Abstracts

Learning Objectives
- Describe antimalarial muscle toxicity in skeletal and cardiac muscle
- Discuss the possible association between antimalarial treatment and QTc prolongation and its possible consequences
- Describe antimalarial deposition in cardiac muscle and its consequences
- Differentiate the role of cardiac biomarkers in the early detection of antimalarial induced cardiomyopathy

REFERENCES

03 LOW DOSE ASPIRIN IN APL-POSITIVE PATIENTS: ARE WE TREATING THE PATIENT OR THE DOCTOR?
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Patients with antiphospholipid antibodies (aPL) are at increased risk for arterial or venous thrombosis. There is, however, significant heterogeneity among patients according to clinical and laboratory features. Therefore, two therapeutic modalities can be discussed for primary prevention of thrombosis in patients: (1) primary prophylaxis in all aPL patients or (2) only in selected high-risk patients. Because aPL are often diagnosed in patients with systemic lupus erythematosus before occurrence of a first thrombosis, primary prophylaxis should be specifically discussed in this setting.

Risk for thrombosis in lupus patients may be increased by additional clinical risk factors, in particular hypertension. Laboratory profile is also important: lupus anticoagulant, double (any combination of lupus anticoagulant, anticardiolipin antibodies or anti-b2 glycoprotein I antibodies) or triple (all three subtypes) aPL positivity, as well as the presence of persistently high aPL titres indicate high risk patients. Specific risk scores may be helpful such as the global antiphospholipid syndrome score (GAPSS).

Observational data indicate that low dose aspirin reduces the risk of first thrombosis in aPL patients, particularly in those with lupus (by 50%) with a low bleeding risk. To improve the risk:benefit ratio, prescribe aspirin in patients with high-risk profiles and low bleeding risk.

Treatment failure may be due to aspirin resistance (insufficient dosage, poor absorption or drug interaction) or poor treatment adherence (long term prophylactic treatment in young patients) of which the attending physician must be aware.

In summary, prophylactic low dose aspirin in aPL positive lupus patients should be considered taking into account thrombotic and bleeding risks. Because of its long-term objectives, this treatment should be carefully explained and discussed with the patient before taking a shared decision.

Learning Objectives
- Explain when primary prophylaxis should be used for aPL
- Describe the risk factors for thrombosis in patients with lupus
- Discuss optimal treatment options for thrombosis risk reduction in patients with aPL

Session 2: The role of interferons in SLE

04 BIOLOGY OF INTERFERONS IN SLE: INSIGHTS FROM LONGITUDINAL DATA ANALYSIS
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Type I interferons (IFNs), including IFN-α, IFN-β, IFN-ω and IFN-κ, represent an essential host defense mechanism stimulated by virus infection.1 3 4 In that setting, type I IFN is tightly regulated with duration of expression limited to several days. When its production is sustained, its protein effects on immune cell function can be damaging. Activation of the type I IFN pathway, typically defined by elevated expression of type I IFN-inducible gene transcripts or their protein products, is a feature of nearly all children diagnosed with systemic lupus erythematosus (SLE), as well as the majority of adult lupus patients. Taken together with insights from murine models, studies of lupus patients have supported the conclusion that type I IFNs comprise a family of pathogenic mediators that contribute to autoimmunity, inflammation and ultimately tissue damage in patients with SLE and some other systemic autoimmune diseases, particularly primary Sjögren’s syndrome and dermatomyositis.

Coordinated expression of type I IFN-stimulated genes is a feature of most patients with SLE, but the relationship of the IFN signature to disease activity has been debated. In addition, the inducers of IFN and the molecular pathways and signaling molecules that result in IFN production have not been well defined. Endogenous nucleic acids have been identified as the relevant drivers of type I IFN production, but the specific features of those nucleic acids have not been well characterized. It is not apparent whether the endosomal toll-like receptors or cytosolic nucleic acid sensors are most relevant to IFN expression in individual patients. Finally, the mechanisms that regulate activation of the IFN pathway – or fail to regulate that pathway in some lupus patients – have not been well defined. To gain insight into these issues, we collected extensive longitudinal clinical, serologic, proteomic and gene expression data to assess the correlates of IFN pathway activation, and to establish new hypotheses regarding the relationship of autoantibody specificity and environmental exposures to production of IFN and induction of IFN-stimulated genes.

Analysis of proteomic and gene expression data collected for up to 4 years on individual patients was analyzed to