer biopsy-negative patients remained on corticosteroids at 12 months following presentation (65% vs 100%) and of those that did remain on corticosteroids, their dosage tended to be lower than for those with positive biopsies (3.4mg/d vs 7.5mg/d, p = 0.002). Fewer biopsy-negative patients were commenced on methotrexate (5.6% vs 34% p = 0.02). There was no difference in the frequency of relapse between biopsy-positive vs biopsy-negative patients (p = 0.40). Biopsy-positive patients were more likely to present in December or January compared to biopsy-negative patients (p = 0.07). There was no difference in corticosteroid duration prior to biopsy (p = 0.42).

Conclusion: Biopsy-positive patients were treated with corticosteroids for longer and at higher doses than those with a negative biopsy. They were also more likely to present in summer and be treated with methotrexate compared to biopsy-negative patients. The seasonal difference in presentation may suggest a different trigger compared to biopsy-negative patients.

REFERENCES:

[1] Grossman C, et al. Baseline clinical predictors of an ultimate giant cell arteritis diagnosis in patients referred to temporal artery biopsy. Clin Rheumatol 2016; 35: 1817-1822.

[2] Hall S, et al. The therapeutic impact of temporal artery biopsy. The Lancet 1983; 322 (8361): 1217-1220.

[3] Dasgupta B, et al. Concise guidance: diagnosis and management of giant cell arteritis. Clin Med (Lond) 2010; 10 (4): 381-6.

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9. Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

THU0324 AXONAL DYSFUNCTION IN CEREBRAL WHITE MATTER IN SYSTEMIC SCLEROSIS: A PROTON MAGNETIC RESONANCE SPECTROSCOPIC IMAGING (^{1}H-MRSI) STUDY

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Background: Systemic sclerosis (SSc) is a diffuse connective tissue disease characterized by varying degrees of cutaneous and visceral fibrosis, presence of autoantibodies and vasculopathy. In addition, central nervous system (CNS) involvements are often observed [1].
Objectives: The aim of the present study was to investigate the presence of axonal dysfunction in systemic sclerosis (SSc) and to determine if clinical, laboratory and treatment features are associated with its occurrence.
Methods: In this longitudinal study we included 38 SSc patients (32 woman, mean age of 50.86, SD±11.66 years; range 31- 74) and 38 healthy volunteers (32 woman, mean age of 49.23, SD±12.03 years; range 26 - 77). All individuals were evaluated (neuropsychiatric evaluation and MRI) at study entry and after 12 months. Cognitive evaluation was performed using the Montreal Cognitive Assessment (MoCA), mood disorders were determined through Beck´s Depression (BDI) and Beck´s Anxiety Inventories (BAI). Individual with scores: MoCA ≤26, BDI ≥11 and BAI ≥7 were considered impaired. SSc patients were further assessed for clinical and laboratory SSc manifestations, disease activity (Valentini Activity Index), severity activity (Medsger Severity Index). We performed multi-voxel ^{1}H-MRSI over the superior-posterior region of the corpus callosum. Our MRI/MRSI protocol consisted of: T1-weighted images; 2D pulse sequence (PRESS); excitation angle of 90˚; Long TE: 144ms and TR: 2000ms; VOI (MRSI) size (mm) ≈ (116 x 79 x 16) grid with 208 spectra. Scans were performed with a Philips 3.0T MRI scanner. We measured signals from *N*-acetyl-compounds (NAA), creatine (Cr), choline (Cho), glutamate (Glu), glutamine (Gln) and Glx (the sum of Glu and Gln) using TARQUIN software.
Statistics was performed according nature of the variable.
Results: We observed a significant reduction in NAA/Cr (mean value=1.72; SD=2.4) and Cho/Cr (mean value=2.4; SD=2.04) ratio in SSc when compared to controls (NAA/Cr mean value=1.85; SD=2.7; p = 0.36; Cho/Cr mean value=0.377; SD=0.169; p<0.001). Reduction in NAA/Cr ratio was associated with cognitive impairment (p = 0.017), presence of migraine (p = 0.001), current use of prednisone (p=0.010) and current use of methotrexate (p < 0.001). NAA/Cr ratio correlated with MOCA scores (r=0.4; p=0,015).
Follow up study showed a reduction in NAA/Cr values when compared to patients´ baseline values (p = 0.0341).
Conclusion: Our results showed a significant reduction in NAA/Cr ratio in SSc patients associated with cognitive impairment and the use of some drugs (MTX and prednisone) during the treatment. Therefore, NAA/Cr ratios may be a useful biomarker in follow-up studies of SSc.

