2nd Familial Mediterranean Fever Meeting

Abstract Book

Cerrahpasa Rheumatology Society 1983

FMF2024.org

SCIENTIFIC SECRETARIAT

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Dear Colleagues,

This is an invitation to all students of familial Mediterranean fever and autoinflammation all over the world. Every aspect of this old disease from genetics to treatment, from pathogenesis to clinical expression and diagnosis has been going through significant evolution during the last two decades. Therefore we are in need of discussing the changing concepts and the needs in FMF. We invite you to get together in İstanbul by the Golden Horn, to exchange and discuss the latest scientific contributions in this field, as well as the consequences of these research in our daily practice, and try to solve our evolving new querries to improve the quality of life of our patients. Each one of your presence is so valuable.
We are looking forward to meet you in Istanbul, between May 3-5, 2024!

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May 3, 2024, FRIDAY

GMT + 3		
16.00-18.00	**Session 1 – Old paradigms, new concepts**	**Chairpersons**: Hasan Yazıcı (*Türkiye*), Isabelle Touitou (*France*)
16.00-16.20	Unmet needs in FMF	Huri Özdoğan (*Türkiye*)
16.20-16.50	Old paradigms and new concepts in FMF	Eldad Ben-Chetrit (*Israel*)
16.50-17.20	What is FMF?	Ahmet Gül (*Türkiye*)
17.20-17.50	Review of the last two year	Yelda Bilginer (*Türkiye*)
19.00	Welcome Reception	

May 4, 2024, SATURDAY

GMT + 3		
08.00 – 10.00	**Session 2 – Update: Genetics and Pathogenesis**	**Chairpersons:** Ahmet Gül (*Türkiye*), Tillmann Kallinich (*Germany*), Banu Peynircioğlu (*Türkiye*)
08.00-08.30	The changing concept of one gene-one phenotype in monogenic autoinflammatory diseases	Ivona Aksentijevich (*USA*)
08.30-09.00	Regulation of pyrin inflammasome	Mohamed Lamkanfi (*Belgium*)
09.00-09.20	Pyroptosis and clinical implications in FMF	Helmut Wittkowski (*Germany*)
09.20-09.40	Pyrin inflammasome and inflammatory cell migration in FMF	Tayfun Hilmi Akbaba (*Türkiye*)
09.40-10.00	Discussion	
10.00-10.30	**Coffee Break**	
10.30-12.00	**Session 3 – Update: Genetic diagnosis, environmental factors and microbiome**	**Chairpersons:** Seza Özen(*Türkiye*), Dorota Rowczenio (*UK*)
10.30-11.00	Update: genetic diagnosis in FMF	Isabelle Touitou (*France*)
11.00-11.20	Non-MEFV gen variants in patients with a FMF phenotype	Eda Tahir Turanlı (*Türkiye*)
11.20-11.40	Syndrome of Undifferentiated Recurrent Fever (SURF)	Marco Gattorno (*Italy*)
11.40-12.00	Impact of enviromental factors and microbiome on the pathogenesis of FMF	Sophie Georgin Lavialle (*France*)

May 4, 2024, SATURDAY

12.00-12.30	**Oral presentations**	**Chairpersons:** Fatoş Önen (*Türkiye*), Ömer Karadağ (*Türkiye*)
12.00-12.07	A clinical overview of unclassified systemic autoinflammatory diseases followed in a Turkish Pediatric Referral Center (Ref: 115)	Şengül Çağlayan (*Türkiye*)
12.07-12.14	Evaluation of patients carrying variants of unknown significance (VUS) in a large FMF cohort: A single center study (Ref: 116)	Taner Coşkuner (*Türkiye*)
12.14-12.21	Exploring S100A8/A9, Neopterin, and MMP3 in Familial Mediterranean Fever: Insights into pathogenesis and diagnostic significance (Ref: 145)	Özgür Can Kılınc (*Türkiye*)
12.21-12.28	Epidemiological features and clinical manifestations in lebanese and Italian subjects with Familial Mediterranean Fever (Ref: 130)	Nour Jaber *(Italy)*
12.30-13.30	**Lunch & Poster Reviewing**	

May 4, 2024, SATURDAY

13.30-15.30	**Session 4 – Criteria, registry, geography**	**Chairpersons:** Helmut Wittkowski (Germany), Fatoş Yalçınkaya (*Türkiye*)
13.30-13.50	Pros and cons of diagnostic and classification criteria for FMF	Isabelle Kone-Paut (*France*)
13.50-14.10	Challenges of preparing a registry for FMF	Marco Gattorno (*Italy*)
14.10-14.20	Discussion	
14.20-15.30	**Round Table: FMF around the world**	**Chairpersons:** Seza Özen (*Türkiye*), Huri Özdoğan (*Türkiye*), Eldad Ben-Chetrit (*Israel*)
14.20-14.35	FMF in Japan	Tomohiro Koga (*Japan*)
14.35-14.50	FMF in Italy	Raffaele Manna (*Italy*)
14.50-15.05	FMF in Saudi Arabia	Sulaiman Al-Mayouf (*Saudi Arabia*)
15.05-15.30	Discussion	
15.30-16.00	**Coffee Break**	
16.00-17.40	**Session 5 – Update: Amyloidosis, associated diseases**	Helen Lachmann (*UK*), Cengiz Korkmaz (*Türkiye*), Melike Melikoğlu (*Türkiye*)
16.00-16.20	Is amyloidosis still a threat in FMF?	Ahmet Gül (*Türkiye*)
16.20-16.40	Early versus late onset FMF	Piero Portincasa (*Italy*)
16.40-17.00	PFAPA and FMF	Özgür Kasapçopur (*Türkiye*)
17:00-17.20	AS and enthesitis in FMF	Servet Akar (*Türkiye*)
17.20-17.40	Behçet's disease and FMF	Emire Seyahi (*Türkiye*)

May 4, 2024, SATURDAY

17.40-18.08	**Oral presentations**	**Chairpersons:** Mikail Kostik (*Russia*), Hakan Babaoğlu (*Türkiye*)
17.40-17.47	Gender differences in the diagnosis delay of familial Mediterranean fever: A JIR cohort study (Ref: 91)	Rim Bourguiba (Tunisia)
17.47-17.54	Cardiovascular comorbidities in patients with Familial Mediterranean Fever over 45 years of age (Ref: 133)	Sejla Karup (*Türkiye*)
17.54-18.01	Male fertility and paternal effect on pregnancy outcomes in FMF (Ref: 150)	Kerem Parlar (*Türkiye*)
18.01-18.08	Menstrual cycle patterns and dysmenorrhea frequency in adolescent girls with familial Mediterranean fever: Cross-Sectional case-control study (Ref: 106)	Fatma Gül Demirkan (*Türkiye*)

May 5, 2024, SUNDAY

GMT + 3		
08.00-10.00	**Session 6a. – Upate:Treatment-I**	**Chairpersons:** Huri Özdoğan(*Türkiye*), Sophie Georgin-Lavialle (*France*), Serdal Uğurlu (*Türkiye*)
08.00-08.20	Mechanism of action of colchicine and its expanding efficacy	Eldad Ben-Chetrit (*Israel*)
08.20-08.40	Colchicine response and tolerance in FMF	Seza Özen (*Türkiye*)
08.40-09.00	Anti-IL1 treatment in FMF	Serdal Uğurlu (*Türkiye*)
09.00-09.15	On-demand anti-IL1 treatment	Ilan Ben-Zvi (*Israel*)
09.15-09.40	Efficacy and safety of anti-IL1β treatment in FMF	Helen Lachmann (*UK*)
09.40-10.00	Anti-IL6 treatment FMF	Tomohiro Koga (*Japan*)
10.00-10.30	**Coffee Break**	
10.30-12.30	**Session 6b. – Update: Treatment II**	**Chairpersons:** Ahmet Gül(*Türkiye*), Isabelle Kone-Paut (*France*)
10.30-10.50	Biologic agent combinations in the management of FMF and other autoinflammatory diseases	Abdurrahman Tufan (*Türkiye*)
10.50-11.10	Treat-to target strategies in FMF	Tillmann Kallinich (*Germany*)
11.10-11.40	Discussion for sessions 6a and 6b	
11.40-12.30	**Session 7 – Transition**	**Chairpersons:** Kenan Barut (*Türkiye*), Gülay Özgön*(Türkiye)*, Amra Adrovich (*Türkiye*)
11.40-12.00	Transition from pediatric to adult FMF clinics	Betül Sözeri (*Türkiye*)

May 5, 2024, SUNDAY

12.00-12.42	**Oral presentations**	
12.00-12.07	Machine learning algorithms to predict colchicine resistance in Familial Mediterranean Fever (Ref: 158)	Admir Öztürk (*Türkiye*)
12.07-12.14	Comparing the effects of treatments during the attack period on clinical and laboratory data in Familial Mediterranean Fever Patients (Ref: 143)	Elif Kılıç Konte (*Türkiye*)
12.14-12.21	Familial Mediterranean Fever: Effective follow-up of patients who ceased colchicine treatment (Ref: 122)	Gülcan Özomay Baykal (*Türkiye*)
12.21-12.28	Canakinumab treatment in patients with colchicine-resistant familial Mediterranean fever: a multicenter observational study (Ref: 83)	Mete Kara (*Türkiye*)
12.28-12.35	Is canakinumab a good tool for the undifferentiated autoinflammatory diseases: the data of retrospective cohort study (Ref: 108)	Mikhail Kostik *(Russia)*
12.35-12.42	Familial Mediterranean Fever from childhood to adulthood (Ref: 163)	Zeynep Balık (*Türkiye*)
12.42-12.50	Discussion	
12.50-13.10	Highlights of the meeting	Sezgin Şahin (*Türkiye*)
13.10-13.30	**Future perspectives, presentation of awards, closing remarks**	Huri Özdoğan (*Türkiye*), Eldad Ben-Chetrit (*Israel*), Serdal Uğurlu (*Türkiye*)

Oral Presentations

OP-01

GENDER DIFFERENCES IN THE DIAGNOSIS DELAY OF FAMILIAL MEDITERRANEAN FEVER: A JIR COHORT STUDY

Rim Bourguiba[1], Samuel Deshayes[2], Gayane Amaryan[3], Isabelle Kone Paut[4], Alexandre Belot[5], Tamara Sarkisyan[6], Rahma Guedri[7], Manel Mejbri[8], Isabelle Melki[9], Ulrich Meinzer[9], Diana Dan[10], Nicolas Schleinitz[11], Véronique Hentgen[12], Sophie Georgin Lavialle[13]

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[4]Pediatric department, Hopital Kremlin Bicetre, Assistance publique des Hôpitaux de Paris
[5]Pediatric department, CHU de Lyon HCL - GH Est-Hôpital Femme Mère Enfant
[6]Department of medical genetics, Yerevan center of medical genetics and primary health care, Armenia
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[11]Internal Medicine department, CHU Timone, Marseille
[12]Pediatric department, Hopital de Versaille, CH de Versailles - Hôpital André Mignot le chesnay cedex, France
[13]Internal medicine department, Tenon Hospital, Centre de référence des maladies auto inflammatoires et amylose AA, Sorbonne University

Familial Mediterranean fever (FMF) is the most common autoinflammatory disease worldwide. Several studies reported that FMF diagnosis may be missed or delayed even in countries with a high prevalence.Our aim was to study a large cohort of European FMF patients to identify the frequency and associated factors of diagnosis delay.

Methods: Clinical data were extracted from the Juvenile Inflammatory Rheumatism (JIR)- cohort. We defined FMF-diagnostic delay (d-FMF) as a duration between the onset of the symptoms and FMF diagnosis of more than 10 years.

Results: We enrolled 960 FMF patients;delayed diagnosis (d-FMF) was noted in 20% of patients (n=200) whereas 80% of other patients (FMF) (n=760) had the diagnosis made within the 10 years from the onset of symptoms. d-FMF patients were significantly older than other FMF with a median age of 46.4 years old versus 15.5 ($p < 0.0001$). Concerning women, the percentage of d-FMF was higher than other FMF patients (56% versus 47%, $p=0.03$).

Regarding the clinical presentation only, erysipelas-like erythema was more frequently observed among d-FMF patients (33% versus 22%, $p=0.0003$).AA amyloidosis was significantly more frequent in d-FMF than FMF (10 % versus 2.6 %, $p< 0.0001$). As well, d-FMF patients received significantly more biotherapy compared to other FMF (18% versus 3.8%, $p<0.0001$).

Discussion and Conclusion: Twenty percent of FMF patients were misdiagnosed before being officially diagnosed as FMF with significantly more women; this could be linked to the differential diagnosis of abdominal attacks with period pains, as frequently reported be women patients.

FMF delay is still significantly high nowadays. To our knowledge, our study is the first cohort study to investigate diagnostic wandering and the factors associated with long diagnostic wandering in a large European cohort. Education and better communication on this disease to patients and practitioners could be fruitful to improve FMF earlier diagnosis.

Keywords: FMF, Delay

OP-02

MENSTRUAL CYCLE PATTERNS AND DYSMENORRHEA FREQUENCY IN ADOLESCENT GIRLS WITH FAMILIAL MEDITERRANEAN FEVER: CROSS-SECTIONAL CASE-CONTROL STUDY

Fatma Gül Demirkan[1], Aylin Yetim Şahin[2], Figen Çakmak[1], Özlem Akgün[1], Vafa Guliyeva[1], Melike Zeynep Tuğrul Aksakal[2], Firdevs Baş[2], Nuray Aktay Ayaz[1]

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[2]Department of Adolescent Medicine, İstanbul School of Medicine, İstanbul University, İstanbul, Türkiye

Objective: Familial Mediterranean Fever (FMF) is an autosomal recessive disease characterized by recurrent fever attacks, peritonitis, and arthritis. Clinical studies have shown that attacks can be triggered by predisposing factors such as emotional stress, cold exposure, or menstruation. However, information regarding the effects of FMF on menstrual cycles is limited. The aim of this study was to investigate the impact of FMF on the menstrual process and the presence of dysmenorrhea symptoms in patients.

Materials and Methods: This study was conducted among 73 adolescent girls diagnosed with FMF and 70 healthy controls. The ages, menstrual cycle characteristics, symptoms, and dysmenorrhea findings of patients and the control group were recorded and evaluated.

Results: There was no significant difference observed between the median age and body mass index of the control group and the patient group. While the age of menarche was similar between the two groups, it was significantly later in the patient group compared to the control group. Additionally, the number of pads used during the first 3 days of menstruation was significantly higher in the patient group compared to the control group ($p=0.001$). (Table 1)

Regarding the localization of pain during dysmenorrhea, the groups exhibited similar characteristics. Dysmenorrhea occurred both during the cycle and before in the patient group, while it predominantly occurred during menstruation in the control group ($p<0.01$). Adolescent girls with FMF had longer and more painful menstrual periods compared to the control group. Additionally, during menstruation, fever, arthralgia, and diarrhea were more common in the FMF group than those in the control group.

Conclusions: Dysmenorrhea symptoms and cycle irregularities are more commonly observed in FMF patients compared to healthy peers. Additionally, menstruation may trigger FMF symptoms. These findings are important for understanding the effects of FMF on menstrual-related hormonal balance and developing treatment strategies.

Keywords: Familial Mediterranean fever, menstruation

Table 1. Demographic Data and Characteristics of Menstrual Cycles of the Groups

	Control (n=70)	Patient (n=73)	p
Age (year) (median, IQR 25-75)	15 (13-17)	16 (14-18)	0,78
BMI (kg/m2) (median, IQR 25-75)	21,11 (19,13-23,64)	20,65 (18,75-23,53)	0,12
Menarche age (year) (median, IQR 25-75)	12 (11-13)	12 (11-13)	0,11
Mother menarche age (year) (median, IQR 25-75)	12 (12-13)	13 (12-14)	0,007*
Menstruation duration (day) (median, IQR 25-75)	5 (5-7)	6 (5-7)	0,15
Duration between cycles (day) (median, IQR 25-75)	28 (28)	28 (24-30)	0,93
Number of pad used in the first three days of menstruation (n) (median, IQR 25-75)	2,5 (2-3,2)	8 (4-10,5)	0,001*
BMI, Body Mass Indeks; IQR, Interquartile range; *p<0,05			

OP-03

IS CANAKINUMAB A GOOD TOOL FOR THE UNDIFFERENTIATED AUTOINFLAMMATORY DISEASES: THE DATA OF RETROSPECTIVE COHORT STUDY

Ekaterina Alexeeva[1], Meiri Shingarova[1], Tatyana Dvoryakovskaya[1], Olga Lomakina[1], Anna Fetisova[2], Ksenia Isaeva[2], Aleksandra Chomakhidze[2], Kristina Chibisova[2], Elizaveta Krekhova[1], Aleksandra Kozodaeva[3], Kirill Savostyanov[2], Aleksandr Pushkov[2], Ilya Zhanin[2], Dmitry Demyanov[2], Evgeny Suspitsin[4], Konstantin Belozerov[5], Mikhail Kostik[5]

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Introduction: the blockade of interleukine-1 is a known highly effective tool for monogenic autoinflammatory diseases (AID). Our study aimed to assess the safety and efficacy of canakinumab for patients with undifferentiated AID (uAID).

Methods: in the retrospective cohort study the information about 32 patients (13 boys and 19 girls) with uAID from two tertial centers was included. NGS (at least PID and AID panel) underwent in all patients and patients with known monogenic AID were excluded.

Results: The age of the first episode was 2.5 (1.3; 5.5) years, and the age of disease diagnosis was 5.7 (2.5;12.7) years. The diagnostic delay was 1.1 (0.4; 6.1) years. Patients have variants in the following genes: IL10, NLRP12, STAT2, C8B, LPIN2, NLRC4, PSMB8, PRF1, CARD14, IFIH1, LYST, NFAT5, PLCG2, COPA, IL23R, STXBP2, IL36RN, JAK1, DDX58, LACC1, LRBA, TNFRSF11A, PTHR1, STAT4, TNFRSF1B, TNFAIP3, TREX1, SLC7A7.The main clinical features were fever (100%), rash (91%), joint involvement (72%), splenomegaly (66%), hepatomegaly (59%), lymphadenopathy (50%), myalgia (28%), heart involvement (31%), intestinal involvement (19%); eye involvement 9%), pleuritis (16%), ascites (6%), deafness, hydrocephalia (3%), failure to thrive (25%).

Initial treatment before canakinumab consisted of non-biologic: NSAID (91%), corticosteroids (88%) and biologic drugs: tocilizumab (62%), sarilumab, etanercept, adalimumab, rituximab, infliximab (all 3%). Canakinumab induced complete remission in 27 (84%), partial in one patient (3%). Two patients (6%) were primary non-responders and two (6%) developed secondary inefficacy further. All patients with partial efficacy or with inefficacy switched to tocilizumab (n=4) and sarilumab (n=1). The total duration of canakinumab treatment was 3.6 (0.1; 8.7) years. During the study, there were no reported SAEs. Patients had non-frequent mild respiratory infections with a similar rate as before canakinumab and one patient developed leucopenia, not required to stop canakinumab.

Conclusion: the treatment of patients with uAID with canakinumab was safe and effective.

Keywords: canakinumab, undifferentiated autoinflammatory disorders

OP-04

A CLINICAL OVERVIEW OF UNCLASSIFIED SYSTEMIC AUTOINFLAMMATORY DISEASES FOLLOWED IN A TURKISH PEDIATRIC REFERRAL CENTER

Şengül Çağlayan, Betül Sözeri

Department of Pediatric Rheumatology, University of Health Sciences, Umraniye Training and Research Hospital, İstanbul

Objective: The aim of our study was to describe a large and homogeneous group of patients diagnosed with systemic unclassified autoinflammatory diseases (USAID) followed by a tertiary referral center and to examine in detail their long-term follow-up and response to treatment by using cluster analysis.

Methods: This was a retrospective study including pediatric patients diagnosed with USAID, who were followed from June 2016 to October 2023 at our center.

