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FRI0495

FOLLOW UP OF INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES – THE EXPERIENCE OF ONE CENTRE

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Background: Interstitial Lung Diseases (ILD) may present features suggesting an underlying autoimmune process, which seem to differentiate them from idiopathic interstitial pneumonias, although without fully meeting the classification criteria (CC) for a specific connective tissue disease. Different terms had been used to describe these conditions and, to reach a consensus, the European Respiratory Society/American Thoracic Society proposed the CC for an entity named Interstitial Pneumonia with Autoimmune Features (IPAF). Clinical evolution and prognosis of this entity are still poorly understood.

Objectives: To evaluate clinical evolution and prognosis of a population of patients with IPAF.

Methods: Retrospective analysis of clinical files of patients followed by the Pulmonology Department since 02/2012 until 06/2019, who met the CC for IPAF, regarding clinical, functional and radiological evolution. Patients were considered to have a progressive phenotype in 24±3 months from their 1st evaluation if they fulfil 1 of the 4 criteria: relative decline in FVC ≥10% predicted; relative decline in FVC ≥5–<10% predicted and worsened respiratory symptoms; relative decline in FVC ≥5–<10% predicted and increased extent of fibrosis on High-resolution Computed Tomography (HRCT); worsened respiratory symptoms and increased extent of fibrosis on HRCT.

Results: 22 (7.4%) of 296 ILD patients met IPAF CC. 59.0% were female with an age at the 1st evaluation of 66.7±12.4 years. They were all non-smokers (63.6%) or ex-smokers (36.4%). Serologic and morphologic criteria were both present in 21 (95.4%) and clinical criteria in 5 patients (22.7%). Antinuclear antibodies (ANA) were identified in 19, rheumatoid factor in 4, SSA in 3 and anti-Jo-1 in 1 patient. HRCT patterns were identified in 21 patients: 15 nonspecific interstitial pneumonia (NSIP), 5 organizing pneumonia (OP) and 2 lymphocytic interstitial pneumonia (LIP). One NSIP and 1 LIP identified on HRCT were confirmed by histopathology. Three patients had inflammatory arthritis and 2 had Raynaud's phenomenon. Immunosuppressive therapy was introduced in most cases (18 patients, including systemic corticotherapy in 17, azathioprine in 4, mycophenolate mofetil in 1), azithromycin was prescribed in 2 patients and 3 remained without therapy. Regarding the follow up at 24±3 months from the 1st evaluation (3 patients were excluded due to too recent follow-up), 4 patients (18.2%) had progressive phenotype, 7 (31.8%) had a favourable evolution and 3 (13.6%) patients had died. During a follow-up of 31.1±19.8 months, this number rose to 6 patients (27.3%), all of them died by respiratory cause and had NSIP pattern. No differences were found in age, last FVC, therapy and time of disease evolution between those who died and the others.

Conclusion: Our study showed that a small proportion of IPAF patients had a progressive phenotype and the NSIP pattern seemed to be a poor prognosis factor for survival.

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FREQUENCY OF POLYAUTOIMMUNITY IN RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERITHEMATOSUS

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Background:

Objectives: To study the frequency of polyautoimmunity and multiple autoimmune syndrome (MAS) in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

Methods: Study design: We performed a cross-sectional study in patients with RA and SLE, and compared them with healthy subjects. Cases: RA

patients classified by ACR/EULAR 2010 criteria and SLE patients classified by ACR/EULAR 2019 criteria. SLE and RA patients were compiled consecutively from a rheumatology clinic of the Regional University hospital of Malaga. Controls: subjects without rheumatologic autoimmune disease (AD) from the same population area. Protocol: All subjects filled out a pre-designed questionnaire for the collection of polyautoimmunity data on the cut-off date. Main variables: polyautoimmunity was defined as co-occurrence of SLE or RA and other AD. Secondary variables: Rheumatologic, cutaneous, endocrine, digestive and neurological AD. MAS was defined as presence of three or more AD. Family history of SLE, RA and other autoimmune diseases were also collected. Statistic analysis: descriptive analysis, bivariate analysis and multivariable analysis were done. (Dependent variable: Polyautoimmunity).

