The 46th patient, seen 5 years after bone marrow transplantation for presumed GATA2 deficiency, was not included in our summary calculations.
32 patients (71%) reported a history of recurrent fevers. 6 patients (13%) had diffuse lymphadenopathy.
Skin involvement was seen in 38 patients (84%) including livedo in 34 (76%), cutaneous polyarteritis nodosa in 27 (60%), and Raynaud's in 9 (20%).
22 patients (49%) had a history of at least one stroke.Brain MRI showed evidence of ischemic infarcts in l6/22 (73%), 5 had both ischemic & hemorrhagic strokes (23%) and 1 had a hemorrhagic stroke (5%). There were 55 strokes in the 22 patients, the majority occurring in the brain stem and cerebellum (38%) and deep brain nuclei (36%). The average age at the time of the first stroke was 5.6 years (range 5 months-20 years). Stroke patients had an average of 3 strokes (range of 1-11). 3 patients manifest severe sequelae of hemorrhagic strokes.
Abdominal ultrasound revealed hepatomegaly in 20 patients (44%) & splenomegaly in 26 (58%). Portal hypertension was observed in 7 patients (16%). Liver biopsies revealed hepatoportal sclerosis in 5 patients and focal nodular regenerative hyperplasia in 2. Abdominal MRA was abnormal in 7/13 patients, revealing arteritis and aneurysms.
Significant peripheral vasculopathy was seen in 4 patients, one requiring multiple amputations of gangrenous digits. Systemic hypertension was observed in 11 patients (24%).
Laboratory evaluation revealed hypogammaglobulinemia in 26 patients (58%). Immunoglobulin replacement was required in 10 patients. Lymphocyte phenotyping revealed arrested B cell class switching in 24/34 patients (71%) and decreased memory T cells in 11/34 (32%). Severe hematologic abnormalities, including anemia, leukopenia, lymphopenia and/or thrombocytopenia in 18 patients (40%), with 6 developing pancytopenia and 3 pure red cell aplasia. Immune mediated neutropenia was observed in 12 patients. ESR and C-reactive protein were elevated in 73% & 86%, respectively.
6 patients underwent bone marrow transplantation with 4 patients successfully engrafted (2 requiring a second transplant), and 2 recently transplanted.
Conclusion: The spectrum of DADA2 continues to expand to include ischemic and hemorrhagic strokes, cutaneous findings, portal and systemic hypertension, hematologic abnormalities, vascular pathology, immune deficiency and bone marrow failure. As the phenotypic presentation is likely to continue to expand, it is important to investigate any new complaints.

Disclosure of Interest
None Declared

O10

Serum S100A8/A9 (calprotectin) in familial mediterranean fever and carriers of MEFV mutations does not correlate with disease activity

Ruth Pepper[1], Mathew Hutchinson[2], Scott R. Henderson[3], Sarah K. Todd[3], Alan D. Salama[3], Philip N. Hawkins[4], Dorota Rowczenio[4], Helen J. Lachmann[4]
[1]Centre for Nephrology, UCL; [2]Rheumatology, University College Hospital; [3]Centre for Nephrology; [4]National Amyloidosis Centre, UCL Division of Medicine and Royal Free Hospital NHS Foundation Trust, London, United Kingdom
Correspondence: Ruth Pepper
Pediatric Rheumatology 2019, **17(Suppl 1):**O10

Introduction: Familial Mediterranean Fever (FMF) is caused by mutations in MEFV. The protein product pyrin is expressed in monocytes, neutrophils and eosinophils. Acute inflammatory attacks are accompanied by a dramatic hepatic acute phase response. S100A8/A9 is damage associated molecular pattern and a TLR4 ligand expressed in neutrophils, monocytes and early infiltrating macrophages.
Objectives: We aimed to investigate S100A8/A9 in 39 patients with FMF, 45 healthy carriers and 16 wild type controls.
Methods: All patients were genotyped. Patients and healthy controls (HC) serum S100A8/A9 levels, cell surface expression on monocytes and neutrophils as well as intracellular peripheral blood mononuclear cells (PBMC) expression were measured by flow cytometry (FACS). CD14 cells were isolated and following overnight incubation with or without LPS, S100A8/A9 was measured in the supernatants by ELISA. Patient and HC monocyte apoptosis was compared.
Results: Serum levels were measures in 84 samples from 31 patients with homozygous or compound mutations (median 9061ng/ml [range 500-38470], 79 samples from 39 symptomatic patients who were MEFV heterozygotes (median 9394ng/ml [range 1744-38119], 80 samples from 45 individuals with MEFV variants but without clinical features of FMF (median 10939ng/ml [range 2447->40000]. There was no difference in calprotectin concentrations between the different mutations and no correlation with levels of the hepatic acute phase response, CRP or SAA. All the groups described had significantly higher levels than healthy controls (n=16 median 2836ng/ml [range 1058-6175])($p<0.001$). Minimal monocyte and neutrophil cell surface expression was detectable. Following LPS stimulation there was significantly more S100A8/A9 detected in the supernatants in patients than healthy control CD14. There was also a trend to an increased intracellular monocyte S100A8/A9 expression.
Conclusion: Patients with pyrin mutations both with and without clinical disease have greatly elevated serum S100A8/A9 levels without detectable cell surface expression in well-controlled disease with a trend to an increased monocyte intracellular expression. Upon monocyte stimulation with LPS, increasedS100A8/A9 is secreted. The exact mechanism by which these patients, especially those with mutations but no clinical disease, demonstrate sustained elevated serum S100A8/A9 remains to be elucidated but does not appear to result in a significant clinical sequelae.

