Background: Multisystem inflammatory syndrome in children (MIS-C) is a rare complication of SARS-CoV-2 infection in the pediatric population, caused by extensive activation of immune system. The understanding of the distorted immune response is still in the early stages.

Objectives: To analyze comprehensively immune profile in MIS-C patients including detailed serologic response to SARS-CoV-2 in comparison with control groups.

Methods: Blood samples of consecutive MIS-C patients were collected at admission. Flow cytometric analysis of all lymphocyte populations including T and B cell differentiation was performed. Immunophenotyping was performed by six-color panels for the detection of lymphocyte subpopulations. Anti-SARS-CoV-2 specific antibodies were measured in the patients' serum. The IgA and IgG antibodies against S protein, the IgG S1 and S2 specific antibodies, antibodies against nucleoprotein and neutralising antibodies were measured. Patients were assessed for a wide range of auto-antibodies, namely ANA, anti-ENA (Jo-1, PL-7, PL-12, SRP, Mi-2, Ku, Pm/Scl 100, Scl-70), myositis specific antibodies (EJ, MDA-5, TIF-1, Ro52, SAE-1, SAE-2, NXP-2), anti-dsDNA, anti-phospholipid antibodies (aCl IgA, IgG, IgM, anti-β2GPI IgG, IgM) and ANCA. Control groups to compare specific antibody response consisted of 14 healthy children and 19 healthy adults, who had SARS-CoV-2 infection in the last 2 months.

Results: Samples of 20 patients were included (14/20 boys, median age 12.4 years). Patients had higher percentage of double negative T cells and low numbers of cytokine producing T cells Th1, Th2 and Th17. Numbers of immune competent and CD21+ transitional B cells were also lowered. All patients had positive antibodies against SARS-CoV-2 including neutralising antibodies. Nine (9/19; 47 %) patients had high titer ($\geq 1:160$) of neutralising antibodies. Results were compared with 2 control groups; 14 healthy children (7/14 boys; median age 8 years,) and 19 healthy adults, who all experienced SARS-CoV-2 infection in the last two months. Patients with MIS-C had significantly higher levels of anti-S IgA ($p<0.0001$), patients with MIS-C and healthy children had significantly higher titers of anti-S1 ($p=0.001$) and significantly lower titers of anti-S2 ($p=0.016$) in comparison to adults (Figure 1). No differences were found in the titers of neutralising antibodies and anti-N antibodies. All patients were ANA negative, 19/20 patients were anti-ENA negative, whereas 1 patient had anti-Ro antibodies in low titre. Three patients had aCL IgG in medium titre and 2 patients anti-β2GPI IgG in low titre. Patients were negative for all other autoantibodies.

Conclusion: The immune response in MIS-C patients is specific with most prominent differences in elevated percentage of double negative T cells and low numbers of Th1, Th2, Th17 and CD21+ transitional B cells. MIS-C patients have distinct serologic response with high anti-S IgA, high anti-S1 and low anti-S2 titres.

Figure 1. Antibody titres in patient group and control groups. Mean value with SEM is shown.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.4109

POS0073

ASSOCIATION OF SAA1 GENE POLYMORPHISM -13T/C (RS12218) WITH CRYOPYRIN ASSOCIATED PERIODIC SYNDROMES (CAPS), BUT NOT FAMILIAL MEDITERRANEAN FEVER (FMF)

L. Guseva¹, E. Fedorov², S. Salugina², M. Krylov¹, E. Samarkina¹. ¹V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology of Rheumatic Diseases, Moscow, Russian Federation; ²V.A. Nasonova Research Institute of Rheumatology, Laboratory of Pediatric Rheumatic Diseases, Moscow, Russian Federation

Background: Autoinflammatory diseases (AIDs) are a group of rare, genetically determined diseases characterized by a periodic events of inflammation, fever,

and clinical symptoms that mimic rheumatic pathology. Laboratory serological markers of AIDs are C reactive protein (CRP) and serum amyloid A (SAA) protein. **Objectives:** We investigated whether SAA1 gene polymorphism -13T/C (rs12218) may affect the susceptibility to pediatric FMF and CAPS patients (pts). We also evaluate whether this polymorphism can affect CRP and SAA protein levels.

