amyloid, and hypochromic mycrocitic anemia. All cultures were negative. He was treated with antibiotics, non-steroid anti-inflammatory drugs (NSAIDs) and prednisone, but relapsed whenever steroids were tapered. Chest CT scan had confirmed presence thick pericardial and pleural effusion while pleural punctate revealed increased number of polymorphonucler cells and increase in protein content without any evidence for infection. Since his mother had a history of neurosensorial hearing loss of undefined etiology and persistently elevated inflammatory markers we suspected on autoinflammatory disease background (possible idiopathic recurrent pericarditis). That is why we have initiated continuous treatment with ibuprofen and colchicine. DNA sample was analyzed but typical MEFV mutations in egzone 2 and 3 were not found. Since boy continued to have periodical attacks of fever and pericardial effusions, approximately on 2 weeks we were forced to add methyl-prednisolon pulses on 10 days. Unfortunately this has not stopped attacks of fever and pericarditis. Additional genetic testing have revealed presence of totally new pathogenic heterozygous missence variant c.1805A > G (NM_001079821.2) in NLRP3 gene causing the substitution of amino acid glutamine with amino acid arginine at position 602. This variant has not been yet reported in previous patient's database with NLRP3 associated autoinflammatory diseases. The presence of this variant was confirmed in the mildly affected mother with sensoneural deafness, and is compatible with the phenotype of NLRP3 associated Muckle-Wells syndrome. Meanwhile, our patient achieved disease remission that is why anakinra was not introduced and steroids could be tapered and stopped, but continued colchicine for one year. Six months after stopping colchicine boy developed persistent arthritis of the right ankle with no response to NSAIDs why methotrexate has been introduced.
Conclusion: Clinical manifestations of some patients can provoke differential diagnostic and treatment dilemmas. We are still in doubt whether our patient had atypical systemic JIA (fever, inflammation and serositis with late onset of arthritis and without skin, lymph node or organ involvement) or autoinflammatory disease that belongs to the cryopyrinopathy group.
Disclosure of Interest
None Declared

P186

A cohort of patients with autoinflamatory diseases followed-up in a unit of paediatric and transitional rheumatology: a descriptive study

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Introduction: The autoinflammatory diseases (AD) are uncommon, most of them are presented as episodes of recurrent fever and may be accompanied by other inflammatory symptoms. This group of diseases includes polygenic entities (without a single known genetic mutation) such as Behçet's disease (BD), systemic-onset juvenile idiopathic arthritis (soJIA), Chronic recurrent multifocal osteomyelitis (CRMO) and PFAPA syndrome. On the other hand, we found the entities that present with specific monogenic mutations, such as Familial Mediterranean Fever (FMF), TNF receptor-associated periodic syndrome (TRAPS), hyper-IgD syndrome and periodic fever (HIDS), cryopyrinopathies (FCAS, MWS, CINCA), Blau's syndrome and PAPA. A group of patients who cannot be classified into a specific diagnosis are clustered as recurrent fever without known genetic anomaly (RFW).
Objectives: To describe and compare the clinical features of monogenic and polygenic AD and RFW seen in a paediatric and transitional rheumatology unit of a Spanish tertiary care hospital.
Methods: We performed a retrospective study including 39 patients with AD followed-up in our center.
Results: The distribution of diagnoses was: sJIA 19 patients (48.72%), BD 5 (12.82%), PFAPA 6 (15.38%), CRMO 3 (7.69%), RFW 4 (10.26%), HIDS 1 (2.56%) and CINCA 1 (2.56%). Patients came from different regions of Spain, being 22 of them boys (56.41%) and 17 girls (43.59%). The genetic study was performed in 12 patients, being positive in 7 (17.95%). Mean age at onset of symptoms was 5 ± 5.65 years in monogenic diseases, 7.96 ± 4.84 years in polygenic disorders and 9.5 ± 5.91 years RFW. Delay in diagnosis in monogenic diseases was higher than in polygenic diseases (67 ± 69.29 months vs. 24.03 ± 30.33 months, respectively). The clinical manifestations more frequently found were fever, followed by joint involvement, being more common in monogenic diseases than in polygenic disorders (Table 6). Haemoglobin levels were lower in monogenic than in polygenic diseases 9.95 g/dL ± 0.63 vs. 11.69 g/dL ± 2, ESR and CRP was higher in monogenic diseases 106 mm/h ± 68.5 and 80.5 mg/L ± 84.14 vs. 56.1 mm/h ± 33.78 and 57.95 mg/L ± 57.95, unlike ferritin that was more elevated in polygenic disease 896 μg/dL ± 1788.34 than in monogenic diseases 183 μg/dL ± 195.7. During his follow up 84.62% of patients received corticosteroids, 51.8% methotrexate and 46.15% biological therapy.
Conclusion: sJIAs was the most frequent AD in our center. All the patients had a similar gender distribution. Delay in diagnosis was greater in monogenic diseases compared with polygenic disorders. Fever and joint involvement were the more common clinical manifestations, especially in monogenic diseases. Ferritin levels were higher in polygenic diseases, whereas CRP and ESR which were higher in monogenic diseases. During the follow-up most patients required treatment with corticosteroids and approximately half of them required biological therapy.
Disclosure of Interest
None Declared

