calcineurin inhibitors was 92% at 5th year. Serious infection occurred in four patients (19%) in the CI +group, and one of them had a fatal course.

Conclusions: Our retrospective analysis suggested that calcineurin inhibitors could be an additional option for AOSD and further prospective studies were desired.

REFERENCES:

- [1] Efthimiou P, et al. Diagnosis and management of adult onset Still's disease. *Ann Rheum Dis* 2006.
- [2] Chen DY, et al. Predominance of Th1 cytokine in peripheral blood and pathological tissues of patients with active untreated adult onset Still's disease *Ann Rheum Dis* 2004.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3180

SAT0613 INCREASED SERUM LEVEL OF IL-36 RECEPTOR ANTAGONIST IS ASSOCIATED WITH ACTIVE DISEASE IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE

H. Kim, J. Kang, B. Nam, J.S. Kim, D.-H. Yoo. *Division of Rheumatology, Hanyang University Medical Center, Seoul, Korea, Republic Of*

Background: Adult onset Still's disease (AOSD) is an inflammatory disorder which was associated with varying level of pro-inflammatory cytokines. However, the role of natural anti-inflammatory molecules has not been evaluated to date. Interleukin (IL) 1 cytokine family is closely related to clinical presentations, disease activity and thus is a target for treatment of AOSD. IL-36 receptor antagonist (Ra) is an anti-inflammatory molecule, but its clinical significance has not been studied in AOSD patients.

Objectives: To figure out the role of IL-36Ra in monitoring disease activity in patients with AOSD.

Methods: The number of 49 AOSD patients meeting Yamaguchi criteria were recruited. Each patient was serially monitored following clinical course of flare and remission, which presented at least 2 points of change in modified Pouchot's score. They were divided into two groups by clinical courses, which were predominant systemic symptoms or arthritis. We compared erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ferritin as disease activity markers between flare and remission. Serum levels of inflammatory cytokines, IL-18, IL-37, and IL-36Ra were measured by enzyme-linked immunosorbent assay (ELISA) in each clinical state of AOSD patients.

Results: Forty-nine patients with AOSD were included in this study; 40 were women (81.6%) and 9 were men (18.3%), with mean age of 49.08 ± 14.17 years old. The mean duration of follow-up was 6.44 ± 3.87 years, and mean difference of modified Pouchot's score was 5.37 ± 1.98 between remission and flare. The number of 33 (67.4%) patients had presented systemic symptoms predominantly, while 16 (32.7%) presented arthritis more frequently in their clinical course. In flare state of AOSD, overall inflammatory markers were elevated, including cytokines

of IL-18 and IL-37. The serum level of IL-36Ra was 164.04 ± 169.03 pg/mL in active state, compared to 125.36 ± 452.0 in inactive state of AOSD patients ($p < 0.001$). IL-36Ra presented positive correlation with modified Pouchot's score and inflammatory markers, including CRP ($r = 0.286$, $p < 0.01$), ferritin ($r = 0.225$, $p < 0.05$) and IL-37 ($r = 0.353$, $p < 0.01$), but was not with level of IL-18 and ESR in active AOSD. Distribution of IL-36Ra level was analysed by each clinical course, however, there was no significant difference in level of IL-36Ra by clinical presentations stratified with predominance of arthritis.

Abstract SAT0613 – Table 1. Comparison of serum IL-36Ra levels in active AOSD patients with other markers for disease activity

	Modified Pouchot's score	ESR	CRP	Ferritin	IL-18	IL-37
IL-36Ra	0.295 ^a	0.086	0.286 ^b	0.225 ^a	0.095	0.353 ^a

Correlation efficient was presented by each inflammatory markers; ^a $p < 0.05$, ^b $p < 0.01$

Conclusions: Serum IL-36Ra level was significantly increased in active AOSD patients compared to inactive AOSD patients, presenting positive correlation with other inflammatory markers. In patients with AOSD, level of IL-36Ra might be another potential serologic marker to estimate disease activity, especially active state of the disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6753

SAT0614 NEW VARIANT IN THE IL1RN-GENE ASSOCIATED WITH LATE ONSET AND ATYPICAL PRESENTATION OF DIRA

J.B. Kuemmerle-Deschner¹, K. Hoernagel², S. Schlipf³, S. Hansmann⁴, A. Hospach⁵, X. Liu⁶, S.M. Benseler⁷, A.N. Weber⁸. ¹Department of Pediatrics, Division of Rheumatology, University Hospital Tuebingen; ²Praxis für Humangenetik Tübingen, Tuebingen; ³Kinderarztpraxis Dr. Lakner, Schwäbisch Gmünd; ⁴Department of Pediatrics, Division of Pediatric Rheumatology, UNIVERSITY HOSPITAL TUEBINGEN, Tuebingen; ⁵Zentrum für Pädiatrische Rheumatologie, Klinikum Stuttgart, Olgahospital, Stuttgart; ⁶Department of Immunology, University of Tübingen, Tübingen, Germany; ⁷Rheumatology, Department of Paediatrics, Alberta Children's Hospital, University of Calgary, Alberta, Calgary, Alberta, Canada

Background: Deficiency of the interleukin-1 receptor antagonist (DIRA) is an autoinflammatory disease characterised by severe systemic inflammation with bone and skin involvement present in the first days of life.

Objectives: We report a novel variant in the *IL1RN*-gene associated an atypical phenotype of DIRA.

Methods: A 3 year-old Caucasian boy presented with recurrent monthly episodes of fever and fatigue, associated with lymphadenopathy, pericarditis, pleuritis, pancreatitis, and arthritis involving sacroiliac, hip, knee and ankle joints in the absence of any skin involvement. Symptoms had started at age one and had progressed over time to life-threatening episodes requiring intensive care therapy. Throughout, inflammatory parameters including ESR, CRP, SAA, S100A8/9, leukocytes, and platelets were highly elevated. Treatment with colchicine and steroids improved symptoms, however did not prevent flares. Immune deficiencies were ruled out; genetic testing for FMF, CAPS, TRAPS, HIDS and DITRA did not reveal variants in the associated genes.

Results: Whole exome sequencing detected a novel homozygous stop variant c.62C>G; p.Ser21* in the *IL1RN* gene (NM_173842.2). Mother, father and brother are heterozygous for the same variant. In addition, three variants of unknown significance were identified in the patient's *PCGF5*, *CPA1* and *SPTA1* genes. Functional studies revealed only marginal secretion of IL-1RA in the patient's unstimulated leucocytes and after stimulation with IL-1 β and LPS, confirming the disease-causing nature of the variant. Subsequently, IL-1 inhibition with anakinra at 2 mg/kg/d was started resulting in complete resolution of clinical symptoms, normal inflammatory markers and dramatically improved energy levels. Intolerance to daily subcutaneous injections prompted a switch to canakinumab at 4 mg/kg/4 weeks. However patient's and mothers assessment of disease activity was inferior on canakinumab compared to anakinra. After four months a flare appeared and lead to return to anakinra.

Conclusions: This is the first report of the novel c.62C>G; p.Ser21* variant in the *IL1RN*-gene primarily causing severe serositis in a homozygous carrier, while heterozygous family members were completely symptom free. Skin disease, one of the most prominent features in other patients with DIRA was not observed in this patient, while IL-1 inhibition was likewise effective.

Pathogenic variants in all reported DIRA patients so far affect all 4 isoforms of IL-1RA.¹ The different phenotype in the patient reported here, may be due to the selective loss of secreted IL1RN.