283

SUPPORTING EVIDENCE TO DIFFERENTIATE PREECLAMPSIA FROM NEPHRITIS IN LUPUS PREGNANCY: AN ELECTRONIC HEALTH RECORDS REVIEW

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Background Pregnancy in women with SLE is associated with a greater risk of both maternal and neonatal complications. Preeclampsia in SLE is particularly tricky because its manifestations and symptoms are nearly indistinguishable from lupus nephritis, a serious SLE manifestation. Renal biopsy is indicated in SLE if active nephritis is suspected, however this is not without risks and many patients and providers prefer to avoid such invasive procedures in later pregnancy. Much of the work on preeclampsia in lupus has relied on clinical documentation and coding, which may be subject to substantial misclassification. We aimed to describe the extent to which the clinical features (purported to support distinguishing between flare/nephritis and preeclampsia) are recorded in electronic health records (EHR).

Methods We identified a cohort of pregnant women with SLE from a tertiary medical teaching hospital using both ICD coded visits and medical record review (excluding drug-induced lupus M32.0) in the EHR. From these pregnancies, we identified 23 women with preeclampsia noted by their treating physician on medical record review. We evaluated documentation and/or measurement of important diagnostic features such as complement, antibodies to double stranded DNA (anti-dsDNA), differential blood counts, the presence of cellular and acellular blood casts, urinalysis, liver function tests, uric acid levels, and the presence of

schistocytes. We recorded the percentage of time that these measures were noted in the EHR. We repeated this restricting to a period with more complete EHR in a sensitivity analysis.

Results Missingness was highest for blood smears to determine the presence of schistocytes (91%). We found that complement levels were not recorded for 51% of patients, while anti-dsDNA was missing in 43% of patients. Differential blood counts were recorded for all patients. We could not find evidence for microscopic urinalysis to rule out casts or hematuria in ~9% of cases. Uric acid levels were not measured in 13% of patients and liver function tests were missing in 39%. We found attenuation of missingness in contemporary cases, but only to a minimal effect.

Conclusions We found that the diagnosis of preeclampsia in this setting was not supported by strong recorded evidence of clinical features upon extensive chart reviews (above and beyond proteinuria and hypertension, two factors that may also be present in nephritis). All of these women diagnosed with preeclampsia also delivered preterm, however, we did not find extensive documentation attempting to distinguish preeclampsia from potential nephritis flare, which would necessitate a different treatment.

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284

T CELLS PRODUCE INTERFERON ALPHA IN A MODEL OF LUPUS-LIKE DISEASE

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Abstract 284 Figure 1 TREX1 D18N T cells spontaneously generate IFN- α . (A) Kaplan-Meier survival curve demonstrating the absence of autoimmune mortality in TREX1 D18N IFNAR KO animals. (B) qRT-PCR measurement of IFN- α gene expression in uninfected WT splenocytes, LCMV +splenocytes, purified LCMV +non innate immune cells, and purified LCMV +innate immune cells (data represents cells from three virally-challenged mice 48 hours after infection). (C) IFN- α gene expression in splenocytes from unchallenged WT and D18N mice (26–30 mice per genotype). (D) IFN- α gene expression in whole splenocytes and purified non-innate and innate immune cells from both WT and D18N mice (3 separations, 6–8 mice per genotype). (E) qRT-PCR measurement of IFN- α expression or ISG expression (F) in whole splenocytes or purified T and B cells from WT and D18N mice (3 separations, 3 mice of each genotype). (G) IFN- α expression in sorted naive or differentiated CD44^{high} CD4 or CD8 T cells from both WT and D18N mice (3 independent sorts, 3 animals of each genotype). All mice were mixed sex and 8–12 weeks of age. Error bars represent SEM. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$ by Log-rank test (A), unpaired student's t-test (C, WT vs. D18N comparisons in D-G), or one-way ANOVA (B, D18N splenocytes vs. other D18N populations in D-G).

Background Failure to properly dispose of self-DNA can inappropriately trigger anti-viral defense systems, leading to autoimmunity. Indeed, mutations in the DNA exonuclease TREX1 are causative for a spectrum of rare lupus-like autoimmune diseases in humans. These disorders involve triggering of the cytosolic dsDNA sensor cyclic GMP-AMP Synthase (cGAS) and the STimulator of INterferon Genes (STING), leading to chronic production of the anti-viral cytokine type I interferon (IFN-I) and the development of autoimmunity. Importantly, the exact cells in which the sensing of undegraded DNA and subsequent production of IFN-I occur remain unknown.

