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POS0886

COULD BE INTERSTITIAL MYOCARDITIS A FEATURE OF THE ANTISYNTHEASE SYNDROME?

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Background: Antisynthetase syndrome (ASS) is characterized by inflammatory myopathy, interstitial lung disease, arthritis, mechanical hands and Raynaud phenomenon, among other features. Recent studies have shown that idiopathic inflammatory myopathies (IIM) may develop cardiac involvement, either ischemic (coronary artery disease) or inflammatory (myocarditis). We wonder if characteristic lung interstitial involvement (interstitial lung disease) that appears in patients with the ASS may also affect the myocardial interstitial tissue. New magnetic resonance mapping techniques could detect subclinical myocardial involvement, mainly as edema (increase extracellular volume in interstitium and extracellular matrix), even in the absence of visible late Gadolinium enhancement (LGE).

Objectives: Our aim was to describe the presence of interstitial myocarditis in a group of patients with ASS.

Methods: Cross-sectional, observational study performed in a tertiary care center. We included 13 patients diagnosed with ASS (7 male, 53%, mean (SD) age at diagnosis 56,8 years ($\pm 11,8$)). The patients were consecutively selected from our outpatient myositis clinic. Myositis specific and associated antibodies were performed by means of line immunoblot (EUROIMMUN[®]). Cardiac magnetic resonance (CMR) was performed on all patients. The study protocol includes functional cine magnetic resonance and standard late gadolinium enhancement (LGE), as well as novel parametric T1 and T2 mapping sequences (modified look locker inversion recovery sequences - MOLLI) with extracellular volume (ECV) calculation 20 minutes after the injection of a gadolinium-based contrast material.

Results: CMR could not be performed in one patient due to anxiety. All patients studied (12) had a normal biventricular function, without alteration of segmental contraction. A third (4 out of 12, 33%) of the studied patients showed elevated T2 myocardial values without focal LGE, half of them (2/4) with an elevated ECV, consistent with myocardial edema. Two patients with normal T2 values showed unspecific LGE focal patterns, one in the right ventricle union points and another with mild interventricular septum enhancement (Figure 1). None of the patients studied refer any cardiac symptomatology. All the four patients with T2 mapping alterations (100%) had interstitial lung involvement, but only 4 out of 8 (50%) of the rest ASS patients without T2 mapping positivity. The autoimmune profile was as follows: 10 anti-Jo1/Ro52, 1 anti-EJ/Ro52, 2 anti-PL12.

Figure 1. Cardiac magnetic resonance images from ASS patients.

Conclusion: Myocarditis, although subclinical, appears to be a feature in ASS patients. T1 and T2 mapping sequences might be valuable to detect and monitor subclinical cardiac involvement in these patients. The possibility that the same etiopathogenic mechanism may be involved in the interstitial tissue in lung and myocardium is raised. More studies must be done in order to assert the prevalence of myocarditis in ASS.

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TRANSCRANIAL ELECTRICAL STIMULATION IS SAFE AND EFFICIENT IN PATIENTS WITH SYSTEMIC AUTOIMMUNE MYOPATHIES

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Background: There is currently few information regarding rehabilitation in patients with systemic autoimmune myopathies (SAMs). Transcranial direct current stimulation (tDCS) has shown promising results for the motor performance of healthy individuals as for patients with, e.g., post-stroke hemiparetic limbs.

Objectives: The present study was aimed to assessing the safety and efficiency of tDCS in patients with SAMs.

Methods: This study is a prospective, randomized, sham controlled, double blind, and clinical trial with ethical approval. Eighteen adult patients with dermatomyositis, polymyositis, antisynthetase syndrome or immune-mediated necrotizing myopathies in remission or with minimal disease activity were enrolled from 2018 to 2019. Patients were allocated randomly in two groups to receive sham or active tDCS with 2mA amplitude submitted for 20 minutes for three consecutive days. The 5x7cm sponge-electrodes were positioned with the anode over the left (C1) or right (C2) - contralateral to the dominant limb, whereas the cathode over the FP2 or FP3, respectively (10-10 EEG electrodes placement). The groups were evaluated in four moments: pre-stimulation, and 30 minutes, 3 weeks and 8 weeks post-tDCS. They were evaluated in the different moments with International Myositis Assessment and Clinical Studies Group set scores, Short-Form health survey (SF-36), state-trait anxiety inventory (STAI), Beck depression inventory (BDI), timed up-and-go test (TUG), time-stands test (TST), isokinetic extension and flexion testing of bilateral knee and elbow. A specific security questionnaire for tDCS was used after the active or sham stimulation in all patients.

Results: The demographic data, kind of myositis, disease duration, and disease status (all with low disease activity) were comparable between both active and sham tDCS groups. After interventions, there was improvement of values of patient's VAS ($P=0.042$) and serum levels of creatine phosphokinase ($P=0.005$), independent of the group. Moreover, in active tDCS group, the physical aspects of SF-36 in week 8 ($P<0.001$), mean and better TST at each evaluation ($P<0.001$), absolute peak tork ($P<0.001$) and peak tork adjusted for body weight values ($P<0.001$) of stimulated inferior limb extension also improved. No differences were observed in the STAI, BDI, or TUG in both groups. The patients' adherence to the protocol was 100% and no adverse event was reported, including disease relapsing.

Conclusion: This unprecedented study evidences the safety of tDCS, besides the potential efficiency in improving rehabilitation of tDCS in SAMs. More studies with a large samples and period of tDCS sessions are necessities to corroborate with the present study.

