Conclusion: SII, CAR, AGR, PNI and FER were can be used as a practical tool for diagnosing AOSD. Among the inflammatory markers, SII was revealed as most powerful marker for diagnosis.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1643

SAT0527

COMBINED EFFECT OF COMMON VARIANTS IN EXON 2 OR EXON 3 AND A PATHOGENIC MUTATION IN EXON 10 OF THE MEDITERRANEAN FEVER GENE ON INFLAMMASOME ACTIVATION IN JAPANESE PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease that is caused by Mediterranean fever (*MEFV*) gene mutations. It is characterized by recurrent and self-limiting febrile attacks within a short period. Although the pathologic significance of *MEFV* exon 2 or exon 3 common variants in patients with FMF is modest and these variants are usually associated with less severe clinical presentations of FMF (1, 2), their combined effects with pathogenic mutation in exon 10 remain to be evaluated.

Objectives: To determine the combined effect of common variants on clinical manifestations and inflammasome activity, we compared the clinical and laboratory characteristics between the coexistence and non-coexistence of *MEFV* exon 2 or exon 3 variants in patients with FMF that had a heterozygous *MEFV* exon 10 mutation.

Methods: We excluded patients with FMF that had two *MEFV* exon 10 mutations in one or more alleles and those with *MEFV* variants in exons other than in exons 2, 3, or 10. Finally, we reviewed 131 Japanese patients with FMF that had a heterozygous *MEFV* exon 10 mutation, and they were divided into the groups with and without *MEFV* exon 2 or exon 3 variants of 34 and 97, respectively. All enrolled patients had only a heterozygous M694I mutation in exon 10 of the *MEFV* gene. We measured serum IL-18 levels at remission without febrile attacks in the groups with and without *MEFV* exon 2 or exon 3 variants of 9 and 31, respectively.

Results: In the univariate analysis, the group with variants in exon 2 or exon 3 had significantly earlier onset (16.0 years v.s. 20.5 years, $p = 0.04$), a higher percentage of thoracic pain with febrile attacks (68% v.s. 44%, $p = 0.02$), a higher frequency of attack (1.0/month v.s. 0.5/month, $p = 0.02$), and a higher IL-18 level in the serum at remission (606.3 pg/ml v.s. 168.4 pg/ml, $p = 0.04$, Figure 1) compared to the group without these variants. Importantly, multivariate analyses showed that the coexistence of *MEFV* exon 2 or exon 3 variants and an exon 10 mutation was independently and significantly associated with earlier onset of FMF ($p = 0.049$) and thoracic pain ($p = 0.03$).

Figure 1.

Conclusion: Our results suggest that the coexistence of *MEFV* exon 2 or exon 3 variants and a *MEFV* exon 10 mutation has combined effects on inflammasome activation in the Japanese population.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5475

SAT0528

CLINICAL PHENOTYPES OF IGG4-RELATED DISEASE REFLECT DIFFERENCES IN EPIDEMIOLOGICAL FEATURES, SEROLOGICAL FINDINGS, AND PROGNOSTIC OUTCOMES

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Background: Four clinical phenotypes of IgG4-Related Disease (IgG4-RD) have been recently identified by Latent Class Analysis (LCA) - Pancreato/biliary (Group 1); Retroperitoneum/Aortitis (Group 2); Head-and-neck limited (Group 3); Micklelicz/Systemic (Group 4) - but the relevance of this classification for patient management remains unknown (1,2).

Objectives: We aimed to assess whether clinical judgment can replicate LCA classification and to evaluate potential differences in epidemiological features, serological findings, and disease outcomes between disease phenotypes.

Methods: The study included 179 patients. Four IgG4-RD experts were asked to classify a validation cohort of 40 patients according to published LCA derived phenotypes based on clinical judgment. Agreement between LCA and clinical clustering was calculated. To assess differences among disease phenotypes, the following variables were recorded on additional 139 patients: serum IgG4 and IgE; inflammatory markers; eosinophils; plasmablasts; IgG4-RD Responder Index (RI); history of atopy, diabetes, osteoporosis, relapses, and tumors; cumulative dose of glucocorticoids and use of rituximab.

Results: Clinical judgment recapitulated LCA classification with strong agreement between IgG4-RD experts ($\kappa = 0.841$, $p < 0.0005$). Group 1 showed the highest levels of serum IgG4 and IgE. Group 2 and 4 had the lowest and highest IgG4-RD RI, respectively (Table 1). Increased cumulative doses of glucocorticoids and higher relapse rate were observed in Group 3 (Fig 1). A higher incidence of diabetes mellitus was observed in Group 1 and 4.

Table 1 Clinical and serological characteristics of patients cohort.

