FRI0306

IDIOPATHIC INFLAMMATORY MYOPATHIES AND ANTISYNTHEASE SYNDROME: CONTRIBUTION OF ANTISYNTHEASE ANTIBODIES TO IMPROVE CURRENT CLASSIFICATION CRITERIA

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Background: The presence of muscle weakness and anti-Jo1 anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies, are evaluated in the new EULAR/ACR proposed classification criteria for adult and juvenile idiopathic inflammatory myopathies (IIM), as well as in the Solomon proposed criteria for antisynthetase syndrome (ASSD) diagnosis (1, 2). That favors an overlapping in both criteria fulfillment; however, the ASSD are not considered among the IIM subgroups classification. Anti-Jo1 ARS positivity is the highest weighted criterion in the EULAR/ACR criteria; nevertheless, other ARS were not included. Any ARS positivity is considered in Solomon's criteria.

Objectives: To evaluate if the detection of non-anti-Jo1 ARS could improve the EULAR/ACR criteria performance, and additionally to contribute to a better classification of the antisynthetase syndromes.

Methods: We performed an observational retrospective study in 2 centers. All patients with clinical suspicion of ASSD or myositis, and positive ARS in the myositis immunoblot (Euroimmun assay) were included. We assessed: 1) The rate of patients meeting EULAR/ACR and Solomon's criteria; 2) The rate of patients with anti-Jo1 and with non-anti-Jo1 ARS that fulfilled them; and 3) The rate of patients with non-anti-Jo1 ARS meeting the EULAR/ACR criteria if we assign to these antibodies the same weight as anti-Jo1 ARS.

Results: A total of 37 patients were included; 70.3% woman, with a mean age at the moment of the ARS detection of 51.4 (SD±14.0) years. The frequency of ARS was: anti-Jo1 (n=17), anti-PL-12 (n=8), anti-PL-7 (n=4), anti-EJ (n=4), and anti-OJ (n=4).

Twenty-two of 34 patients (59.5%) met EULAR/ACR criteria and 17 (45.9%) met Solomon's criteria. Thirteen patients (35.1%) fulfilled both criteria, representing the 59.1% of those who met EULAR/ACR criteria and the 76.5% of those who met Solomon's criteria.

Analyzing by antibodies, all patients with anti-Jo1 ARS (n=17) met EULAR/ACR criteria. Among the patients with non-anti-Jo1 ARS (n=20), only 5 (25%) met the criteria; however, if we gave the anti-Jo1 weight to the other ARS when applying the EULAR/ACR criteria, 19 of the 20 cases (95%) would meet them.

Besides, considering the clinical features, 10 of the 20 patients with non-anti-Jo1 ARS (50%) presented clinically objectified muscle weakness, and only 4 of them met EULAR/ACR criteria; nevertheless, weighing any ARS as anti-Jo1, the other 6 cases would be reclassified as IIM.

Conclusion: All cases with anti-Jo1 positivity met EULAR/ACR criteria, but not those with other ARS. Nevertheless, when we applied the EULAR/ACR criteria assigning to all ARS the same weight as anti-Jo1, all except one patient fulfilled the criteria; thus, the most important result was that all patients with clinically objectified muscle weakness and non-anti-Jo1 ARS that initially did not meet the EULAR/ACR criteria could be re-classified as IIM.

In this way, our results suggests that the detection of non-anti-Jo1 ARS in patients with myopathy suspicion, could increase the sensitivity of the EULAR/ACR classification criteria; and that the ASSD, when presents myositis, should be considered among the IIM classification subgroups.

REFERENCES:

- [1] Lundberg IE, et al. *Annals of the rheumatic diseases*. 2017;76(12):1955-64.
- [2] Solomon J, et al. *Jornal brasileiro de pneumologia*. 2011;37(1):100-9.