Results: A total of 76 patients were involved in the study. The median current age of the patients, age of onset of the complaints, and age of diagnosis were 124 months (interquartile range, IQR: 83-179), 53 months (IQR:36-95), 94 months (IQR: 60-140), respectively. The most frequently observed clinical symptoms accompanying fever episodes were arthralgia (69.7%), abdominal pain (68.4%), myalgia (53.9%), and rash (38.2%). According to NGS and WES analyses, no mutation was observed in 54 patients (71%). In the remaining 22 patients (29%), sequence variants classified as benign or variants of undetermined significance (VUS) were identified in various genes. Colchicine was used in 69 (90.7%) patients in the study. Of these, 34 patients (49.2%) had a complete response, 27 patients (39.1%) had a partial response, and 8 patients (11.6%) had no response. Additionally, IL-1 blockers were used in 10 patients (13.1%). According to the two-step cluster analysis, three clusters had been identified with distinct features. There were no significant differences between clusters in terms of gender distribution, age at onset of symptoms, age at diagnosis, number of annual attacks, duration of the episode, response to colchicine treatment, or biological agent use.

Conclusion: This study highlights the complex and diverse nature of USAID, highlighting challenges in diagnosis, genetic characterization, and treatment. Future research should focus on improving our understanding and management of this heterogeneous group of diseases by expanding genetic analyses and investigating new treatment options.

Keywords: unclassified autoinflammatory diseases, cluster analysis

OP-05

EVALUATION OF PATIENTS CARRYING VARIANTS OF UNKNOWN SIGNIFICANCE (VUS) IN A LARGE FMF COHORT: A SINGLE CENTER STUDY

Taner Coşkuner, Kadir Ulu, Betül Sözeri

Health Sciences University, Umraniye Training and Research Hospital Division of Pediatric Rheumatology Istanbul, Turkey

Objective: Familial Mediterranean Fever (FMF) is caused by mutations in the MEFV (Mediterranean fever) gene located on chromosome 16p.13.3. The MEFV gene has 10 exons. However, clinical complaints can also be seen with variants of unknown significance (VUS), most of which are located in exons 2 and 3, although the frequency is low. In this study, we aimed to present the demographic and clinical characteristics of patients with VUS alleles who were followed up in our clinic with a diagnosis of FMF.

Materials-Methods: In this study, the demographic and clinical characteristics of patients who were followed up in our clinic between 2016 and 2023 with a diagnosis of FMF, received colchicine treatment and were followed up for at least 6 months were retrospectively analyzed.

Results: The study included 355 patients with VUS alleles out of 2325 patients followed up with a diagnosis of FMF in our clinic. Of the patients, 50.4% (n:179) were female and 49.6% (n:176) were male. The mean age at attack onset was 5.7 ± 3.9 years and the mean age at diagnosis was 7.3 ± 4.8 years. The mean number of attacks per year was 9.5 ± 7.2. The most common VUS allele was E148Q with 67.6% (n:299). The most common mutation was E148Q heterozygosity 62.2% (n:221). In E148Q heterozygosity, fever was observed in 81.4%, abdominal pain in 87.3% and arthralgia in 60%. Colchicine resistance, the need for biologic therapy and amyloidosis were not observed in any of the patients.

Conclusion: In our country, VUS alleles are observed to a considerable extent in FMF patients and cause clinical findings with similar frequency to pathologic alleles. We think that more studies should be conducted on this subject for the follow-up and treatment of patients with the increasing number of patients with the VUS allele.

Keywords: VUS, E148Q

OP-06

FAMILIAL MEDITERRANEAN FEVER: EFFECTIVE FOLLOW-UP OF PATIENTS WHO CEASED COLCHICINE TREATMENT

Gülcan Özomay Baykal, Sıla Atamyıldız Uçar, Betül Sözeri

Umraniye Training and Research Hospital

Introduction: Familial Mediterranean Fever (FMF) is an autosomal recessive inherited disease. We aimed to identify sociodemographic and disease characteristics of patients with heterozygous mutations displaying an FMF phenotype who ceased colchicine treatment after a certain period.

Results: Retrospective analysis was conducted on data from 44 patients, out of 1241, with heterozygous mutations monitored with FMF between 2016 and 2023 at Umraniye Training and Research Hospital. 20 were female (45.5%) and 24 were male (54.5%). The median follow-up period was 64 months (min. 1, max. 89). The median age of initiation of colchicine is 87.5 months (7–196). The median time elapsed until discontinuation of colchicine was 29 months (range, 2–140 months). When MEFV mutations were examined, M694V was 31.8% (n = 14), E148Q was 29.5% (n = 13), V726A was 11%, and M680I was 9.1% (n = 4) heterozygous. 70.4% (n = 31) of the patients were discontinued because they had been without attacks for at least 6 months, and 29.6% (n = 13) left colchicine voluntarily. The mean follow-up period without attacks after discontinuation of colchicine was 26.5 months (6–102). 13.6% (n = 6) of the patients who discontinued colchicine started colchicine again after an average of 45.8 (4–60) months due to having an attack. Of the 44 patients, 36 (82%) had fever, 32 (73%) had abdominal pain, 27 (61%) had arthralgia, 14 (32%) had leg pain symptoms.

Conclusion: Most of the FMF patients who discontinued colchicine did not need to start the drug again. On average, they remained attack-free for 2 years. However, those who resumed the medication did so after an average period of 4 years, with a maximum range of 5 years. For this reason, it is recommended that FMF patients who have stopped colchicine be closely monitored for at least 5 years.

Keywords: Colchicine Cessation, FMF attacks

Drug Discontinuation probabilities for MEFV Mutation Types

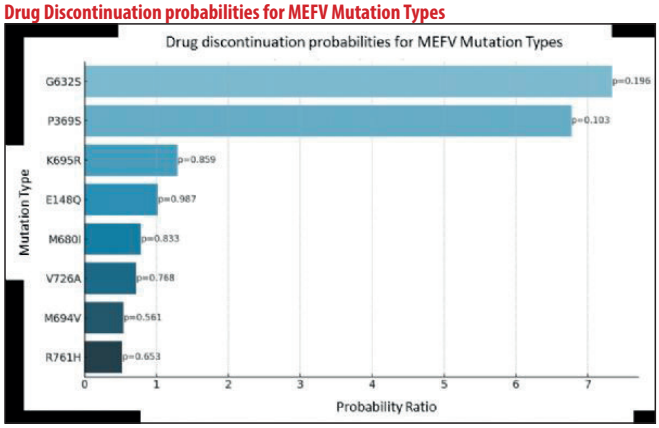

Figure. Comparison of the types of MEFV mutations in patients who were followed up with the diagnosis of FMF and patients who discontinued treatment with Colchicine

MEFV mutation distribution

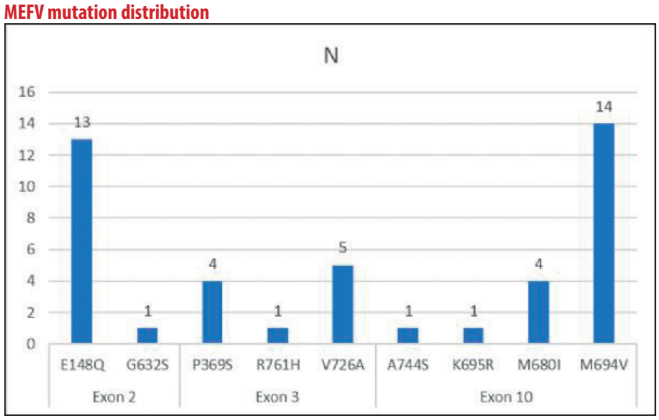

Figure. MEFV mutation distribution in patients diagnosed with FMF whose Colchicine treatment was discontinued

OP-07

EPIDEMIOLOGICAL FEATURES AND CLINICAL MANIFESTATIONS IN LEBANESE AND ITALIAN SUBJECTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory monogenic disease with recurrent febrile painful attacks due to serositis. FMF manifestations can greatly change across the Mediterranean basin. We assessed two well-characterized FMF groups living in Italy (Apulia) and Lebanon.

Methods: 142 Lebanese patients (females 66.2%) and 53 Italian patients (females 60.4%) followed at referral centers were interviewed by a 55-item questionnaire for demographic, clinical, and genetic features.

Results: At entry, Italian patients were older than Lebanese patients (44.3±SEM2.3 yrs. vs. 22.0±1.2 yrs., $p<0.0001$). In Italian and Lebanese patients, the age at FMF diagnosis was 30.6±2.1 yrs and 13.5±0.9 yrs., with a diagnostic delay of more than 5 years in 50% and 20%, respectively ($p<0.05$). Genetic testing revealed that the most common MEFV variants were E148Q (53.1%), R761H

(46.9%) in Italians, and E148Q (29.9%), and M694V (28.4%) in Lebanese Subjects. Besides fever, the prevalence of other symptoms (chest, abdominal pain, arthralgias, erysipelas-like dermatitis) was lower in Italians (25%-96%) than in Lebanese patients (44%-99%) ($p<0.05$). For diagnosis and management, Italian patients visited an internist, while Lebanese patients visited gastroenterologists or pediatricians. Misdiagnoses occurred more often in Italian than Lebanese patients (71.7% vs 46.5%, $P=0.002$), mostly as appendicitis and other gastrointestinal disorders. Colchicine was the first-line treatment while anti-IL-1 agents (canakinumab, anakinra) were used in 6.1% and 0.8% of Italian and Lebanese patients, respectively.

Conclusion: FMF epidemiological and clinical profiles show that Italian patients more often experience initial misdiagnosis and delayed diagnosis. Lebanese patients exhibit more symptoms, likely due to severe mutation types. The role of gene-environment interaction across different geographical areas requires more studies.

Keywords: Familial Mediterranean fever, Rare disease

OP-08

CARDIOVASCULAR COMORBIDITIES IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER OVER 45 YEARS OF AGE

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Objective: The relationship between Familial Mediterranean Fever (FMF) and cardiovascular diseases (CVDs) remains unclear. This study explored the relationship between FMF and CVDs.

Materials-Methods: The study targeted individuals aged 45 and above diagnosed with FMF. Those who also had coronary artery disease, cerebrovascular disease, or hypertension were classified as having cardiovascular disease (CVD). The diagnosis of FMF was confirmed using the Tel-Hashomer criteria. The Turkish Government Statistical Organization (TUIK) data was utilised as a control group to ensure robust comparisons and reliable results.

Results: Among the 522 patients examined, 201 were found to have CVD. Patients without CVD had a mean age of 53.00 ± 6.43 years, while those with CVD had a mean age of 60 ± 8.33 years. Hypertension was present in 188 patients (36%), while 51 patients (9.8%) had coronary artery disease, and 10 patients (1.9%) had cerebrovascular disease. Diabetes was the most common comorbidity among patients with CVD (30.3%). All 522 patients were on colchicine treatment, with 35 patients with CVD (17.2%) and 25 patients without CVD (7.8%) showing resistance to colchicine. Amyloidosis was present in 5% of patients, but none exhibited cardiac involvement.

Conclusions: Patients with CVD displayed a higher incidence of colchicine resistance compared to those without CVD. The colchicine resistance within the patient group may enhance the risk of cardiovascular disease development. Both colchicine and anti-interleukin-1 therapies show promise in reducing the risk of CVDs in patients with FMF.

Keywords: Familial Mediterranean Fever, cardiovascular disease

Table 2. Distribution of Cardiovascular Disease Among Individuals Diagnosed with FMF

	Patients (n=522)
Hypertension n (%)	188 (36%)
Cerebrovascular disease (%)	10 (1.9%)
Coronary artery disease (CAD) n (%)	51 (9.8%)
I CVD n (%)	156 (29.8%)
II CVD n (%)	42 (8.0%)
III CVD n (%)	3 (0.6%)

Table 1. Presentation of Demographic Data of the Patients

	Patients with CVD (n=201)	Patients without CVD (n=321)
Age(mean±SD)[a]	57.60±8.33	53.00±6.42
Female[b]	143 (71.1%)	192 (59.9%)

[a]p<0.001 and [b]p=0.009.

Table. Cardiovascular Comorbidities and Medication Use in Study Participants

	Patients (n=201) with CVDs	Patients (n=321) without CVDs
History of smoking n(%)	84 (41.8%)	151 (46.8%)
Diabetes n(%) p<0.001	61 (30.3%)	33 (10.3%)
Arrhythmia n(%)	11 (5.5%)	8 (2.5%)
Colchicine response n(%) p=0.021	183 (91.0%)	308 (95.9%)
Colchicine resistance n(%) p<0.001	35 (17.2%)	25 (7.8%)
Biological therapy n(%)	25 (12.4%)	18 (5.7%)
Total number of medications (mean ± SD) p=0.006	4.20±2.28	1.74±1.55
VAS score (mean ± SD)	2.73±3.08	2.59±3.04

Table. Comparative Analysis of Findings between the TEKHARF Study and Our Study

	TEKHARF	Our study (n=522)
Hypertension p<0.01	6401/2955 (46.1%)	522/188 (36%)
Coronary Artery Disease	7457/587 (7.8%)	522/51 (9.7%)
Cerebrovascular Disease p=0.016	7457/302 (4%)	522/10 (1.9%)

OP-09

COMPARING THE EFFECTS OF TREATMENTS DURING THE ATTACK PERIOD ON CLINICAL AND LABORATORY DATA IN FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Objective: Familial Mediterranean fever (FMF) is the most common inherited autoinflammatory disease. Attacks of FMF are usually self-limiting; however, due to restrictions in daily life, treatments are used to reduce symptoms and shorten the duration of the attacks. This study aimed to compare the effectiveness of treatment methods for FMF attacks.

Materials-Methods: The study included patients with compound heterozygous or homozygous mutations in exon 10. Demographic data, laboratory parameters, attack symptoms, and VAS scores were prospectively recorded. The clinic offered three protocols for FMF attacks, as decided by the paediatric rheumatologist: Anakinra, NSAID, and intravenous 0.9% saline. VAS scores were monitored by phone call every two hours, and CRP levels were measured at the time of treatment and 24 hours later. The data was analyzed using the Mann-Whitney U-test for non-normally distributed VAS scores and the paired t-test for normally distributed CRP values.

Results: Of 56 patients, 23(50%) were female. The median ages for symptom onset, diagnosis, and last visit were 14.8(9.8-18.5), 3(1.5-6), and 4(2.5-7) years, respectively. The median number of attacks was 3.5(2-10). More than half(53.5%) had a history of irregular colchicine use. Common symptoms during the attack included abdominal pain(85.7%), chest pain(57.1%), fever(53.5%), vomiting(32.1%), and diarrhoea(21.4%)(Table 1). Lymphopenia was present in 26(46%) patients and leucocytosis in 12(21.4%) patients. The median duration of the attack was 24(6-48) hours after treatment initiation. The CRP values at 0 and 24 hours were (118.7±78) and (100.5±52) respectively, with no statistically significant difference(p=0.21). The patient group receiving anakinra had statistically lower VAS values at 6-12 and 24 hours(Table 2).

Conclusion: Since anakinra treatment provides significant improvement in symptom scoring in the first 24 hours and a decrease in the requirement for hospitalisation in FMF attack patients, we recommend single-dose anakinra treatment for attack patients with high VAS scores.

Keywords: anakinra, attack

Table 1. Clinical and demographic characteristics of FMF patients

	Total N=56 (%) Medium (Q1-Q3)	Anakinra N=22 (%) Medium (Q1-Q3)	NSAID/ iv hydration N=25 (%) Medium (Q1-Q3)	Combined N= 9 (%) Medium (Q1-Q3)
Female	28 (50%)	12 (54,5%)	11 (44%)	5 (55%)
Age (year)	14.8 (9.8- 18.5)	14.8 (9.1-17.7)	14,1 (8.7-18.9)	17.4 (11- 19)
Symptom onset age (year)	3 (1.5-6)	3 (1.5-5.25)	4 (2.75- 8)	4 (1.5-10)
Diagnosed age (year)	4 (2.5-7)	3 (2.37-6.5)	4 (2.75- 7)	6 (4-11.5)
Fever	30 (53.5%)	12 (54.5%)	10 (40%)	8 (88.8%)
Abdominal pain	48 (85.7%)	18 (81.8%)	23 (92%)	7 (77.7%)
Pleurit	32 (57.1%)	16 (72.7%)	9 (36%)	7 (77.7%)
Pericarditis	1 (1.7%)	1 (4.5%)	0 (0%)	0 (0%)
Arthritis	2 (3.5%)	0 (0%)	2 (8%)	0 (0%)
Arthralgia	11 (19.6%)	3 (13.6%)	5 (20%)	3 (33.3%)
Vomitting	18 (32.1%)	8 (36.3%)	7 (28%)	3 (33.3%)
Diarrhea	12 (21.4%)	6 (27.2%)	4 (16%)	2 (22.2%)
Attack ceased time (hours)	24 (6-48)	18 (4-54)	24 (18-48)	24 (9-48)

Table 2. The change in Visual Analogue Scale (VAS) scores according to treatment choice

	Anakinra N=22 Median (Q1-Q3)	NSAID/ iv hydration N=25 Median (Q1-Q3)	P- value
VAS 6	3 (0-5)	6 (3-8)	0.032
VAS 12	1.5 (0-4)	4 (2-6)	0.028
VAS24	0 (0-2)	2 (0.5-5)	0.016
DeltaVAS 2	1 (0.75-3)	0 (0-1.5)	0.014
Delta VAS 6	4.5 (2-6.25)	2 (0-5)	0.03

OP-10

EXPLORING S100A8/A9, NEOPTERIN, AND MMP3 IN FAMILIAL MEDITERRANEAN FEVER: INSIGHTS INTO PATHOGENESIS AND DIAGNOSTIC SIGNIFICANCE

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Background and Objectives: Familial mediterranean fever (FMF) is characterized by inflammatory attacks due to overactivation of pyrin inflammasome. This study aimed to investigate the role of S100A8/A9, neopterin, and MMP3 in the pathogenesis of FMF and their reliability at monitoring subclinical inflammation and disease activity, and at differentiating FMF attacks from appendicitis, the most common misdiagnosis among FMF patients.

Methods: Blood samples (n=75), comprising from FMF patients during an attack (n=20), the same FMF patients during the attack-free period (n=14), patients with appendicitis (n=24), and healthy volunteers (n=17) were obtained. Duplicate determinations of S100A8/A9, neopterin, and MMP-3 levels were conducted using the enzyme-linked immunosorbent assay (ELISA).

Results: FMF patients with and without attack and patients with appendicitis had significantly elevated S100A8/A9 levels compared to healthy volunteers (p-values: <0.001, 0.036, 0.002, respectively). Patients with appendicitis and FMF patients with and without attack had significantly increased serum neopterin levels compared to healthy volunteers (p-value: <0.001). MMP3 levels were significantly higher among patients with appendicitis and FMF patients during

attack compared to healthy controls (p-values: <0.001, 0.001). Serum levels of S100A8/A9, neopterin, and MMP3 were increased significantly during attacks compared to attack-free periods among FMF patients (p-values: 0.03, 0.047, 0.007).

Conclusions: S100A8/A9 emerges as a potential marker for disease activity and target for novel treatment options. Neopterin and S100A8/A9 might help physicians to monitor subclinical inflammation during the attack-free periods of FMF patients. MMP3 might aid in diagnosing FMF attacks when distinguishing between attack and attack-free periods is challenging.

Keywords: S100A8/A9 Neopterin

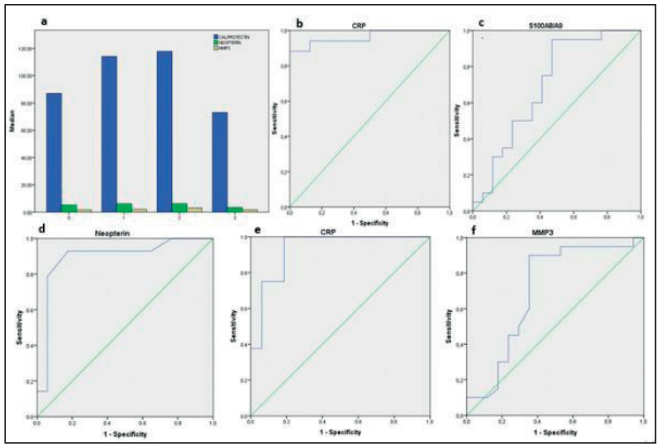

Figure. Clustered bars and ROC curves for studied parameters. a: Clustered bars showing studied parameters across study groups, blue indicates S100A8/A9, green neopterin, orange MMP3 b, c, and f indicate ROC curves of CRP, S100A8/A9, and MMP3 at differentiating FMF attack from attack-free periods, respectively. d and e indicate ROC curves of neopterin and CRP at differentiating attack-free FMF patients from healthy controls

Table. Demographic features and laboratory parameters across study groups.

