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P040

Evaluation of CD9 blood levels in pediatric patients with familial mediterranean fever (FMF)

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Introduction: Familial Mediterranean Fever (FMF) is a clinically diagnosed autoinflammatory disease in which CD9, a tetraspanin protein involved in immune regulation, may play a role in its underlying inflammatory mechanisms.
Objectives: The objective of this study is to investigate CD9 levels in FMF patients and examine their asssociation with clinical features, genetic findings and inflammatory characteristics.
Methods: Clinical, genetic, and laboratory data (serum amyloid A (SAA), white blood cell count (WBC), fibrinogen, C- reactive protein (CRP), estimated sedimentation rate (ESR), 24-hour urine) were collected from pediatric FMF patients (subdivided into attack and remission groups) and compared with a healthy control group. CD9 blood levels were measured by ELISA and re-tested after 15 days in the attack group. Data were analyzed using Mann–Whitney U, Chi-square, and correlation tests via SPSS.
Results: The study included 40 FMF patients (23 girls, 17 boys; mean age 11.3 ± 3.8 years) (6 during attack, 34 in remission) and 28 healthy controls (20 girls, 8 boys; mean age 9.1 ± 4.8 years). The most common clinical manifestations were abdominal pain (78%) and arthritis (50%). The most common genetic mutations were M694V (27,5%) and E148Q (17,5%). CD9 levels were significantly lower in the FMF patients compared to the control group ($p<0.01$). No significant difference was observed between the remission group and the attack group ($p > 0.05$). CD9 levels did not correlate significantly with inflammatory markers (CRP, ESR, SAA), nor were they associated with gender, genetic variations or symptoms ($p > 0.05$).
Conclusion: Despite the limitations in sample size and the restricted attack group due to the study's prospective design, the findings indicate that CD9 may have a significant role in the pathophysiology of FMF. Further large-scale, multicentered studies are required to comprehensively elucidate its role.
Disclosure
None declared

P041

Subclinical inflammation in pediatric familial mediterranean fever: predictors and follow-up results

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Pediatric Rheumatology, **23(2):** P041

Introduction: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease of childhood. Subclinical inflammation, characterised by persistently elevated acute phase reactants in the absence of clinical episodes, is an increasingly recognised risk factor for long-term complications. Undetected inflammation can lead to severe outcomes such as amyloidosis, organ damage such as renal failure, and growth retardation. Despite the significant clinical relevance of the issue, there is a paucity of research on the predictors and outcomes of subclinical inflammation in paediatric FMF patients.
Objectives: The aim of this study was to determine the frequency and clinical predictors of subclinical inflammation in pediatric FMF patients and to evaluate the response to treatment adjustments for subclinical inflammation.
Methods: The medical records of FMF patients followed up at our clinic between December 2011 and February 2024 were retrospectively reviewed. Patients were grouped according to the presence or absence of subclinical inflammation, defined as elevated CRP levels during attack-free periods at more than 75% of follow-up visits. The clinical and genetic results of the two groups were compared.
Results: 572 FMF patients were included in the study, 288 (50.3%) of whom were female. Mean age was 168 ± 60 months. Subclinical inflammation was found in 15.6% of patients (n=89). Patients with subclinical inflammation had a significantly earlier age at diagnosis (p=0.038), longer duration of disease ($p<0.001$), more frequent attacks of fever (p=0.004) and arthritis ($p<0.001$), higher frequency of comorbid inflammatory diseases (p=0.027), and more frequent attacks per year ($p<0.001$). Independent predictors of subclinical inflammation included longer disease duration (OR=1.09, p=0.023), biallelic exon 10 mutations (OR=3.90, p=0.020), colchicine resistance (OR=2.60, p=0.048), arthritis (OR=7.06, $p<0.001$), and higher disease severity scores (ISSF) (OR=5.67, $p<0.001$). Maximum tolerated dose escalation of colchicine controlled inflammation in 45% of cases (n=40), while 55% (n=49) required biologics. Of those treated with biologics, 87.7% (n=43) achieved normalisation of inflammatory markers.
Conclusion: In paediatric FMF patients, subclinical inflammation can be seen with appropriate treatment doses of colchicine. Earlier age at diagnosis, carrying a biallelic exon 10 mutation, presence of arthritis, and higher ISSF scores seem to be related with subclinical inflammation. Increasing colchicine to the maximum tolerated dose is effective in almost half of these cases. Anti-IL-1 treatments are effective in those who are resistant to colchicine.
Disclosure
None declared