Methods: 26 FMF pts - 8 boys, 18 girls; age - M(SD) 7.37(5.32) years and 24 CAPS pts - 12 girls, 12 boys; age - 4.76(5.83) years, and 95 healthy individuals (controls) were included in this study. The diagnosis of FMF was based on Turkish paediatric criteria for the diagnosis of familial Mediterranean fever [1] and was confirmed by the detection of pathogenic mutations of the MEFV gene in the homozygous or compound-heterozygous states. The diagnose of CAPS was made on the basis of characteristic clinical signs and was confirmed by the detection of a pathogenic mutation in the NLRP3 gene. SAA1 gene polymorphism -13T/C was genotyped using allele-specific RT-PCR assay. SAA protein concentration was measured using nephelometry in FMF and CAPS pts.

Results: Table 1 shows the genotypic and allelic frequencies of SAA1 gene in FMF, CAPS and controls. There were no significant differences between FMF pts and controls in the genotypic and allelic distributions of -13T/C gene polymorphism. The frequency of -13C allele was significantly higher in CAPS pts compared with controls (OR=2.03 [CI 1.02-4.03], $p=0.03$). Moreover, a statistically significant difference was revealed in the genotypic and allelic distributions between FMF and CAPS pts groups ($p=0.047$ and $p=0.02$ respectively). The CRP levels did not correlate with SAA1 -13T/C polymorphism. The SAA protein concentration was associated with SAA1 gene polymorphism in FMF pts ($p=0.036$).

Table 1. The distribution of genotypes and alleles of SAA1 gene polymorphism -13T/C in FMF, CAPS and control groups.

Genotypes/Alleles	FMF n=26 (%)	CAPS n=24 (%)	Controls n=95 (%)
TT	12 (46,2)	4 (16,7)	39 (41,1)
TC	12 (46,2)	14 (58,3)	42 (44,2)
CC	2 (7,7)	6 (25,0)	14 (14,7)
P (pts vs controls)	>0,05	>0,08	
T	24 (63,2)	21 (50,0)	80 (61,5)
C	14 (36,8)	21 (50,0)	50 (38,5)
P (pts vs controls)	>0,05	0,03	

Conclusion: Our preliminary study in small groups of pediatric FMF and CAPS pts revealed that SAA1 gene polymorphism -13T/C (rs12218) is associated with susceptibility to CAPS, but not FMF. The influence of this polymorphism on SAA protein levels in FMF pts was also shown. Further investigations are required to clarify the role of SAA1 gene polymorphism -13T/C in susceptibility to FMF and CAPS in large studies in different ethnic and population groups.

REFERENCES:

[1] Yalcinkaya F, Ozen S, Ozcakar ZB, et al. Rheumatology (Oxford). 2009;48(4):395-8. doi: 10.1093/rheumatology/ken509.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3910

POS0074

CAN WE PREDICT THE DEVELOPMENT OF NEPHRITIS IN PEDIATRIC IGA VASCULITIS PATIENTS?

E. Sag^{1,2}, S. Demir^{1,2}, Y. Bilginer^{1,2}, S. Özen^{1,2}. ¹Hacettepe University Faculty of Medicine, Department of Pediatric Rheumatology, Ankara, Turkey; ²Hacettepe University Faculty of Medicine, Translational Medicine Laboratories, Pediatric Rheumatology Unit, Ankara, Turkey

Background: IgA vasculitis (IgAV) is the most common systemic vasculitis of childhood, characterized by palpable purpura, arthritis, gastrointestinal and renal involvement¹. It is a relatively self-limited disease apart from the renal involvement which is associated with the long term morbidity.

Objectives: We aimed to define a marker at disease onset to predict the renal involvement.

Methods: In this pilot study, we analyzed a targeted panel of vascular inflammation markers (sT2, RAGE, TIE-2, sCD40L, TIE-1, sFIt-1, LIGHT, TNF-α, PIGF, IL6, IL18, IL10 and MCP-1) in the plasma samples of eight patients IgAV at the onset of the disease, before any treatment was initiated. At the time of sample collection, none of the patients had renal involvement; four of these patients subsequently developed nephritis and were defined as the IgAVN group. The levels of the markers were studied by a cytometric bead-based multiplex assay panel according to manufacturer's instruction (LEGENDplex HU Vascular Inflammation panel 2 (13-plex); catalogue number 740966, Biolegend) and analyzed by Novocyte 3005 flow cytometer.

Results: There were no significant differences in gender, age, clinical manifestations, and laboratory findings between IgAV and IgAVN patients (Table 1). sCD40L levels were higher (median 1938.1 vs 754.9 pg/mL, $p=0.04$) whereas sST2 levels were lower (median 862.8 vs 2302.8 pg/mL, $p=0.02$) in the patients who developed IgAV nephritis (Figure 1). sRAGE levels were higher and IL18 levels were lower in IgAVN patients but did not reach statistical significance, probably due to the low number of patients. The other parameters did not show any specific pattern.