	FMF (during attack) (Median + IQR) (n=20)	FMF (attack-free) (Median + IQR) (n=14)	Appendicitis (Median + IQR) (n=24)	Healthy control (Median + IQR)
Age (years, mean ± SD)	36.6 ± 13.51	39.54 ± 14.0	41.8 ± 23.05	35.71 ± 7.8
Gender (females, %, n)	40 (8)	50 (7)	41.7 (10)	64.7 (11)
S100A8/A9 (ng/mL)	114.1 (91.88-160.83)	87.1 (74.9-115.6)	117.75 (75.25-280)	73 (64.15-87.85)
Neopterin (nmol/L)	6.15 (5.18-8.48)	5.2 (4.9-5.93)	6.2 (4.23-14.25)	3.5 (2.9-4.1)
MMP3 (ng/mL)	2.21 (2.03-3.4)	1.77 (1.68-2.4)	3.15(2.05-5.88)	1.8 (1.45-2.05)
CRP (mg/L)	43.73 (13.42-64.43)	2.71 (1.66-3.8)	22 (6.5-89)	0.95 (0.55-1.00)
WBC	8.8 (6.7-11)	7.0 (6.4-8.9)	11.88 (7.59-14.42)	6.9 (5.6-8.4)
NEUT	6 (4.6-8.75)	4.1 (3.5-4.7)	9.14 (5.38-11.55)	5.6 (3.9-6.2)
LYMPH	1.6 (1.1-2.05)	2.2 (1.9-2.9)	1.69 (0.95-2.47)	1.6 (0.65-2.05)

OP-11

EFFECT OF FAMILIAL MEDITERRENEAN FEVER ON MALE FERTILITY AND PATERNAL EFFECT OF FAMILIAL MEDITERRENEAN FEVER ON PREGNANCY OUTCOMES AND COMPLICATIONS

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Background: Familial Mediterranean Fever (FMF) is the most common hereditary periodic fever worldwide. Male infertility is a rare complication of FMF; however, some studies have suggested that FMF does not decrease male fertility. This is the first study to explore the paternal effects of FMF on pregnancy outcomes and complications.

Objectives: To investigate the effect of FMF on male fertility and the paternal effect of FMF on pregnancy outcomes and complications. To determine the effects of MEFV mutation status and drugs used in the treatment of FMF on these outcomes.

Methods: In this study, 282 adult male patients with FMF were interviewed. Relevant data were collected from archives and interviews.

Results: A total of 180 patients attempted pregnancy and only three (1.7%) could not conceive. The remaining 177 patients managed to conceive 451 times. These 451 pregnancies resulted in 384 (85.1%) live births, 52 (11.5%) miscarriages, seven (1.6%) abortions, four (0.9%) ectopic pregnancies, three (0.7%) stillbirths and one (0.2%) anembryonic pregnancy. Pregnancy complications and their relationship with the MEFV mutation status and treatment used during conception are shown in Table 1. The presence of the M694V allele was not statistically significant for any parameter. There were no statistically significant differences in miscarriage, stillbirth, and preterm birth rates between our patient population and the Turkish population.

Conclusions: The presence of FMF did not lead to a decrease in male fertility. FMF did not have a paternal effect on pregnancy outcomes or complications. Using colchicine during conception led to a significant increase in non-elective cesarean section rates, and not using any drugs during conception led to a significant increase in miscarriage rates. Uncontrolled inflammation may be the underlying mechanism of this increase in miscarriage rates. In patients who stop using colchicine during pregnancy attempts, anti-IL-1 agents can be used to prevent miscarriages.

Keywords: pregnancy, infertility

Table. Pregnancy complications and their relationship with MEFV mutation status and treatment used during conception

	Colchicine only	Colchicine + canakinumab	Sulfasalazine only	No drug	p	M694V allele present	M694V allele not present	p
Preterm birth, n (%)	11 (9.7)	0 (0)	0 (0)	5 (7.7)	1	3 (5.5)	9 (14.3)	0.136
Gestational hypertensive disorders, n (%)	0 (0)	0 (0)	0 (0)	3 (4.6)	0.07	0 (0)	1 (1.6)	1
Gestational diabetes, n (%)	4 (3.5)	0 (0)	0 (0)	5 (7.7)	0.346	3 (5.5)	3 (4.8)	1
Non-elective c-section, n (%)	60 (53.1)	1 (100)	0 (0)	21 (32.3)	0.031	30 (54.5)	32 (50.8)	0.71
Fetal growth restriction, n (%)	3 (2.7)	0 (0)	0 (0)	2 (3.0)	1	1 (1.8)	1 (1.6)	1
Perinatal asphyxia, n (%)	1 (0.9)	0 (0)	0 (0)	0 (0)	1	0 (0)	0 (0)	1
Postterm birth, n (%)	1 (0.9)	0 (0)	0 (0)	0 (0)	1	1 (1.8)	0 (0)	0.46
Fetal anomalies, n (%)	3 (2.7)	0 (0)	0 (0)	0 (0)	0.567	1 (1.8)	1 (1.6)	1
Miscarriage, n (%)	27 (23.9)	0 (0)	1 (100)	24 (36.9)	<.001	15 (27.3)	15 (23.8)	0.67
Ectopic pregnancy, n (%)	2 (1.8)	0 (0)	0 (0)	2 (3.0)	0.555	1 (1.8)	0 (0)	0.46
Anembryonic pregnancy, n (%)	1 (0.9)	0 (0)	0 (0)	0 (0)	1	0 (0)	1 (1.6)	1
Stillbirth, n (%)	0 (0)	0 (0)	0 (0)	3 (4.6)	0.07	0 (0)	0 (0)	1

OP-12

MACHINE LEARNING ALGORITHMS TO PREDICT COLCHICINE RESISTANCE IN FAMILIAL MEDITERRANEAN FEVER

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Objective: This study aimed to develop machine learning algorithms for predicting colchicine resistance in patients with Familial Mediterranean Fever (FMF).

Materials-Methods: We conducted an analysis of medical records from 1300 FMF patients, extracting various features including chest pain, presence of compound heterozygous mutations in MEFV gene, presence of M694V homozygous mutation, attacks per month before treatment, age of symptom onset, erysipelas-like rash associated with attacks, presence of arthritis with erythema, presence of recurrent arthritis, and colchicine resistance status.

Results: The cohort included both pediatric and adult-onset FMF patients, with 113(8,6%) classified as colchicine-resistant and 1187(91,4%) as colchicine-responsive. Logistic regression exhibited the best performance, utilizing features such as the presence of compound heterozygous mutations in the MEFV gene, chest pain during attacks, number of attacks per month before treatment, M694V homozygous mutation, and presence of recurrent arthritis, achieving an AUC of 0.76. (Figure 1) Deep neural network models also performed well, with the features of the number of attacks per month before treatment, the presence of M694V homozygous mutation, and the presence of recurrent arthritis, yielding an AUC of 0.75. (Figure 2) (Table 1)

Conclusion: Machine learning algorithms, offering a probability output for colchicine resistance risk, can function as sensitive and specific tests with adaptable thresholds. Enhancing AUC may require training deep learning models on larger datasets or incorporating additional features associated with colchicine resistance risk.

Keywords: Familial Mediterranean Fever, Colchicine resistance

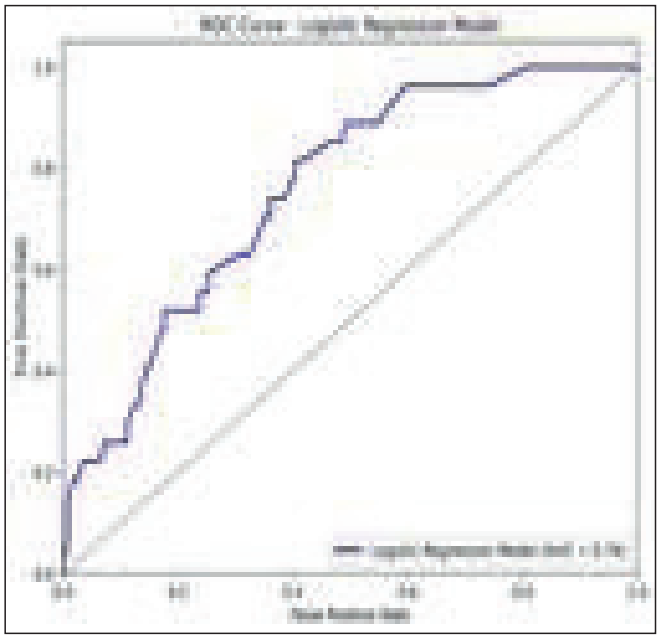

Figure 1. ROC Curve of Logistic Regression Model (AUC = 0.76)

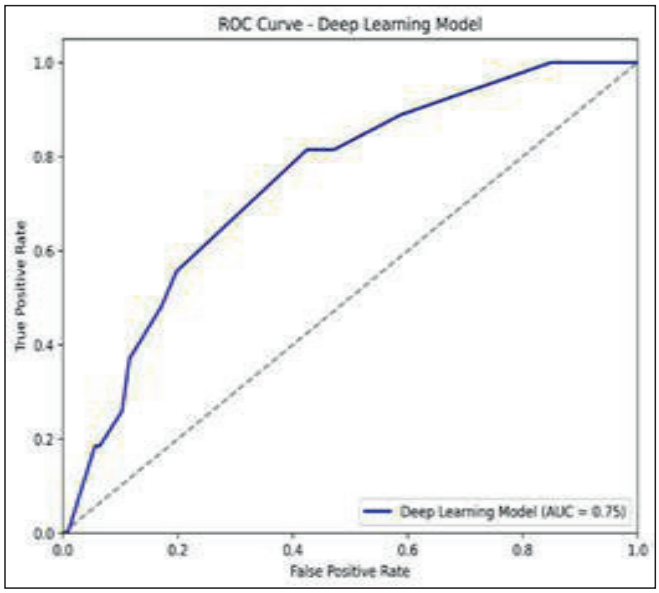

Figure 2. ROC Curve of Deep Learning Model (AUC = 0.75)

Table 1. Summary of the Results of Machine Learning Models

Model	Features	AUC
Logistic Regression	presence of compound heterozygous mutations in the MEFV gene, chest pain during attacks, number of attacks per month before treatment, M694V homozygous mutation, presence of recurrent arthritis	0.76
Deep Neural Network	number of attacks per month before treatment, presence of M694V homozygous mutation, presence of recurrent arthritis	0.75

OP-13

FAMILIAL MEDITERRANEAN FEVER FROM CHILDHOOD TO ADULTHOOD

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Objectives: With the development of diagnostic and treatment methods, more children with familial Mediterranean fever (FMF) are transitioning to adulthood. This study aims to evaluate the characteristics of patients followed in the pediatric rheumatology department from childhood to adulthood.

Materials and methods: The medical records of patients who were planned to be transferred to the adult rheumatology department and completed pediatric rheumatology follow-up at Hacettepe University between January 2015 and May 2023 were reviewed retrospectively. Patient demographics, disease characteristics, MEFV mutations, treatments, comorbidities, and the last pediatric visit characteristics were recorded.

Results: In total, 232 patients with FMF were included in the study. 115 (49.6%) patients were female. The median age at onset of symptoms was 4.0 years, the median duration from the onset of symptoms to diagnosis was 2.6 years and the age at diagnosis was 8.4 years, respectively. The median follow-up duration in the pediatric rheumatology department was 8.9 years. Comorbidities were present in 74 (32%) of the patients. The most common comorbidity was juvenile idiopathic arthritis (n=20; 8.6%) followed by inflammatory bowel disease (n=7; 3.0%). MEFV gene mutation was homozygous in 178 (76.7%), heterozygous in 49 (21.1%), and negative in 5 (2.2%) patients. The median age at the first pediatric rheumatology visit was 9.8 years and 18.6 years at the last visit. At the last visit, 24

(10.3%) patients had active disease. Six patients were off medication, while others were on colchicine treatment. Nineteen patients (8.2%) resistant to colchicine were on anti-interleukin 1 treatment. Also, 19 patients (8.2%) were using additional treatments for accompanying comorbidities.

Conclusions: Despite treatment, some patients still have active disease and comorbidities are common. Evaluating the patient with a holistic approach, analyzing the findings during the transition period, and continuing follow-up without interruption may contribute to the improvement of the prognosis in adulthood.

Keywords: Familial Mediterranean fever

Poster Presentations

PP-01

ASSESSING THE EFFICACY OF BUZZY® IN PAIN REDUCTION DURING CANAKINUMAB ADMINISTRATION FOR FAMILIAL MEDITERRANEAN FEVER

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Objective: Between 5-15% of patients with Familial Mediterranean Fever (FMF) exhibit resistance to colchicine treatment. In instances of colchicine resistance, alternative therapies administered parenterally are employed. The current pain experienced by patients can be alleviated through treatment interventions. Consequently, a comprehensive approach to pain management is crucial in the care of FMF patients. Buzzy® is a device designed to reduce pain during needle procedures. This innovative device combines an ice pack with a vibration motor, allowing clinicians to apply cold therapy, tactile stimulation, and distraction techniques simultaneously. By leveraging the effects of cold and vibration on the skin, Buzzy® effectively reduces the perception of pain. This study aimed to measure the effectiveness of Buzzy® in reducing pain during the subcutaneous administration of canakinumab in FMF.

Method: The study enrolled patients with colchicine resistance, including those undergoing canakinumab treatment. Pain scores were assessed both before and after the administration of Buzzy® by using the Visual Analog Score(VAS), the Faces Pain Scale-Revised(FPS-R) Scale, and the Children's Fear Scale(CFS)(Figure 1)

Results: A total of 15 patients enrolled in the study. Of them, 9(60%) were girls and 6(40%) were boys. The median age of patients was 9 (5-18) years. Before Buzzy®, the median VAS, FPS-R, and CFS scores were 4(0-8), 4(0-8), and 1 (0-4), respectively. After Buzzy®, the median VAS, FPS-R, and CFS scores were 2 (0-6), 2 (0-6), and 0 (0-3), respectively. The VAS and FPS-R scores were significantly decreased (p=0.04 and 0.008) while CFR scores were decreased, but did not reach the statistically significant (p=0.526) (Figure 2)

Discussion: According to the gate control theory of pain, these methods temporarily block pain signals from reaching the central nervous system by closing the "gates". In patients necessitating continual injections, applications akin to Buzzy can mitigate both the pain and apprehension experienced by these individuals.

Keywords: FMF, pain

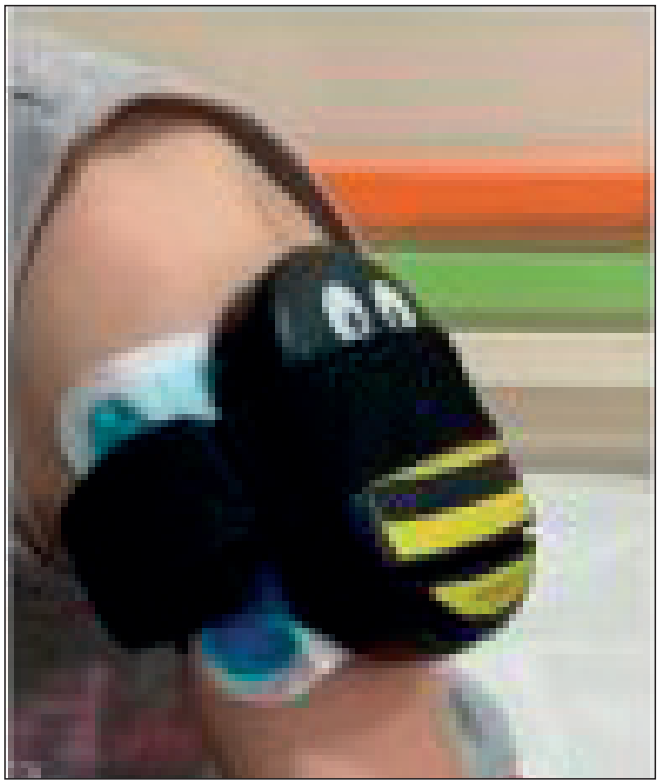

Figure 1

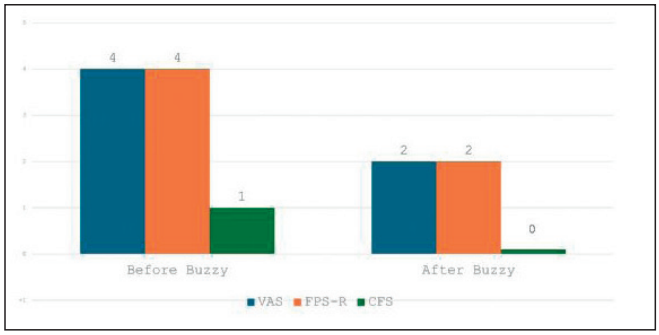

Figure 2

PP-02

TONSIL PROTEOMICS PROFILE OF PATIENTS WITH PERIODIC FEVER, APHTHOUS STOMATITIS, PHARYNGITIS, AND ADENITIS SYNDROME (PFAPA)

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Introduction: Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome is a recurrent fever syndrome of unknown etiology characterized by regular episodes of fever, pharyngitis, oral aphthosis, and cervical lymphadenopathy. However, PFAPA syndrome is considered as the most common periodic fever syndrome, the exact etiopathogenesis of PFAPA syndrome remains unknown. Biological fluids or tissues may provide disease-specific biomarkers that may help clinicians to find new pathogenic pathways or potential drug candidates.

Material-Methods: Tonsil tissues of seven patients with PFAPA were collected during the tonsillectomy. Seven patients with obstructive sleep apnea enrolled as a control group. All patients were inactive and treatment-free. The nHPLC LC-MS/MS system was used

for protein identification and label-free quantification. Bioinformatics analysis was carried out using the UniProt accession numbers of the identified proteins.

Results: The label-free proteome analysis revealed that 23 proteins were upregulated while 57 were downregulated when the two-fold change, a standard fold of change criteria were applied between the two groups (in log2 scale). STRING analysis highlighted alterations in the mitochondrial electron transport chain (ETC) suggesting a regulatory effect on the ATP biosynthesis process. Western Blot analysis was used for verification of the LC-MS/MS data. An anti-OXPHOS antibody cocktail clearly showed that complex III and IV were substantially, and complex II and V were moderately downregulated in the PFAPA group. Furthermore; Western Blot analysis of pyruvate dehydrogenase complex (PDHC) showed downregulation in all PDHC subunits (E1α, E1β, E2, and E3bp).

Conclusion: Herein bioinformatics analysis underlined the importance of mitochondrial ETC and regulation of the ATP biosynthetic process. The discovery of immunometabolism has the potential to serve as a central regulator of inflammation and opens up new possibilities for addressing inflammation-related disorders by modulating the metabolism of vascular and immune cells.

Keywords: PFAPA, proteomics

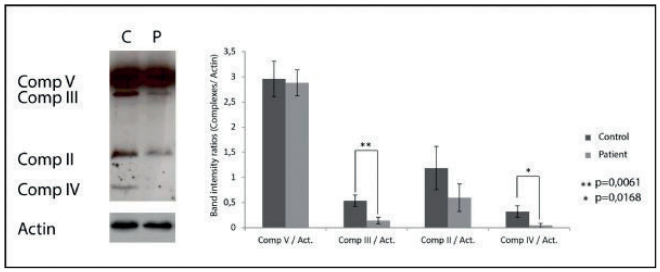

Figure 1.

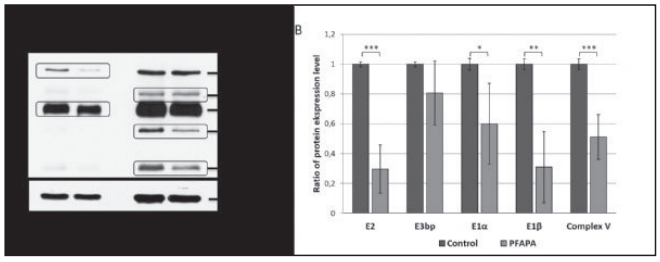

Figure 2.