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LENABASUM, A CANNABINOID TYPE 2 RECEPTOR AGONIST, REDUCES CD4 CELL POPULATIONS AND DOWNREGULATES TYPE 1 AND 2 INTERFERON ACTIVITIES IN LESIONAL DERMATOMYOSITIS SKIN

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Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 (CB2) agonist that activates resolution of innate immune responses. CB2 is a G-protein coupled receptor found primarily on activated immune cells. In vitro, it has shown to affect T-cell activity, alter Th1 and Th2 cytokine production, and decrease type 1 interferon activity.

Objectives: We sought to characterize the in vivo effect of lenabasum on inflammatory cells and cytokines thought to be involved in the itch and disease pathogenesis of dermatomyositis (DM).

Methods: 22 adult patients with refractory, skin-predominant DM on stable standard-of-care treatments were recruited for a double-blind, placebo-controlled, randomized trial. Treatment was initially administered orally at a dose of 20 mg a day for 4 weeks, and subsequently raised to 20 mg twice a day for an additional 8 weeks. In a subset of subjects, lesional skin biopsies were collected at baseline and at Week 12. Tissues were stained via immunohistochemistry for IFN-beta, IFN-gamma, IL-4, IL-13, IL-33, IL-31, IL-31 RA, CB2 receptor, PPAR-gamma, CD4, CD8, CD69, CD11c, and mast cells. RT-PCR for IFN-beta, IFN-gamma, IL-31, IL-4, STAT6, and ST2 was performed on tissue RNA. Protein expression was quantified either by percent area positive or cells per HPF in the dermis. Statistical analyses were performed using the Wilcoxon signed-rank test.

Results: CD4 expression in the skin biopsies from lenabasum-treated subjects significantly decreased at Week 12 compared to the placebo group (p<0.05). There were significant reductions in IFN-beta mRNA and protein, as well as IFN-gamma mRNA and protein at Week 12 in subjects on lenabasum compared to placebo (p < 0.05). IL-31 protein (p < 0.01) was reduced at Week 12 in subjects who received lenabasum, but IL-31RA protein did not change. CB2 protein decreased significantly in the lenabasum group compared to placebo. There were no changes in IL-4, IL-13, IL-33, and PPAR-gamma protein, or the number of CD8, CD69, CD11c, or mast cells in either group. There was no significant difference in IL-31, IL-4, STAT6, or ST2 mRNA expression.

Conclusion: Lenabasum reduces Type 1 and 2 interferon levels as well as T-helper cell inflammation in subjects with DM. These effects have the potential to inhibit underlying disease pathways in DM, thus contributing to clinical improvement.

REFERENCES:

- [1] Kim, H.J., Zeidi, M., Bonciani, D., Pena, S.M., Tiao, J., Sahu, S. and Werth, V.P. Itch in dermatomyositis: the role of increased skin interleukin-31. *British Journal of Dermatology*. 2018;179(3):669-678.
- [2] Robinson ES, Alves P, Bashir MM, Zeidi M, Feng R, Werth VP. Cannabinoid Reduces Inflammatory Cytokines, Tumor Necrosis Factor- α , and Type I Interferons in Dermatomyositis In Vitro. *J Invest Dermatol*. 2017;137(11):2445
- [3] Wong D, Kea B, Pesich R, Higgs BW, Zhu W, Brown P, et al. Interferon and biologic signatures in dermatomyositis skin: specificity and heterogeneity across diseases. *PLoS One*. 2012;7(1):e29161.

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HIGH LEVEL OF SERUM NEOPTERIN IS ASSOCIATED WITH RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE AND REDUCED SURVIVAL IN DERMATOMYOSITIS

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Background: Neopterin is primarily synthesized and released by activated macrophages/monocytes upon stimulation with interferon- γ and is considered as a marker for macrophage activation.

Objectives: This study aimed to analyze the serum levels of neopterin in patients with dermatomyositis (DM) in association with clinical manifestations, laboratory data and patient prognosis.

Methods: One hundred and eighty-two consecutive DM patients and 30 healthy controls were retrospectively enrolled in the study. Serum levels of neopterin were detected by using the ELISA method. Clinical and laboratory data and patient prognosis were obtained and analyzed in association with serum neopterin.