Methods We generated a mouse expressing the catalytically inactive TREX1 D18N allele, which causes familial chilblain lupus in humans. We examined anti-viral gene expression and the phenotype of these mice to study the immunological effects of losing TREX1 activity. We performed bone marrow transplants to determine if autoimmune pathogenesis in this model was dependent on hematopoietic or non-hematopoietic cells. Finally, we measured expression of type I interferon in various purified cell populations to identify specific cellular producers contributing to autoimmune pathogenesis.

Results In this study, we demonstrate that TREX1 catalytic inactivity induces IFN-I signaling and lupus-like autoimmunity in a mouse. Moreover, we show that TREX1 deficiency within bone marrow-derived cells causes IFN-I activation and the development of autoimmunity. We provide evidence of spontaneous IFN- production within both innate immune and T cells. T cell IFN-α expression was observed in all T cell populations, but was most enriched within naive T cells. We also demonstrate that D18N T cells express all components of the cGAS-STING pathways and generate IFN-I protein, both spontaneously and in response to small-molecule activation of STING.

Conclusions Our findings demonstrate that TREX1 enzymatic activity is crucial to prevent inappropriate DNA-sensing and IFN-I production. TREX1 inactivity within hematopoietic cells was both necessary and sufficient to induce lupus-like autoimmunity, indicating that TREX1 normally acts within immune cells to suppress inappropriate activation of anti-viral signaling. Both innate immune and T cells respond to TREX1 dysfunction by spontaneously synthesizing IFN-, a surprising result given that T cells are not canonically thought to be major IFN-producing cells. These results expand our understanding of the pathogenesis of lupus-like disease, and indicate that small molecule inhibition of TREX1 could represent an appealing strategy for anti-viral and cancer immune-therapies.

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285

LUPUS NEPHRITIS PRESENTING AS TUBERCULOSIS INFECTION: A CASE REPORT

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Background Lupus nephritis, a form of glomerulonephritis, is the inflammation of kidneys attributable to systemic lupus erythematosus (SLE). It is an autoimmune disorder in which kidney tissue insult is triggered predominantly by the

complement system. Herein, we report the case of a 24 years old female with atypical manifestations of SLE.

Methods Case Presentation: A female aged 24 years was presented with the complaint of fever, cough (with sputum) and dyspnea for the past one month. The preliminary physical examination was suggestive of pneumonia. Her laboratory investigations revealed anisocytosis and normochromic anemia (Hb 9.3 g/dL, HCT 30%). Lymphocytes (12%) were decreased while neutrophils (84%), platelets ($439 \times 103/\mu\text{L}$) and ESR (75 mm/hr) were increased. A serum biochemistry test showed elevated urea (92 mg/dL), creatinine (1.5 mg/dL) and sodium (145 meq/L). The chest X-ray demonstrated a right sided pleural effusion which directed towards a possible Tuberculosis (TB) infection. However, pleural biopsy efficiently excluded an active TB infection. Nephrological investigations exhibited evidence of protein (0.3 g/L) and blood traces in the urine. Her proteinuria (2+) was within nephrotic range which was confirmed through qPCR (3.9 U). Moreover, serum TSH (8.054 mU/L) was also elevated and cardiolipin test was positive for IgM (1.10). SLE specific diagnostic tests anti-dsDNA was positive and ANA was also reactive. Left kidney biopsy exhibited characteristics of diffuse endocapillary proliferative glomerulonephritis. SLE diagnosis was established, and patient was treated with cyclophosphamide pulse therapy along with corticosteroid methylprednisolone and achieved complete remission.

Results CASE REPORT

Conclusions To date, this is the first case report of SLE simulating as a TB infection in a developing country. The patient did not display classic triad of SLE; joint pain and malar rash aside from fever. This case reiterates the implication of considering unusual case presentations of SLE and undertaking rigorous clinical workup to minimize the probability of missed cases and improve patient clinical outcomes.

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286

MATERNAL SYSTEMIC LUPUS ERYTHEMATOSUS AND THE RISK OF CRYPTORCHIDISM IN MALE OFFSPRING

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Background Background: Systemic lupus erythematosus (SLE) is one of the most prevalent autoimmune rheumatic diseases affecting young women of childbearing age. The disease is characterized by elevated levels of systemic inflammation and high levels of circulating autoantibodies, potentially affecting multiple organs and tissues. Women suffering from SLE have decreased fecundity, and increased risk of adverse pregnancy outcomes such as miscarriage and preeclampsia. This risk is further elevated with increasing disease activity, and seems less pronounced when disease is well managed. SLE is not in itself considered a risk factor for specific birth defects; however, not all congenital anomalies are diagnosed immediately after birth, and might thus be overlooked in most studies on reproductive outcomes. Cryptorchidism (undescended testis) is a common genital anomaly, often diagnosed throughout childhood. It arises from an imperfect genital development in the