Table 1.

	IgAV (n=4)	IgAVN (n=4)	p value
Gender	2F, 2M	1F, 3M	0.49
Age at disease onset	9.0±5.4	10.3±3.4	0.68
Arthralgia/arthritis	50%	75%	0.49
GIS involvement	75%	50%	0.49
Haemoglobine (gr/dL)	12.4±2.3	12.3±0.6	0.95
White blood cells, $\times 10^9/L$	11150±1933	8525±1497	0.08
Platelets $\times 10^9/L$	290250±87328	269250±38741	0.68
Erythrocyte sedimentation rate (mm/hr)	10.5±9.1	21.0±14	0.26
C-reactive protein (mg/dL)	0.63±0.03	1.16±0.96	0.39

Data are given as mean±SD

Figure 1.

Soluble CD40 ligand (sCD40L) is expressed on platelets and released on activation. It is proinflammatory for endothelial cells and promotes coagulation by inducing expression of tissue factor on monocytes and endothelial cells². It was investigated in acute coronary syndrome and was suggested as a risk factor for vascular damage.² Furthermore, the levels of sCD40L were shown to be correlated with disease activity in ANCA-associated vasculitis³. Thus in IgAV, sCD40L may be associated with the involvement of the kidney vasculature, which represents the more severe form of the disease. Receptor for advanced glycation end-products (RAGE) is another marker for endothelial damage and vasculitis which was higher in IgAVN, as well.

IL33 is expressed by epithelial and endothelial cells and overexpression of IL33 have been shown in large vessel vasculitis⁴. sST2 acts as a decoy receptor and inhibits IL33 signalling⁴. It was interesting to see that the levels of the IL-18 and sST2, which are members of IL-1 family, were lower in IgAVN patients.

Conclusion: Although the number of the patients were limited in this pilot study, we suggest that sCD40L and sRAGE might be used to predict the development of renal disease in IgAV patients. Further studies with larger number of patients are needed to confirm our findings.

REFERENCES:

- [1] Sag E, Batu ED, Ozen S. Childhood systemic vasculitis. *Best practice & research Clinical rheumatology* 2017;31(4):558-75.
- [2] Heeschen C, Dimmeler S, Hamm CW, et al. Soluble CD40 ligand in acute coronary syndromes. *The New England journal of medicine* 2003;348(12):1104-11.
- [3] Tomasson G, Lavalley M, Tanriverdi K, et al. Relationship between markers of platelet activation and inflammation with disease activity in Wegener's granulomatosis. *The Journal of rheumatology* 2011;38(6):1048-54.
- [4] Desbois AC, Cacoub P, Leroy AS, et al. Immunomodulatory role of Interleukin-33 in large vessel vasculitis. *Sci Rep* 2020;10(1):6405.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.1306

Pediatric Rheumatology - Clinical

POS0075

SAFETY AND EFFICACY OF GOLIMUMAB FOR THE TREATMENT OF POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS - AN UPDATE FROM THE BIKER REGISTRY