PP-03

IRON DEFICIENCY IN FAMILIAL MEDITERRANEAN FEVER: A STUDY ON 211 ADULT PATIENTS FROM THE JIR COHORT

Ilenia Di Cola[1], Alessandra Bartoli[2], Léa Savey[3], Fatima Bensalek[2], Marion Delplanque[3], Rim Bourguiba[2], Isabelle Kone Paut[4], Linda Rossi Semerano[4], Isabelle Melki[5], Guilaine Boursier[6], Véronique Hentgen[7], Sophie Georgin Lavialle[3]

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Objectives: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease worldwide. Fatigue is known to trigger FMF attacks. So far, no association has been reported between iron deficiency and fatigue in FMF patients. Our aim was to evaluate the prevalence of iron deficiency in FMF patients and its association with clinical features, laboratory parameters, disease activity and outcomes over time.

Methods: A retrospective evaluation of prospectively followed homozygous FMF patients at the French National Reference Centre was performed.

Results: Of 211 patients, 67 (31.8%) had a serum ferritin level < 27 ng/mL and were defined as iron deficient. Of these, 61 (91%) were female with a mean age of 36.81 (± 17.03) years. FMF patients with iron deficiency had lower Hb ($p < 0.001$) and BMI ($p=0.023$) and were significantly younger than those without iron deficiency ($p=0.004$), but they did not have more elevated inflammatory biomarkers. Female gender ($p=0.0015$) was associated with lower ferritin levels.

Conclusion: Iron deficiency, which mainly affects young women regardless of their level of inflammation, may be secondary to excessive gynaecological losses. Iron-deficient FMF patients may be more tired, which may lead to an increase in FMF attacks. Thus, it may be important to correct iron deficiency because this condition alone can cause asthenia, even in the absence of anaemia. Interestingly, ferritin doesn't seem to have pro-inflammatory properties in FMF. In conclusion, this work highlights the importance of measuring ferritin levels in FMF patients to detect iron deficiency in the absence of anaemia.

Keywords: FMF, iron deficiency

PP-04

THE NEEDED DAILY DOSE OF COLCHICINE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER MAY BE HIGHER IN WOMEN

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Objectives: Colchicine is the gold standard treatment to prevent Familial Mediterranean Fever (FMF) disease attacks. We aimed at investigating the daily colchicine dose in FMF patients and at describing the clinical characteristics of patients taking the maximum daily dosage (2.5 mg).

Methods: From 2016 to June 2023, a retrospective evaluation of prospectively followed homozygous FMF patients at the French National Reference Centre was performed.

Results: Out of 272 patients, 30 (11.03%) were treated with a daily colchicine dose of 2.5 mg. Of these, 23 (76.67%) were women with a mean weight of 61.74 (± 12.27) kg, and a mean BMI of 22.83 (± 4.12). In this context, 20 patients (76.92%) weighed<50 kg. In multivariate analysis, female gender was associated with higher values of daily colchicine dose (p=0.0208). Amyloidosis (p<0.0001) and age (p=0.0009) were associated with lower values of daily colchicine dose. Weight (p= 0.4073) was not associated with colchicine dose.

Conclusion: No toxicity has been noted in patients treated with 2.5 mg of colchicine, including patients weighting<50kg. Of note, most of these patients were women. This gender difference may be since women require a higher dose of colchicine because of a more demanding clinical picture. It has been described an unconventional activation of pyrin, caused by endogenous steroid catabolites. We may speculate that in our cohort the clinical picture of female patients requiring an increased daily dose of colchicine may be related to the hormonal background, with a possible exaggeration of pyrin activation. This is the first study to examine the question of colchicine dosage and weight in FMF adult patients and to highlight a possible link with female gender. We advise clinicians to explain that colchicine treatment may be used daily up to 2.5 mg without toxicity if renal function is normal and no drug interactions are present.

Keywords: colchicine, gender diversity

PP-05

ASSESSING THE READINESS OF PEDIATRIC PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER TO TRANSITION TO ADULT-ORIENTED TREATMENT IN A REGION ENDEMIC TO FMF

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Objective: Transition is the planned process of pediatric patients moving from child-centered to adult-oriented treatment. Transitional care is crucial for patients with chronic diseases. Since the majority of patients referred to the pediatric rheumatology clinic are diagnosed with FMF in our region, it is essential to transition these patients to adult care for the continuity of their treatment. The objective of this study was to assess the readiness of patients with FMF for the transition process.

Materials and methods: This study is a cross-sectional study. All patients were surveyed regarding their awareness of and willingness to undergo transitional care. The Transition Readiness Assessment Questionnaire (TRAQ) was administered to all participants. Colchicine-responsive and colchicine-resistant cases were compared.

Results: A total of 110 patients were enrolled. Of them, 67 (60.9%) were girls and 43 (39.1%) were boys. Seventy-four (67.3%) patients were colchicine-responsive while 36 (32.7%) were colchicine-resistant. The median age of the patients was 17.7 years (15-22). The median total TRAQ score was 3.9 (1.95-5). When we compared TRAQ scores between colchicine-responsive and colchicine-resistant cases; the median TRAQ score was 3.9 (2.2-5) in colchicine-responsive and 3.1 (1.95-4.8) in colchicine-resistant patients (p=0.003).

Conclusions: Assessing the readiness of patients with FMF for transition care will enhance the awareness of patients and help determine the optimal time for transition. Having a more severe illness can influence the preparatory processes of the disease.

Keywords: Familial Mediterranean Fever, transition

PP-06

THE EVALUATION OF HEALTH STATUS OF FAMILIAL MEDITERRANEAN FEVER PATIENTS HAVING HOMOZYGOUS M694V MUTATION

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Objective: In our study, we aimed to evaluate the health status of our patients diagnosed with Familial Mediterranean Fever (FMF) with M694V homozygous mutation based on age, gender, clinical symptoms, treatments used, comorbidities, and development of amyloidosis.

Materials-Methods: The data of the patients were analyzed retrospectively. We found 183 FMF patients with M694V homozygous mutation who were 18 years of age or older. However, we could access the data of 178 patients completely. Missing data of patiens were accessed via patient information system and telephone.

Results: Of the 178 patients included in the study, 97 were male and 81 were female. The most common clinical symptom was abdominal pain with 88.2%. This was followed by arthralgia with 74.7% and arthritis with 42.1%. The frequency of chest pain was 39.2%. Proteinuria was seen in 23.0% of patients, while the percentage of amyloidosis was 7.9%. In 12 of 178 patients, sacroiliitis

were determined. The number of patients receiving biological therapy was 26.4%. 22.5% of them was taking interleukyn-1 antagonists (anakinra, canakinumab) while 3.9% of them was receiving TNF-alpha inhibitors (golimumab, etanercept, certazilumab). 32 of our 178 patients had a history of laparoscopic surgery. 8 of our patients were deceased. 5 of them had developed amyloid. 4 of them were renal transplants.

Conclusion: The most frequently detected mutation in patients with familial Mediterranean fever is M694V. FMF patients having homozygous M694V mutation are reported to be more severe. In this study, we aimed to describe the important clinical features of our M694V homozygous patients in our single center cohort. Two of our prominent results in M694V homozygous FMF patients are as follows; The frequency of proteinuria and the need for biological treatment is significantly higher.

Keywords: Familial Mediterranean fever, M694V

PP-07

UNUSUAL CAUSE OF HEPATOMEGALY IN A ROMANIAN WOMAN

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A 41-year-old Romanian woman was referred for investigation of hepatosplenomegaly. Her history included 4 early miscarriages. Clinical examination revealed hepatomegaly and splenomegaly. Blood count showed microcytic anemia, lymphopenia at 600 E/mm3 and platelets at 163,000. Renal and liver function tests and C-reactive protein were normal in the absence of crisis. A thoracic-abdominopelvic CT scan showed non-dysmorphic hepatomegaly at 21 cm and splenomegaly at 17 cm. She reported abdominal pain during work changes and under stress, without diarrhea, nausea or vomiting. Etiological investigations for gonococcus, mycoplasma, chlamydia, brucellosis and tuberculosis were negative. Serologies for hepatitis B and C, HIV, parvoB19, HTLV1 and HHV8, leishmania, bilharzia and parasites were negative. Nuclear antibodies were 1/100 positive with no specificity, anti-ECT and liver kit were negative. Blood and urine tests were normal. Liver biopsy showed no inflammatory infiltrate, fibrosis or granuloma. Perls staining showed no hemosidic deposits, and congo red staining detected no amyloidosis. On further questioning, the patient reported febrile abdominal pain lasting 2 days since the age of 9, occurring 4 times a year, with arthritis and erythematous lesions of the ankles and legs (pseudoerysipelas). C-reactive proteine was 28 mg/l during the flare-up period. An autoinflammatory disease responsible for recurrent inflammatory abdominal pain was suggested (FMF). Genetic analysis of exon 10 of MEFV by Sanger sequencing showed a homozygous M694V mutation. Colchicine treatment was introduced at a dose of 1 mg/day, with good clinical progression and normalization of CRP. Hepatomegaly and splenomegaly persisted on follow-up CT scan. Our case report illustrates a diagnosis of FMF in a patient of Romanian origin with no family history of FMF, although Romania once belonged to the Ottoman Empire. Hepatic involvement in FMF has been rarely reported.Apart from AA amyloidosis, rare cases of hepatic cytolysis and cryptogenic cirrhosis associated with FMF have been described.

Keywords: hepatomegaly, FMF

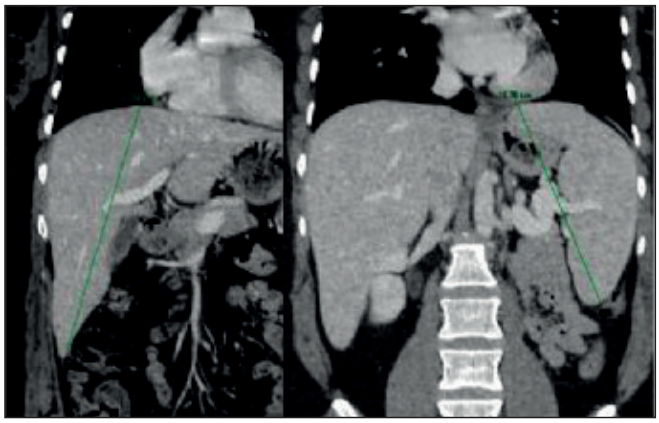

Figure 1. Homogenous hepatomegaly and splenomagaly

PP-08

AUTOINFLAMMATORY DISEASES: A DIAGNOSTIC CHALLENGE IN THE MAGHREB COUNTRIES: EXPERIENCE FROM TUNISIA

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Familial Mediterranean fever (FMF) is the most common Autoinflammatory diseases AID. Access to genetic analysis remains limited and costly in the Maghreb countries and in Tunisia, making AID under-diagnosed in our country. Genetic analysis of exon 2 and 10 of the MEFV gene in Sanger is available in most of Tunisia.

The aim of our work was to report on Tunisia's experience in diagnosing AID other than FMF.

Methods: Descriptive multicenter study of patient with suspected AID over the period from July 2021 to September 2023. All patients had MEFV gene sequencing.

Results: We enrolled 18 patients. Median age at study inclusion was 31.5 +/- 13.67 years. Median age at onset of symptoms was 5 years +/- 13.5. All patients had recurrent fever. Digestive symptoms were noted in 16 patients:abdominal pain (n=16) Twelve patients had joint involvement, with arthralgia (n=12) and arthritis (n=4). Skin involvement was reported in 6 patients: urticaria related to neutrophilic dermatosis (n=2) and oral aphthosis (n=6). The median duration of flare was 4 days +/- 6.4. Median CRP during a flare was 59 mg/l +/- 57. No cases of AA amyloidosis were reported. Genetically, all patients underwent MEFV sequencing. The presence of at least one mutation in the MEFV gene was reported in 7 patients. The other patients were heterozygous for FMF or carried the E148Q variant (n=4). Autoinflammatory disease remained unclassified in 11 (61%) patients.

Conclusion: In 2024, the diagnosis of AID has largely evolved thanks to precision medicine

In our series, 61% of patients had IAD that remained unclassified, with significant impact on quality of life due to lack of diagnosis and limited access to biotherapies.

Keywords: Delay, Auto-inflammatory disease

PP-09

NAVIGATING COMPLEXITY: A NUANCED PRESENTATION OF PORPHYRIA, FMF, BEHÇET'S, AND CELIAC DISEASE

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Introduction: Autoimmune diseases are conditions in which the immune system mistakenly targets normal tissue, causing inflammation, cellular damage, and dysfunction in various organs and systems, resulting in a wide array of signs and symptoms. The prevalence of these diseases varies geographically, suggesting environmental and genetic risk factors. For instance, Familial Mediterranean fever (FMF), and Behçet's disease are among those most prevalent in Turkey. Although the presence of one autoimmune disease increases the risk of having another, the coexistence of porphyria, familial Mediterranean fever (FMF), Behçet's disease, and celiac disease in a single patient is profoundly rare, as it has not been previously reported.

Case presentation: A 44-year-old male from the Black Sea region of Turkey, presented with abdominal pain, nausea, and vomiting. Laboratory tests revealed elevated inflammatory markers and positive autoimmune profiles. When combined with the patient's ethnicity, these results raised suspicions of autoimmune disease. As a result, genetic testing was conducted and consequently confirmed the presence of specific mutations associated with each disease, such as E148Q mutation in the MEFV gene, HLA-B51, and HLA-DQ2 alleles.

Conclusion: The significance of this case lies in the rare coexistence of porphyria, familial Mediterranean fever (FMF), Behçet's disease, and celiac disease within a single patient, highlighting the complex nature of autoimmune and inflammatory disorders. The overlapping symptomology and heterogeneous presentations of these four diseases pose formidable challenges in their recognition, diagnosis, and subsequent management. By reporting this case, we aim to contribute to the growing body of literature on complex autoimmune presentations, and emphasize the need for heightened clinical awareness and interdisciplinary collaboration in managing patients with such rare and challenging medical presentations.

Keywords: Combined autoimmune disorders, Abdominal pain

PP-10

CAN THE M694V HOMOZYGOUS GENOTYPE OF FAMILIAL MEDITERRANEAN FEVER BE PREDICTED BASED ON CLINICAL FINDINGS?

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Objective: The aim of this study is to determine the clinical phenotype associated with the possibility of having the M694V homozygous genotype in patients diagnosed with FMF clinically.

Materials and methods: This study was a retrospective analysis of pediatric FMF patients followed at our pediatric rheumatology clinic between 2016 and 2023. A total of 472 pediatric patients diagnosed with FMF and having a homozygous genotype in exon 10 were included in the study. Demographic and clinical data were recorded from the patients' medical charts. The patients were divided into two groups: those who had the M694V homozygous mutation and others.

Results: A total of 472 children (251 girls and 221 boys) were included in the study. The median (IQR; 25 - 75) of age disease onset and age at diagnose was 3.5 (1.8-6) years and 5 (3-8) years, respectively. Parental consanguinity was present in 36.2% of patients and 58% had a family history of FMF. The median of following time was 32 (18-43) months. The mean (±SD) of attack duration was 70.2 (±39.2) hours. The main clinical findings of 472 patients in our study were abdominal pain in 89%, fever in 87.5%, arthralgia in 57.4%, arthritis in 28.8%, myalgia in 47.5%, exertional leg pain in 25.6%, chest pain in 25.6% and erysipelas-like erythema in 22.2%.

The comparison of groups was presented in Table 1 of the study. Multivariable logistic regression model for prediction of M694V genotype was presented in Table 2.

Conclusion: The predictability of the M694V homozygous genotype at the time of presentation for FMF patient was based on clinical findings; which are the patient's young age at the onset of the first attack, and symptoms of arthralgia, arthritis, chest pain, and erysipelas-like erythema.

Multicentre, larger patient cohorts are needed to confirm this.

Keywords: familial Mediterranean fever, genotype-phenotype correlation

Table 1. Comparison of the M694V homozygous group and the other group with a homozygous genotype at exon 10

	Group 1 (n:402)	Group 2 (n:70)	p
Genotypes	M694V/M694V n:402	M680I/M680I n:38 V726A/V726A n:23 R761H/R761H n:8 I641F/I641F n:1	
Age at disease onset, median (IQR; 25 - 75)	3 (2-6) years	4 (2-9) years	0.044
Age at diagnose, median (IQR; 25 - 75)	5 (3-7) years	7 (3-10) years	0.031
Attack duration, mean (±SD)	71.7 (±39.5) hours	62.4 (±35.8) hours	0.046
Parental consanguinity*, n (%)	143 (35.6)	24 (34.3)	0.835
Family history of FMF**, n (%)	236 (58.7)	32 (45.7)	0.043
Fever, n (%)	356 (88.6)	57 (81.4)	0.096
Abdominal pain, n (%)	358 (89)	62 (88.5)	0.905
Arthralgia, n (%)	244 (60.7)	27 (38.6)	0.002
Arthritis, n (%)	127 (31.5)	9 (12.8)	0.001
Myalgia, n (%)	199 (49.5)	25 (35.7)	0.033
Exertional leg pain, n (%)	113 (28.1)	8 (11.4)	0.003
Chest pain, n (%)	111 (27.6)	10 (14.2)	0.018
Erysipelas-like erythema, n (%)	104 (25)	1 (1.4)	0.001
Diarrhea, n (%)	71 (17.7)	6 (8.6)	0.057
Vomiting, n (%)	32 (8)	5 (7.1)	0.814
Constipation, n (%)	15 (3.7)	2 (2.9)	0.857
Protracted febrile myalgia syndrome, n (%)	7 (1.7)	0 (0)	0.266
Colchicine resistance, n (%)	63 (15.7)	0 (0)	0.001
FMF: familial Mediterranean fever *: 11 patient missing value **:10 patient missing value			

Table 2: Multivariable logistic regression model for prediction of M694V genotype

	p value	Odds ratio, 95% confidence interval (lower-upper)
Age at disease onset (year)	0.002	0.892 (0.832-0.958)
Family history of FMF	0.095	1.578 (0.923-2.698)
Parental consanguinity	0.671	0.883 (0.498-1.564)
Attack duration (hour)	0.297	1.004 (0.996-1.012)
Abdominal pain	0.721	0.845 (0.335-2.126)
Fever	0.350	1.451 (0.664-3.170)
Arthritis	0.028	2.565 (1.109-5.934)
Myalgia	0.667	1.142 (0.623-2.093)
Exertional leg pain	0.158	1.923 (0.775-4.771)
Chest pain	0.023	2.351 (1.123-4.922)
FMF: familial Mediterranean fever		

PP-11

ANTI-TNF USAGE IN FAMILIAL MEDITERRANEAN FEVER

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Tumor necrosis factors(TNF) inhibitors have been used in colchicine-resistant familial Mediterranean fever(FMF) patients, especially in those with articular involvement and sacroiliitis. Approximately 5% of the FMF patients have chronic joint involvement, majority resembling spondyloarthritis with mono/oligo arthritis of lower extremities and sacroiliitis. Although there are several case reports and observational studies demonstrating the effectiveness of various TNF inhibitors in articular symptoms FMF, the role of TNFantagonists in FMF has not been exactly clarified yet. Here we would like to present the clinical findings and treatment outcomes of 29 colchicine-resistantFMF patients who are on TNFinhibitors

All of the patients met the Tel Hashomer criteria. All had recurrent FMF attacks and subclinical inflammation in attack-free periods despite proper colchicine usage. But none had any sign of amyloidosis. Mean age of the patient group was 32.9±11years. Mean age at diagnosis was 22.6±12.5years. Mean age for starting an anti-TNF was 27.8±11.5years. Majority of the patients were females (20females, 9 males). Median duration of TNFinhibitor usage was 16months(8.5-49.5months).

Regarding FMF-related gene mutations data was present for 22 patients. Of those 10 had homozygous, 9 had compound heterozygous mutations. 8 patients were homozygous for M694V and 15 patients had at least one copy of M694V mutation.