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EPIDEMIOLOGICAL AND CLINICAL DIFFERENCES BETWEEN ANTI-MDA5 PHENOTYPES: DATA FROM A LARGE COHORT (MEDRA5) STUDY

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Background: Idiopathic inflammatory myopathies are a heterogeneous group of systemic autoimmune diseases. Several phenotypes have been linked to specific autoantibodies. Clinically amyopathic dermatomyositis with rapidly progressive interstitial lung disease, the most severe form of ILD, is associated with the anti-MDA5 antibodies. However not all the patients with dermatomyositis and anti-MDA5 positive antibodies develop this severe condition.

Objectives: We aim to define different phenotypes from a large cohort of patients diagnosed with dermatomyositis who were positive to anti-MDA5 antibodies.

Methods: We retrospectively analyzed the clinical and immunological data of 90 anti-MDA5 patients [50 female, 55.6%, mean (SD) age at diagnosis 47 (15.4) yrs.] with dermatomyositis recruited from a multicenter register in Spain (MEDRA5) including 30 hospitals. All the patients fulfill de International Myositis Classification Criteria (EULAR/ACR) for dermatomyositis (score >90%). Anti-MDA5 were detected by means of commercial immunoblot (EUROIMMUN®). The chi-square test was used to assess the relationships between qualitative variables. The Kruskal-Wallis test was used to compare medians between groups.

Results: Sixty-six patients (73.3%) were diagnosed with clinically amyopathic dermatomyositis. Three different phenotypes linked with the anti-MDA5 antibody were identified. Group 1: patients with rapidly-ILD phenotype (28 patients, 31.1%), group 2: antisynthetase-like phenotype (23 patients, 25.5%), and group 3: non-ILD phenotype (39 patients, 43.3%). Clinical and immunological comparison between the groups disclosed that age at disease onset was higher (median, IQR) in patients from group 1 [53 (43-60)] vs. group 2 [46 (40-56)] or group 3 [42 (41-51)] ($p=0.01$); disease onset was more frequent in spring in patients from group 1 (46.5%) than in the rest of the groups (21.7% and 28.9%) ($p<0.01$). Cancer was detected in 7 patients, only associated with myositis in 3 cases (3 years interval between cancer and dermatomyositis) without significant differences between phenotypes. Vasculitis (one case ANCA positive) was detected in 9 cases (6 limited to skin, 1 renal and 1 intestinal), 6 of them in the group 3 (statistical significance, in comparison with group 1 and 2, $p<0.01$). Mortality rate was higher in group 1 (51.9%, 16 out of 17 due to refractory respiratory failure) vs group 2 (12.5%) or 3 (0%) ($p<0.001$). Anti Ro52 positivity was more frequent in group 1 (65.4%) vs. group 2 (25%) or 3 (35.5%) ($p<0.017$), although it did not reach statistical significance in terms of mortality ($p=0.173$) or patients admitted in the intensive care unit ($p=0.173$). Mechanic hands were more frequent in group 2 (40.6%) than in groups 1 (25%) and 3 (34.4%) ($p=0.05$). Fever was significantly most frequent in group 1 (52.6%) than in group 2 (21.1%) and 3 (26.3%) ($p=0.001$). Other clinical or immunological features such as arthritis, myositis, or the number of characteristic skin lesions among others were not more frequent in one group or another.

Conclusion: Three different phenotypes of patients positive to anti-MDA5 were identified. The presence or not of ILD, or the different type (rapidly progressive or not) of ILD were the main feature that allow to differentiate these phenotypes, which are relevant in clinical practice.

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POS0889

CO PRESCRIPTION OF ANTI-ACID THERAPY REDUCES THE BIO AVAILABILITY OF MYCOPHENOLATE MOFETIL IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Mycophenolate mofetil (MMF) is an effective treatment option for systemic sclerosis (SSC). However, many patients require co administration of proton pump inhibitors (PPI) or H2 receptor blockers (HRB) because of significant gastrointestinal manifestations in SSC. Co-treatment with PPI or HRB have shown to be associated with reduced drug exposure in post-transplant patients.^{1, 2} There is scarcity of data among patients with SSC. We evaluated the drug concentration of MMF over 12 hours of exposure and assessed the impact of ranitidine and PPI in twenty patients with SSC.

Objectives: To assess the effect of esomeprazole or ranitidine on the bioavailability of MMF in SSC patients who are on a stable dose of MMF.

Methods: Twenty SSC patients, who were on a stable dose of MMF (1.5-3 g) for the past 3 months were selected for the study after obtaining informed written consent. All patients were given either MMF (without PPI or HRB), MMF + esomeprazole, MMF + ranitidine for one month each. At the end of each month, EDTA plasma samples were collected at various time points including 0, 1/2, 1, 1½, 2, 2½, 3, 4, 5, 6, 8 and 12 hours following drug administration to determine the 12-hour area under curve (AUC) of mycophenolic acid (MPA) levels. Estimation of MPA levels was carried out using reverse phase high performance liquid chromatography (HPLC). Total gastrointestinal score was calculated at the end of each month using UCLA Scleroderma Clinical Trial Consortium GIT 2.0 scoring. To compare the mean AUC, linear mixed effect model was fit by considering treatment as the fixed effect and subject as the random effect. MMF was set as the reference treatment for the other three treatments and these were analysed together using Linear mixed effect model.

Results: All patients were females with mean age of 45 years. Addition of either ranitidine or esomeprazole significantly reduced the mean AUC and C max of the MMF over 12-hour time period. On the other hand, PPI or HRB helped in reduction of the total GI score at the end of 1 month. Details of pharmacokinetics are depicted in the table 1.