THU0334

EFFECT OF THE DELAY FROM INITIAL SYMPTOMS TO DIAGNOSIS OR THERAPY INITIATION, ON DISEASE CONTROL AND MORTALITY, IN INFLAMMATORY MYOSITIS PATIENTS FROM THE INFLAMMATORY MYOSITIS REGISTRY FROM THE MADRID COMMUNITY (REMICAM)

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Background: In inflammatory diseases, such as rheumatoid arthritis, early treatment has demonstrated to improve disease control and decrease mortality. It is not known if an early treatment could have similar effects on inflammatory myositis (IM) patients.

Objectives: To analyze if the delay between initial symptoms and diagnosis or therapy initiation influences disease control or mortality in IM patients.

Methods: All patients from REMICAM were included (1). The influence of time elapsed between initial symptoms and diagnosis or start of therapy, and the year of diagnosis (before or after 2000), on mortality and disease control (defined as the possibility of glucocorticoid (GC) withdrawal due to IM improvement), was studied by means of survival analysis and regression proportional hazard bi and multivariate Cox models. All factors with $p < 0.2$ in bivariate were included in multivariate models. The mortality analysis was controlled for age, sex, and other known mortality factors: cardiovascular risk factors, interstitial lung diseases (ILD), cardiac involvement and cancer. The disease control analysis was controlled for age, sex and other known severity factors such as ILD, cardiac involvement and IM subtypes.

Results: From 479 patients (74% females, 52% polymyositis, 44±22 years at diagnosis, 10±8 years follow up), 208 (43%) were diagnosed before 2000, and 473 (99%) received any treatment: 473 (99%) oral GC, 50/344 (15%) GC pulses, 78 (16%) HCL, 355 (74%) immunosuppressants (IS) (MTX 228, LF 10, AZA 190, CYP 44, MP 38, CyS 32), 55 (12%) biologics (RTX 45, abatacept 2, aTNF 16) and 79 (17%) IVIG. Disease control was more frequent in younger patients, diagnosed after year 2000, and was independently associated with less ILD presence, lower n° of therapies and a shorter time between the initial symptoms and the start of IS therapy (Table 1). Risk factors for mortality were age, male sex and cancer, but not the delay in diagnosis or in the start of therapy (Table 2)

Abstract THU0334 –Table 1.

	Bivariate		Multivariate	
	HR (IC95%)	p	HR (IC95%)	p
Age at diagnosis	0.97 (0.96-0.98)	<0.0001	0.97 (0.96-0.98)	<0.0001
ILD	0.3 (0.2-0.5)	<0.0001	0.4 (0.3-0.8)	0.006
Diagnosis < 2000		0.07	1.9 (1.2-3.1)	0.006
N therapies	0.8 (0.7-0.9)	<0.0001	0.7 (0.6-0.8)	<0.0001
Any IS	0.6 (0.4-0.8)	0.004	0.08 (0.01-0.6)	0.02
Initial symptoms to IS	0.987 (0.981-0.993)	<0.0001	0.98 (0.97-0.99)	<0.0001

Abstract THU0334 –Table 2.

	Bivariate		Multivariate	
	HR (IC95%)	p	HR (IC95%)	p
Sex	0.5 (0.3-0.8)	0.003	0.56 (0.36-0.87)	0.01
Age at diagnosis	1.05 (1.04-1.07)	<0.0001	1.05 (1.04-1.06)	<0.0001
Cancer	3.4 (2.2-5.2)	<0.0001	1.9 (1.2-2.9)	0.003

Conclusion: In the REMICAM cohort, disease control is more frequent in younger patients, diagnosed after 2000, with early initiation of IS therapy. Mortality was not associated with the delay in diagnosis or therapy in our study. Our data support the hypothesis that, in IM, as in other inflammatory diseases, an early treatment is essential to decrease inflammation and achieve disease control.

REFERENCE:

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THU0335

FIBROSIS IS NOT JUST FIBROSIS – TGF-B AND PDGF INDUCE DIFFERENT EXTRACELLULAR MATRIX PROFILE: A MODEL OF DERMAL FIBROBLASTS WHICH MIMICS SYSTEMIC SCLEROSIS POTENTIAL FOR EVALUATION OF ANTI-FIBROTIC COMPOUNDS WITH TRANSLATIONAL BIOMARKERS

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Background: Fibroblasts are responsible for the excessive extracellular matrix formation (ECM) observed in systemic sclerosis (SSc). These cells are activated by stimulants from both the vascular and immune systems, including platelet derived growth factor (PDGF) and transforming growth factor beta (TGF-β). While both TGF-β and PDGF induces extracellular matrix (ECM) formation, there is a need to understand the quantitative differences to allow for more optimal drug development and patient targeted therapies. This may be accomplished by using translational tools in cell culture systems for the evaluation of potential anti-fibrotic compounds in SScs.

Objectives: This study investigated the ability of dermal fibroblast to produce ECM that mimics SSc though the use of clinical validated biomarkers.

Methods: Primary human dermal fibroblasts were grown in DMEM media containing 0.4% fetal calf serum, FICOLL (to produce a crowded environment) and ascorbic acid for 14 days. The cells were stimulated with PDGF [0.04-4 nM], TGF-β [0.01-4 nM], a combination of interleukin 6 (IL-6) [3 nM] and the soluble IL-6 Receptor (sIL-6R) [0.3 nM], or a combination of TGF-β [1 nM], IL-6 [3 nM], and sIL-6R [0.3 nM]. An ALK-5 (TGF-β receptor) inhibitor (iALK-5, [1 nM-10 μM]) was added together with 1 nM TGF-β with or without 7 days pretreatment and stimulated for 17 days in total. Media were changed twice a week. Unstimulated cells (w/o) were used as controls. Type I, III and VI collagen formation (PRO-C1, PRO-C3, PRO-C6) and fibronectin (FBN-C) were evaluated by ELISAs in the supernatant collected at each media change. Staining with hematoxylin and eosin (H&E) together with immunohistochemical staining were performed. Kruskal-Wallis tests were used to examine the difference between treatments at different days.

Results: Stimulation with TGF-β induced type I collagen formation from day 3, with a 4-fold change (FC) detected on day 10 compared to w/o ($P < 0.0001$, Figure 1), and type III collagen formation in a dose dependent manner from day 10 (4.4-FC, $P < 0.0001$). TGF-β did not induce type VI collagen formation. PDGF induced type III collagen formation from day 6, with an 8.3-FC by day 10 ($P < 0.0001$) and type VI collagen formation from day 3 with a 6.0-FC by 10 ($P = 0.0006$). PDGF did not induce type I collagen formation. Media alone did not induce any collagen formation. H&E staining showed that fibroblasts treated with PDGF and TGF-β were more confluent and disorganized compared to untreated cells. Visual examination showed type I collagen attachment to the bottom of the wells and this increased in response to stimulants.

Abstract THU0335 – Figure 1