The reason for starting a TNFinhibitor was inflammatory back pain and sacroiliitis in 14 cases, chronic arthritis in 6 cases. Six cases had both sacroiliitis and chronic arthritis. Three cases did not have articular symptoms, they had colchicine-resistant FMF activity but could not tolerate IL-1 inhibitors.

The first TNFinhibitor was etanercept in 15(51.7%) cases, adalimumab in 6(20.7%), infliximab in 3(10.3 %), certolizumab-pegol in 3(10.3%) and golimumab in 2(6.9%)patients. During the follow-up switch between TNFinhibitors was required only in 3 cases due to secondary-failure.

TNFinhibitors were well-tolerated and effective in all of the patients. Subclinical inflammation in attack-free periods subsided, frequency of attacks significantly decreased (Table-1).

TNFinhibitors have a promising role in treatment of colchicine-resistant FMF patients.

Keywords: antiTNF, Familial Mediterranean Fever

Table 1. Treatment outcomes of 29 colchicine -resistant FMF patients

	Before TNF inhibitor usage Median(IQR)	After TNF inhibitor usage Median(IQR)	p value
Erythrocyte sedimentation rate mm/hour	42(22-55)	19(17-24)	<0.001
C-reactive protein mg/L	17.4(3-19.6)	3(3-5.3)	0.001
Attack frequency	3(3-5.3)	1(0-2)	<0.001
Visuel Analoque Scale (VASpain) (0-10)	6(5-7)	2(0.5-3)	<0.001

PP-12

BESCHET'S DISEASE IN RUSSIA: THE RETROSPECTIVE PRELIMINARY DATA OF MULTICENTRAL STUDY

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Background: Beçet's disease (BD) is a rare systemic vasculitis, associated with certain nationalities, related to Great Silk Road. BD in Russia is rare and the data about BD in Russia is scarce.

Methods: in the retrospective cohort study we included data from patient's case histories. We evaluated demography, family history, clinical and laboratorial features, treatment options and outcomes. The diagnosis was made according to the criteria of the International Study Group for BD, 1990.

Objectives: to describe clinical course of BD in Russia.

Results: from 44 patients with inclusion age 21.5 years (15.7; 38.6) 59.0% (26/44) had pediatric onset (11 females) and 41% (18/44) adult onset (12 females). Asians/Causacians was 9 (20.5%)/ 35 (79.5%) patients. BD positive family history was in 4 patients (9%). The most frequent first symptom of BD was oral ulcers in 31/44 (70.5). Among clinical features patients with BD had the following organ and system involvement: oral ulcers-95%, genital ulcers-53%, ulcers of both localizations -52%, eye involvement -45%, skin-48.7%, positive pathergy phenomenon-50%, CNS-23%, GI-39%, joints-59%, thrombotic events/large vessel vasculitis-7%. Laboratorial features: ESR-21.0 (12.5; 27.8) mm/h, CRP-3.9 (0.4; 14.5) mg/l, patients with increased ESR-55%, with increased CRP-55%, with anemia-36.4%. 50% had HLAB51, HLAB27-40%, RF-18.2%. The main comorbidity was Crohn's disease 4 (9%)

Treatment options included: corticosteroids-67%, colchicines-42%, TNF-a inhibitors 37% (etanercept 6.25%, adalimumab 43.75%, golimumab and infliximab 25% each), azathioprine- 26%, cyclophosphamide and methotrexate-10% each. Also less frequent medications used: canakinumab (n=1), tocilizumab (n=2), tofacitinib (n=1), cyclosporine (n=1), MMF (n=1), hydroxychloroquine (n=2), sulfasalazine (n=3), apremilast (n=3). In 5 patients biologics were switched and apremilast initiated in 3 patients.

Conclusion: the data about BD in Russia is limited, prevalence underestimates, big diagnostic delay is typical and further investigations are required.

Keywords: Beschet's disease

PP-13

EARLY DIAGNOSIS IN FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean fever (FMF) is characterized by recurrent attacks of polyserositis. Untreated, it can lead to recurrent episodes and amyloidosis.

Objectives: This study aimed to assess the clinical profiles of patients diagnosed early versus those diagnosed late.

Methods: We recruited 143 FMF patients aged 18 and above who met the Tel-Hashomer Criteria. Through face-to-face surveys, we collected data on patients' demographic characteristics, educational background, smoking habits, family history of FMF and amyloidosis, as well as the features, duration, and frequency of FMF attacks. Additionally, we recorded the age at first FMF attack, age at first specialist visit, time between the first FMF attack and the first specialist visit, and the medical specialties consulted for symptoms. Information on MEFV gene mutations, time between the first specialist visit and diagnosis, and clinical decisions made by specialists at the time of diagnosis were obtained from hospital records. Early diagnosis was defined as occurring within three years of the first symptom.

Results: The mean diagnostic delay was 12.03±10.43 years. Age at first FMF attack (p=0.020), time between the first FMF attack and the first specialist visit (p=0.003), and the year of the first specialist visit (p=0.001) were statistically significant factors associated with early diagnosis in regression analysis. MEFV mutation was the primary factor influencing doctors' diagnostic decisions for FMF, particularly after 2000.

Conclusions: Beyond demographic, clinical, and genetic variations, early diagnosis may be linked to heightened patient awareness of the disease. Moreover, the availability of MEFV mutation testing may positively impact doctors' diagnostic decisions, potentially facilitating early FMF diagnosis and supplanting reliance on clinical features alone. However, this approach may result in diagnostic challenges for gene-negative FMF cases.

Keywords: Familial Mediterranean Fever

PP-14

INSIGHTS INTO THE CLINICAL MANIFESTATIONS AND GENETIC PROFILE OF FAMILIAL MEDITERRANEAN FEVER AMONG ADULT PATIENTS: A MULTICENTRIC STUDY IN TUNISIA

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Familial Mediterranean Fever (FMF) is the most common auto inflammatory disease.

Tunisia is a high-prevalence country for FMF. To date, we have no prevalence for FMF in Tunisia, and few studies have been published on the subject.

Methods: We conducted a multicenter cross-sectional study over the month of March 2024 including adult patients with genetically confirmed FMF.

Results: We included 48 patients with a genetically confirmed diagnosis of FMF. The sex ratio was 1.6. Median age at inclusion was 32 years [11-74].Median age of onset was 12.50 [1-50].Mean age of FMF diagnosis was 24 years [3-55]. The mean age at FMF diagnosis was 24 years [3-55]. A delay of more than 10 years between onset of symptoms and FMF diagnosis was reported in 20 patients (41%). Febrile abdominal pain was noted in all patients. The median white blood cell count during crisis was 9800Elements/ mm3 [5940-35000].Median crisis CRP was 103 mg/l [5-290].

Genetic mutations in the MEFV gene were M694V/M694V homozygous (n=12), M694V/M694I (n=5), M680I/M680I (n=1), M680V/M690V V726A/E148Q and I692del/- (n=1), E148Q/I692del (n=1), V726A/E148Q (n=1). Heterozygos mutation in MEFV was noted in 8 patients.

The diseases associated with FMF were distributed as follows Ankylosing spondylitis (n=3), IgA vasculitis (n=1), FMF coxitis (n=1). AA amyloidosis was noted in 3 patients. Therapeutically, 43 patients were on colchicine and 2 patients were on TNF blockers for associated spondylarthritis. The disease was well controlled in 36 patients, and poorly controlled in 6 (13%). One patient was in chronic renal failure without recourse to hemodialysis.

Discussion and Conclusion: Despite Tunisian physicians' awareness of FMF, 40% of patients in our cohort were in diagnostic wandering. Six patients (13%) in our cohort had poorly controlled disease, given the unavailability of anti-Il1 drugs in our country, which represents a therapeutic challenge.

Keywords: FMF, Tunisia

PP-15

A CASE OF PROTRACTED FEBRILE MYALGIA SYNDROME WITH ATYPICAL COURSE AND SEVERE ASYMMETRIC LOSS OF MUSCLE STRENGTH

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Introduction: Protracted febrile myalgia syndrome (PFMS) is a rare form of familial Mediterranean fever (FMF) characterised by prolonged myalgia. The duration of PFMS is much longer than a typical 2–5-day attack familial Mediterranean fever and lasts for 2-6 weeks until they treated with corticosteroids. Colchicine is not effective for control of PFMS's attacks. The attacks typically resolve with corticosteroid and/or IL-1 receptor blockers. Herein, we present a young adult without typical FMF clinic but with severe asymmetric muscle strength loss.

Case presentation:A 25-year-old Caucasian male patient presented with intermittent recurrent myalgia, especially in the gastrocnemius and thigh region, for the last 5 years. There was no known chronic disease or drug use, and similar family history. In many previous emergency service visits with similar pain attacks, C-reactive protein(CRP) was between 30 and 100 mg/dl, erythrocyte sedimentation rate(ESR) between 50-60 mm/h, creatinine kinase(CK) were found to be normal(Table 1). He stated that the pain lasted for 2-4 weeks and was localized in all four extremities, most prominently in the proximal lower limbs. The last six months, attacks have become more frequent, and severity of muscle pain increased as well. Fever, abdominal, flank or chest pain suggesting serositis was not accompanying this complaint. All serology was negative but In the MEFV gene analysis, P369S mutation was found to be homozygous.

Thigh magnetic resonance imaging confirmed inflammation and oedema and muscle biopsy showed no pathological findings (Figure 1). Electromyography revealed myopathic findings during attack-period, despite normal results in attack-free study. The patient was treated successfully with anakinra and remarkable rapid recovery in both muscular findings and acute phase reactants were observed.

Conclusion: PFMS should be considered even in the absence of apparent FMF attack pattern and in the presence of unexpected severe muscle weakness, especially in areas endemic for FMF and long-lasting myalgia attacks.

Keywords: Familial Mediterranean fever; protracted febrile myalgia

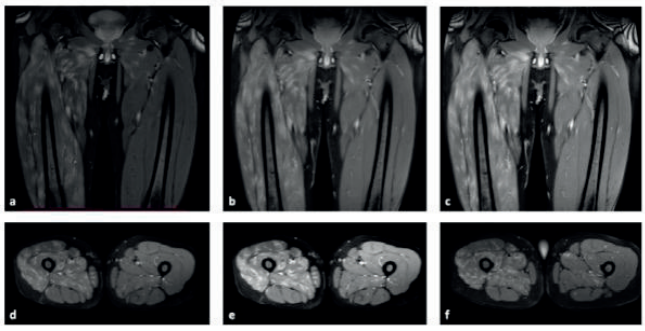

Figure 1. Coronal (a) proton density weighted (PDW) with fat saturation, (b) contrast enhanced T1-weighted fat saturation and (c) T1-weighted; and axial (d) proton density weighted (PDW), (e) contrast enhanced T1-weighted fat saturation and (f) T1-weighted MRI of the thigh muscles at presentation. There is remarkably increased intensity and swelling within the muscles representing severe oedema and inflammation more prominent on the right side.

Table 1. Laboratory parameters of the patient during follow-up

Parameter	At hospitalisation	At attack-time	At the 1st week of anakinra
ESR (mm/h)	87	N/A	9
CRP (mg/dL)	48	137	1
Serum amyloid A mg/dl (ULN <0.5)	80.3	N/A	N/A
Urine erythrocyte	1	1	1
Urine leucocyte	1	1	1
uPCR	88 mg/day	376 mg/day	125 mg/day
Serum creatinine (mg/dL)	0.77	0.66	0.71
Serum creatinine kinase(U/L)	33	26	53
Ferritin (ng/mL)	319	780	440
WBC 10^6/L	8900	14900	5600
Neutrophil 10^6/L	5900	12700	3100
Lymphocyte 10^6/L	2600	1930	1900
Haemoglobin g/dL	14.1	12.1	13.0
Platelets 10^9/L	443	323	405

PP-16

ARTHRITIS AND ITS CHARACTERISTICS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Introduction: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease characterized by recurrent attacks of fever and serositis. Many of the FMF patients also present with arthritis during the attacks, which may vary in its characteristics. In this study, we aimed to describe and characterize arthritis in FMF patients.

Methods: We used our hospital's record system to retrospectively identify FMF patients with joint involvement who presented to our clinic between 2005-2020. The prevalence, laboratory results of attack and remission periods, genetic mutation analysis, demographic data, characteristics of attacks, characteristics of joint involvement, comorbidities, treatments and treatment responses of patients were recorded.

Results: 954 patients from a cohort of 2350 FMF patients had joint involvement (40%). The male/female ratio was 0.49 (male patient n=316, female patient n=638). In patients with FMF and joint involvement, the frequency of at least one exon 10 was high. Female sex was more common compared to general FMF population and the age of onset of symptoms was earlier. Monoarthricular pattern was more frequent than oligoarthricular and polyarhticular pattern. Colchicine resistance was higher, and the required colchicine dose for disease control and the frequency of use of biological agents were high.

Conclusion: Since M694V mutation is common and the colchicine dose required for disease control is high, we can conclude that the disease activity is high in FMF patients with arthritis. The frequency of sacroiliitis and spondyloarthropathy is significantly increased, especially in individuals with M694V mutation, and joint involvement features are similar, suggesting that there may be a common point in their pathogenesis. FMF should be included in the differential diagnosis in patients presenting with arthritis in FMF endemic regions.

Keywords: Familial Mediterranean Fever, arthritis

Table 1. Demographic characteristics of the patients

Characteristic	Value
Gender, n (M/F)	954 (316/638)
Age, (mean±SD), (years)	38,43±11,29
Age of diagnosis, (mean±SD), (years)	23,79±12,55
Disease duration, (mean±SD), (years)	14,13±7,32
Comorbidities, n	412
Ankylosing Spondylitis	97
Hypertension	69
Diabetes Mellitus	33
Hypothyroidism	31
Fibromyalgia	21
Inflammatory Bowel Disease	18
Rheumatoid Arthritis	17
Chronic Kidney Disease	17
Psoriasis	14
Systemic Lupus Eritematosus	9
Malignancy	5

Table 2. Comparison of patients with at least one M694V mutation (group 1) and those without M694V mutation (group 2)

Characteristic	Group 1 (n=517)	Group 2 (n=437)	p value
Gender (F:M)	353:164 (2,14:1)	285:152 (1,87:1)	0,327
Symptom onset age (mean±SD), (years)	12,5±0,73	14,8±0,96	0,022
Family history of FMF n(%)	355 (69)	225 (52)	<0,001
Arthritis at first attack n (%)	318 (67)	214 (49)	<0,001
Monoarthritis n(%)	309 (61)	214 (49)	0,001
Oligoarthritis n(%)	162 (32)	152 (35)	0,272
Polyarthritis n(%)	36 (7)	64 (15)	<0,001
Red arthritis n(%)	311 (61)	200 (45)	<0,001
Knee joint n(%)	249 (48)	246 (56)	0,015
Ankle joint n(%)	413 (80)	286 (65)	<0,001
Hip joint n(%)	41 (8)	30 (7)	0,520
Sacroiliac joint n,(%)	48 (9,3)	49 (11,2)	0,337
Surgery for arthritis n(%)	7 (1,3)	6 (1,4)	0,775
CRP value in attack (mean±SD), (mg/L)	56,41±3,82	51,7±3,49	0,916
Sedimentation rate in attack (mean±SD), (mm)	38,3±1,7	38,46±2,75	0,014
Last visit colchicine dose (mean±SD), (mg/day)	1,57±0,327	1,42±0,49	0,009
Colchicine response n(%)	427 (83)	394 (90)	0,002
Anti IL-1 therapy use n,(%)	47 (9)	34 (8)	0,457
NSAID use n(%)	64 (12,4)	56 (12,8)	0,859
Corticosteroid use n(%)	19 (3,7)	35 (8)	0,004
cDMARD use n(%)	24 (4,7)	48 (11)	<0,001
Anti-TNFα use n(%)	22 (4,3)	24 (5,5)	0,382

PP-17

COMORBIDITY PROFILE OF FAMILIAL MEDITERRANEAN FEVER PATIENTS VARIES BY TREATMENTS

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Aim: In familial Mediterranean fever (FMF) treatment choice may be an indirect indicator of disease activity. As treatment resistance/failure increases in FMF, comorbidities related to inflammation/damage are expected to increase. So, we aimed to evaluate the comorbid conditions of patients according to treatment steps.

Methods: We retrospectively reviewed 740 FMF patients treated at our institute between May 2019 and March 2024. Demographics, comorbidities, presence of sacroiliitis, family history of FMF, and FMF treatments of patients were evaluated. FMF treatment was evaluated in 3 groups: coated colchicine, compressed colchicine and IL-1 inhibition. Coated colchicine treatments were switched to a compressed colchicine preparation due to colchicine resistance or intolerance. Colchicine resistance was defined as the presence of at least one attack/month despite administration of the maximum tolerated dose of colchicine for at least 3 months, and C-reactive protein and serum amyloid A levels above the normal range between attacks. If resistance or intolerance to compress colchicine treatment persists we add or switch IL-1 inhibition to FMF patients.

Results: The mean age (SD) of FMF patients was 40.7 (13.3) and 62.4% were female. Of the 44.7% all patients had at least 1 comorbidity. The three most common comorbidities are hypertension (20%), hyperlipidemia (7%) and depression (6.8%). The initial coated colchicine treatment was changed in a total of 24.5% of the patients, including 11.3% compressed colchicine and 13.2% IL-1 inhibition. Demographic characteristics and comorbidities of the FMF patients are shown in the Table.

Conclusion: The frequency of comorbidities was highest in the IL-1 inhibition group, the majority of them related to FMF disease activity such as hypertension and chronic kidney disease. The fact that some comorbidities are proportionally less in the compressed colchicine group compared to coated colchicine group suggests that switching colchicine preparations in suitable FMF patients may prevent the development of comorbidities.

Keywords: FMF

Table. Demographic characteristics and comorbidities of the FMF patients

	Coated colchicine, n=558	Compressed colchicine, n=84	IL-1 inhibition, n=98	p
Age, year, mean (SD)	41.5 (13.6)	38.1 (12.1)	38.2 (11.9)	0.020
Female, n (%)	355 (60)	54 (64)	53 (54)	0.350
Family history of FMF, n (%)	73 (13)	19 (23)	12 (12)	0.035
Sacroiliitis, n (%)	141 (24)	5 (6)	13 (13)	<0.001
Any comorbidity, n (%)	238 (41)	37 (32)	56 (57)	0.002
Hypertension, n (%)	111 (19)	10 (12)	28 (29)	0.015
Diabetes mellitus, n (%)	36 (6)	4 (5)	5 (5)	0.900
Hyperlipidemia, n (%)	39 (7)	6 (7)	7 (7)	0.970
Coronary artery disease, n (%)	11 (2)	2 (2)	1 (1)	0.800
Arrhythmia, n (%)	9 (2)	1 (1)	0	0.640
Chronic kidney disease, n (%)	13 (2)	0	20 (20)	<0.001
Non-renal amyloidosis, n (%)	2 (0.3)	0	1 (1)	0.560
Chronic obstructive pulmonary disease, n (%)	7 (1)	3 (4)	1 (1)	0.170
Asthma, n (%)	33 (6)	3 (4)	3 (3)	0.580
Thyroid disease, n (%)	29 (5)	4 (5)	1 (1)	>0.999
Depression, n (%)	44 (8)	4 (5)	3 (3)	0.200
Demyelinating diseases, n (%)	3 (1)	1 (1)	0	0.430
Neuropathy (non-diabetes mellitus), n (%)	4 (1)	0	0	>0.999
Cerebrovascular disease, n (%)	3 (1)	0	3 (3)	0.060
Osteoporosis, n (%)	13 (2)	1 (1)	1 (1)	0.900
Malignancy, n (%)	3 (0.5)	1 (1)	2 (2)	0.150
FMF: familial Mediterranean fever, IL-1: Interleukin-1, SD: Standard deviation				

PP-18

CLINICAL FEATURES OF PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER OVER 50 YEARS OF AGE: A SINGLE-CENTER EXPERIENCE

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Objective: This cross-sectional study aims to explore the impact of aging on the clinical manifestations and progression of Familial Mediterranean Fever (FMF), focusing on patients above 50 years old, utilizing data from a single tertiary center.