Results: We recruited 109 patients with RA, 105 with SLE and 88 controls. Fifteen patients with RA (13.8%), 43 with SLE (41%) and 2 controls (2.2%) reported polyautoimmunity. Table 1 describes the epidemiological characteristics, comorbidities and polyautoimmunity in study population. The most frequent AD associated with RA was Sjögren's syndrome (SS) (53.3%) and SS (55.8%) followed by the antiphospholipid syndrome (30.2%) were associated with SLE. Hashimoto's thyroiditis and psoriasis were the next most frequent AD. According to family history, 5 patients with RA (33.3%) and 12 with SLE (27.9%) had a family history of first degree of other AD. Obesity was associated with polyautoimmunity in RA (OR = 3.362, p = 0.034). In SLE, joint damage (OR = 2.282, p = 0.038) and anti-RNP antibodies (OR = 5.095, p = 0.028) were factors associated with polyautoimmunity and taking hydroxychloroquine was a protective factor (OR = 0.190, p = 0.004).

Conclusion: Polyautoimmunity in RA and especially in SLE is frequent. It was associated with obesity in RA and in SLE with joint damage and anti-RNP antibodies. The hydroxychloroquine appeared as a protective factor.

Variables	RA (N=109)	SLE (N=105)	Controls (N=88)	P value
Epidemiological characteristics				
Sex: female, n (%)	85 (78.0)	99 (94.3)	68 (77.3)	0.001
Age, mean (SD), years	56.5 (10.8)	50.8 (13.2)	57.1 (10.6)	0.133
Caucasic race, n (%)	107 (98.2)	105 (100)	88 (100)	0.168
Comorbidities				
Smoking				0.001
No smoking, n (%)	55 (50.5)	78 (74.3)	56 (63.6)	
Smoking history, n (%)	54 (49.5)	27 (25.7)	32 (36.4)	
Obesity, n (%)	38 (34.9)	21 (20.0)	22 (25.0)	0.044
Dyslipidemia, n (%)	24 (22.0)	22 (21.2)	17 (19.3)	0.896
Hypertension, n (%)	27 (24.8)	28 (26.7)	23 (26.1)	0.746
Diabetes mellitus, n (%)	7 (6.4)	1 (1.0)	1 (1.1)	0.031
Polyautoimmunity, n (%)	15 (13.8)	43 (41)	2 (2.2)	<0.001
MAS, n (%)	1 (0.9)	9 (8.6)	0 (0.0)	<0.001
FH polyautoimmunity, n (%)	19 (17.6)	26 (24.8)	15 (17.0)	0.060

RA: rheumatoid arthritis; SLE: systemic lupus erythematosus; SD: standard deviation; MAS: multiple autoimmune syndrome; FH: Family history

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FRI0497

THERAPEUTIC STRATEGIES AND LONG-TERM OUTCOME IN PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES: A SINGLE CENTER LARGE-SCALE OBSERVATIONAL COHORT STUDY

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Background: Patients with idiopathic interstitial pneumonia (IIP) may have features of connective tissue diseases (CTDs). The term interstitial pneumonia with autoimmune features (IPAF) has been recently proposed for such patients [1]. To date, only few studies have comprehensively described outcomes over a long-term period and choices of treatment [2-4].

Objectives: The aim of this study was to investigate the therapeutic strategies and long-term outcome among patients with IPAF, IIP, and CTD-ILD.

Methods: Six hundreds- and seventy-two patients who had visited our department between April 2009 and March 2019 and were evaluated by chest HRCT scan. They were clinically and radiologically diagnosed as having interstitial lung disease (ILD), including IIP, CTD-ILD, undifferentiated connective tissue diseases associated ILD or other ILD. Then, we applied IPAF criteria to these patients, 68 patients were diagnosed as IPAF. We extracted the

treated patients from IPAF patients. Then, the treated patients were divided into two groups, which were treated with monotherapy (glucocorticoid: GC) and with combination therapy (GC and immunosuppressant: IS). Clinical, laboratory and imaging data were collected from medical records and statistically analyzed.

