162 HOMOCYSTEINE LEVEL IN PATIENTS WITH LUPUS NEPHRITIS

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Background In SLE, both disease-specific and traditional risk factors are important. Increased serum homocysteine levels are seen in approximately 15% of patients with systemic lupus erythematosus and are associated with an increased risk of atherothrombotic events in this population. The serum level of homocysteine in patients with lupus nephritis has not been well described.

Methods We performed a retrospective review of patients who had both, a biopsy proven lupus nephritis (class II-VI), and measured homocysteine levels for the first time during routine evaluation. Clinical and laboratory data were obtained from review of medical records.

Results Five patients with lupus nephritis had homocysteine level measured. The ages ranged from 29–47 years and were predominately African Americans. There were two patients with class III, one with class III-V, one with class IV, and one with class V lupus nephritis. All were female, with positive anti-dsDNA, low C4 and on hydroxychloroquine. Of the five patients, all had elevated homocysteine levels.

Conclusions This study demonstrates that patients with lupus nephritis are at a high risk for developing elevated homocysteine levels.

Funding Source(s): None

163 BACTERIAL BIOFILM PRODUCT CURLI/EDNA INDUCES NETS AND SERUM ANTI-CURLI/EDNA LEVELS CORRELATE WITH BACTERIURIA AND LUPUS ACTIVITY

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Background Infections are a major contributor to lupus disease. We have previously demonstrated that bacterial amyloid

curli, produced by *E.coli*, can accelerate disease in mouse models of lupus. Interestingly curli incorporates extracellular DNA, which in turn can be both adjuvant and a self-antigen in lupus. Finally, uropathogenic *E. coli* (UPEC) is responsible for the majority of urinary tract infections in SLE.

Methods Based on our previous results, we hypothesize that exposure to UPEC triggers anti-curli/eDNA antibodies and curli/eDNA complexes can trigger the innate immune system. We investigated 98 lupus patients who met at least 4 SLICC criteria. Results were compared to 54 age, sex and race matched healthy controls. We tested the production of anti-curli/DNA complex for both IgG and IgA subclasses. We also correlated the levels of anti-curli/DNA antibodies with clinical parameters. Finally, we treated human neutrophils with curli/eDNA complexes.

Results We found that curli/eDNA induces neutrophil extracellular traps in a ROS manner. Anti-curli/eDNA IgG levels were detected in lupus and controls plasma and the levels correlated with persistent bacteriuria ($p < 0.05$) and disease flares in lupus patients. In addition, anti-curli/eDNA antibodies could bind to DNA demonstrating a potential molecular mimicry mechanism in lupus. Finally IgA anti-curli/eDNA levels were higher ($p < 0.01$) in lupus donors compared to controls.

Conclusions We conclude curli/eDNA complexes can activate the innate and adaptive immune system and could be a mechanism to sustaining disease in lupus.

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164 URINARY ALCAM AS A NOVEL BIOMARKER FOR RENAL PATHOLOGY IN LUPUS NEPHRITIS

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Background Lupus nephritis is one of the most common and severe complications of SLE affecting more than 60% patients. The management of lupus nephritis largely depends on renal histopathologic findings. Due to the invasive feature and complications of renal biopsy, it is significantly urgent to develop novel biomarkers to predict renal pathology.

Abstract 164 Figure 1 Urinary ALCAM levels were elevated in active LN patients. (A) Group comparison showed significant increase of urinary ALCAM in active LN patients (14 IQR (6.97-24.8) ng/mg) when compared to those in active SLE without renal involvement patients (3.54 IQR (1.31-7.58) ng/mg), inactive SLE patients (2.75 IQR (1.45-5.67) ng/mg), and healthy controls (1.29 IQR (0.665-1.89) ng/mg). (B) Receiver Operating Characteristic (ROC) curve analysis indicated a good performance of urinary ALCAM in discriminating active LN from active SLE without renal involvement, inactive SLE, and healthy controls. Group Description: A=Active LN group; N=Active SLE without renal involvement group; C=Inactive SLE group; H=healthy control group

Abstract 164 Figure 2 Correlation between urinary ALCAM and (A) rSLEDAI, (B) SLEDAI, (C) SLICC RAS, (D) 24 hour urine protein level, (E) hemoglobin, and (F) complement 3 level. rSLEDAI = renal SLEDAI, SLICC RAS = SLICC renal activity score, Hb = hemoglobin. C3 = complement 3

Abstract 164 Figure 3 Urinary ALCAM levels were elevated in proliferative LN patients. (A) Group comparison between proliferative (Class III and Class IV) LN patients (16.3 IQR (8.01-28.5) ng/mg) and membranous patients (Class V LN) (4.47 IQR (2.63-6.54) ng/mg). (B) Receiver Operating Characteristic (ROC) curve analysis indicated a good discriminative performance of urinary ALCAM in proliferative LN versus membranous LN

Abstract 164 Figure 4 Correlation analysis between urinary ALCAM and renal pathology. (A) Urinary ALCAM correlated positively with activity index (AI) in renal pathology. (B) Urinary ALCAM didn't correlate with chronicity index (CI) in renal pathology

Abstract 164 Table 1 Demographic characteristics of study subjects

	Active LN	Active Non-LN	Inactive SLE	Healthy Control
N	75	61	73	28
Age (years) (mean±SD)	35.0±11.15	36.0±14.62	40.0±14.0	32.0±11.6
Female, n (%)	72 (96.0%)	57 (93.4%)	69 (94.5%)	23 (82.1%)
Disease Duration (years)	6.8	6.33	6.63	0
Clinical Characteristics, n (%)				
Fever	7(9.3%)	11(18.0%)	10(13.47%)	N/A
Lymphadenopathy	3(4%)	2(3.3%)	1(1.4%)	N/A
Malar rash	13(17.3%)	17(27.9%)	10(13.47%)	N/A
Mucosal ulceration	1(1.3%)	3(4.9%)	1(1.4%)	N/A
Alpecia	5(5.3%)	3(4.9%)	0(0%)	N/A
Vasculitis	4(5.3%)	4(6.6%)	0(0%)	N/A
NPSLE	0(0%)	0(0%)	0(0%)	N/A
Myositis	0(0%)	1(1.6%)	0(0%)	N/A
Arthritis	4(5.3%)	3(4.9%)	1(1.4%)	N/A
Myocarditis/Endocarditis	9(12.0%)	4(6.6%)	4(5.5%)	N/A
Serosal effusion	9(12.0%)	4(6.6%)	7(9.6%)	N/A
ILD/pneumonitis	3(4.0%)	3(4.9%)	3(4.1%)	N/A
Pulmonary haemorrhage	5(6.7%)	4(6.6%)	0(0%)	N/A
Gastrointestinal vasculitis	0(0%)	0(0%)	5(6.8%)	N/A
Lupus nephritis	75(100%)	0(0%)	9(12.3%)	N/A
Leukocytopenia	10(13.3%)	18(29.5%)	6(8.2%)	N/A
Hemolytic anemia	0(0%)	1(1.6%)	1(1.4%)	N/A
Thrombocytopenia	6(8.0%)	14(23.0%)	9(12.3%)	N/A
rSLEDAI, median (IQR)	8(4-12)	0(0-0)	0(0-0)	N/A
SLEDAI, median (IQR)	12(9-16)	8(6-12)	4(2-4)	N/A
Laboratory Tests				
24h Urine Protein (g/24h)	3.4(2.2-7.0)	0.2(0.1-0.3)	0.2(0.1-0.4)	N/A
eGFR* (mL/min/1.73 m ²)				N/A
Positive ANA/ total tested	64/75	52/61	67/73	N/A
Positive anti-dsDNA/ total tested	51/75	62/61	36/73	N/A
Hypocomplementemia/ total tested	67/75	54/61	30/73	N/A

