Abstracts

MANAGEMENT OF PREGNANCY IN SLE AND APS

JIB Buyon, New York University Grossman School of Medicine, Division of Rheumatology, New York, NY, USA

Since systemic lupus erythematosus (SLE) primarily affects women of childbearing age, therefore pregnancy assumes great importance for these patients. Accordingly, proper pre-conception counselling is highly relevant to management and can set the stage for a more favourable outcome.

Women of childbearing age with SLE should be advised of medications safe to continue during pregnancy and told that disease should be in remission or at least not acutely active. Hydroxychloroquine is strongly recommended for all women during pregnancy despite a concern raised regarding a very slight increase in malformations, which was not confirmed in a subsequent study. Low dose aspirin to prevent pre-eclampsia should be highly reinforced. The issues related to pregnancy outcome for the maternal-fetal dyad comprise three components, maternal, placental and fetal with the latter clearly influenced by the two former. With the completion of a large prospective US based study,1 factors associated with poor pregnancy outcomes in patients who are generally stable at the time of conception have emerged and include being Hispanic or non-white, taking blood pressure medications, low platelet counts, active disease even if stable, and the presence of a lupus anticoagulant. In the absence of these factors, pre-eclampsia still occurs at a greater frequency than in the otherwise healthy population, with estimates of about 9%, as does small for gestational age at about 10%. In patients with no risk factors at baseline, the adverse pregnancy outcome rate is about 8% and fetal/neonatal mortality 3.9%. In patients who are either lupus anticoagulant (LAC) positive, or LAC negative but non-white and treated with anti-hypertensives, the adverse pregnancy outcome rate approaches 60%; fetal/neonatal mortality at 22%. In general, patients with prior kidney disease but in remission do well without an increased risk of flare with de novo kidney disease being quite uncommon with risk under 3%. Severe flares in patients stable at conception approach less than 3% at any time during pregnancy and postpartum, and approximately 10% intrapartum and 25% postpartum for mild/moderate flares (most not requiring intervention).2

Promising biomarkers, which may identify women early in pregnancy at risk for poor outcomes, include angiogenic factors and alternative and terminal complement activation factors. Turning to neonatal lupus, newer research supports the contribution of Type I interferon in the pathogenesis. A prospective study supports the use of hydroxychloroquine to decrease the recurrence of congenital heart block in half.3 Data suggest that low titre anti-SSA/Ro antibodies do not confer risk of fetal cardiac injury but defining low and high titres in commercial laboratories is not well established since many do not provide a broad range of values. New approaches to surveillance are being addressed leveraging home heart rate and rhythm monitoring by the mothers.4 The NIH has launched a recent US and Canada based study to evaluate whether the titre of anti-SSA/Ro 60 or 52 antibodies confers higher risk and if home Doppler monitoring can identify a transition period of conduction slowing that is reversible with dexamethasone and IVIG if administered within 12 hours of a Doppler abnormality confirmed by echocardiogram. Overall, the landscape for women with lupus contemplating pregnancy is favourable after achievement of stability or remission prior to conception. Prevention of reversible cardiac damage in those women with SLE and anti-SSA/Ro antibodies may be on the horizon.

REFERENCES

Case 1: A 36-year-old white female

A 36-year-old white female who has occasional dry eyes, no dry mouth, and no other symptoms was tested for anti-SSA/Ro antibodies, given the dry eyes and a family history of...
Lupus nephritis (LN) is a common manifestation of systemic lupus erythematosus (SLE) that can lead to irreversible renal impairment. Lupus nephritis is initiated by the deposition of nucleic acid-containing material in the glomeruli, which triggers the engagement of complement, the activation of renal stromal cells and the recruitment of circulating pro-inflammatory cells. Disease progression is associated with tubulointerstitial hypoxia, metabolic dysfunction of the tubular epithelium, tubulointerstitial capillary rarefaction, accumulation of mixed lymphoid infiltrates and fibrosis. Each of these abnormalities may require different therapeutic approaches. In addition, loss of renal homeostatic programs contributes to morbidity including anemia, hypertension and increased cardiovascular risk.

Forty percent of patients with moderate to severe renal lymphoid infiltrates progress to end stage renal disease over 2–5 years. Immune infiltrates in LN kidneys can occupy several niches. Glomerular infiltrates consist mainly of macrophages, with T cells present in the more severe crescentic forms. Glomerular macrophages are recruited from the pool of circulating monocytes and include both classical and non-classical subtypes. Endothelial cells that are activated via nucleic acid-sensing toll-like receptors (TLRs) such as TLR 7 preferentially recruit non-classical monocytes. Macrophages change their phenotype upon glomerular entry and take on a phagocytic phenotype that is associated with disease activity.

Mixed tubulointerstitial leukocyte infiltrates, sometimes with features of lymphoid organisation, are found in LN, particularly in chronic disease. B cell and T cell clones are present in LN tissue, and T peripheral helper cells that express high amounts of inducible T-cell costimulator and interleukin (IL)-21 are located next to B cells in the renal infiltrates. Lupus nephritis kidneys also contain large numbers of CD8 T cells and natural killer cells that produce interferon (IFN)γ. Interestingly a predominance of B cells over T cells is associated with a better prognosis. The presence of antigen presenting cells such as myeloid dendritic cells (DCs) and plasmacytoid DCs, is associated with more advanced disease in LN.

In addition to infiltrating cells, the kidneys have a network of tissue resident macrophages located around glomeruli and in the tubular interstitium that are involved in immune surveillance. Peritubular renal macrophages are particularly susceptible to immune complex-mediated activation owing to their anatomic location near to small peritubular vessels that lack an intervening basement membrane. These cells expand and become both inflammatory and pro-fibrotic during LN, suggesting a dysregulated repair process.

Overall, many types of immune cell are found in the kidneys of individuals with LN. A better understanding how each infiltrating cell type contributes to renal injury is now needed so that pathogenic cells can be targeted, whereas those involved in organ protection and repair can be spared.

**Learning Objectives**
- Explain clinical and laboratory risk factors for adverse pregnancy outcomes in women with SLE
- Assess flare rates in pregnancies of women with SLE
- Manage SLE pregnancies complicated by anti-SSA/Ro antibodies

**Prime time session: treatment targets and novel therapies**

**CELLS INVOLVED IN SLE: BEYOND B CELLS**

Anne Davidson. Institute for Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, New York

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**Learning Objectives**
- Describe the heterogeneity of immune cells in lupus nephritis kidneys
- Discuss the spatial organization of immune cells in lupus nephritis kidneys

**References**

3. Kassianos AJ, et al. Increased tubulointerstitial recruitment of human CD141(hi) DCs, is associated with more advanced disease in LN.

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