BACKGROUND: Hydroxychloroquine (HQC) cardiotoxicity remains an underrecognized condition. Diagnosis ultimately relies on invasive endomyocardial biopsy (EMB) and non-invasive screening methods are warranted. Strain imaging is a novel tool to detect early subclinical left ventricular (LV) dysfunction and may have a role in screening for HQC cardiotoxicity (1). Strain measures systolic deformation indices that when decreased can predict cardiovascular outcomes more accurately than LV ejection fraction (2).

OBJECTIVES: We assessed whether high HQC cardiotoxicity risk is associated with a specific strain pattern in a group of patients with SLE and end-stage renal disease (ESRD).

METHODS: This was a retrospective study in a tertiary care center in New York on a group of patients with an established diagnosis of SLE, ESRD and cardiomyopathy on the index echocardiogram followed between years 2003 and 2019. The patients were stratified into two groups: high risk HQC toxicity group, defined as either cumulative HQC dose ≥1000g and/or an endomyocardial biopsy confirming HQC toxicity. Low/moderate risk group was defined as a cumulative dose of HQC <1000g. Clinical, demographic, electrocardiographic and echocardiographic strain parameters were compared between the groups.

RESULTS: A total of 16 patients were included. Two patients had EMB consistent with HQC induced toxicity and 3 patients had cumulative HQC doses ≥1000g. There were no significant differences in the baseline demographic characteristics between the two groups. Compared to patients with low/moderate risk, patients in the high risk group had a lower heart rate at the time of the echocardiogram (69 vs 87 beats per minute, p<0.08) and a higher frequency of LV hypertrophy (40% vs 9.1%, p=0.02), Strain analysis showed that both groups had compromised LV global longitudinal strain (GLS) and global cross-sectional strain (GCS). However, compared to the low/moderate risk group, the high risk group had a weaker LV GLS (-12.3% vs -14.9%, p=0.02).

CONCLUSION: We report an association of higher HQC cardiotoxicity risk and impaired strain in a set of SLE ESRD patients. Standard echo measures did not differentiate between high and low/moderate risk patients. Although the findings did not reach statistical significance, given the small sample size, results are still suggestive of a possible utility of strain echocardiography for detection of early HQC toxicity.

References:

Disclosure of Interests: None declared

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THE EXPRESSION OF IFNα, IFNβ AND INFγ SERUM LEVELS OF THOSE CYTOKINES IN SJÖGREN’S SYNDROME PATIENTS

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Background: In the pathogenesis of autoimmune mediated diseases, such as Sjögren’s syndrome (SS), interferons (IFN) and IFN pathway activation play a vital role.

Objectives: We planned to assess IFNα, IFNβ and INFγ expression and IFNα serum levels in SS patients and correlation of these parameters with: autoantibodies specific for SS, serum concentration of C3, C4 component of complement C3, C4, Gamma factor (RF), gammaglobulins, focus score (FS) and eye dryness methods.

Methods: Whole blood RNA was isolated from 77 SS patients [F91%vSSM9%]; mean age 49.69±15.36; SS diagnosis according to EULAR/ACR 2016 criteria. The analysis of IFNα-, β- and γ-expression levels was based on validated TaqMan probes by ΛCT methods. Serum concentrations of rheumatoid factor (RF), C3 and C4 complement components (mg/dL) and gammaglobulins (g/dL) were assessed. Anti-Ro/SSA and/or anti-La/SSB autoantibodies were assessed by semiquantitative immunoblotting evaluation. The eye dryness and keratoconjunctivitis sicca were confirmed with Schirmer’s test (score of less than 5 mm/5”) and the ocular staining score (OSS) using lissamine green and fluorescein staining. The biopsy of minor salivary gland was performed with the histopathological evaluation of FS. The study was approved by the Bioethics Committee. Differences between groups of patients were determined using non-parametric Mann-Whitney U test or Kruskall-Wallis test with Dunn’s post hoc. Correlations were determined using non-parametric Spearman test. The level of statistical significance was set at p < 0.05.

Results: IFNα had the highest expression levels among IFNs and IFNβ serum concentrations were higher than those of IFNα and γ. In cases with high HQC serum concentration lower IFNβ expression was observed. There was a highly significant correlation between IFNα and IFNβ expression (r = 0.6;p<0.001). IFNβ expression (p<0.059) was higher in the group of younger (<45 y.o.) patients (n= 23; 29.9%) as compared to the group of older individuals (at least 45 y.o.). In patients with SS-A / Ro antibodies with strong antigen binding affinity (3) IFNβ expression and IFNγ serum levels were highest of all IFNs. The presence of anti La/SS-B antibodies was associated with the increased IFNγ expression while not with the increased IFNβ serum concentration. In terms of IFNα expression and protein level, RF(+) patients had average higher values compared to RF(-) patients. The average mRNA level of IFNα was about 3 times lower in patients with low Schirmer’s test (<5mm/5”) in comparison to patients with Schirmer’s test<5mm/5”; Schirmer’s test ≥5mm/5” was associated with higher IFNβ serum concentration.

Conclusion: Type I IFN signature predominates in the peripheral blood of studied patients. Presented results confirmed the pivotal role of type I IFN in the disease process. The serum concentration of IFNα and the expression of IFNβ were the highest values of those parameters for cytokines assessed in this study. A positive correlation between IFNα and IFNβ mRNA levels has been observed.

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