A. Zimmer¹, A. Klein², K. Minden³, T. Hospach⁴, F. Weller-Heinemann⁵, J. Kuemmerle-Deschner⁶, M. Fasshauer⁷, N. Hofmann⁸, H. Koessel⁹, I. Foeldvari¹⁰, S. Mrusek¹¹, D. Windschall¹², N. Onken¹³, M. Hufnagel¹⁴, D. Foell¹⁵, N. Brueck¹⁶, P. T. Oommen¹⁷, F. Dressler¹⁸, A. Helling-Bakki¹⁹, G. Horneff². ¹Kinderklinik St. Augustin, Paediatric Rheumatology, Sankt Augustin, Germany; ²Kinderklinik St. Augustin, Paediatric Rheumatology, St. Augustin, Germany; ³Charité Universitätsklinik Berlin, Paediatric Rheumatology, Berlin, Germany; ⁴Klinikum Stuttgart- Olgahospital, Paediatric Rheumatology, Stuttgart, Germany; ⁵Klinikum Bremen-Mitte, Professor-Hess-Kinderklinik, Paediatric Rheumatology, Bremen, Germany; ⁶Universitätsklinikum Tübingen, Paediatric Rheumatology, Tübingen, Germany; ⁷Klinikum St. Georg gGmbH, Paediatric Rheumatology, Leipzig, Germany; ⁸Klinikum Bamberg, Sozialstiftung Bamberg, Paediatric Rheumatology, Bamberg, Germany; ⁹Städtisches Klinikum Brandenburg GmbH, Paediatric Rheumatology, Brandenburg, Germany; ¹⁰Hamburger Zentrum für Kinder- und Jugendrheumatologie am Klinikum Eilbek, Paediatric Rheumatology, Hamburg, Germany; ¹¹Praxis für Kinder- und Jugendrheumatologie, Paediatric Rheumatology, Baden-Baden, Germany; ¹²Klinik für Kinder- und Jugendrheumatologie, Paediatric Rheumatology, Sendenhorst, Germany; ¹³Kinder- und Jugendärztliche Gemeinschaftspraxis, Paediatric Rheumatology, Lüneburg, Germany; ¹⁴Universitätsklinikum Freiburg, Paediatric Rheumatology, Freiburg, Germany; ¹⁵Universitätsklinikum Münster, Paediatric Rheumatology, Münster, Germany; ¹⁶Universitätsklinikum Carl Gustav Carus, Paediatric Rheumatology, Dresden, Germany; ¹⁷Universitätskinderklinikum Düsseldorf, Paediatric Rheumatology, Düsseldorf, Germany; ¹⁸Medizinische Hochschule Hannover, Paediatric Rheumatology, Hannover, Germany; ¹⁹Universitätsklinikum Heidelberg, Paediatric Rheumatology, Heidelberg, Germany

Background: Golimumab (GOL) is approved for treatment of polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years and older. Data on long-term safety of GOL in this indication are limited.

Objectives: To assess long-term safety and efficacy of GOL in pJIA patients.

Methods: In this ongoing non-interventional observational study, clinical characteristics, disease activity and safety parameters were analysed using the German Biologics in Paediatric Rheumatology (BiKeR) registry. 81 pJIA-patients treated with GOL were body weight-matched with 162 patients receiving alt. tumor necrosis factor inhibitors (TNFi) and 81 biologic-naïve patients under methotrexate (MTX)-therapy.

Results: Baseline parameters of GOL patients differed from the alternative TNFi and MTX cohorts. In patients starting with GOL treatment, disease duration was longer, corticosteroid use was less and disease activity, measured by the mean number of active joints and the JADAS10, was lower (Table 1).

The long-term clinical efficacy of GOL in pJIA is highlighted by a decrease of the mean JADAS 10 from 11.6 (baseline) to 5.2 after 24 months. After 2 years, a JADAS 10 minimal disease activity was reached by 44.4 % of patients, whereas 22.2 % of patients were in remission and the JIA ACR 30/50/70/90 response rates were 77.8/72.2/66.7/55.6% respectively.

AE, SAE and infectious AE rates between the three cohorts were comparable (Table 1). In the GOL cohort, 4 SAE (1 uveitis, 1 arthritis flare, 1 fibromyalgia syndrome and 1 abscess) were reported, while in the alt. TNFi group 7 SAEs and in the MTX cohort 1 SAE were noted (Table 1). One serious infectious event (1 abscess) was documented in the GOL cohort, 2 alt. TNFi patients had influenza and no serious infectious events were seen in the MTX control group.

Few autoimmune processes occurred: 2 incident events in the GOL cohort (1 uveitis, 1 psoriasis), 3 cases in the alt. TNFi group (2 uveitis, 1 psoriasis,) and 1 event in MTX-patients (celiac disease) (Table 1). Out of the 20 GOL patients with preexisting uveitis at baseline, 6 had flare events; there were no reported uveitis flares of the 17 patients in the alt. TNFi group and no patients with preexisting uveitis in the MTX-group. No malignancies or deaths were reported.

Conclusion: Our interim results show an acceptable safety profile of GOL therapy, comparable to treatment with alt. TNFi or MTX. No new safety signals occurred. The efficacy outcome data confirm long-term benefits of GOL treatment in pJIA patients.

Acknowledgements: We greatly appreciate the kind support of Z. Huang, S. Calhoun.

Disclosure of Interests: Angela Zimmer: None declared, Ariane Klein: None declared, Kirsten Minden: None declared, Toni Hospach: None declared, Frank Weller-Heinemann: None declared, Jasmin Kuemmerle-Deschner: None declared, Maria Fasshauer: None declared, Nadja Hofmann: None declared, Hans Koessel: None declared, Ivan Foeldvari: None declared, Sonja Mrusek: