0%, $p=0.046$). Of note, three of the five LN patients with cerebrovascular accidents or venous thrombosis were anti-MPO/PR3 positive.

Conclusions Positive ANCA by IIF was common in LN, however, only a fifth of LN patients had anti-MPO/PR3 antibodies which were associated with anti-cardiolipin IgG antibodies. Anti-MPO/PR3 negative patients were more likely to have a positive ANCA IIF with nuclear staining. We are currently comparing ANCA positivity between SLE patients with and without LN.

Funding Source(s): The Arthritis Society Chair in Rheumatic Diseases at the Cumming School of Medicine, University of Calgary

21 IS LUPUS NEPHRITIS ONSET DELAYED IN OLDER CAUCASIAN FEMALES WITH LESS AGGRESSIVE PATHOLOGY?

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10.1136/lupus-2019-lsm.21

Background Lupus Nephritis (LN) usually presents within five years of SLE diagnosis. Male gender, Hispanic and African American race, and childhood-onset SLE portend greater risk of early nephritis. However, patients with late-occurring nephritis are poorly characterized. Since proliferative nephritis is a more aggressive class of nephritis than membranous and mesangial, we hypothesized that female gender, Caucasian race, adult-onset SLE, and membranous pathology would be associated with a later onset of nephritis.

Methods A single large urban medical center was the source for retrospective record review of patients who underwent kidney biopsy between 1999 and 2015. Patients with biopsy-proven LN were evaluated to determine whether gender, race, age at SLE diagnosis, age at first biopsy, or histopathologic classification were associated with time between SLE diagnosis and first renal biopsy.

Results 630 patients were screened. After elimination of duplicates, those without initial biopsy, biopsy findings other than LN, and unknown date of SLE diagnosis, 293 subjects had adequate data available for analysis. Those with late onset SLE, diagnosis after age 50, were excluded from further analysis due to known differences in this subgroup. The remaining 278 patients had characteristics shown in table 1. Twenty-nine percent of patients in this cohort developed nephritis more than 5 years after initial SLE diagnosis. Multivariable linear regression identified greater age at first biopsy and race as the strongest predictors of time between SLE diagnosis and first renal biopsy. Hispanic patients were more likely to present with LN earlier in their course and Asian patients were more likely to present later, with African American and Caucasian groups between them. The model accounts for 27% of the variability in the time elapsed between diagnosis and biopsy. Histopathologic class did not make a significant contribution, and proliferative nephritis was noted in similar numbers of patients who developed LN after 5 years and those in the early presenting group.

Conclusions Surprisingly, more than a quarter of known LN patients at this large US center present after 5 years of SLE, higher than expected based on low numbers of late onset nephritis in other cohorts. This appears to be more common in Caucasian and Asian subgroups. Older patients are more likely to develop nephritis later, but aggressive histopathology is not less likely in later presentations. The data underscore

Abstract 21 Table 1 Patient Characteristics

Characteristic	Total (n = 278)	≤5 Years (n = 197)	>5 Years (n = 81)	>10 Years (n = 45)	>15 Years (n = 22)
Female (n, %)	242 (87.05)	167 (84.77)	75 (92.59)	42 (93.33)	21 (95.45)
Race/Ethnicity (n, %)					
Asian	18 (6.47)	9 (4.57)	9 (11.11)	5 (11.11)	2 (9.09)
White/Caucasian	27 (9.71)	17 (8.63)	10 (12.35)	7 (15.56)	5 (22.73)
Black/African American	121 (43.53)	84 (41.12)	40 (49.38)	21 (46.67)	12 (54.55)
Hispanic/Latino	112 (40.29)	90 (45.69)	22 (27.16)	12 (26.67)	3 (13.64)
Age at SLE (median, IQR)	25.45 [19.12, 33.20]	25.64 [19.49, 35.03]	25.16 [18.31, 30.22]	24.36 [18.12, 29.34]	24.5 [19.16, 27.03]
Age at Lupus Nephritis (median, IQR)	29.78 [22.26, 38.43]	26.88 [20.49, 36.49]	36.24 [30.02, 44.78]	42.34 [33.06, 48.88]	45.38 [38.34, 51.75]
Histopathologic Class (n, %)					
II	33 (11.87)	24 (12.18)	9 (11.11)	6 (13.33)	5 (22.73)
III	65 (23.38)	45 (22.84)	20 (24.69)	14 (31.11)	7 (31.82)
III+V	41 (14.75)	25 (12.69)	16 (19.75)	5 (11.11)	1 (4.55)
IV	64 (23.02)	49 (24.87)	15 (18.52)	7 (15.56)	3 (13.64)
IV+V	24 (8.63)	16 (8.12)	8 (9.88)	4 (8.89)	1 (4.55)
V	51 (18.35)	38 (19.29)	13 (16.05)	9 (20.00)	5 (22.73)
Proliferative (III, III+V, IV, IV+V)	194 (69.78)	135 (68.53)	59 (72.84)	30 (66.67)	12 (54.55)

The initial group is the total cohort, followed by the cohort divided into <5 years between SLE and first LN biopsy and >5 years. All >10 years patients are also included within the >5 years group, and >15 years patients are also in >5 years and >10 years groups. Groups are presented for illustrative purposes only. Time between SLE and biopsy was analyzed as a continuous outcome variable to prevent unnecessary loss of power.

the importance of remaining vigilant about nephritis risk in patients of diverse demographics five years and more after diagnosis with SLE.