Materials and Methods: Patients diagnosed with FMF according to Tel Hashomer criteria and aged over 50 by 2022 were included.We retrospectively screened the digital records and files of the included patients. Patient demographics, age at symptom onset, age at diagnosis, diagnostic delay, follow-up duration, mutations, attack characteristics, attack frequency, Visual Analogue Scale (VAS) score, comorbidities, treatment, and usage of biological drugs were investigated during the search.

Results: In this study, 343 patients were evaluated (Table 1). Table 2 shows the attack characteristics, and significant differences were found in the frequency of fever, abdominal pain, arthralgia, arthritis, and chest pain between three periods ($p<0.001$).A significant difference was found in the number of attacks before treatment, after treatment, and during the last year ($p<0.001$). The patients' VAS disease severity scores were evaluated for before treatment, after treatment, and the latest attacks. Before treatment, after treatment, and the latest VAS scores were compared and there was a significant decrease in the VAS score in the latest attack ($p<0.001$).

Conclusions: Our retrospective study on Familial Mediterranean Fever (FMF) patients aged 50 and above sheds light on the impact of aging on disease severity and colchicine therapy. Through our analysis, we observed a notable decrease in both attack frequencies and Visual Analog Scale (VAS) scores among older patients. Additionally, there was a discernible correlation between the reduction in patient complaints and the corresponding decrease in colchicine doses administered. These findings suggest a potential association between aging and milder FMF symptomatology, indicating the possibility of reduced reliance on colchicine therapy in aging FMF patients.

Keywords: aging, colchicine

Table. Clinical characteristics of the attacks

Attack Characteristics	Before treatment n (%)	After treatment n (%)	Latest n (%)	p-value
Fever	266 (77.6)	253 (73.8)	52 (15)	<0.001
Abdominal pain	293 (85.4)	299 (87.2)	223 (65)	<0.001
Arthralgia	56 (16.3)	82 (23.9)	33 (9.6)	<0.001
Arthritis	87 (25.4)	100 (29.2)	32 (9.3)	<0.001
Chest pain	71 (20)	79 (23)	24 (7)	<0.001
Myalgia	23 (6.7)	34 (9.9)	46 (13.5)	0.14
Erysipelas like erythema	11 (3.2)	12 (3.5)	7 (2)	0.487

Table. Demographic characteristics of the patients

	All (n:343)	Female (n:224)	Male (n:119)
Age (years), mean ± SD	57.6 ± 6.5	57.4 ± 6.42	58.1 ± 6.65
Age at symptom onset (years), mean ± SD	24 ± 14.4	23.5 ± 14.8	24.8 ± 13.6
Age at diagnosis (years), mean ± SD	40.8 ± 10.8	42 ± 10.6	38.6 ± 10.8
Diagnostic delay (years), mean ± SD	16.8 ± 14.5	18.5 ± 14.8	13.8 ± 13.5
Follow-up duration (years), mean ± SD	16.8 ± 9.79	15.4 ± 8.98	19.4 ± 10.7

PP-19

INFLAMMATORY COMORBIDITIES IN PEDIATRIC FAMILIAL MEDITERRANEAN FEVER; A SINGLE REFERRAL CENTER EXPERIENCE

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Ankara Etlik Şehir Hastanesi, Çocuk Romatoloji Kliniği

Introduction: Familial Mediterranean fever (FMF), most common autoinflammatory disease, is characterized by recurrent episodes of fever and serosal inflammation with high acute phase response. The MEFV mutations that are usually associated with FMF may sometimes be associated with quite different diseases and clinical entities. Many inflammatory or rheumatic diseases are increased compared to the healthy population.

The aim of this study was to evaluate inflammatory diseases associated with FMF patients.

Material and Methods: Patients with a diagnosis of FMF followed up in a tertiary hospital rheumatology department between 2017 and 2022 were included in the study. The diagnosis was based on Yalçınkaya-Özen and Eurofever criteria. Juvenile idiopathic arthritis, immunoglobulin A vasculitis, poluarteritis nodosa,Behçet's disease, inflammatory bowel disease, and systemic lupus erythematosus were considered inflammatory diseases. Non-inflammatory comorbidities were not included in the study. Disease severity was classified using the Pras et al. and Mor et al. severity scores.

Results: A total of 725 patients with FMF were included in this study. Of 725 patients, 54 had an inflammatory comorbidity. IgA vasculitis was the most frequent comorbidity in FMF patients. In FMF patients without comorbidities, the age at disease onset and diagnosis was younger. Demographics, clinical characteristics and concomitant disease were summarized in Table 1. The disease severity score was higher in patients with comorbidities. Laboratory parameters were summarized in Tables 2.

Conclusion: Similar to the literature we found that 7.4% of the patients with FMF have concomitant comorbid diseases and IgA vasculitis is the most frequent comorbid disease. Patients without comorbidities were younger than the patients with comorbidities. Patients with comorbidities had a lower percentage of using biological DMARDS. However, those patients had a more severe disease than the patients without comorbidity.

Keywords: Inflammatory disease, comorbidity

Table 1. Demographic characteristics of FMF patients with and without comorbidity

	Group 1 n=54	Group 2 n=671	p
Sex			0.96
Female, n(%)	29 (53.7%)	358 (53.4%)	
Male, n(%)	25 (46.3%)	313 (46.6%)	
Age at disease onset (years), median (IQR)	4,5 (5)	3 (3,3)	**0,015**
Age at diagnosis (years), Imedian (IQR)	7,3 (3,3)	6 (5,4)	**0,015**
Attack frequency at diagnosis (year), median (IQR)	12 (4,5)	12 (12)	0,07
Attack duration at diagnosis (day), median (IQR)	2 (1)	2 (1)	0,136
MEFV mutations			0.8
Exon 10*, n(%)	35 (64.8%)	424 (63.2%)	
Other mutations, n(%)	19 (35.2%)	247 (36.8%)	
Colchicine response			0.3
Complete or partial response, n(%)	50 (92.6%)	641 (95.5%)	
Resistant, n(%)	4 (7.4%)	30 (4.5%)	
Biological DMARDS, n(%)	12 (25%)	36 (75%)	<0.001
Disease severity			
MOR			<0.001
Mild, mean, n(%)	17 (%32)	321 (47.8%)	
Moderate, mean, n(%)	15 (%27.8)	229 (34.1%)	
Severe, mean, n(%)	22 (%40)	199 (17.7%)	
PRAS			<0.001
Mild, mean, n(%)	9 (16.7%)	203 (30.3%)	
Modarate, mean, n(%)	29 (53.7%)	391 (58.3%)	
Severe, mean, n(%)	17 (29.6%)	74 (11%)	
Inflammatory comorbidities, n (%)	54 (7.4%)		
IgA vasculitis	34 (4.7%)		
Inflammatory bowel disease	2 (0.3%)		
Juvenile idiopathic arthritis	15 (2.1%)		
Polyarteritis nodosa	3 (0.4%)		
Systemic lupus erythematosus	1 (0.1%)		
Uveitis	2 (0.3%)		

*Homozygosity or compound heterozygosity for exon 10 MEFV mutations.
DMARDS Disease modifying anti-rheumatic drugs; IQR Interquartile range; FMF Familial Mediterranean fever.

Tablo 2. Laboratory assesments of FMF patients with and without comorbidity

	Group 1 n=54	Group 2 n=671	p
ESR[a], mm/h*	54 (39)	40 (25)	**<0.001**
CRP[a], g/dL*	72 (69.3)	77.8 (89)	0.6
WBC[a], 10^9/L*	8930 (7350)	9410 (4880)	0.4
HB[a],gr/dL*	11,8 (2)	12,1 (1,7)	**0.02**
PLT[a], 10^9/L*	354000 (185000)	323000 (123000)	0.1
ESR, mm/h*	8 (7)	7 (7)	0,4
CRP, g/dL*	3 (1.15)	3 (0.02)	0,8
WBC, 10^9/L*	6940 (2060)	6770 (2215)	0,7
HB, gr/dL*	12,8 (1,75)	13,3 (1,5)	0,13
PLT, 10^9/L*	276000 (122000)	300000 (98500)	0,16

[a] During FMF attack period
* Median, Interquartile range
CRP C- reactive protein, ESR Erythrocyte sedimentation rate, HB haemoglobin concentration, WBC White blood cell count, PLT, Platelet count

PP-20

LONG TERM EFFICACY OF ANTI IL1 INHIBITION IN SEVERE JOINT INVOLVEMENT IN FMF PATIENT

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Objective: FMF has been considered a model for inflammatory diseases as osteoarticular diseases. The current treatment of osteoarthritis is aimed to control symptoms. Histological investigations have demonstrated that many soluble inflammatory mediators, including IL-1, are increased in synovial fluid in osteoarthritis. Therefore disease-modifying agents able to inhibit catabolic pathways would be considered.

Subject and Method: We report a case of a 53-year old woman, who suffered from recurrent hip pain, fever and abdominal pain from the infancy. Only 20 years later, the diagnosis of FMF was established by the help of Montpellier Laboratory (M680I homozygosis). Since the starting of colchicine, no further episodes of fever or hip pain have occurred. However, due to coxarthrosis caused by the persistence of untreated inflammation for many years, total hip replacement was necessary bilaterally. In 2020, she had also knee osteoarthritis (more on the left leg) despite normal SAA and CRP parameters with colchicine 2 mg a day. After a brief treatment with NSAID, anakinra 100mg a day was introduced and a clinical and radiological improvement was obtained; afterward a dose 300 mg per week was kept.

Results: The MRI performed after 3 years of anakinra therapy showed clear reduction in joint effusion, synovial thickening and arthro-synovitic inflammation.

Conclusions: It has demonstrated that IL-1beta inhibits anabolic activities and stimulates chondrocytes to produce proteolytic enzymes, whereas IL-1alpha behaves like "alarmin", since, in case of damage, it is released from the cells, determining the local inflammation. If IL1beta is a pivotal cytokine of systemic inflammation after the inflammasome activation and in this subject was controlled by colchicine, in contrast anakinra (as anti ILalpha) has demonstrated a local anti-inflammatory effect. This optimal and persisting effect of anakinra in osteoarthritic knee opens to new therapeutic possibilities in patients suffering from osteoarthritis resistant to classical therapies before anatomical abnormalities.

Keywords: IL-1, joint involvement

PP-21

REPORT ON A COHORT OF ITALIAN PATIENTS AFFECTED BY FAMILIAL MEDITERRANEAN FEVER: PHENOTYPE AND GENOTYPE CHARACTERIZATION, WITH A SPECIFIC FOCUS ON ASSOCIATED IMMUNE MEDIATED DISEASE

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Objectives: Aim of the present study is to investigate the clinical presentation and the genetic background of an Italian cohort of Familial Mediterranean Fever (FMF) patients, with a focus on the immune mediated conditions associated with this disease.

Materials-Methods: A total of 321 patients affected by FMF have been enrolled, all of them were attending the Periodic Fevers Research Centre of Rome, Catholic University, 'A.Gemelli' Hospital, Italy.

The diagnosis of FMF was made using Tel Hashomer criteria and all individuals underwent a genetic test for MEFV mutation.

Results: The main clinical features of our study population are reported in Table1. The most common clinical manifestation are: fever presents in 306 patients (95.3%), abdominal pain in 264 patients (82.2%), joint pain in 226 patients (70.4%), chest pain in 148 patients (46.1%), skin manifestations in 112 patients (34.9%) and oral aphthosis in 101 patients (31.5%).

The results of genetic investigation showed no mutations in 30% of patients, while the most frequent genotype was simple and compound heterozygosity of M694V, complete results are summarized in Figure 1. Of the entire cohort, 48 patients (15%) had received a diagnosis of an immune mediated condition as reported in Figure 2. Considering two subgroups of our population, those with FMF associated with immune mediated disease (48), and that with FMF without immune mediated disease (273), no significant difference were found in regards to features of flare, age of onset and dose and effectiveness of colchicine. Skin manifestation and arthritis were found to be prevalent in the group of FMF associated with immune mediated disease ($p < 0.05$). Table 2.

Conclusions: This study is a panoramic of FMF disease in an Italian cohort of patients, we described the phenotype and genotype features and the immune mediated associated conditions of our FMF patients.

Keywords: Familial Mediterranean fever, auto-inflammatory disease

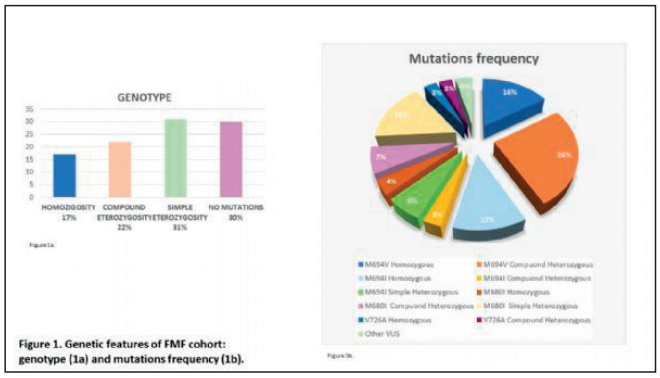

Figure 1. Genetic features of FMF cohort.

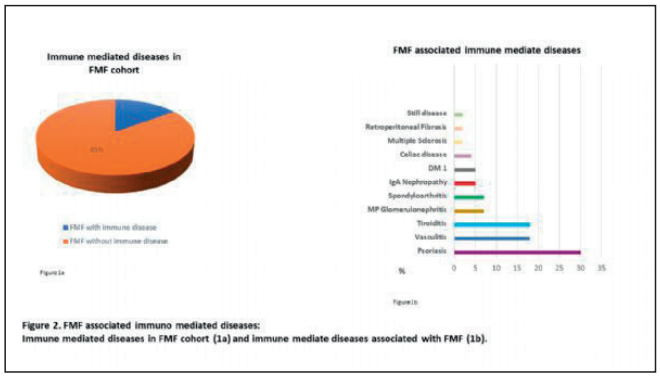

Figure 2. FMF associated immune mediated diseases

Table1. Clinical features of FMF cohort

CLINICAL FINDINGS	FMF COHORT n = 321 (%)
SEX Male Famale	170 (52,9) 151 (47,1)
FEVER	306 (95,3)
JOINT PAIN	226 (70,4)
ABDOMINAL PAIN	264 (82,2)
CHEST PAIN	148 (46,1)
ORAL APHTHOSIS	101 (31,5)
SKIN MANIFESTATION	112 (34,9)
TEMPERATURE (C°)	39 ± 0,08 SD
DURATION OF ATTACKS (DAYS)	3,7 ± 2,77 SD
PERIODICITY OF ATTACKS (DAYS)	32,39 ± 38,32 SD
AGE ONSET (YEARS)	15,07 ± 12,77 SD
AGE OF DIAGNOSIS (YEARS)	28,70 ± 16,24 SD
DIAGNOSTIC DELAY (YEARS)	13,50 ± 13,25 SD
MEAN DOSE COLCHICINE (mg/day)	1,34 ± 0,34 SD

Table 2. Features of two subgroups of FMF cohort.

CLINICAL FINDINGS	FMF PATIENTS WITH IMMUNOMEDIATED CONDITION N (%)	FMF PATIENTS WITHOUT IMMUNOMEDIATED CONDITION N (%)	P VALUE
SEX Male Famale	24 (50) 24 (50)	127 (51,8) 118 (48,2)	N.S.
FEVER Yes Not	43 (89,6) 5 (10,4)	237(96,7) 8 (3,3)	N.S.
JOINT PAIN Yes No	37 (77,1) 11 (22,9)	177 (74,3) 61 (24,9)	N.S.
ABDOMINAL PAIN Yes Not	40 (83,3) 8(16,7)	201 (84,1) 38 (15,9)	N.S.
CHEST PAIN Yes Not	32 (66,7) 16 (33,3)	117 (49,3) 120 (50,7)	N.S.
ORAL APHTHOSIS Yes Not	16 (33,3) 32 (66,7)	83 (33,2) 153 (66,8)	N.S.
ARTHRITIS Yes Not	22 (45,8) 26 (54,2)	24 (10,1) 214 (89,9)	P 0.001
SKIN MANIFESTATION Yes Not	25 (52,1) 23 (47,9	79 (33,1) 159 (66,8)	P 0.02
TEMPERATURE (°C)	38,69 ± 0,81 SD	39,02 ± 0,86 SD	N.S.
DURATION OF ATTACKS (DAYS)	3,45 ± 2,5 SD	3,64 ± 2,74 SD	N.S.
PERIODICITY OF ATTACKS (DAYS)	29,06 ± 30,39 SD	34,44 ± 42,18 SD	N.S.
AGE ONSET (YEARS)	18,07 ± 14,57 SD	14,60 ± 12,55 SD	N.S.
AGE OF DIAGNOSIS (YEARS)	33,41 ± 15,42 SD	28,32 ± 16,21 SD	N.S.
DIAGNOSTIC DELAY (YEARS)	15,60 ± 14,44 SD	13,37 ± 13,20 SD	N.S.
MEAN DOSE OF COLCHICINE	1,34 ± 0,45 SD	1,37 ± 0,45 SD	N.S.

PP-22

GENETIC FEATURES IN ITALIAN AND LEBANESE SUBJECTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background and Aims: Familial Mediterranean Fever (FMF) is an autoinflammatory monogenic disease caused by recessively inherited mutations in Mediterranean Fever (*MEFV*) gene with noticeable variation among ethnicities. We investigated the spectrum of *MEFV* variants in FMF subjects living in Italy and Lebanon.

Methods: Genetic data and FMF symptoms were collected from 156 Italian (females 54.5%) and 127 Lebanese subjects (females 69.3%) previously diagnosed with FMF.

Results: Italians, as compared to Lebanese patients, were older (age 38.7±SEM1.7 yrs. vs 20.5±1.2 yrs., resp., p<0.001), had similar heterozygosity (44.2% vs 54.3%, resp, p=NS), lower homozygosity (7.7% vs 16.5%, resp, p=0.02), and higher compound heterozygosity (48.1% vs 29.2%, resp, p=0.01). In Italian subjects, 55.8% of mutations were variants of uncertain significance, while in Lebanese 61.4% were pathogenic variants. The most common variant among homozygote and heterozygote subjects was only R202Q (69.2% and 43.5%, respectively) in Italians, and M694V (57.1%) and E148Q

(30.4%) respectively, in Lebanese patients. In the compound heterozygous group, E148Q/R761H was the most frequent in Italians (53.3%), and M694V/V726A (10.8%) and M694V/E148Q (10.8%) in Lebanese. The most frequent variants were R202Q (34.2%) in Italians and E148Q (27.6%) in Lebanese. In patients carrying the E148Q variant, Italians showed a significantly lower prevalence of fever, abdominal pain, thoracic pain, arthralgia, and myalgia (18.2%-69.1%) compared to Lebanese (82.9%-94.3%, $p<0.05$).

Conclusion: Our results show a variation in *MEFV* mutation between two Mediterranean countries. Lebanese subjects have more pathogenic variants and a higher prevalence of symptoms compared to Italians carrying the same mutation. Our future studies will investigate the genotype-phenotype correlation focusing on environmental epigenetic factors.

Keywords: Familial Mediterranean Fever, MEFV variants

PP-23

ANAKINRA TREATMENT IN A PATIENT WITH END-STAGE RENAL FAILURE DUE TO FMF-ASSOCIATED AMYLOIDOSIS: 5.5 YEARS OF EXPERIENCE

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IL-1 inhibition serves as an alternative treatment in patients with colchicine-resistant FMF attacks and amyloidosis secondary to FMF. Anakinra is a recombinant human IL-1 receptor antagonist.Its clearance is affected by the glomerular filtration rate. So in FMF patients with end stage renal insufficiency, administering anakinra every other day is recommended.In patients on hemodialysis anakinra is usually given three times a week following the dialysis sessions. Long term safety of this application has not yet been studied in detail.The main safety concern relates to the risk of infection,as both presence of renal failure and the use of IL-1 antagonists increases the risk of infections. Herelong-termfollowupofapatientwhoisonhemodialysisforend-stage renal failure secondary to FMF-associated amyloidosis is presented. Case: A 45-year-old female patient was admitted due to recurrent FMF attacks. It was learned that she had been on hemodialysis three times a week because of renal failure caused by FMF-associated amyloidosis.She had been diagnosed to have FMF at the age of 11.She was homozygous for M694V mutation.Poor treatment compliance and lack of follow-up in terms of health care had caused renal amyloidosis when she was 36years old and since progression to end-stage renal failure could not be prevented she had been on hemodialysis since she was 42.Despite colchicine treatment 0,5mg/day she had been having FMF attacks 3-4times a month and had been using steroids to releave the attacks.Anakinra 100 mg/3 times a week after hemodialysis sessions were started.The attacks dramatically subsided.Subclinical inflammation resolved, steroids were stopped.Since 5.5 years she has been followed in remission for FMF.Anakinra had an excellent safety profile in our patient.She had no serious infection, no need for hospitalization although she was diagnosed to have Covid infection in two seperate occasions. Anakinra is an effective and safe treatment option in patients on hemodialysis.