	Group 1 (59 pts - 45%)	Group 2 (29 pts - 22%)	Group 3 (25 pts - 19%)	Group 4 (18 pts - 14%)	P value
Female n° (%)	12 (20%)	8 (28%)	11 (44%)	5 (28%)	0.18
Age	67 (61-73)	61 (56-70)	52 (40-62)	57 (51-62)	<0.0001
Serum IgG4 (mg/dL)	331 (184-575)	155 (49-258)	150 (80-255)	282 (166-460)	0.0009
IgG4-RD RI	9 (6-9)	6 (6-9)	9 (6-12)	9 (6-13)	0.004
Definite diagnosis n° (%)	20 (34%)	18 (62%)	20 (80%)	10 (55%)	0.0008
Probable diagnosis n° (%)	1 (0.59%)	0 (0%)	1 (0.19%)	1 (0.14%)	0.6
Possible diagnosis n° (%)	38 (64%)	10 (34%)	4 (16%)	7 (39)	0.0003
Emergency n° (%)	37 (63%)	14 (48%)	7 (28%)	10 (55%)	0.03
Department n° (%)	7 (12%)	4 (14%)	7 (28%)	6 (23%)	0.09
History of atopy n° (%)	20 (8-39)	40 (14-59)	38 (14-54)	12 (8-21)	0.04
ESR (mm/h)	5 (2-8)	10 (3-52)	8 (3-28)	3 (2-6)	0.03
CRP (mg/L)	200 (200-500)	200 (100-275)	300 (200-475)	200 (100-500)	0.3
Eosinophils (cell/mm ³)	283 (97-723)	69 (28-264)	120 (41-412)	219 (54-657)	0.02
IgE (U/mL)	1765 (627-4000)	1890 (1020- 4000)	2000 (370- 4780)	2690 (140-5130)	0.99
Plasmablast (cell/mL)	4 (2-9)	7 (4-12)	10 (3-18)	11 (2-38)	0.04
Diagnostic delay (months)	60 (37-70)	50 (40-75)	65 (40-90)	40 (30-70)	0.8
Starting prednisone dose (mg, range)	10 (17%)	1 (3%)	2 (8%)	2 (11%)	0.09
Diabetes at disease onset

Figure 1. Relapse free survival of the four different IgG4-RD phenotypes.

Conclusion: Clinical phenotypes of IgG4-RD reflect differences in epidemiological features and prognostic outcomes.

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Disclosure of Interests: Marco Lanzillotta: None declared, Emanuel Della Torre: None declared, Corrado Campochiaro Speakers bureau: Novartis, Pfizer, Roche, GSK, SOBI, Gaia Mancuso: None declared, Lorenzo Dagna Grant/research support from: The Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR) received unrestricted research/educational grants from Abbvie, Bristol-Myers Squibb, Celgene, Janssen, Merk Sharp & Dohme, Mundipharma Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI., Consultant of: Prof Lorenzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Roche, Sanofi-Genzyme, and SOBI.

DOI: 10.1136/annrheumdis-2020-eular.1438

SAT0529

CLINICAL CHARACTERISTICS AND TREATMENT PATTERNS IN A PATIENT GROUP WITH INTERSTITIAL LUNG DISEASE.

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Background: Diffuse interstitial lung disease (ILD) is frequently associated with connective tissue diseases (CTD) and is one of the main causes of morbidity and mortality in these patients. Recently, the concept of Interstitial Pneumonia with Autoimmune Features (IPAF) has been defined to characterize ILD associated with systemic manifestations limited to subtle serological and clinical autoimmune abnormalities and not fulfilling the international criteria for the diagnosis of a given CTD.

Objectives: The objective of this study is to describe the clinical, serological and radiological characteristics, as well as the treatment patterns of patients with ILD referred to a Rheumatology Service for suspected CTD

Methods: Observational, cross-sectional study of 43 patients with ILD referred for evaluation to the medical consultation of CTD of the Rheumatology service at the Reina Sofia Hospital. Patients were classified as patients with defined CTD, patient with IPAF and patients with other types of pneumopathy. We conducted a descriptive study of all patients and compared the clinical-analytical-radiological characteristics and treatment patterns of the first two groups.

Results: Of the 43 patients, 67.40% were women with a mean age at diagnosis of 65.65 (10.42) years and 53.50% of smoking patients. Of the total of patients, 16 (37.2%) were included in the CTD group, 17 (39.5%) met criteria for IPAF and 10 (23.3%) had another type of pneumopathy. In the CTD group scleroderma was the most frequent disease (6/16), followed by inflammatory myopathy (4/16), Sjögren's syndrome (3/16), rheumatoid arthritis (2/16) and polymyalgia rheumatic (1/16). In this group of patients, the most common symptom was Raynaud's phenomenon (RP) (7/16), followed by arthritis (7/16) and mechanic's hands (3/16). Regarding the most frequently antibodies were ANA (100%), anti-RO (41.7%), anti-citrullinated protein antibodies (30%) and rheumatoid factor (RF) (28.6%). In patients with IPAF, as in the CTD group, the most observed clinical criterion was RP (5/17), followed by arthritis (1/17) and mechanic's hands (1/17). Among the serological criteria the most common antibodies were ANA (100%), followed by anti-RO (33.3%), anti-RNA synthetase (28.6%) and RF (22.2%).