Table 6 (Abstract P186). See text for description

	Monogenic	Polygenic	Recurrent fever
Fever	100%	81.25%	100%
Joint involvement	100%	62.5%	75%
Rash	100%	59.38%	0%
Lymphoadenopathy	50%	46.88%	25%
Splenomegaly	100%	12.5%	0%
Abdominal involvement	30%	21.88%	25%

P187

Genetic and clinical profile of a paediatric population with FMF in Sicily

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Introduction: Familial Mediterranean fever (FMF) is an Autoinflammatory syndrome that is common in children in Mediterranean countries.
Objectives: The real prevalence of FMF in Sicilian children is unknown and need a wide population study. Furthermore, there are no data on the real prevalence of the different mutations between FMF patients and the concordance and/or discordance in clinical and biochemical parameters between patients of different generations.
Methods: We collected clinical, biochemical and genetic data of 77 patients in paediatric age (1-16 years) affected by recurrent attacks of fever (about 3 days long) with variable association with the clinical symptoms typical of the disease (abdominal pain, serositis, arthralgia and/or arthritis, myalgia, erysipelas like erythema, oral aphthosis).
Results: We found 38 patients with clinically relevant mutations and 39 patients with polymorphism in the MEFV gene (R202Q and or Nt1588-69G > A, homozygous or heterozygotes; 33 R202Q heterozygotes and 6 R202Q homozygous patients. The most frequent mutations that we observed in our patients were: E148Q (11 heterozygotes); R408Q (6 heterozygotes); P369S (6 heterozygotes); M694V (5

heterozygotes, 1 homozygous patient); I591T (3 heterozygotes). Some of them had 2 or more mutations in association. All the patients were treated with colchicine with a complete (95%) or partial response to the treatment. None of the patients developed amyloidosis. Three patients from unrelated families, had a vasculitis (2 Kawasaki Disease; 1 Schoenlein-Hoenoch Purpura) and all presented the same association: P369S and R408Q.
Conclusion: This finding verifies the importance of molecular diagnosis and detailed sequencing which is recommended to perform in particular for the countries with a high risk of FMF.
In several instances, family studies provided the prevalence of a single mutation in patients experiencing a pathogenic effect, with molecular evidence for pseudodominant transmission. We evidenced a variable clinical and serological pattern between patients in the same family; the genetic study was in fact extended to parents and brothers of the index case, with the recommendation to dose Serum amyloid A (SAA), blood pressure and evaluate an urine analysis to exclude proteinuria.
The M694V homozygous and heterozygous genotype was found to be associated with a higher prevalence of amyloidosis and arthritis and higher levels of SAA. The parents of our patients with M694V mutation have more severe clinical manifestations and a lower response to colchicine.
Further studies are needed to highlight generational differences of clinical spectrum and SAA levels in FMF patients of the same family, carrying the same mutations.
Disclosure of Interest
None Declared.