Disclosure of Interest
None Declared

O11

PAPA syndrome: novelties from the Eurofever registry

Roberta Caorsi, Daniela Marotto, Antonella Insalaco, Angelo Marzano, Joost Frenkel, Graciela Espada, Immaculada Calvo Penades, Marijia Jelusic, Maria Cristina Maggio, Joost Swart, Esther Hoppenreijs, Ozgur Kasapcopur, Fabrizio De Benedetti, Marco Gattorno, The Pediatric Rheumatology International Trial Organization (PRINTO) and the Eurofever Project
Center for Autoinflammatory Diseases and Immunodeficiency, Istituto G. Gaslini, Genova, Italy
Correspondence: Roberta Caorsi
Pediatric Rheumatology 2019, **17(Suppl 1):**O11

Introduction: PAPA syndrome is a very rare autoinflammatory condition. Few data are nowadays available about the clinical characteristic, the response to treatment and the outcome of this disease.
Objectives: To analyse the data of the PAPA patients enrolled to the Eurofever registry.
Methods: the data analysed in the study were extracted from the Eurofever registry, which is hosted in the PRINTO website (www.printo.it). The patients were included in the study in the presence of mutations in the PSTPIP1 gene or, in genetically negative patients, in the presence of at least two of the following clinical manifestation: recurrent pyogenic arthritis, pyoderma gangrenousm or skin abscess with negative cultural tests. Demographic data, clinical manifestations and response to treatment were analysed.
Results: In may 2018 baseline and clinical information were available of near 4000 patients in the Eurofever registry. Of the 36 patients classified as PAPA syndrome, 2 were excluded from the study. 34 PAPA patients, from 11 different centers, were analysed: the genotype was confirmatory in 29 patients, while in 5 was not available. 10 patients were of the same family, in 4 cases one parent was affected (2 included in the registry), while in other 8 patients the family history was negative. At the time of enrolment, 15 patients were in the paediatric age, while 19 were adults. The mutations detected in the PSTPIP1 gene were E250Q (13 pts), E250K (5 pts), A230T (3 pts), G258A (3 pts), E277D (2 pts), E257G (1 pt), G940A (1pts) and R365W (1 pts).

The disease course was recurrent in 24 patients, while the other 10 presented a chronic disease course with periodic recrudesces. Joint and skin involvement were present at disease onset in 24 and 9 patients respectively. In other 12 patients skin involvement appeared over time. 20 out of the 34 patients presented clinical manifestations not typical of PAPA syndrome (psoriasis, uveitis, osteolytic bone lesions, chronic renal failure, muscular abscesses, gastrointestinal symptoms anaemia and hepatosplenomegaly).
10 patients were treated with NSAID with partial and poor response in 6 and 4 patients respectively, while steroids caused a complete or partial control of disease manifestations in 6 and 10 patients respectively. Five patients were treated with methotrexate with partial response. Etanercept was used in 6 patient with complete response in 2 and partial in 4, adalimumab in 4 patients (1 partial and 1 complete responders, 2 failure) and anakinra in 9 patients (3 partial and 6 complete responders). 2 patients were treated with Canakinumab with complete response.
Conclusion: This study enlightens the phenotypic variability of PAPA syndrome. The unusual clinical manifestations and the lack of the clinical triad of the disease may be responsible for the under recognition of this disease. Between biologic drugs, IL-1 inhibitors were more effective in the analysed cohort of patients.

Disclosure of Interest
None Declared

O12

New classification criteria for recurrent autoinflammatory diseases applied to an independent cohort: experience from the JIR cohort database

Glory Dingulu[1], Sophie Georgin-Lavialle[2], Isabelle Koné-Paut[3], Pascal Pillet[4], Anne Pagnier[5], Etienne Merlin[5], Daniela Kaiser[6], Alexandre Belot[7], Michael Hofer[8], Véronique Hentgen[9]
[1]Centre Hospitalier Versailles, Le Chesnay; [2]Service de Médecine Interne-CEREMAIA, Centre Hospitalier Universitaire Tenon, Paris; [3]Service de Rhumatologie Pédiatrique-CEREMAIA, Centre Hospitalier Universitaire Le Kremlin Bicêtre, Le Kremlin Bicêtre; [4]Service d'Accueil des Urgences Pédiatriques, Centre Hospitalier Universitaire Pellegrin, Bordeaux; [5]Service de Pédiatrie Générale, Centre Hospitalier Universitaire Clermont Ferrand, Clermont Ferrand, France; [6]Service de Pédiatrie Générale, Centre Hospitalier Cantonal Luzern, Luzern, Switzerland; [7]Service de Néphrologie-Rhumatologie Pédiatrique, Centre Hospitalier Universitaire Mère-Enfant, Bron, France; [8]Service de Rhumatologie Pédiatrique, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [9]Service de Pédiatrie Générale-CEREMAIA, Centre Hospitalier Versailles, Le Chesnay, France
Correspondence: Glory Dingulu
Pediatric Rheumatology 2019, **17(Suppl 1):**O12