Regarding the radiological pattern, in both groups the most frequent was nonspecific interstitial pneumonia, followed by the indeterminate pattern and usual interstitial pneumonia (UIP) in third place. There were no significant differences by gender and age, between the group of CTD and IPAF, observing in both groups a predominance of women with a similar mean age, being the upper smoking habit in the IPAF group (70.6% vs 31.5%, $p = 0.02$). Regarding the treatment used, the use of immunosuppressants (IS) was more frequent in CTD group (56.3% vs 11.8%, $p = 0.007$).

Conclusion: The clinical-serological and radiological characteristics were similar among patients with IPAF and CTD, which supports the notion of a similar pathophysiology in both groups. In our cohort patients with CTD received IS more frequently than IPAF group, however, future work would be necessary to assess whether the response to treatment is similar in these populations and if IS can benefit patients with IPAF to long term. In addition, it could be useful to include the UIP pattern within the IPAF classification criteria, not currently included, since it is the third most frequent radiological pattern.

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Disclosure of Interests: Rafaela Ortega Castro: None declared, Pérez Sánchez Laura: None declared, Font Ugalde Pilar: None declared, Jerusalem Calvo Gutierrez: None declared, Antonio Requejo-Jimenez: None declared, Simona Espejo-Pérez: None declared, Teresa Gonzalez-Serrano: None declared, María del Carmen Castro Villegas: None declared, Gómez García Ignacio: None declared, Alejandro Escudero Contreras: None declared, Eduardo Collantes Estevez Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene, Maria A Aguirre: None declared

DOI: 10.1136/annrheumdis-2020-eular.5812

SAT0530

DESCRIPTION AND OUTCOMES OF A SERIES OF 21 PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES IN A MULTIDISCIPLINARY UNIT.

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Background: A significant proportion of patients with idiopathic interstitial pneumonia shows autoimmune features, but do not meet the criteria to be classified as a systemic autoimmune disease. In 2015, a joint working group of the European Respiratory Society (ERS) and the American Thoracic Society (ATS) proposed classification criteria for the category called interstitial pneumonia with autoimmune features (IPAF).

Objectives: To evaluate the clinical, serological and morphological characteristics of a series of 21 patients with IPAF as well as the treatment that was applied and the evolution they presented.

Methods: A retrospective cohort study was conducted. The patients who met ERS/ATC IPAF classification criteria in the period from 2012 to 2019 were collected from our interstitial lung disease (ILD) database, including 546 patients. All cases were systematically assessed in a multidisciplinary committee. Clinical, serological, morphological, as well as treatment and outcome variables were collected. A Descriptive analysis is shown.

Results: 21 patients were included in the study, 12 of them (57.1%) women. The mean age at diagnosis was 61.6 years (SD 14.0), and the median follow-up time was 2.9 years (IQR 4.9). All showed ILD by HRCT, 10 (47.6%) patients had autoimmune features at the moment of the diagnosis, and 20 (95.2%) were positive for some auto-antibody. 12 (57.1%) fulfilled two of the three domains, and 9 (42.9%) fulfilled the three IPAF domains. Characteristics are described in Table 1. Lung biopsy was performed in 9 cases (42.9%). The mean FVC at diagnosis was 70.4% (DS 21.0) and DLCO 46.7% (DS 21.5). Regarding the treatment during the disease, mofetil mycophenolate (MMF) was used in 8 (38.1%) patients, cyclophosphamide (CYC) in 3 (14.3%), rituximab (RTX) in 2 (9.5%) and azathioprine in 2 (9.5%). In 1 case (4.8%), CYC and RTX were used in combination. Oral glucocorticoids (GCC) were prescribed in 14 patients (66.7%), 4 of them alone, and 6 cases (28.6%) required high-dose methylprednisolone in 250-1000mg regimens. Antifibrotic drugs (nintedanib or pirfenidone) were used in 5 cases (23.8%) in combination with immunosuppressants and/or GCC. Five patients (23.8%) required home oxygen supplementation. Outcomes to date: 7 (33.3%) patients had readmissions due to ILD acute exacerbation; 2 (9.5%) required lung transplantations, and 3 (14.3%) died during follow-up, 1 (4.8%) due to respiratory causes.