EMERGING CONCEPTS IN THE RECOGNITION AND MANAGEMENT OF SLE

Question 1. What is the potential for cardiotoxicity with hydroxychloroquine?

Answer: The first thing to remember is that we should not alarm patients about antimalarial-associated cardiotoxicity. Antimalarials can be associated with hypertrophic or restrictive cardiomyopathy, or conduction disturbances; these are difficult to differentiate from the cardiomyopathy associated with SLE, and cardiotoxicity has been less-well characterized than retinopathy. However, cardiotoxicity is unheard of in patients taking doses ≤5 mg/kg in the first 10 years of treatment, and thereafter, maybe 1 in 1000 patients have clinically-relevant cardiotoxicity. Advanced age, female sex, higher cumulative dose, higher daily dose, comorbid cardiac disease, and renal dysfunction are all thought to be risk factors. We do not have any formal recommendations for screening and monitoring, but ECG and echocardiography are good first steps to assess the patient for cardiac conduction disorders, ischemia, left ventricular function, and structural abnormalities due to either the disease process or to antimalarial treatment. Neither technique is particularly helpful in clarifying the etiology of any abnormalities that are identified. T2 cardiac magnetic resonance imaging can be a sensitive method for identifying myocardial relaxation abnormalities, but endomyocardial biopsy is the gold standard for diagnosing cardiomyopathy in patients with SLE as the histological findings can differentiate the causation.

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Question 2. What is the relevance of blood level testing for hydroxychloroquine?

Answer: Monitoring hydroxychloroquine levels may be able to differentiate refractory disease from nonadherence to treatment, allowing us the opportunity to improve treatment adherence and make informed decisions when faced with a patient who is not responding to first-line treatments. Nonadherence is common in patients with lupus, and hydroxychloroquine levels are suggestive of treatment adherence. Even though hydroxychloroquine levels are only roughly correlated with response, patients with more active disease have been shown to have lower hydroxychloroquine levels, presumably due to poor adherence. In a patient with active disease and low hydroxychloroquine levels, serial monitoring and follow-up with clinical counseling can improve medication adherence, and we believe that this will lead to a long-term improvement in renal outcomes, and a reduction in flares and thrombotic events.

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Question 3. At what time during the diagnosis should you consider a kidney biopsy?

Answer: Even though there are recommendations for when to do renal biopsies, we believe they should only be contemplated if the result would actually guide or change management. That said, the American College of Rheumatology recommends renal biopsy for patients with proteinuria ≥500 mg/day, an active urinary sediment with persistent hematuria and/or cellular casts, or a rising serum creatinine. Similarly, the American Society of Nephrology suggests biopsy in the presence of proteinuria ≥500 mg/day, or any level of proteinuria or hematuria with impaired kidney function. For untreated patients with clinical evidence of lupus nephritis, biopsy should be done within the first month after disease onset and before starting immunosuppressive treatment. Currently, renal biopsy is not indicated at the completion of induction therapy. For patients who have successfully completed maintenance therapy, renal biopsy can be used to identify insidious, active lupus nephritis, and biopsy should be considered whenever a patient experiences a flare.

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