P39 LONGITUDINAL CHANGES OF CEREBRAL WHITE MATTER TISSUE MICROSTRUCTURE IN EARLY-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Diffusion tensor imaging (DTI) studies revealed alterations of cerebral white matter (WM) tissue microstructure in patients with established Systemic Lupus Erythematosus (SLE), highlighting longitudinal changes in DTI metrics. The main aim of this study was to evaluate longitudinal variations of DTI metrics in different WM tracts of newly-diagnosed SLE patients.

Methods In a prospective single-centre observational study (2013–2018), patients meeting revised ACR or SLICC classification criteria, aged less than 55, within 24 months from diagnosis, were evaluated with brain MRI (1.5T Philips Achieva) at baseline (T0) and after at least 12 months (FU). DTI data (15 directions, b-value 800s/mm²) were analysed using ExploreDTI software. Automatic lesion segmentation was performed using Lesion Prediction Algorithm (Matlab16). An in-house developed semi-automated WM tracts segmentation algorithm was used to assess fractional anisotropy (FA), mean (MD), radial (RD), axial diffusivity (AD) values in different normal-appearing WM tracts. Variations in neuroimaging data were analysed by Wilcoxon matched-pairs signed-ranks test.

Results 17 early SLE patients were included. After mean 456.3 (87.1) days, mean(SD) FA values significantly decreased at left corticospinal tract (T0: 0.483(0.032); FU: 0.470(0.034), $p=0.0040$) and posterior limb of left internal capsule (0.590

(0.020) vs 0.580(0.024), $p=0.0396$), with increase in MD (0.755 vs 0.770, $p=0.0023$) and RD values (0.467 vs 0.482, $p=0.0019$) (figure 1). Increase in MD and RD values was independent of baseline neurologic symptoms, disease activity and comorbidities.

Conclusions Longitudinal decrease in FA and increase in MD start in early phases of SLE course, even in absence of overt NP symptoms, reflecting a compromised WM tissue microstructure.

P40 PROMISING SALIVARY PROTEIN BIOMARKERS IN KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by the production of auto-antibodies. We aimed to find salivary protein biomarkers in Korean patients with SLE.

Methods The salivary proteins were subjected to 2-dimensional gel electrophoresis (2-DE). The spots exhibiting >2-fold intensity change between SLE and healthy subjects (HSs) were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MS) analysis. The amounts of candidate proteins in saliva of patients with SLE and rheumatoid arthritis (RA), and HSs were analyzed using western blotting and enzyme-linked immunosorbent assay.

Results The proteomic analysis using 2-DE and MS revealed 10 differentially expressed protein spots, which included immunoglobulin gamma-3 chain C (IGHG3), protein S100, lactoferrin, leukemia-associated protein 7, and 8-oxoguanine DNA glycosylase. The patients with SLE exhibited enhanced salivary IGHG3 (3.9 ± 2.15 pg/mL) and lactoferrin ($4.7 \pm$

Abstract P39 Figure 1 Axial FA and MD maps with overlying WM tracts (thresholded by the WM probability map), showing posterior limb of left internal capsule (arrows); variation of main DTI parameters (FA, MD, RD, AD) between T0 and FU at posterior limb of left internal capsule

1.8 pg/mL) levels than patients with rheumatoid arthritis (RA) (1.8 ± 1.01 pg/mL and 3.2 ± 1.6 pg/mL, respectively, $p < 0.001$ for both) or HCs (2.2 ± 1.64 pg/mL and 2.2 ± 1.7 pg/mL, respectively, $p < 0.001$ for both). The levels of salivary IGHG3 correlated with erythrocyte sedimentation rate ($r = 0.26$, $p = 0.01$), anti-dsDNA antibody levels ($r = 0.25$, $p = 0.01$), and nephritis ($r = 0.28$, $p = 0.01$).

Conclusions The levels of salivary IGHG3 and lactoferrin were higher in patients with SLE. In addition, salivary IGHG3 levels correlated with SLE disease activity markers.

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P41 PREDICTING AUTOIMMUNE CONNECTIVE TISSUE DISEASES: THREE YEAR FOLLOW UP OF AN AT RISK COHORT IDENTIFIES LATE PROGRESSION AND BIOMARKERS TO PREDICT NEED FOR THERAPY

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Background Autoimmune connective tissue diseases (AI-CTDs: SLE, pSS, IIM, Scleroderma, MCTD) are preceded by asymptomatic ANA positivity. We previously recruited a cohort of new ANA-positive referrals without AI-CTD. 17% met criteria by AI-CTD at 12 months, and this was predicted an IFN Score. This study includes 3 year follow up of that cohort with more detailed analysis of the 'non-progressor' group and predictors.