Introduction: New classification criteria for the inherited periodic fever syndromes Cryopyrin Associated Periodic Syndrom (CAPS), Tumour Necrosis Factor Receptor Associated Periodic Syndrom (TRAPS), Familial Mediterranean Fever (FMF), Mevalonate Kinase Deficiency (MKD), have recently been developed during a Consensus Conference held in Genoa in March 2017.
Objectives: The aim of our study was to compare these new classification criteria for monogenic recurrent fever syndromes with the diagnoses of clinicians in a real-life setting.For this purpose we used the JIRcohort database, an international platform gathering data of patients with pediatric inflammatory disease.
Methods: Patients with recurrent fever syndrome and complete clinical and genetic data were enrolled to the study from the autoinflammatory module of the JIRcohort database. Patients genotype were characterized with HRF pathogenicity classification. A score from 0 to 2, 0 (no mutation), 1 (non-confirmatory genotype) and 2 (confirmatory genotype) was attributed to each gene screened in one patient. The new Genoa classification criteria were applied to all the patients and then compared to the diagnosis of the treating physician. The treating physician diagnosis was considered as standard reference. If the treating physician hesitated between two or more diagnoses, patients were redefined as Syndrome of Unexplained Recurrent Fever (SURF). SURF and PFAPA patients were pooled together. Finally, for each criteria sensitivity and specificity were determined before an analytical study, describing true positive, false positive and false positive patients.
Results: 455 patients were included:10 CAPS, 11 MKD, 27 TRAPS, 122 FMF and 285 SURF/PFAPA patients.
CAPS classification criteria showed a 60 % sensitivity and 98% specificity. 6 patients were true positive patients with confirmatory and non-confirmatory *NLRP3* genotype. 4 were false negative patients with non-confirmatory genotype or no mutation in NLRP3. 8 were false positive with no mutation in *NLRP3*.
TRAPS classification criteria showed a 100 % sensitivity and 98% specificity. 22 were true positive patients with confirmatory and non-confirmatory *TNFRSF1A* genotype. 5 patients were false positive with non-confirmatory genotype or no mutation in *TNFRSF1A*.
FMF classification criteria showed a 96 % sensitivity and 88% specificity. 117 patients were true positive with confirmatory, non-confirmatory and non mutated *MEFV* genotype. 5 were false negative with non-confirmatory and non mutated genotype. 37 werefalse positive patients with patients with non-confirmatory genotype or non mutated genotype or no *MEFV* screening.
MKD classification criteria showed a 64 % sensitivity and 66% specificity. 7 patients were true positive patients with confirmatory MVK genotype.4 were false negative patientswith non-confirmatory genotype or non mutated MVK genotype. 148 were false positive patients with non mutated MVK genotype.
Conclusion: This work is the first to study Genoa criteria, in real-life setting, in a cohort of patients seen with recurrent fever. Genoa criteria showed tremendous performance for patients with confirmatory genotype and helped classifying patients with non-confirmatory genotype.
Genoa classification criteria were less effective when patients did not display at least one genetic variant. Implementation of biological criteria in MKD might improve MKD criteria performance.
The major limit of our study is the lack of a proper gold standard when genotype is not confirmatory. Nevertheless our study shows that the new classification criteria are of a high risk of misclassification in patients displaying a recurrent fever syndrome without genetic test.

Disclosure of Interest
None Declared

O13

Impaired platelet functions in patients treated with colchicine

Özlem Çimen[1], Selcan Demir[2], Erdal Sağ[2], Armağan Keskin[1], Yelda Bilginer[3], Şule Ünal Cangül[3], Seza Özen[2]
[1]Department of Pediatrics; [2]Department of Pediatric Rheumatology; [3]Department of Pediatric Hematology, Hacettepe University Medical Faculty, Ankara, Turkey
Correspondence: Selcan Demir
Pediatric Rheumatology 2019, **17(Suppl 1):**O13

Introduction: Colchicine has been used in the treatment of Familial Mediterranean Fever (FMF) since 1972. Apart from the inhibiting mitosis in all cells, colchicine has an anti-inflammatory effect by inhibiting activation and migration of neutrophils. Colchicine is a safe drug at recommended doses, but it can cause rare side effects including hematological findings such as lymphopenia, thrombocytopenia and neutropenia.
Objectives: In this study we aimed to define the adverse effect of colchicine on platelet function and its clinical relevance.
Methods: A total of 220 FMF patients between June 2016-2017, followed at Hacettepe University Pediatric Rheumatology Department and were on colchicine treatment for at least one year, were included to the study.
Results: Among the selected 220 FMF patients, 100 of them (54% female) described hematological symptoms when questioned in detail. The mean age of these patients was 11.74 ± 4.86 years. The mean cumulative colchicine exposure was 5.7±3.8 years.