Funding Source(s): Mallinckrodt Research Fellowship, NIH: T32DK007257,UL1TR001105,U54GM104938,P30AR053483, U01AI101934,U19AI082714

22 BARICITINIB INHIBITS B CELL ACTIVATION AND AMELIORATES MURINE LUPUS

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10.1136/lupus-2019-lsm.22

Background B cells carry out central roles in the pathogenesis of SLE by triggering tissue inflammation through autoreactive antibody-dependent responses. Baricitinib is a JAK1/2 inhibitor that blocks the downstream of multiple cytokine receptor signaling implicated in lupus pathogenesis.

Methods We investigated the effect of Baricitinib to the differentiation of B cells *in vitro*. And female MRL/lpr mice were administered baricitinib (10 mg/kg) or vehicle (0.5% methyl cellulose) by gavage twice daily for 8 weeks, when determined serum levels of anti-ds DNA antibodies and pro-inflammatory cytokines (BAFF, IL-6 and IL-17), proteinuria, renal inflammation and IgG-C3 deposit. *In vitro*, Baricitinib suppressed the mRNA expression of AID, Bcl6, XBP-1, IRF4 and the production of IgG in B cells.

Results In MRL/lpr model, Baricitinib-treated mice showed reduced levels of anti-dsDNA antibodies, proteinuria, and cytokines as compared with those of control mice. In addition, Baricitinib prevented renal pathology, as judged by changes in the histopathological scores of glomeruli with PAS stain and IgG-C3 deposition by confocal microscope. Finally, Baricitinib treatment significantly inhibited downstream of Jak/STAT signals in CD19 +B cells from spleen. In conclusion, this study revealed the regulatory effects of baricitinib on B cells and ameliorates murine lupus.

Conclusions These results indicate that Jak inhibitors have the potential therapeutic approach for SLE.

Funding Source(s): None

23 TREATING LUPUS-PRONE MICE WITH A COENZYME Q10 ANALOG DECREASES DISEASE PARAMETERS INDICATING A THERAPEUTIC ROLE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2019-lsm.23

Background Immune dysregulation and organ damage are characteristic of systemic lupus erythematosus (SLE). We previously reported that mitochondrial reactive oxygen species (ROS) and the release of oxidized mitochondrial DNA (mtDNA) may be involved in autoimmunity and contribute to the generation of type I IFN responses, important mediators in the pathogenesis of SLE. Mitochondrial dysfunction

Abstract 23 Figure 1 Effects of idebenone treatment on lupus-prone mice. Idebenone treatment showed improvements such as reduction of skin ulcers and attenuation in mortality

and an imbalance in ROS production may lead to oxidative stress, mitochondrial lipid, protein and DNA modifications, and alterations in the production of adenosine triphosphate (ATP). Idebenone is a coenzyme Q10 synthetic analog with antioxidant properties previously tested in humans to treat different diseases where mitochondrial function is compromised. This study aimed to assess if idebenone mitigates murine lupus.

Methods Two different doses of idebenone were given orally to MRL/lpr mice for 8 weeks. At euthanasia, treated and untreated mice were analyzed and compared for clinical, immunologic and metabolic parameters including autoantibody generation, proteinuria, kidney function and pathology, renal immune complex deposition, endothelium-dependent vasorelaxation, assessment of pro-inflammatory gene expression, quantification and characterization of neutrophil extracellular trap (NET) formation and mitochondrial ROS, measurement of complex II-specific activity and cardiac lipid peroxidation.

Results Idebenone was well tolerated and led to significant attenuation in mortality and an improvement of glomerular inflammation, renal function, skin ulcers and splenomegaly. The levels of proinflammatory cytokines and inflammasome-related genes were significantly decreased by idebenone. In addition, we observed inhibition of NET formation both in lupus mice bone marrow neutrophils and in neutrophils from lupus patients. Enhanced complex II-specific activity and mitochondria specific gene transcription were shown in cells isolated from idebenone-treated lupus-prone mice, suggesting improved mitochondrial function and reduction of oxidative stress. Idebenone-treated mice also displayed reduced heart lipid peroxidation.

Conclusions Idebenone improves murine lupus. These results suggest that idebenone and other drugs that improve mitochondrial function may have a therapeutic role in SLE.

Funding Source(s): This study was supported by the Intramural Research Program, NIAMS/NIH (ZIA AR041199) and the Alliance for Lupus Research.