Results: Serum levels of neopterin were significantly increased in DM patients (median 21.2 nmol/L, IQR 13.9-35.2 nmol/L) compared to healthy controls (median 4.3 nmol/L, IQR 2.9-5.6 nmol/L, $P < 0.01$). High serum neopterin levels were associated with anti-MDA5 antibody, rapidly progressive interstitial lung disease (RP-ILD), and cutaneous involvement including skin ulcer and heliotrope rash. Longitudinal assessment of serum samples revealed that the serum neopterin levels were closely correlated with disease severity. In addition, a significant increase in serum neopterin concentration of non-survivors (median 38.7 nmol/L, IQR 23.5-65.3 nmol/L) was observed when compared to that of survivors (median 19.0 nmol/L, IQR 12.5-29.0 nmol/L) ($P < 0.01$). ROC curves showed that serum neopterin could distinguish non-survivors and survivors at an optimal cut-off level of 22.1 nmol/L with a sensitivity and specificity of 0.804 and 0.625 respectively ($P < 0.01$). Kaplan-Meier survival curves revealed that DM patients with serum neopterin > 22.1 nmol/L had a significantly higher mortality compared to patient group with serum neopterin < 22.1 nmol/L (logrank $P < 0.01$). Multivariate Cox regression analysis identified high serum neopterin concentration to be an independent risk factor for poor prognosis in DM (adjusted HR=4.619, 95%CI: 2.092-10.195, $P < 0.01$).

Conclusion: Increased serum levels of neopterin were significantly associated with RP-ILD and reduced survival in DM patients, suggesting it as a promising biomarker in the disease evaluation of DM. These findings highlight the role of cellular immune activation and macrophage activity in the pathogenesis of DM.

REFERENCE:

- [1] Murr C, Widner B, Wirltner B, et al. Neopterin as a marker for immune system activation. *Current drug metabolism* 2002; 3: 175-87.

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FR10309 SEVERE ABDOMINAL MANIFESTATIONS IN JUVENILE DERMATOMYOSITIS

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Background: Juvenile dermatomyositis (JDM) is a rare and heterogeneous children-onset idiopathic inflammatory myopathy. It primarily affects skeletal muscle and skin, but also pulmonary, cardiac and gastrointestinal systems in a subset of patients. Gastrointestinal (GI) involvement occurs in 22 to 37% of JDM patients and have been described only in a few case reports.

Objectives: To describe causes of severe abdominal manifestations in JDM patients.

Methods: Retrospective monocentric study. Inclusion criteria were (i) diagnosis of JDM according to the modified Bohan and Peter criteria before 16 years of age, (ii) occurrence of severe involvement of any intra-abdominal organ, (iii) follow-up at Necker Hospital from 2005 to 2018. Severe abdominal manifestation was defined as a potential life-threatening abdominal organ event, need for abdominal surgery and/or parenteral nutrition. Gastrointestinal (GI) involvement was defined by severe abdominal pain, dysphagia, digestive hemorrhage, obstruction, ulceration and/or perforation. Severe hepatitis was defined by an elevation of liver enzymes exceeding five times the upper limit associated with an elevation of γ -glutamyl transferase (γ GT) activity and/or liver failure. Abdominal manifestations were classified as certain or probable primary JDM involvement, therapy-related event or infection-related event.

Results: Nine patients with 19 abdominal complications were identified among 110 JDM patients followed during the study period (8.3%).