P044

Clinical course and treatment indications in mefv heterozygous children without fmf phenotype: a single-center experience

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Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease in childhood. Although FMF is typically associated with the presence of two pathogenic variants in the MEFV gene, a diagnosis can also be established in the presence of a single pathogenic variant if characteristic clinical features are present. The diagnosis of FMF is primarily based on clinical findings, with genetic analysis serving as a supportive tool. However, the management of individuals who carry only a single MEFV mutation but do not exhibit clinical features of FMF remains controversial. Therefore, defining the long-term clinical course and treatment indications in MEFV heterozygous individuals without FMF phenotype is a significant unmet need in clinical practice.
Objectives: This study aims to evaluate the clinical course, laboratory features, and reasons for initiating treatment in pediatric patients who are heterozygous for MEFV mutations and do not present with FMF clinical findings at baseline.
Methods: We retrospectively reviewed the medical records of 116 pediatric patients with heterozygous MEFV mutations who were asymptomatic for FMF at initial presentation and followed at our center between 2015 and 2024. Demographic data, family history, presenting complaints, genetic findings, laboratory parameters, and follow-up data were analyzed. The primary outcome was the indication for initiating colchicine or other anti-inflammatory treatment during follow-up. *Group 1* comprised patients who, despite being asymptomatic for FMF at baseline, required the initiation of colchicine or other anti-inflammatory treatment during the follow-up period due to the development of clinical symptoms or persistent laboratory abnormalities. *Group 2* consisted of patients who remained untreated throughout the entire follow-up duration, as they did not exhibit any

clinical or laboratory indications warranting treatment. The decision to initiate treatment was made by the treating physician based on a comprehensive assessment of the patient's clinical presentation, laboratory findings, and family history, in accordance with established clinical guidelines.
Results: The median age of the 116 patients included in the study was 13.3 years (min: 3.7; max: 24.3), and the mean follow-up duration was 3.1 years. The most common presenting complaints were abdominal pain (34.5%), fever (13.8%), and family history (8.6%). The most frequent MEFV mutations identified were M694V/- (47.4%), V726A/- (15.5%), and E148Q/- (14.7%). A positive family history was present in 63.8% of patients, most commonly FMF (34.5%) and FMF+amyloidosis (3.4%). During follow-up, 51.7% of patients were diagnosed with FMF and treatment was initiated, while 48.3% continued to be monitored without treatment. The most common reasons for initiating treatment were recurrent attacks, persistent elevation of acute phase reactants, and a strong family history of severe FMF/Amyloidosis. A comparison of the clinical and genetic characteristics between Group 1 (patients who required treatment) and Group 2 (patients who remained untreated) revealed several notable differences. Patients who required treatment had significantly higher baseline ESR (26.9 vs. 16.2 mm/h, p=0.009) and CRP (22.1 vs. 7.8 mg/L, p=0.005) values compared to the untreated group. Among the 116 patients, the most frequent mutation was M694V/- in both groups. However, the compound heterozygous M694V/E148Q mutation was significantly more common in the treated group (9.8% vs. 0%, p=0.049).
Conclusion: A significant proportion of MEFV heterozygous children without FMF phenotype may develop clinical or laboratory indications for treatment during follow-up. Family history, persistent subclinical inflammation, and specific mutation types are prominent predictors of treatment initiation. Early identification of high-risk patients and proactive management may be critical to prevent long-term complications.
Disclosure
None declared

P045

Lung-only involvement in sting-associated vasculopathy with onset in infancy: a diagnostic pitfall in the absence of cutaneous vasculitis

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Pediatric Rheumatology, **23(2):** P045