Results: Proportion of treatment received patients with IPAF, IIP, or CTD-ILD was 44.1%, 28.1%, and 88.0%, respectively. Then we compared long-term outcomes among patients with IPAF, IIP, and CTD-ILD, 5-year non-exacerbation rate in IPAF patients, IIP patients, and CTD-ILD patients was 53.7%, 28.3%, and 59.5%, respectively (Figure 1.). No significant difference between IPAF and CTD-ILD group was found ($P=0.71$). Next, we focused on IPAF and compared characteristics at diagnosis between the treatment group ($n=30$) and non-treatment group ($n=38$) in patients with IPAF. Interestingly, treatment group was significantly associated with signs of mechanic's hands, arthritis, anti-SS-A antibody positivity, and anti-ARS antibody positivity ($P=0.009$, 0.05, 0.05, and 0.007). Among the treatment group, GC monotherapy was received in 46.7% ($n=14$), whereas GC+IS combination therapy group was 50% ($n=15$). When we compared long-term outcomes between two groups, 3-year non-exacerbation rate was 70.1%, 43.5%, and 83.3% (Figure 2.). No significant difference was not seen between two different treatment groups ($P=0.24$).

Conclusion: Our large-scale cross-sectional cohort study identified that the prognosis of IPAF patients was poor as same as that of CTD patients, and even though GC mono or GC+IS combination treatment was applied for IPAF patients, prognosis was still poor and thus new intervention for IPAF should be needed to improve their prognosis.

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Figure 1. Kaplan-Meier survival curves of interstitial pneumonia with autoimmune features (IPAF) ($n=68$), idiopathic pulmonary fibrosis (IIP) ($n=170$) and connective tissue disease (CTD)-interstitial lung disease (ILD) ($n=92$).

Figure 2. Kaplan-Meier survival curves of interstitial pneumonia with autoimmune features (IPAF) with monotherapy ($n=14$), with combination therapy ($n=15$) and without treatment ($n=38$).

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DOES TESTING FOR SAA IS MORE BENEFICIAL THAN CRP FOR THE FOLLOW-UP OF FMF PATIENTS WITH M694V HETEROZYGOUS OR M694V HOMOZYGOUS MUTATIONS?

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Background: In order to follow subclinical inflammation and adjust the therapy for an optimal Familial Mediterranean Fever (FMF) disease control, clinicians seek for readily accessible, affordable and reproducible markers. C-reactive protein (CRP) is widely used for this purpose. Some suggest that CRP measures are not conclusive in all cases, especially at initial stages of inflammation. It is suggested that Serum Amyloid A (SAA) may be more reliable and sensitive in predicting an ongoing inflammation.

Objectives: In order to evaluate and to compare the sensitivity of SAA and CRP in FMF patients with M694V homozygous and M694V heterozygous mutations respectively.

Methods: Blood samples from 28 patients with M694V homozygous mutation and from 15 patients with M694V heterozygous mutation were obtained during a mean follow-up of 1 year. Multiple samples were drawn in both attacks and attack-free periods of FMF (153 from M694V Homozygous and 31 from M694V Heterozygous). For the analysis of the correlation, the folds of normal CRP and SAA levels were used. Serum levels of the given markers were measured with nephelometric kits (normal CRP levels <5mg/L and SAA levels <6,8mg/L). More than one-and-a-half-fold increase of CRP and SAA was defined as an active inflammation.

Results: Except in one patient, all patients in the whole cohort were on prophylactic colchicine. Among 28 patients with M694V homozygous mutation, one patient was treated with adalimumab, and 12 patients with anti-IL-1 regimens. Among 15 patients with M694V heterozygous mutation, 4 were under anti-IL-1 treatment. There were a total of 183 measurements of CRP and SAA from 43 patients. Twenty-three measurements were obtained during the attack period in M694V homozygous group and the remaining 160 measurements were obtained in attack-free period. The figure demonstrates the correlation between CRP and SAA results ($r=0.745$, $p<0.001$). Both acute phase reactants were increased in 69 measurements, while in 13, CRP was high but SAA was normal and in 31, SAA was high however CRP was within normal limits. The mean increase in CRP of the whole cohort was $2,37 \pm 3,22$ -fold of the normal, whereas mean increase in SAA was $6,77 \pm 13,23$ -fold of the normal.

Conclusion: According to these results, serial testing of SAA does not provide any additional advantages over CRP. As it is readily accessible and affordable, CRP seems to be sufficient for the follow-up of FMF patients.

Figure:

$P<0,001$, $r=0,745$

Figure. The folds CRP and SAA in whole M694V homozygous and heterozygous mutant population

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