P188

Anti-IL1 in patients with low penetrance mutations for autoinflammatory diseases: tuscany and sicilian case series from paediatric to adult age

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Introduction: Patients with low penetrance mutations for Autoinflammatory syndromes (AID) can have severe clinical manifestations, which require to be treated with biological drugs anti-IL-1.
Objectives: To evaluate the response of AID to treatment with the recombinant human IL-1 receptor antagonist anakinra or with the anti-IL-1b.
Methods: We enrolled from 3 centers (U.O. of Rheumatology, Universitary Hospital "S. Maria Le Scotte", Siena; S.O.D.C. of Paediatric Rheumatology, "A. Meyer" Hospital, Florence and U.O. of Paediatric Clinic, Children Hospital "G. Di Cristina", Palermo) 26 patients with SAI and low penetrance mutations, with age: 0.8-58 years (11 M, 15 F; age:4-62 years; medium age of paediatric patients: 11.2 years). The symptoms started in paediatric age in all the patients; however adult patients received the diagnosis in adult age.
Results: All the patients (9 CAPS, 10 TRAPS, 2 HIDS, 2 FMF, 3 sJIA) received anti-IL-1b drugs (anakinra or canakinumab). The subjects kept a diary of symptoms at the diagnosis and at the outset, and underwent clinical and laboratory assessments, including measurement of the SAA, ESR, CRP, blood count, urinalysis.
At the outset, the 84.6% showed recurrent episodes of fever, variously associated with: rash (61.5%), abdominal pain (50%), arthralgia and/or myalgia (88%), arthritis (46%). All the patients, before starting anti-IL-1b drugs, were treated with NSAIDs, steroids, DMARDs, colchicine with a poor control of the disease. The 30.7% associate the anti-IL-1b to one or more of other drugs. The 57.7% (38.5% between children, 19.2% between adults) showed a complete remission; the 19.2% incomplete, the 23.1% did not respond. SAA was increased in 88.5% (M: 155,86; n.v. < 6,4 mg/l), reduced in 58%. CRP was increased before anti-IL-1b drug in the 50%, with a normal value in the 92% after the drug was started. ESR was increased in the 69.2%, with a normal value in the 42.3%.
Proteinuria was detected in the 8% before the anti-IL-1b drug was started and was in the normal range after they was treated with the biological drug.
In children, prevalent clinical manifestations were abdominal pain and arthritis; in adults thorax pain and pericarditis were more frequent.
Conclusion: The clinical features of the AID were correlated with age, also in patients with low penetrance mutations: some manifestations were more frequent in adults, others in childhood. The remarkable response on clinical and haematological parameters (76.9% of all the patients) to anakinra or canakinumab suggests that IL-1β has a fundamental role in the pathogenesis of inflammation associated with low penetrance mutations as well. In paediatric age, IL-1 blockade higher efficacy was probably linked to a more severe clinical phenotype.
Disclosure of Interest
None Declared.

P189

Genetic and clinical profile of a sicilian population with R92Q mutation

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Introduction: Gene TNFRSF1A mutation is linked to TRAPS, autosomal dominant Autoinflammatory Disease (AID) with recurrent attacks of fever (2-3 weeks long), abdominal pain, vomiting, serositis, arthralgia and/or arthritis, myalgia, fasciitis, rash. The disease starts precociously and amyloidosis is reported in the 25% of the patients. Patients carrying the mutation R92Q usually show a mild clinical phenotype, with an extreme interindividual variability. Arthralgia and serositis are frequently less severe, however oral ulcers and pharyngitis are recurrent.
Objectives: We studied the clinical and biochemical impact of the mutation R92Q in our population and the treatment outcome in all the patients with clinical relevant symptoms.
Methods: We followed 15 patients (6 M and 9 F), 11 children and 4 adults, carrying the R92Q heterozygous mutation of the gene TNFRSF1A. The diagnosis of children were done at the age of 4-14 years, o the adults was performed following the sons diagnosis. SAA levels were significantly high in 8/11 children and in 2/4 adults.
Results: All the symptomatic patients were treated with NSAIDs, steroids, colchicine with a variable control of the disease. The colchicine was not sufficient in 4/5 patients and 2 of them were treated with the anti-IL-1 β biological drug canakinumab.
Conclusion: Functional studies performed on R92Q evidenced a changed conformational structure vs. the wild type.
Our patients showed polymorphic clinical features: some of them are asymptomatic, other record different symptoms with an intrafamilial variability. In paediatric age, the clinical phenotype is more severe also in correlation with the symptoms of parents carrying the same mutation. We stress the data that all our patients underwent the genetic study because they recorded symptoms linked to AID.
Disclosure of Interest
None Declared.

P190

A paediatric FMF patient with recurrent priapism during attacks

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