Introduction: STING-associated vasculopathy with onset in infancy (SAVI) is a type 1 interferonopathy, characteristically represents with unprovoked fever episodes and systemic inflammation along with skin and lung inflammation. Lung involvement is encountered in nearly %75 of patients with SAVI, mostly interstitial lung disease, resultant from non-specific fibrosis. there is arising information on patients only manifesting as interstitial lung disease (ILD) without any skin lesions, which makes the diagnosis more difficult and broadening the differential diagnosis of the disease to the ILD spectrum.
Objectives: We aimed to present our experience with a case of SAVI syndrome without cutaneous vasculitis.
Methods: Case presentation
Results: A 10-months old male patient, born to nonconsanguineous parents, was admitted to our hospital with cough and respiratory distress. His past medical history indicated that respiratory distress and tachypnea was present since birth and treated with antimicrobial agents at different occasions. He had a pediatric intensive care unit (PICU) hospitalization when he was 5 months old, lasting for 4-months in another medical center. Initial physical examination revealed hypotonia, pallor, bilateral crackles, tachypnea, and retractions.
High resolution thorax computerized tomography (HRCT) showed large, consolidated areas with air bronchograms, prominent in the lower lobes, compatible with infection along with ground-glass opacities and white circles reveal microcystic appearance in peripheral zones, suggestive for ILD.
At 14 months of age, whole exome sequencing revealed a heterozygote c.461A>G (p.Asn154Ser) variant in *STING1* gene (NM_198282.4) and a heterozygote c.2020G>C (p.Met680Ile) variant in *MEFV* gene (*NM_000243.3)*. Baricitinib was commenced at 3 mg/g per day, in three divided doses, but did not lead to any improvement in respiratory symptoms. Therefore, we aimed to suppress other inflammatory pathway, nuclear factor kappa B (NFKB) and initiated intravenous tocilizumab at a dosage of 12 mg/kg during the 3rd week of baricitinib. However, the patient deteriorated and deceased 1 months later. Parental testing confirmed that the variant was de-novo.
Conclusion: SAVI syndrome should be considered in differential diagnosis of ILD in every age, even in the absence of skin involvement. Consent to published had been obtained.
Disclosure
None declared

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P046

Efficacy of colchicine treatment in children with periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome

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Pediatric Rheumatology, **23(2):** P046

Introduction: PFAPA syndrome is the most common periodic fever disorder in children, characterized by recurrent episodes of fever associated with cervical adenitis, pharyngitis, and aphthous stomatitis. Growing evidence suggests a connection between PFAPA and Familial Mediterranean Fever (FMF), with both having associations with IL-1β pathways. Colchicine, a standard treatment for FMF, may potentially benefit PFAPA patients, but limited evidence exists on its efficacy for preventing recurrent PFAPA episodes.
Objectives: To evaluate the efficacy of colchicine prophylaxis in children diagnosed with PFAPA syndrome by comparing attack frequency in colchicine-treated patients versus standard care controls.
Methods: We conducted a retrospective analysis of 55 PFAPA patients (15 in the colchicine group and 40 in the control group). Demographics, clinical characteristics, FMF genetic profiles, and attack frequency before and after intervention were collected. The primary outcome was the time interval between fever episodes. Statistical significance was set at P<0.05.
Results: Both groups were comparable regarding age at diagnosis (5.33 [3.71-6.96] vs. 4.63 [3.94-5.32] years, P=0.4), age of symptom onset (3.00 [2.02-4.57] vs 2.59 [2.16-3.03] years, P=0.42), and duration of fever before diagnosis (3.75 [2.93-4.57] vs 4.345 [3.90-4.99] days, P=0.14). The colchicine group demonstrated a significant increase in the time between attacks after treatment (83.00 [58.56-107.44] days) compared to pre-treatment intervals (27.92 [24.68-31.15] days, P=0.002). MEFV mutations were more prevalent in the colchicine group (58.33% vs 26.32%, P<0.05), with heterozygous M694V (5/11) and V726A (4/11) being most common. Within genetic subgroups, patients with mutations receiving colchicine experienced shorter fever duration (3.25 [2.66-3.84] days) compared to controls (4.45 [3.00-4.00] days, P<0.05. Notably, both genetically positive and negative patients responded favorably to colchicine treatment, although the magnitude of improvement was greater in those with MEFV mutations.
Conclusion
Conclusion: Colchicine prophylaxis significantly extended the interval between fever episodes in all PFAPA patients, with enhanced efficacy in those with MEFV gene mutations. The nearly three-fold increase in attack-free intervals in genetically positive patients demonstrates that genetic testing may be an important factor in predicting treatment response. These findings suggest colchicine as an effective