Keywords: Anakinra, hemodialysis

PP-24

RECURRENT ORAL ULCERS FOUND TO BE CAUSED BY FAMILIAL MEDITERRANEAN FEVER 20 YEARS AFTER ITS ONSET: CASE REPORT

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It is important to consider a broad spectrum of auto-inflammatory diseases when one is suspected, as despite each having its own typical presentation, they occasionally appear atypically. Oral ulcer, a symptom that is often associated with viral and specific rheumatological diseases, is presented in a 21-year-old male who has been suffering from it since he was a year old. In addition, he kept encountering some other symptoms of unknown causes throughout his life, which left him being inaccurately diagnosed and with the wrong treatment. Furthermore, he was admitted with complications of FMF that are rare to occur, like pneumonia and significantly elevated amyloid A levels, which could have been avoided if the right diagnosis had been established at the time when the disease manifested with mild symptoms.

Keywords: Chronic recurrent oral ulcers, Familial mediterranean fever (FMF)

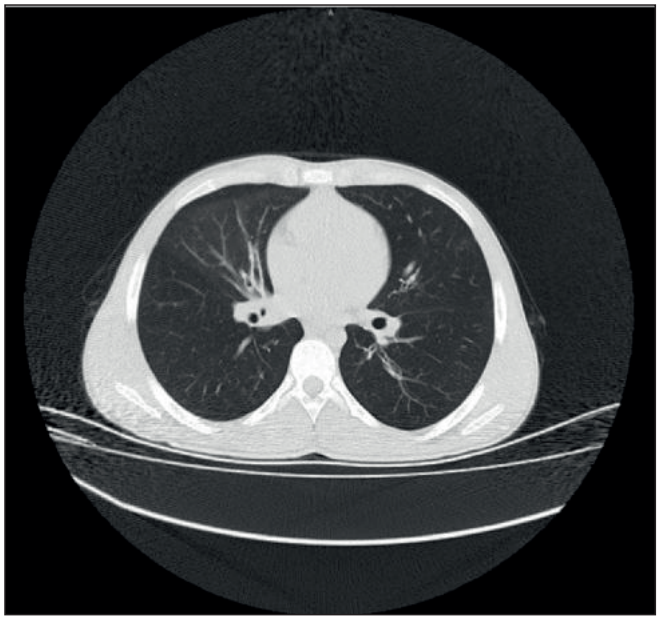

Figure 1. Ground glass opacity at the upper lobe of the right lung.

PP-25

REFRACTORY SWEET SYNDROME IN ASSOCIATION WITH FAMILIAL MEDITERRANEAN FEVER: A CASE REPORT

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Background: Familial Mediterranean fever (FMF), the most common hereditary monogenic autoinflammatory disease, manifests through short-term inflammatory attacks that spontaneously heal within 1-4 days. Sweet syndrome, also known as acute febrile neutrophilic dermatosis, is a rare disorder and usually coexisted with other infectious, inflammatory, and malignant diseases.

Case Presentation: A 63-year-old patient with a 3-year history of recurrent, abrupt onset of tender, annular skin lesions was admit-

ted to the dermatology outpatient clinic with arthralgia and fever (Figure 1a). The laboratory is significant for high erythrocyte sedimentation rate; high C-reactive protein level, and neutrophilia. Skin lesions were biopsied, pathology was consistent with neutrophilic dermatosis and the clinical presentation was compatible with Sweet syndrome. On the third day of the methylprednisolone regime (tapered from 35 mg to 5 mg), the patient's fever subsided, and skin lesions regressed (Figure 1b). With the patient's history of recurrent arthralgia, fever, and erysipelas-like erythema, also heterozygous MEFV gene mutation; an FMF diagnosis was made. Twice a day 0.5mg colchicine dispert was added treatment regimen as a maintenance treatment. However, after cessation of methylprednisolone treatment; the patient became symptomatic with high fever, arthritis in the right metacarpal joint, diffuse arthralgia skin lesions, and high levels of acute phase reactants. 3-gram pulse steroid treatment began and tapered in three months. Thus, the patient was considered as having refractory Sweet syndrome and treated with anakinra, skin lesions regressed under anakinra treatment.

Learning Points for Clinical Practice: FMF and Sweet syndrome have similar clinics and pathophysiologic manifestations. In cases of Sweet syndrome associated with FMF, it is seen that FMF has an atypical clinical course. It could be due to processing neutrophilic activation, inflammasome dysregulation, and overproduction of IL-1B. Because of this; if the patient is unresponsive to the colchicine treatment; anakinra could be beneficial.

Keywords: FMF, Sweet

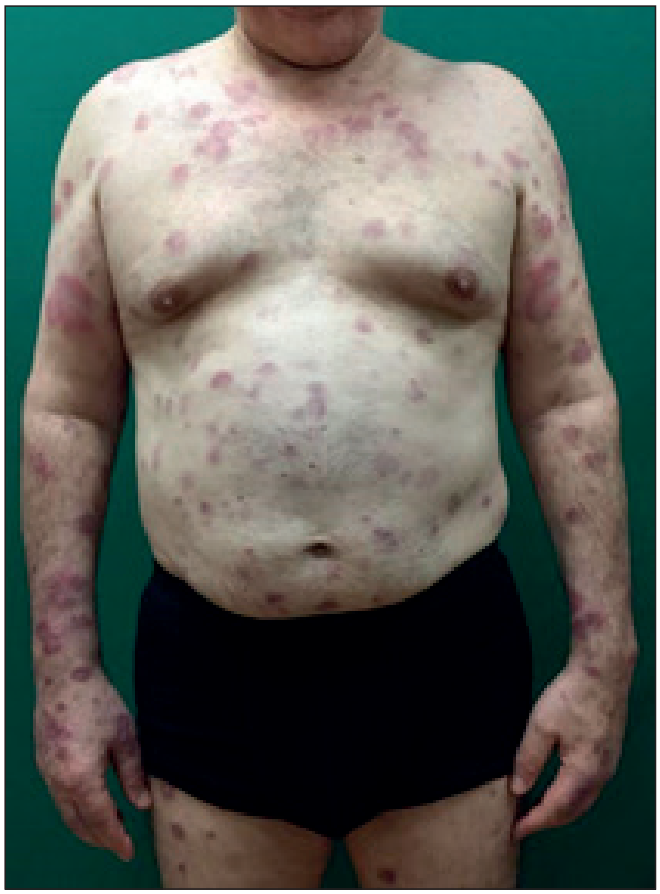

Figure 1a. Tender annulary skin lesions prominent in distal extremities

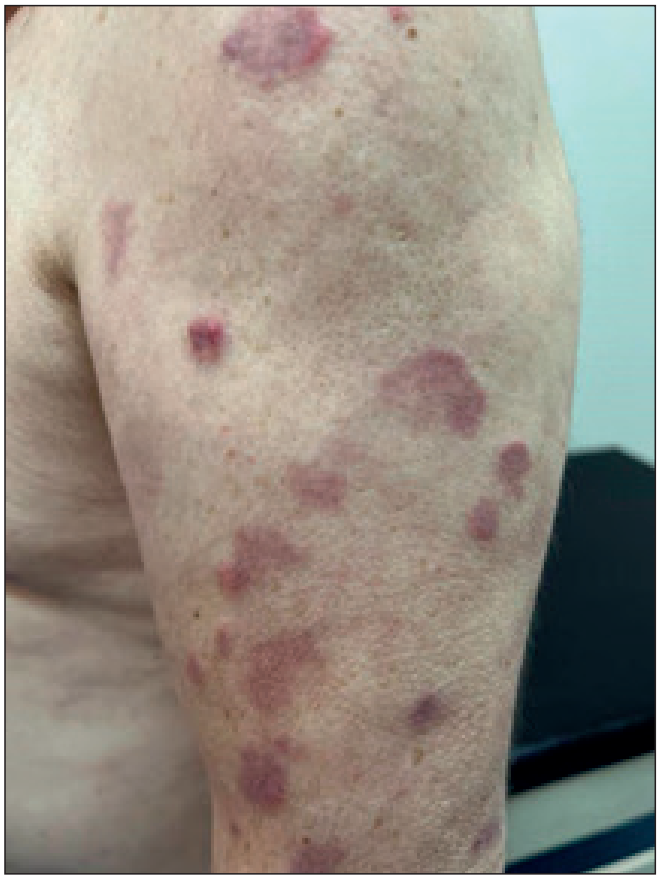

Figure 1b. Lesions of the left upper arm after tapering methylprednisolone dosage to 5 mg.

PP-26

IMPACT OF DISEASE ACTIVITY ON HEPATITIS B VACCINATION RESPONSES IN PATIENTS WITH COLCHICUM RESISTANT FAMILIAL MEDITERRANEAN FEVER

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Aim: The study aims to explore the correlation between the disease activity and subclinical inflammation with anti-Hbs titers in FMF patients.

Methods: This is a retrospective study at the Umraniye Training and Research Hospital's pediatric rheumatology clinic. 88 colchicum resistant FMF patients who had the anti-Hbs levels and HbsAg levels were included in the study. All the demographic data, clinical finding, and MEFV gene sequencing results were retrospectively collected from patients' files. For control group, Anti-Hbs titer greater than 10 IU/L was accepted indicative of seroprotection against HBV.

Results: A total of 88 patients with FMF were included in the study. 52 (59.1%) were female, 36 (40.9%) were male. The median of symptom age was 3.5 years (IQR 2, 7) and the median of diagnosis age was 5.25 years (IQR 3, 9). The follow-up period had a median of 139 months (IQR 91.5, 171.75). Most frequent symptoms were abdominal pain (85, 96.6%), fever (84, 95.9%), and arthralgia (57, 64.8%). The most common MEFV gene mutation was homozygous M694V genotype with 67 (76.1%) patients. All the patients were colchicum resistant and started on biological agents afterwards. Of these patients, 43 (48.9%) had positive anti-Hbs levels, with a median titer of 58.5 IU/L (IQR 22.2, 114.71). The median symptom age of anti-Hbs positive patients were 4 (IQR 2, 7) years and for negative patients were 3 (IQR 2, 6.65) years. By comparing anti-Hbs positiv-

ity percentages with healthy pediatric patients' data (72.9% n=200) provided from another study, we found a significant correlation with FMF patients' anti-Hbs antibody positivity rate (p=0.0005). No correlation was observed between the age of symptom onset and anti-Hbs titers (R2=0.501). There was no statistical significance between the median age at symptom onset and diagnosis between anti-Hbs levels (p=0.375, p=0.257,respectively). Frequency of attacks did not show a significant correlation with anti-Hbs seropositivity.

Keywords: FMF, Anti-hepatitis B surface antibody

PP-27

EVALUATION OF THE HEALTH-RELATED QUALITY OF LIFE SCALE (FMF-QOL) IN PEDIATRIC PATIENTS DIAGNOSED WITH FAMILIAL MEDITERRANEAN FEVER

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Aim: The aim was to assess the difficulties experienced by paediatric patients with FMF, focusing on the physical, emotional and social dimensions of health using the FMF Quality of Life Scale (FMF-QoL).

Results: The familial Mediterranean fever quality of life scale was applied to 187 patients with FMF and 50 control subjects. The median age (IQR) was 13 (10.3-15.8) years in the FMF group and 11 (9-13) years in the control group. The female/male ratio was 90/97 (48.1% female) in the patient group and 25/25 (50% female) in the control group. Forty-three (22.9%) patients with FMF were colchicine resistant. FMF quality of life total median score was 16 (9-32) for colchicine-resistant FMF patients, 20.5 (10.2-31) for patients receiving only colchicine treatment and 9.5 (6-14) for the control group. Quality of life score was statistically significantly lower in the control group compared to the patient group (p=0.00). It was observed that 15 questions with differences were especially related to physical activity and social support. There was no significant difference between colchicine-resistant and colchicine-only patients (p=0.62). Quality of life score showed no difference in terms of gender in the patient group with FMF (p=0.18). There was no correlation between age and total quality of life score (p=0.62).

Conclusion: This study illustrates the substantial effect of FMF on patient quality of life, with treatment resistance presenting as a notable concern. The lack of significant differences in quality of life across gender and age groups suggests that FMF's impact is broadly consistent among patients, emphasizing the need for effective management strategies to improve the quality of life for all affected individuals.

Keywords: quality of life scale, paediatric

PP-28

THE IMPACT OF DIFFERENT MEFV GENOTYPES ON CLINICAL PHENOTYPE OF PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: SPECIAL EMPHASIS ON JOINT INVOLVEMENT

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Introduction: Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease worldwide [1]. Joint involvement is one of the common and important findings of FMF [2]. In this study, we aimed to evaluate the clinical features of patients and characteristics of arthritis in children with FMF and investigate the influence of MEFV gene variants on their clinical features.

Material and methods: In total, 782 patients with FMF were categorized into 3 groups according to the MEFV mutation; Group 1: Patients homozygous for M694V; Group 2: Patients carrying other pathogenic MEFV variants (M694I, M680I, V726A) in exon 10 in homozygous or compound heterozygous states; and Group 3: FMF patients with other variants or without mutations. Clinical and demographic findings were compared between groups.

Results: Among the 782 FMF patients, total frequency of arthritis was 237 (30.3%): 207 (26.4%) were acute monoarthritis and 67 (8.5%) were chronic arthritis. All 3 groups were compared regarding the frequency of arthritis (acute and/or chronic), acute monoarthritis, and chronic arthritis. The frequency of arthritis (40.4% vs. 24.8% vs. 26.7%; p:0.001) and acute monoarthritis (35.4% vs. 20% vs. 23.7%; p:0.001) was found to be significantly higher in Group 1 than in the other groups. The average duration of acute monoarthritis (2 days vs. 1 day; p:0.001) was longer in patients with the M694V homozygous mutation. The rate of arthralgia and chronic arthritis did not differ between groups. FMF patients with chronic arthritis showed a distinct juvenile idiopathic arthritis (JIA) distribution pattern with a more frequent juvenile spondyloarthropathy (JSpA) subtype (43.2%) (Table I-II).

Conclusion: Homozygous M694V mutation is associated with a more frequent and longer acute monoarthritis comparing to other MEFV genotypes. In countries where FMF carrier frequency is high, JSpA patients with negative HLA-B27 antigen should also be assessed for polyserositis episodes of FMF.

Keywords: Arthritis, familial Mediterranean fever

Table 1: Demographic data, symptoms and clinical presentations of patients in our cohort study

	n (%) or mean ± SD or median (min -max; IQR, 25th—75th percentiles)
Total number of patients	782
Gender (female)	384 (49.1%)
Age at last visits (years)	14.2±4.4
Age of symptom onset (years)	3 (0-16)
Age of disease diagnosis (years)	6 (1-17)
Fever	619 (79.2%)
Abdominal pain	648 (82.9%)
Chest pain	164 (21%)
Arthritis	237 (30.3%)
-Acute monoarthritis	207 (26.5%)
-Chronic Arthritis	67 (8.5%)
Arthralgia	496 (63.4%)
Erysipelas-like erythema	30 (3.8%)
Prolonged febrile myalgia	8 (1%)
Renal amyloidosis	2 (0.2%)
Colchicine resistance	52 (6.6%)
The dose of colchicine (mg/day)	1.47±0.6
Biological agent requirement	91 (11.6%)
Canakinumab	40 (5.1%)
Adalimumab	27 (3.4%)
Etanercept	15 (1.9%)
Anakinra	7 (0.9%)
Tocilizumab	1 (0.1%)
Certolizumab	1 (0.1%)

SD standart deviation min. minimum, max. maximum

Table 2: Comparison of the characteristics of familial Mediterranean fever-related arthritis according to genotype

	Total n (%)	Group 1* n (%)	Group 2* n (%)	Group 3* n (%)	p value
Arthritis	237 (30.3%)	91 (40.4%)	31 (24.8%)	115 (26.7%)	p=0.001
Acute monoarthritis	207 (26.5%)	79 (35.4%)	25 (20%)	103 (23.7%)	p=0.001
Chronic Arthritis	67 (8.5%)	22 (9.8%)	15 (%12)	30 (6.9%)	0.35
JSpA	29 (43.2%)	12 (54.5%)	3 (20%)	14 (46.7%)	0.27
oJIA	13 (19.4%)	4 (18.2%)	3 (20%)	6 (20%)	0.72
PolyJIA	8 (11.9%)	1 (4.5%)	4 (26.7%)	3 (10%)	p<0.05
sJIA	2 (3%)	1 (4.5%)	-	1 (3.3%)	0.72
JPsA	1 (1.5%)	-	-	1 (3.3%)	0.67
Undifferentiated JIA	14 (20.9%)	4 (18.2%)	4 (26.7%)	6 (20%)	0.40
Acute monoarthritis attack duration (day) (median, min-max)	2 (0-30)	2 (0-30)	1 (0-7)	1 (0-14)	p<0.05

JSpA juvenile spondyloarthropathy, oJIA oligoarticular juvenile idiopathic arthritis, PolyJIA polyarticular juvenile idiopathic arthritis, sJIA systemic juvenile idiopathic arthritis, JPsA juvenile psoriatic arthritis SD standart deviation min. minimum, max. maximum *Group 1: Patients homozygous for M694V Group 2: patients carrying other pathogenic MEFV variants (M694I, M680I, V726A) in exon 10 either in a homozygous or compound heterozygous state Group 3: Patients with other variants (homozygous, heterozygous or compound heterozygous) or without any mutation.

PP-29

SERUM LEVELS OF CITRULLINATED HISTONE H3 AS A MARKER OF NEUTROPHIL EXTRACELLULAR TRAPS AMONG PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is the most frequent autoinflammatory disease stemming from mutations in the MEFV gene, characterized by overactivation of innate immune system. Neutrophil extracellular traps (NETs) are shown to play a role in the pathogenesis of FMF. Citrullinated Histone H3 (CitH3) is a specific marker of NETosis.

Objectives: This study aims to evaluate formation of NETs among FMF patients with and without attack and FMF patients with amyloidosis by assessing serum levels of CitH3.

Methods: Blood samples (n=79) were collected from four groups, FMF patients during attack (n=18), the same FMF patients during the attack-free period (n=12), FMF patients with amyloidosis (n=28) and healthy volunteers (n=21). CitH3 levels were determined in duplicate by the enzyme-linked immunoabsorbent assay (ELISA).

Results: Serum levels of CitH3, CRP, NLR, urea, and creatinine are summarized in the table. Males constituted 55.2% of the FMF patients and the average age was 37.5 ± 11.8. All FMF patients had at least one Exon-10 mutation.

Median level of CitH3 was 82.9 (IQR, 59.9-106.6) among FMF patients with attack and 65.4 (IQR, 53.85-76.0) among healthy volunteers (p-value: 0.043). FMF patients without attack had a significantly increased median CitH3 level compared to healthy controls (74.75 [IQR, 67.7-79.0] vs 65.4 [IQR, 53.85-76.0], p-value: 0.048). Median CitH3 level of FMF patients with amyloidosis was significantly higher than healthy volunteers (77.2 [IQR, 69.48-90.53] vs 65.4 [IQR, 53.85-76.0], p-value: 0.004). Serum CitH3 levels were higher during attacks compared to attack-free period, but the difference did not reach statistical significance (p-value:0.42). Serum CitH3 levels positively correlated with NLR (p-value < 0.001, r: 0.748).

Conclusions: The results showed increased CitH3 levels among FMF patients during attack and attack-free periods indicating formation of NETs. Additionally, patients with amyloidosis had increased CitH3 levels which remarks increased formation of NETs in FMF patients with amyloidosis.