REFERENCES:

[1] Hietaharju A, Jaaskelainen S, Hietarinta M, Frey H. Central nervous system involvement and psychiatric manifestations in systemic sclerosis (scleroderma): clinical and neurophysiological evaluation. Acta neurologica Scandinavica. 1993
[2] Mountford, C. E., Stanwell, P., Lin, A., Ramadan, S., and Ross, B., Neurospectroscopy: the past, presente and future," Chemical reviews, 2010
[3] Wilson, M., Reynolds, G., Kauppinen, R. A., Arvanitis, T. N., and Peet, A. C., A constrained least-squares approach to the automated quantitation of in vivo 1h magnetic resonance spectroscopy data," Magnetic resonance in medicine, 2011.

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THU0325 THE HMGB1/AGE-RAGE AXIS IN SYSTEMIC SCLEROSIS PATIENTS: A POTENTIAL ROLE IN ITS VASCULOPATHY?

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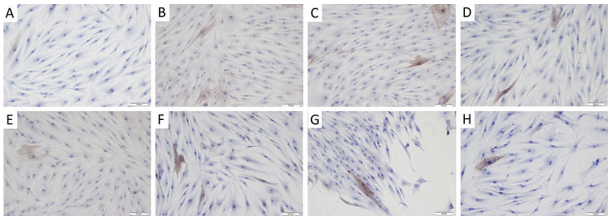
Background: Systemic sclerosis (SSc) is a progressive fibro-inflammatory autoimmune disease of which the pathogenetic pathways are incompletely understood. Advanced glycation endproducts (AGEs) are oxidative stress derived compounds with potential proinflammatory effects. Their exact role in fibrosis remains unknown. The receptor for AGEs is RAGE, which is also the receptor for high mobility group box 1 (HMGB1), a nuclear protein, which is proinflammatory when released from activated or apoptotic cells. We hypothesize that AGEs and HMGB1 may promote inflammation and profibrotic processes, presumably mediated by RAGE.
Objectives: To study the role of the HMGB1/AGE-RAGE axis in the pathogenesis of SSc.
Methods: Distribution of N-(carboxymethyl)lysine (CML) and N^{δ}-(5-hydro-5-methyl-4-imidazolon-2-yl)-ornithine (MG-H1) was assessed by immunohistochemistry in skin biopsies of 12 SSc patients [median age 56 years (IQR 52-61); 6 of affected, 6 of unaffected skin]. The intensity was assessed semi-quantitatively on endothelium and fibroblasts. In vitro experiments were performed on healthy human dermal fibroblasts, which were stimulated by HMGB1, AGE-BSA or TGF-β1 as control. Inflammatory and profibrotic markers were measured by ELISA and rt-PCR. Differentiation to myofibroblasts was assessed by staining of α-smooth muscle actin (α-SMA). In an additional clinical study, we included 20 SSc patients [51 years (44-58)] and 20 age- and sex-matched healthy controls [(HC) 52 years (45-62)]. Sera were obtained to determine CRP, ESR, HMGB1 and soluble RAGE (sRAGE) levels. AGE accumulation in skin was assessed as skin autofluorescence (SAF) by the AGE Reader.
Results: MG-H1 staining was more intense on all skin structures in SSc patients, compared to HC, while CML staining showed no differences. MG-H1 was more pronouncedly detected on endothelium and fibroblasts in affected compared to unaffected skin. In vitro stimulation of fibroblasts with AGE-BSA resulted in increased expression of IL-6, collagen-1α and connective tissue growth factor. Finally, HMGB1 and AGE-BSA induced myofibroblast differentiation and formation of SMA fibers (Fig. 1, 2). In regards to the clinical study CRP (SSc: median 1.8 mg/l (IQR 0.8-3.5), HC: 0.7 (0.4-1.8), p=0.04), ESR (SSc: 8.5 mm/h (5.3-15.5), HC: 5.0 (3.0-7.0), p=0.02), HMGB1 (SSc: 3.4 ng/ml (1.6-6.1), HC: 1.6 (0.8-2.8), p=0.03), sRAGE (SSc: 956.3 pg/ml (717.9-1670.0), HC: 684.9 (517.0-890.5), p=0.02) and SAF (SSc: 2.2 AU (1.8-2.5), HC: 1.8 (1.4-2.1), p=0.02) were significantly increased in SSc patients, compared to HC.
Conclusion: This is the first translational study that might indicate a prominent role of the HMGB1/AGE-RAGE axis in systemic sclerosis by promoting inflammation and fibrosis. Further studies investigating this pathway are ongoing.



Abstract THU0325 – Figure 1. Smooth muscle actin (α-SMA) expression by immunohistochemistry in stimulated and unstimulated human skin fibroblasts. Fibroblasts were treated with 0 **(A)**, 1 **(B)**, 10 **(C)** or 50 **(D)** ng/ml TGF-β1, 10 **(E)** or 100 **(F)** μg/ml AGE-BSA or 1 **(G)** or 10 **(H)** μg/ml HMGB1. All cells were treated for 24 hours. Detection was performed with 2 μg/ml anti α-SMA. Bar 100 μm.