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MEETING ABSTRACTS

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O01

Reconstitution of the B cell compartment following anti-CD19 CAR-T cell therapy in refractory patients with Juvenile Dermatomyositis (JDM)

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Pediatric Rheumatology, **23(2):** O01

Introduction: CD19 CAR T-cell therapy is an innovative strategy to induce profound B cell depletion in patients with refractory idiopathic inflammatory myopathies (IIM). However, its effects on B cell phenotypes in pediatric patients remain largely unknown.
Objectives: To characterize the reconstitution profile of B cell subsets in three patients with juvenile dermatomyositis (JDM) treated with anti-CD19 CAR T-cell therapy.
Methods: Three patients with refractory JDM received a single infusion of autologous, second-generation anti-CD19 CAR T cells (1×10^6 CAR T cells/kg; lentiviral vector), manufactured on the CliniMACS Prodigy system. Lymphodepletion was achieved using cyclophosphamide (1000 mg/m^2 over 2 days) and fludarabine (90 mg/m^2 over 3 days). B cell immunophenotyping was performed according to standard operating procedures (SOPs) before and after CAR T-cell infusion. A comparator group of five JDM patients treated with rituximab (RTX) was included.
Results: B cell reconstitution occurred at a median of 8 weeks (IQR: 8.0-12.0) post-CAR T therapy, with an immature transitional B cell phenotype. B cell subsets distribution was assessed at a median of 27.3 weeks (IQR: 22.5–40.2) after treatment, when all B cell subsets were present for each patient, and compared to pre-treatment profiles. In the RTX group, B cell phenotyping was performed at a median of 47 weeks (IQR: 33.4–50.7) post-treatment. The proportion of CD19$^+$ B cells among lymphocytes was similar before and after CAR T-cell treatment (pre: 32% [IQR: 23–40], post: 21% [IQR: 20–24]). B cell subset analysis showed comparable levels of transitional, naïve and plasmablast populations pre- and post-treatment. However, there was a notable reduction in total memory B cells (MBCs) post-treatment (pre: 6.4% [IQR: 6.3–9.1], post: 3.9% [IQR: 3.1–4.0]), particularly in the switched MBC subset. Interestingly, JDM patients treated with RTX showed higher frequencies of switched MBCs during B cell reconstitution compared to those treated with CAR T cells: CAR T treated-patients 16.0 % [IQR: 8.5-18.0], RTX group 52.0% [IQR: 28.0, 60.0].
Conclusion: These data show that following CAR T cell treatment, the memory B cell compartment presents a lower frequency of switched MBCs when compared to pre-treatment levels and to patients treated with RTX, suggesting a specific effect of CAR T cell treatment in regulating the memory B cell compartment in JDM patients.
Disclosure
None declared

O02

Anti-CD19 Car-T cell therapy in refractory juvenile dermatomyositis (JDM): a single-center case series

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Pediatric Rheumatology, **23(2):** O02

Introduction: CD19 CAR T-cell therapy represents an innovative approach emerging as a promising treatment option in patients with refractory idiopathic inflammatory myopathies (IIM), but the experience in children so far is limited.
Objectives: To report on the safety and efficacy of anti-CD19 CAR T-cell therapy in 3 JDM patients.
Methods: All 3 patients received a single infusion of fresh, autologous second-generation anti-CD19 CAR T product (lentiviral vector) manufactured on the Prodigy device ($1x10^6$ CAR T cells/kg), after lymphodepletion with cyclophosphamide (1000 mg/m^2 over 2 days) and fludarabine (90 mg/m^2 over 3 days).
Results: Maximum follow-up after CAR T-cell therapy was 20 months. Patients 1 and 2 had a history of severe chronically active disease with extensive calcinosis and ulcerations. Patient 3 presented interstitial lung disease (ILD) and persistently active muscle and skin disease with ulcerations. Short-term effects of CAR T-cell therapy on Patient 1 have been previously reported (Nicolai A&R 2024). All patients were refractory to multiple immunosuppressive treatment lines and presented significant side effects from chronic glucocorticoid treatment. After infusion, CAR T cells rapidly expanded, reaching peak concentrations after a median of 7 days (range 7-9). At peak, the median number of circulating CAR T cells was 32.69 per microliter (range 31.04-535.02). CD19+ B cells were undetectable in peripheral blood after a mean of

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