

Conclusions Serum CIC and IL-6 significantly correlated with clinical SLEDAI, which is higher degree of correlation than anti-dsDNA, C4 and C3 levels. Our study suggested that CIC and IL-6 can be used as alternative biomarkers to determine SLE activity.

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IMMUNE COMPLEX GLOMERULONEPHRITIS ASSOCIATED WITH LYSINURIC PROTEIN INTOLERANCE: A CASE REPORT AND REVIEW OF THE LITERATURE

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10.1136/lupus-2017-000215.324

Background and aims Patients with lysinuric protein intolerance (LPI) due to inherited defect of cationic amino acid transport in intestine and renal tubules may have aberrant immune responses leading to multiple organ involvement. The renal involvement with immune complex glomerulonephritis in LPI is albeit rare and has not been well established.

Methods We report a 4-year-old boy manifested nephrotic syndrome with renal histological findings showing immune complex glomerulonephritis highly suggested of lupus nephritis, but the initial serology survey excluded the diagnosis of SLE initially. The diagnosis of lysinuric protein intolerance was established and SLE developed 1 year later. Renal manifestations in patients with LPI and the coexistence of LPI with SLE are reviewed.

Results The initial renal involvement in LPI included renal tubular dysfunction, nephritic and nephrotic syndrome. During follow-up, some patients developed renal function impairment and may progress to end stage renal disease. Glomerulus was the major involved lesion with the most common histological finding was immune complex glomerulonephritis. Five patients, including our patient, with LPI coexisted with SLE have been reported during follow-up. These patients characterised female predominant, young onset age, predominant renal involvement, and poor prognosis. Our patient supported the suggested mechanism of macrophage activation. Treatment with steroid and cyclosporine accordingly led to remission of nephritis.

Conclusions LPI was not only a disorder of amino acid wasting but also a complex multisystemic disease with aberrant immune responses. LPI-associated glomerulonephritis shares similar characteristics on renal histology with lupus nephritis. Both macrophage activation and excess arginine accumulation might play roles on the pathogenesis.

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IS LUPUS AN INFLAMMATION RESOLUTION DEFICIENCY DISORDER?

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10.1136/lupus-2017-000215.325

Background and aims Lupus and lupus nephritis progression and flares are difficult to predict. Recently, osteoprotegerin, endothelin-1, CXCR3⁺ CD4⁺ T cells and MCP-1 mRNA expression in urine sediments have been described as possible

biomarkers of lupus and lupus nephritis. But their relationship with histological activity has not been sufficiently explored. It is desired that biomarkers of a disease should more rapidly reflect disease progression which would allow shorter clinical proof of concept trials and should be able to predict flares, measure current disease activity and severity, predict progression of disease and prognosis.

Methods It is likely that continued inflammatory events seen in lupus could be due to failure of the resolution of inflammation. Thus, the balance between inflammation and resolution is tilted more in favour of pro-inflammatory events and/or failure of production of pro-resolution molecules at the most appropriate time leading to non-resolution of inflammation. One such endogenous pro-resolution and anti-inflammatory molecule is lipoxin A₄, whose deficiency could lead to continuation of inflammation in lupus and lupus nephritis.

Results It was noted that low plasma and urinary lipoxin A₄ indicated disease activity and progression of disease, while a fall in its levels were noted prior to impending flares and increase in disease activity; and an increase in the levels of lipoxin A₄ suggested resolution of inflammation and amelioration of disease process.

Conclusions It is suggested that measurement of plasma and urinary lipoxin A₄ will be a good biomarker to predict flares, measure current disease activity and severity, predict progression of disease and prognosis.

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ROLE OF BIOACTIVE LIPIDS IN AUTOIMMUNE DISEASES INCLUDING LUPUS

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10.1136/lupus-2017-000215.326

Background and aims To evaluate whether a regimen of corticosteroids and cyclophosphamide, and methods designed to enhance endothelial NO synthesis and augment antioxidant defenses can lead to long-lasting remission of lupus and other autoimmune diseases.

Methods Patients with established lupus, dermatomyositis and rheumatoid arthritis are selected for the study. Their plasma phospholipid content of unsaturated fatty acids, nitric oxide, anti-oxidants and cytokines are measured before and after treatment.

Results Plasma phospholipid content of arachidonic, eicosapentaenoic and docosahexaenoic acids (AA, EPA and DHA respectively) were found to be low and so also plasma nitric oxide levels and anti-oxidants with a concomitant increase in plasma IL-6 and TNF concentrations. These patients were given pulses of methylprednisolone and cyclophosphamide based on their disease status and response to therapy followed by oral supplementation of GLA/EPA/DHA daily.

Conclusions All patients who entered the study went in to full remission that was found to be associated with restoration of plasma phospholipid content of AA/EPA/DHA, antioxidants and nitric oxide and cytokines to normal. All these patients were in full remission even after stopping immunosuppressive drugs but are continuing GLA/EPA/DHA orally.