Abstract 164 Table 1 (continued)

Renal Pathology (ISN/RPS Classification)				
Class I	0(0%)	N/A	N/A	N/A
Class II	1(1.3%)	N/A	N/A	N/A
Class III/ III+V	16(21.1%)	N/A	N/A	N/A
Class IV/ IV+V	48(65.8%)	N/A	N/A	N/A
Class V	9(12.3%)	N/A	N/A	N/A
Class VI	0%	N/A	N/A	N/A
Comorbidity				N/A
Hypertension	15(20%)	1(1.6%)	6(8.2%)	N/A
Diabetes mellitus	0(0%)	1(1.6%)	1(1.4%)	N/A
Hyperlipidemia	4(5.3%)	0(0%)	0(0%)	N/A
Hypothyroidism	2(2.7%)	1(1.6%)	0(0%)	N/A
Pulmonary embolism	0(0%)	1(1.6%)	0(0%)	N/A

Abstract 164 Table 2

	Cutoff	AUC	SEN	SPE	PPV	NPV
Urinary ALCAM (ng/mg)	>7.17	0.86 ***	79.37%	88.90%	98.04%	38.10%
Anti-dsDNA Ab (IU/ml)	>28.3	0.59 ns	52.50%	62.50%	84.00%	17.39%
C3 (g/L)	<0.574	0.77 *	60.66%	87.50%	97.37%	22.58%
C4 (g/L)	>0.755	0.50 ns	69.49%	50.00%	91.11%	18.18%
AUC = area under the curve, SEN = sensitivity, SPE = specificity, PPV = positive predictive value, NPV = negative predictive value.						

Methods In this cross-sectional study, a total of 77 biopsy-proven active LN, 61 active SLE without LN and 75 inactive SLE patients and 28 age and gender matched healthy controls were recruited. Urinary levels of activated leukocyte cell adhesion molecule (ALCAM) were determined by enzyme-linked immunosorbent assay in urine samples of the above-mentioned subjects. Renal histopathology was reviewed by an experienced renal pathologist. Urinary ALCAM levels were normalized by urine creatinine. For active LN patients, all samples were collected at the time of renal biopsy.

Results Urinary ALCAM levels were significantly increased in active LN patients when compared to those in active SLE without renal involvement patients, inactive SLE patients,

and healthy controls (figure 1A). ROC analysis showed a good performance of urinary ALCAM in discriminating active LN from active SLE without renal involvement and inactive SLE and healthy controls (figure 1B). Further correlation analysis revealed a positive correlation between urinary ALCAM and general disease activity-SLEDAI score, as well as renal disease activity-rSLEDAI and SLICC-RAS (figure 2A-C). Urinary ALCAM also correlated with lab parameters including 24 hour urine protein, hemoglobin, and complement 3 (C3) (Figure 2D-F). More interestingly, we found a good prediction value of urinary ALCAM in renal histopathological findings. Urinary ALCAM levels were significantly increased in proliferative LN (Type III and IV) as compared

to those in membranous LN Type V (Figure 3). It outperformed conventional biomarkers (anti-dsDNA antibody, C3, C4) in discriminating the two different types of LN. Urinary ALCAM levels correlated positively with activity index (AI) in renal histopathology, indicating a role in guiding clinical management of LN.

Conclusions Urinary ALCAM is a promising biomarker for predicting renal histopathological changes in LN, which may serve as a valuable surrogate of renal biopsy. These findings should be confirmed in a larger cohort to further validate the utility of urinary ALCAM as a biomarker.

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IDENTIFICATION OF SERUM BIOMARKERS FOR SYSTEMIC LUPUS ERYTHEMATOSUS USING A LIBRARY OF PHAGE DISPLAYED RANDOM PEPTIDES AND DEEP SEQUENCING

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Abstract 165 Figure 1 Schematic diagram and workflow. A. The schematic for phage display screening and next generation sequencing. B. This study is composed of three major phases, i.e., screening phase, validation phase I, and validation phase II