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	20 (34%)	18 (62%)	20 (80%)	10 (55%)	0.0008
n° (%)					
Probable diagnosis	1 (0.59%)	0 (0%)	1 (0.19%)	1 (0.14%)	0.6
n° (%)					
Possible diagnosis	38 (64%)	10 (34%)	4 (16%)	7 (39)	0.0003
n° (%)					
Emergency	37 (63%)	14 (48%)	7 (28%)	10 (55%)	0.03
Department n° (%)					
History of atopy	7 (12%)	4 (14%)	7 (28%)	6 (23%)	0.09
n° (%)					
ESR (mm/h)	20 (8-39)	40 (14-59)	38 (14-54)	12 (8-21)	0.04
CRP (mg/L)	5 (2-8)	10 (3-52)	8 (3-28)	3 (2-6)	0.03
Eosinophils (cell/mm ³)	200 (200-500)	200 (100-275)	300 (200-475)	200 (100-500)	0.3
IgE (U/mL)	283 (97-723)	69 (28-264)	120 (41-412)	219 (54-657)	0.02
Plasmablast (cell/mL)	1765 (627-4000)	1890 (1020- 4000)	2000 (370- 4780)	2690 (140-5130)	0.99
Diagnostic delay (months)	4 (2-9)	7 (4-12)	10 (3-18)	11 (2-38)	0.04
Starting prednisone dose (mg, range)	60 (37-70)	50 (40-75)	65 (40-90)	40 (30-70)	0.8
Diabetes at disease onset	10 (17%)	1 (3%)	2 (8%)	2 (11%)	0.09