Diagnosis of JDM was made at a median age of 10.7 years-old [range, 3.7 – 14.4], with a median CMAS of 7 [range, 2 – 48], median MMT of 47 [range, 38 – 76], a median creatine kinase level of 3 812 UI/L [range, 170 – 14 054], and a median follow-up of 3 years [range, 0.4 – 6.3]. Seven patients were positive for either anti-NXP2 ($n = 4$), anti-TIF1- γ ($n = 2$) or anti-MDA5 ($n = 1$) antibodies. JDM-related abdominal disease comprised GI involvement ($n = 10$), acute pancreatitis ($n = 4$) and hepatitis ($n = 3$). The revealing symptom for GI involvement and acute pancreatitis was abdominal pain. Five patients with severe abdominal pain, vomiting and/or obstruction, underwent abdominal imaging revealing thickening of colon ($n = 2$) and/or ileum mucosa ($n = 2$). Hepatitis was found in 3 patients with an uncommon extensive steatosis with moderate inflammation and perisinusoidal fibrosis ($n = 2$). Treatment-related complications were considered certain for methotrexate-induced liver toxicity (1 patient) and possible for duodenal perforations (1 patient) 3 days after a methylprednisolone pulse. At last visit, JDM was clinically inactive in four patients. Three patients died from refractory JDM, 2.9 years [range, 2 – 3.6] after the JDM diagnosis, among the 9 patients identified in this study *versus* only 1/92 of the other JDM patients from our cohort.

Conclusion: Primary JDM involvement was the main cause of severe abdominal manifestations and associated to a high mortality rate. We highlight for the first time that pancreatitis should be considered as a main diagnosis in JDM patients who develop severe and/or sustained abdominal pain.

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FR10310 UNIVERSITY OF CALIFORNIA LOS ANGELES SCLERODERMA CLINICAL TRIALS CONSORTIUM GASTROINTESTINAL TRACT 2.0 REFLUX-SCALE ASSOCIATES WITH IMPAIRED ESOPHAGEAL SCINTIGRAPHY FINDINGS IN SYSTEMIC SCLEROSIS

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Background: The University of California Los Angeles Scleroderma Clinical Trials Consortium gastrointestinal tract 2.0 (UCLA SCTC_GIT 2.0) questionnaire is a self-reported tool including 7-multi-item scales and measuring GI quality of life both in clinical trials and day-to-day clinic care of systemic sclerosis (SSc) patients (1). Scarce data are available on the correlation between patient reported GI symptoms and motility dysfunction as assessed by esophageal scintigraphy.

Objectives: To evaluate the UCLA SCTC_GIT 2.0 score in SSc patients undergoing esophageal scintigraphy and correlate their findings.

Methods: Data of SSc patients admitted to our clinic, undergoing esophageal scintigraphy, were reviewed. The score of UCLA SCTC_GIT 2.0, usually administered to all attending SSc patients, was calculated. Data were expressed as percentage (%) and mean $\pm$ standard error. Pearson's test was used for Prism 7 correlation analysis. $P < 0.05$ was considered significant.

Results: Of all the SSc patients admitted to our clinic from 1st Sept 2017 to 31st December 2018, twenty underwent esophageal scintigraphy. Seventeen were female, 4 with diffuse subset, mean age was 51 (± 3.4) years, disease duration of 6.8 (± 1.2 years) years. Twelve (60%) patients reported esophageal (reflux, dysphagia) symptoms, 5 (25%) stomach (early satiety, vomiting) and 9 (45%) intestinal (bloating, diarrhea, constipation) symptoms while 3 (15%) reported no symptoms. Mean $\pm$ SE scores of UCLA SCTC_GIT 2.0 items were: reflux 0.8 $\pm$ 0.2, distention 0.9 $\pm$ 0.2, fecal soiling 0.5 $\pm$ 0.2, diarrhea 0.5 $\pm$ 1, social 0.5 $\pm$ 0.1, emotional 0.5 $\pm$ 0.2, constipation 0.5 $\pm$ 0.1, and total UCLA SCTC_GIT 2.0 0.6 $\pm$ 0.1. Nine (45%) patients had no-mild, 4 (20%) moderate and 7 (35%) severe to very-severe reflux score. Esophageal scintigraphy showed hypomotility in 16 (80%) patients who had a higher UCLA SCTC_GIT 2.0 reflux score compared with the remaining 20% patients (1