THU0276

HIGH HYDROXYCHLOROQUINE EXPOSURE IS ASSOCIATED WITH ABNORMAL STRAIN IMAGING IN LUPUS PATIENTS WITH END-STAGE RENAL DISEASE

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Background: Hydroxychloroquine (HCQ) 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 HCQ 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 HCQ 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 HCQ toxicity group was defined as either cumulative HCQ dose ≥ 1000 g and/or an endomyocardial biopsy confirming HCQ toxicity. Low/moderate risk group was defined as a cumulative dose of HCQ < 1000 g. 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 HCQ induced toxicity and 3 patients had cumulative HCQ doses ≥ 1000 g. 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%, $p=0.2$). 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% , $p=0.27$).

Characteristics overall and stratified by HCQ risk group

	Characteristic	Overall (n=16)	Low/Moderate HCQ Risk (n=11)	High HCQ Risk and/or Positive EMB (n=5)	P value
Demographics	Age, years	47.5 (36.5,60.7)	50.0 (33.9,60.5)	42.5 (42.7,61.0)	0.95
	Female, n(%)	14 (87.5)	9 (90)	5 (83.3)	0.99
Clinical Features	SLE duration, years	7.4 (4.3,17.5)	5.5 (3.5,13.2)	15.6 (11.6,19.3)	0.15
	HCQ cumulative dose, g	422.8 (224.2,422.8)	285.4 (110.8,523.6)	1140 (1006,1625.4)	0.005
	HCQ therapy duration, years	3.4 (2.5, 8.9)	3.2 (1.5,5.1)	7.8 (6.8,11.6)	0.06
	HCQ daily dose, mg/d	226 (200,394.9)	200 (179.4,253.7)	400 (389.8,400)	0.007
	Hypertension, n (%)	14 (87.5)	10 (90.9)	4 (80.0)	0.99
	Diabetes, n (%)	3 (18.8)	2 (18.8)	1 (20.0)	0.99
Echocardiogram	CAD, n (%)	3 (18.8)	2 (18.8)	1 (20)	0.99
	EF, %	55 (42.5,60)	55 (40,60)	55 (55,70)	0.45
	LA size, cm	3.8 (3.4,4.3)	3.8 (3.4,4.2)	4.3 (3.4,4.9)	0.30
	LVEDD, cm	4.9 (4.4, 5.5)	4.8 (4.2,5.5)	5.0 (4.9,5.4)	0.43
	E/E'	12.3 (8.8,16.3)	12 (8.8,14.9)	16.9 (4.9,21.8)	0.43
	Moderate-severe LV hypertrophy, n(%)	3 (18.7)	1 (9.1)	2 (40.0)	0.20
Strain echocardiography	GLS, %	-13.9 (-16.7,-12.3)	-14.9 (-16.7,-12.9)	-12.3 (-15.4,-12.2)	0.27
	Base/Apex Ratio	0.8 (0.7,0.9)	0.76 (0.68,0.86)	0.76 (0.66,0.83)	0.95
	GCS, %	-20.2 (-21.7,-17)	-19.7 (-20.5,18.0)	-21.7 (-23.9,-20.9)	0.16
	RV GLS, %	-20.19 (-22.1,-17.5)	-20.2 (-22.3,-17.1)	-19.8 (-22.1,-17.5)	0.99

Conclusion: We report an association of higher HCQ 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 HCQ toxicity.

References:

- [1] Buss SJ, et al. J Rheumatol. 2010;37(1):79-86
- [2] Kalam K, et al. Heart. 2014;100(21):1673-80

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THU0277

THE EXPRESSION OF IFNA, INFβ AND INFγ AND 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, INFβ and INFγ expression and IFNs 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), rheumatoid factor (RF), gammaglobulins, focus score (FS) and eye dryness symptoms.

Methods: Whole blood RNA was isolated from 77 SS patients [F91%vsM9%]; 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 ΔCT 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 Kruskal-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: IFNβ had the highest expression levels among IFNs and IFNβ serum concentrations were higher than those of IFNα and -γ. In cases with high IFNβ 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) IFN β expression and IFNβ serum levels were highest of all IFNs. The presence of anti La/SS-B antibodies was associated with the increased IFNβ 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 C3 serum concentration compared to patients with normal C3 serum concentration values. IFNβ mRNA level was 2.5 times lower in patients with low Schirmer's test ($< 5\text{mm}/5'$) in comparison to patients with Schirmer's test $\geq 5\text{mm}/5'$; Schirmer's test $< 5\text{mm}/5'$ 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 IFNβ 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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THU0278

NAILFOLD CAPILLAROSCOPY IN SJÖGREN'S SYNDROME: A SYSTEMATIC LITERATURE REVIEW AND STANDARDISED INTERPRETATION

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