Methods Patients were recruited if they had: (i) ANA; (ii) did not meet criteria for AI-CTD; (iii) symptoms less than 12 months. Diagnostic criteria for AI-CTDs and therapies were assessed at baseline then 12-monthly for 3 years. We categorised progression as:

1. Absolute-non-progressors (no clinical criteria at all time points: 0–36 months)
2. Undifferentiated-CTD (≥ 1 clinical criterion at baseline and/or at follow up but not meeting criteria)
3. Year-1-progressor (meeting criteria for AI-CTD within 12 months)
4. Late-progressor (meeting criteria for AI-CTD later than 12 months)

Interferon Score A and Interferon Score B were measured at baseline using taqman as previously described.¹

Results 3-year follow up was available in 146/150. Proportions in the above categories were: Absolute-non-progressors: 33/146 (23%); Undifferentiated-CTD: 86/146 (59%); Year-1-progressors: 21/146 (14%); Late-progressors: 5/146 (3%). No patient progressed or required immunosuppression after 2 years. 6/86 patients with Undifferentiated-CTD received an immunosuppressant. The present work therefore defines a larger group of 32/146 (22%) with clinically significant disease including 21 Year-1-progressors, 5 late-progressors, and 6 undifferentiated-CTD who needed an immunosuppressant.

Clinical features had limited utility in predicting these outcomes. Of 31 patients with no clinical criteria at baseline, 1 progressed to meet criteria within 1 year, 2 progressed at 1–2 years, 3 were prescribed hydroxychloroquine and 1 was prescribed an immunosuppressant. The 108 patients with at least 1 criterion at baseline had the highest risk: 20 progressed to meet criteria within 1 year, 2 progressed at 1–2 years, the others all had U-CTD. 35 were prescribed hydroxychloroquine and 13 were prescribed an immunosuppressant. There was also no association between ENA, C3 or C4 and clinical outcome.

The association between interferon scores and progression was stronger when comparing Year 1 progressors with absolute non-progressors ($p = 0.007$). Late progression was not predicted by baseline IFN Scores. However, within U-CTD, patients who required an immunosuppressant had higher expression of IFN Score A ($p = 0.011$) and IFN Score B ($p < 0.001$) than those who did not.

Conclusions Among ANA-positive referrals, no clinical feature or routine laboratory test could rule out development of clinically significant disease, but IFN Scores had a unique value in predicting these outcomes. At-Risk individuals who ultimately developed clinically significant disease are therefore immunologically but not clinically distinctive. Future work will incorporate biomarkers into clinically applicable risk models to allow earlier exclusion of AI-CTD or trials of preventative treatment.

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P42 DISEASE ACTIVITY, IMPAIRED IRON TRANSPORT AND FAILED SEQUESTRATION: A NOVEL MECHANISM FOR ANAEMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Haematological manifestations are a frequent feature of systemic lupus erythematosus (SLE) yet the role of abnormal iron metabolism is poorly understood. In this study, we investigated the role of key regulators of iron metabolism including ferritin (an iron carrier protein), transferrin (which facilitate iron transport to cell surface receptors), hepcidin (which prevents iron release from stores under the influence of IL6 and IL1 β) and lipocalin-2 (LCN2, which is released by innate immune system activation and induces iron sequestration).

Methods Serum samples were collected from SLE patients without a history of haemolytic anaemia attending University College London Hospital, UK ($n = 39$). Clinical parameters including Haemoglobin (Hb), dsDNA, complement C3 and SLEDAI-2K were recorded. Levels of IL1 β , IL6, hepcidin, ferritin, LCN2 and transferrin in addition to other iron regulators including erythropoietin (EPO), soluble transferrin receptor (sTfR), haptoglobin (Hp) and NRAMP2, were measured by ELISA. Following normalisation of data, hierarchical correlate cluster was performed to produce a heatmap using MeV Software.

Results The results demonstrate a surprising negative correlation between LCN2 and SLEDAI-2K ($P < 0.001$, $r = -0.40$), which suggests iron is not being appropriately sequestered in