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GENETIC POLYMORPHISM +1444CT IN THE C – REACTIVE PROTEIN IS ASSOCIATED WITH THE SUSCEPTIBILITY FOR SYSTEMIC LUPUS ERYTHEMATOSUS AND DISEASE ACTIVITY

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10.1136/lupus-2017-000215.327

Background and aims The gene *C-reactive protein* (CRP), located at 1q23-24, is a candidate to be investigated as a susceptibility locus for systemic lupus erythematosus (SLE). The aim of the study was to evaluate the association between the +1444CT CRP polymorphism with the susceptibility for SLE, disease activity, and CRP serum levels.

Methods The study enrolled 176 SLE patients and 223 healthy controls from Brazilian population. SLE disease activity (SLEDAI), clinical and laboratorial characteristics were evaluated. The +1444CT CRP polymorphism was determined using polymerase chain reaction and restriction fragment length polymorphism.

Results The frequency of CC vs. TT genotypes and the C vs. T allele among the patients differed from the controls ($p=0.0201$ and $p=0.0072$, respectively). Patients carrying the T allele presented higher CRP ($p=0.017$) and showed a trend toward higher IL-6 compared with patients carrying the C allele ($p=0.057$). The increased CRP was independently of the IL-6 in these subgroups of patients. SLE patients carrying the CC genotype showed positive correlation between CRP and C4 levels ($p=0.039$), while those with T allele presented a trend toward a negative correlation between CRP and C3 and C4 ($p=0.056$ and $p=0.073$, respectively); and a trend toward positive correlation with anti-nucleosome and anti-dsDNA ($p=0.052$ and $p=0.091$, respectively).

Conclusions Our data showed that +1444CT CRP polymorphism was associated with SLE susceptibility and CRP levels, as well as CRP levels were associated with disease activity, suggesting that this polymorphism may play a role in the pathophysiology of SLE, which may be used as a possible marker of disease activity.

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CCR5Δ32 (RS333) POLYMORPHISM IS ASSOCIATED WITH SUSCEPTIBILITY TO SYSTEMIC LUPUS ERYTHEMATOSUS IN FEMALE BRAZILIAN PATIENTS

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10.1136/lupus-2017-000215.328

Background and aims The role of CCR5Δ32(rs333) polymorphism in the pathogenesis of systemic lupus erythematosus

(SLE) has been evaluated worldwide. The aim of this study was to determine the association between CCR5Δ32 polymorphism with the susceptibility to SLE and the activity of disease in female Southern Brazilian patients.

Methods The study enrolled 169 female SLE patients and 132 unrelated female healthy individuals. Baseline clinical, laboratorial characteristics, and the SLE activity (determined using the SLEDAI) were evaluated according to the CCR5Δ32 genotypes. The CCR5Δ32 polymorphism was determined from genomic DNA using a polymerase chain reaction.

Results The frequencies of the genotypes CCR5/CCR5, CCR5/CCR5Δ32 and CCR5Δ32/CCR5Δ32 were 87.6%, 11.8%, and 0.6%, respectively, among the patients, and 96.2%, 3.8%, and 0.0%, respectively among the controls, [$p=0.0116$, odds ratio:3.432 (95% confidence interval:1.252–9.40). Patients carrying the CCR5/CCR5Δ32 and CCR5Δ32/CCR5Δ32 genotypes presented earlier age of onset of disease ($p=0.0293$) and higher levels of anti-dsDNA ($p=0.0255$), than those carrying the wild type genotype. When the analysis was adjusted for ethnicity, only the age at onset of disease remained associated with the CCR5Δ32 polymorphism ($p<0.05$); patients with variant CCR5Δ32 allele (heterozygous and homozygous), presented lower age at onset of disease than those with the wild type genotype.

Conclusions The results suggest that the CCR5Δ32 polymorphism might be associated with SLE genetic predisposition among female Brazilian patients and the age at onset of the disease; however, this genetic variant was not associated with the activity of SLE in this population.

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ELEVATED IFIT3 IN MONOCYTES CONTRIBUTED TO HYPERACTIVE cGAS-STING SIGNALLING PATHWAY IN SLE

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10.1136/lupus-2017-000215.329

Background and aims IFIT3 is one of the Interferon-stimulated genes showed significantly increase in PBMCs of SLE patients. However, the functions of IFIT3 in dysregulated immune responses of SLE are not fully understood. SLE is featured by over production of nuclear antigens, such as dsDNAs, from debris of numerous dead cells, which give rise to autoantibody production. cGAS-STING signalling pathway has been proposed to play an important role in sensing DNA and producing inflammatory cytokines in SLE. Our study is IFIT3's function in regulating cGAS-STING signalling pathway in SLE. **Methods** Monocytes were isolated from SLE patients or healthy controls by Ficoll-paque method and CD14+ magnetic beads. The expression of IFNβ and phosphorylation of IRF3 were measured in either IFIT3 over-expressing or knockout cells upon VACV-70 stimulation by Q-PCR and Western blot. We used Co-IP to identify the interaction between IFIT3 and its interaction proteins.

Results cGAS-STING signalling pathway was over-activated in monocytes from SLE patients compared to healthy controls. The expression of IFIT3 was significantly elevated in SLE patients and was positively correlated with the activity of cGAS-STING signalling pathway. *In vitro*, we revealed that the expression of IFNβ and phosphorylation of IRF3 could be reduced by knocking down IFIT3, while over-expression of