Keywords: Familial Mediterranean fever, NETosis

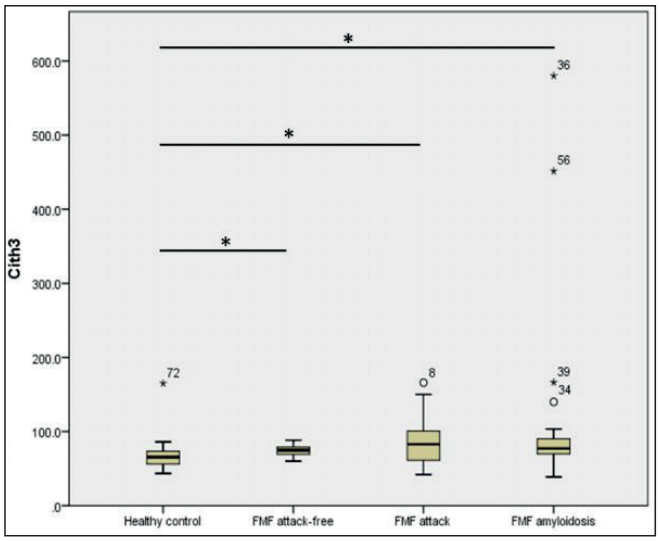

Figure 1. Boxplot illustration of serum CitH3 and its comparisons across study groups

Table 1. Demographic features and laboratory parameters across study groups

	FMF (during attack) (Median + IQR)	FMF (attack-free) (Median + IQR)	FMF (amyloidosis) (Median + IQR)	Healthy control (Median + IQR)
Age (years, mean ± SD)	34.47 ± 12.63	37.18 ± 13.57	40.1 ± 10.0	35.53 ± 8.29
Gender (female, %, n)	33.3 (6)	41.7 (5)	53.6 (15)	66.7 (14)
Cit-H3 (ng/mL)	82.9 (59.9-106.6)	74.75 (67.7-79.0)	77.2 (69.48-90.53)	65.4 (53.85-76.0)
CRP (mg/L)	44.4 (14.5-63.5)	2.6 (1.8-3.5)	3.3 (0.995-9.1)	0.95 (0.54-1.56)
NLR	4.9 (3.0-7.0)	1.9 (1.4-3.1)	-	-
Urea (mg/dL)	28.0 (21.0-32.5)	27.5 (22.3-34.0)	43.0 (31.5-58.0)	21.5 (19.0-27.0)
Creatinine (mg/dL)	0.77 (0.65-0.98)	0.85 (0.66-0.99)	1.1 (0.73-1.9)	0.68 (0.51-0.8)

PP-30

FABRY DISEASE ACCOMPANIED BY FAMILIAL MEDITERRANEAN FEVER: A CASE REPORT

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Introduction: Familial Mediterranean fever (FMF) is classified as an autoinflammatory disorder characterized by recurrent episodes of febrile serositis. Fabry disease (FD) is an X-linked lysosomal storage disorder resulting from mutations in the alpha-galactosidase A gene. The manifestations of FD consist of gastrointestinal, cutaneous, vascular, renal, and neurological symptoms. FMF and FD exhibit overlapping clinical manifestations, potentially resulting in diagnostic challenges and the misidentification of one condition as the other. This report presents a case initially diagnosed as FMF, which was later reevaluated and identified as FMF with FD through clinical evaluation.

Case report: An eighteen-year-old female presented to our clinic with pyrexia and abdominal discomfort. She exhibited elevated levels of acute phase reactants during attacks. No proteinuria was determined. Hearing impairment was not found. Bilateral corneal verticillata was noted during ocular examination, alongside optic disc

edema observed in the left eye. After genomic DNA sequence analysis, we showed that the patient had c.289G>C (p.A97P) heterozygous and M694V heterozygous mutations. She stated that she had mild extremity pain and numbness in her hands and feet. Following electromyographic assessment, she was diagnosed with sensory polyneuropathy. The activity of the α-galactosidase A (AGALA) enzyme and the analysis of the GLA gene were undertaken. The deficiency of AGALA was identified. Consequently, additional family members exhibiting similar manifestations underwent assessment for FD but did not exhibit aberrant results. As a result, the patient was evaluated as a sporadic FD case coexisted with FMF. Enzyme replacement therapy for FD was initiated, concurrently with colchicine treatment.

Discussion: FD is a rare disease mimicking FMF. The distinguishing between the two diseases for therapeutic approaches, follow-up procedures, and genetic counseling is needed. However, it is worth noting that, in exceptional cases such as the one presented in our study, the coexistence of these two entities can occur.

Keywords: Fabry disease, Familial Mediterranean fever

PP-31

COLCHICINE COMPLIANCE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER-RELATED AMYLOIDOSIS

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Purpose: In this retrospective cohort, we evaluated the colchicine compliance of patients diagnosed with Familial Mediterranean Fever (FMF)-related amyloidosis in our outpatient clinic between 1986 and 2016.

Method: A survey was administered to forty-one patients (18 males/23 females) regarding colchicine compliance. Additionally, the characteristics of the patients were noted from their files.

Results: There were 3 groups in our cohort; patients diagnosed with FMF before amyloidosis, patients diagnosed with FMF and amyloidosis simultaneously, and patients diagnosed with amyloidosis before FMF. The age of symptomatic onset of FMF was 7.13±5.24 years(as shown). The average age of starting colchicine treatment was 21.42±14.75 years, and the average age of amyloidosis diagnosis was 29.57±12.14 years. The duration of delayed diagnosis was 14.35±13.84 years. The maximum colchicine dose was 2.1 mg/day. In the follow-up of patients diagnosed with FMF before amyloidosis, colchicine compliance was poor (11/25, 44%), while dose skipping rates were also high (15/25, 68%); It was observed that colchicine compliance was better (12/13, 91%) and dose skipping rates were lower (2/13, 14%) in patients in whom FMF and amyloidosis were diagnosed simultaneously. One of the patients diagnosed with amyloidosis before FMF was compliant, and the other two were not; with missed doses. After the diagnosis of amyloidosis was confirmed, 31 (75%) of the patients complied with the treatment, and dose-skipping rates were low (12/41, 30%). Amyloidosis developed in five patients despite good compliance.Thirty-two patients (%78) had heterozygous or homozygous M694V.

Conclusion: Overall, diagnostic delay was high. Especially; compliance rates were lower in patients diagnosed with FMF before amyloidosis. There was also a group of patients who were diagnosed despite adequate and appropriate compliance. It was emphasized that early diagnosis and adequate treatment are important in preventing amyloidosis, while close follow-up is also important in the treatment of FMF patients.

Keywords: familial mediterranean fever related amyloidosis, compliance

Table 1. Clinical characteristics of patients

No. of patients, n (Male/Female)	41(18/23)
Age of symptoms onset, mean±SD, year	7.13±5.24
Age at diagnosis of FMF, mean±SD,year	21.21±14.85
Age at initiation of colchicine, mean±SD, year	21.42±14.75
Age at diagnosis of amyloidosis proven by biopsy, mean±SD, year	20.57±12.14
Disease duration, mean±SD, year	31.7±11.84
Delay at diagnosis, mean±SD year	14.35±13.84
FMF; familial mediterranean fever	

E-POSTERS

EP-01

TUBERCULOUS ARTHRITIS IN RHEUMATOLOGY PRACTICE: A CASE REPORT

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Introduction: Tuberculosis (TB) is a granulomatous infection caused by Mycobacterium tuberculosis. We present one patient with TB arthritis diagnosed in our clinic in 2022.

Case: A seventy-six-year-old woman complaining of swelling in her left ankle for 1 year was referred to an outside centre, where she was started on sulfasalazine, diclofenac, and adalimumab, but her symptoms persisted despite 2 months of treatment. The laboratory tests of our patient, who had arthritis in her left ankle, were unremarkable, PPD:0 mm, lung and sacroiliac radiography were normal. X-ray of the left ankle showed severe narrowing of the tibial-talar joint space and marked destruction of the distal tibia and talus. Contrast-enhanced computed tomography (CT) scan showed a nondisplaced fracture at the posterior malleolus of the tibia extending into the joint space and a periosteal reaction at the posterior distal tibia. Under ultrasound guidance, a 10 cc cloudy fluid sample was taken from the swelling at the level of the left ankle. Sampling revealed a positive tuberculosis ARB.

Discussion: Although pulmonary TB cases account for the majority of TB cases in our country, a high rate of 34.3% consists of extrapulmonary TB involvement (1). Although TB arthritis occurs in almost all joints, it usually occurs as monoarthritis in the hip or knee. Clinical findings usually include slowly progressive swelling, pain and loss of joint function. Constitutive symptoms such as fever and weight loss can be observed in only about 30% of cases (2). Our patient also had monoarthritis and no constitutional symptoms. In rheumatology practise and considering that tuberculosis cases are still common in our country and the PPD test is not reliable, we think it is important to perform sampling in patients with monoarthritis whenever possible and to exclude possible infectious causes, especially tuberculosis.

Keywords: arthritis, tuberculosis

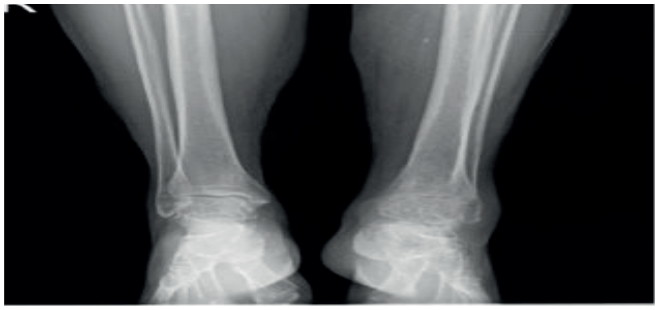

Figure 1. Left ankle radiograph of case

EP-02

RHEUMATOID ARTHRITIS AND SECONDARY AMYLOIDOSIS

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Introduction: In this presentation, we will discuss a case of seropositive rheumatoid arthritis (RA) in which secondary amyloidosis develops in a relatively short period of time.

Case: A 77-year-old male patient diagnosed with seropositive RA presenting with anemia and acute phase reactant elevation, was admitted to the hospital for etiological investigation. Apart from pleural effusion, no pathology was found and amyloidosis wasn't detected in the rectal biopsy (Figure-1). Sample was taken from pleural effusion was exudative but no pathology was found in microbiological and histopathological examinations. Despite antibiotic therapy, neighter clinical nor laboratory response was seen. Pleural effusion was considered to be related to RA. He was discharged with certolizumab therapy. The patient was readmitted with fever, left-sided flank pain, and hypotension less than a month later. Fluid sample from the persisting pleural effusion was found to be purulent. After diagnosed with empyema broad-spectrum antibiotics were started and surgical decortication was planned. During follow-up, the patient developed pretibial edema, proteinuria. Therefore, rectal biopsy was repeated. Staining with Amyloid-A (AA) was observed which was indicating secondary amyloidosis. After completion of antibiotic treatment and decortication operation, tocilizumab therapy was initiated.

Discussion: Amyloid storm (AS); defined as a more than 2-fold increase in serum creatinine and proteinuria and a 10-fold increase in C-reactive protein (CRP) within less than 2 weeks, usually following an infection in individuals with amyloidosis. In our case, there was an increase in serum creatinine (from 1.05 mg/dl to 1.77 mg/dl), proteinuria (from 410 mg/day to 2297 mg/day), elevated acute phase reactants and rapid development of amyloidosis within a period of less than a month. Although our case did not fulfill the criteria for AS, we wanted to report the case due to the rarity of such a presentation in RA.

Keywords: Rheumatoid Arthritis, Secondary Amyloidosis

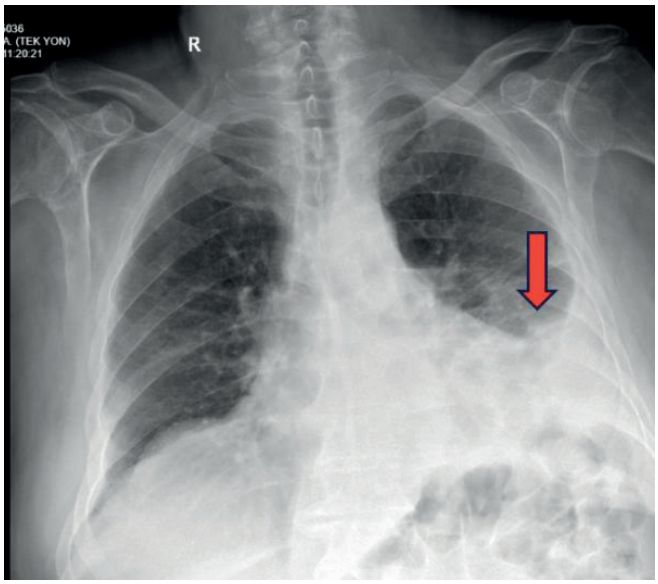

Figure 1. Pleural Effusion (Red Arrow)

EP-03

TREATMENT RESISTANT ADULT ONSET STILL CASE

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Introduction: Adult-onset Still disease is a rare clinical entity that can occasionally overwhelm all available therapeutic options, posing a fatal risk. We would like to share a clinical course of a treatment-resistant case.

Case: An eighteen-year-old female patient was diagnosed with adult-onset Still's disease, presenting with splenomegaly, generalized lymphadenopathy, fever, rash, sore throat, elevated ferritin, and hypertriglyceridemia without proof of malignancy or infectious cause on comprehensive work-up. Thus, 100 mg per day of Anakinra and pulse methylprednisolone were administered. After seven months, the treatment regimen had to be switched to tocilizumab due to in-

creased plasma ferritin and C-reactive protein levels. Canakinumab was the next course of action, yet the administration of canakinumab had to be stopped due to elevated liver function tests. Uncontrolled inflammation led to the development of a second MAS; tofacitinib was prescribed as a course of action.

After three months, she revealed shortness of breath, which was attributed to concomitant primary pulmonary hypertension, as proved by right cardiac catheterization. As the treatment refraction was marked, regimens were altered in the following order; anakinra 200 mg/day, then tocilizumab 8 mg/kg/twice a month with cyclosporin A, and finally baricitinib.

Ultimately, a combination of the 100 mg/day of anakinra and the 4 mg/day of baricitinib was decided. Despite four flare-ups in one year, we achieved clinical and biochemical remission with the current combination protocol. No adverse events were observed during the long treatment courses. Pulmonary capillary wedge pressure and mean pulmonary artery pressure were dramatically decreased with the treatment of pulmonary hypertension as well as systemic inflammation control.

Conclusion: This was the first case of adult-onset still disease treated by anakinra and baricitinib together. In the future, it might be possible to use combinatory regimens to target multiple cytokines in unresponsive patients in this disease.

Keywords: Adult-onset still disease, Baricitinib

EP-04

TREATMENT WITH RUXOLITINIB IN VEXAS SYNDROME: A CASE REPORT

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Introduction: VEXAS (Vacuoles, E1 Enzyme, X-Linked, Autoinflammatory, Somatic) syndrome is a rare, adult-onset multisystemic autoinflammatory syndrome caused by a somatic mutation in the UBA-1 gene on the X chromosome. Here, we present a case of VEXAS Syndrome diagnosed and treated with Ruxolitinib in our clinic.

Case: A 65-year-old male patient presented with weakness, fatigue, and a weight loss of 15 kilograms over the past 2 months. Thyrotoxicosis was diagnosed, and the patient was admitted to the endocrinology service. Investigations during hospitalization revealed macrocytic anemia, leukocytosis, splenomegaly, elevated sedimentation rate, and high CRP levels. The patient developed high fever during the hospital stay, but cultures were negative. Bone marrow biopsy were normal. Abdominal CT scan revealed hepatosplenomegaly and a hypodense lesion in the spleen (infarct?). Thoracic CT scan showed left pleural effusion. Orbital MRI was performed due to ptosis, revealing inflammation in bilateral retrobulbar fat tissue. Despite classic immunosuppressive therapies, the patient's condition progressed. Biopsy of painful erythematous lesions on the left ear, behind the ear, and scalp revealed findings consistent with acute neutrophilic dermatosis. EMG revealed ulnar nerve neuropathy on the left side. Due to poor response to conventional immunosuppressive therapies and progressive clinical course, VEXAS syndrome was considered. Bone marrow biopsy was repeated, revealing vacuoles consistent with VEXAS syndrome. Mutation analysis of UBA-1 sent from bone marrow came back positive. The patient was started on ruxolitinib 1x10 mg, and clinical and laboratory responses were observed after treatment initiation.

Conclusion: VEXAS Syndrome can present with diverse clinical manifestations and may mimic rheumatological and hematological disorders. Especially in elderly male patients presenting with clinical features suggestive of rheumatological disease accompanied by macrocytic anemia and refractory elevation of acute phase reactants, VEXAS Syndrome should be considered. While data on the treatment of VEXAS syndrome are limited, ruxolitinib shows promise.

Keywords: Ruxolitinib, VEXAS syndrome

EP-05

A CASE OF BEHÇET'S SYNDROME PRESENTING WITH ACUTE CORONARY SYNDROME

Gamze Akkuzu, Bilgin Karaalioğlu, Duygu Özgür, Rabia Deniz, Fatih Yıldırım, Cemal Bes

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Introduction: Behçet's Syndrome (BS) is a systemic vasculitis that can affect both veins and arteries. Cardiac involvement is rare in BS, but the important point is that cardiac involvement may be the first manifestation of BS. We present a young male case diagnosed with BS after acute coronary syndrome caused by coronary artery aneurysms and thrombosis.

Case: A 26-year-old male patient presented to the emergency department with the complaint of severe retrosternal chest pain that started that morning. Meanwhile, in the laboratory tests at the time of admission, troponin t was 27.4 ng/L (<14) and c-reactive protein (CRP) was 73 mg/L (<5). CAG revealed a total occlusion of the left anterior descending artery (LAD) from the mid-segment (Figure 1), and balloon dilatation, thrombectomy, intracoronary tirofiban were performed. The patient's chest pain decreased. Control CAG was planned after tirofiban infusion due to the presence of coronary saccular aneurysm and continuation of dense thrombus, and thrombolysis in myocardial infarction grade II/III flow (TIMI-II/III). Upon regression of dense thrombus and TIMI-III flow monitoring in CAG, a 2.75X 24 mm stent was implanted distally and a 4.0X28 mm stent proximally overlapped with the distal. Optimal patency was achieved (Figure 1). The patient stated that he had recurrent genital ulcers for 2 years and oral aphthous lesions since earlier times. Pulmonary, coronary and abdominal CTA were performed. There were thrombosed appearances accompanied by aneurysmatic dilatation on the right in the branches going to the bilateral lower lobe of the pulmonary arteries. The treatment of the patient was continued with methylprednisolone (with gradual dose tapering) and monthly cyclophosphamide. Hemoptysis did not recur in the ongoing follow-up of the patient.

Conclusion: The presence of cardiac involvement worsens the prognosis of BS and therefore early diagnosis and early initiation of immunosuppressive therapy are vital.

Keywords: Coronary aneurysm, Behçet's syndrome

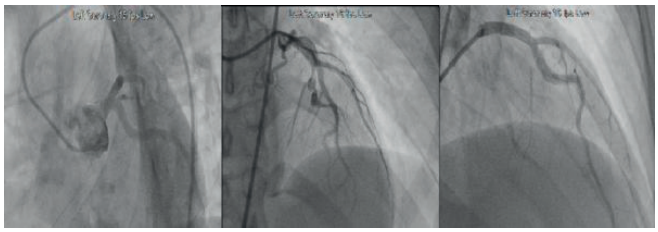

Figure 1. Coronary interventions, respectively (the aneurysm is increasing in the middle image, flow delivered by stents in final image).

EP-06

A FAMILY, TWO INTERFERONOPATHIES: AICARDI-GOUTIÈRES SYNDROME

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Introduction: Type 1 interferonopathies are disorders stemming from the dysregulation of the interferon response. This dysregulation gives rise to both autoinflammatory and autoimmune pathologies. These conditions often present with characteristic features found in connective tissue diseases, including panniculitis, livedo reticularis, chilblains, and interstitial lung disease. Recently, the use of Janus kinase(JAK) inhibitors has been reported as potential therapeutic interventions for certain rare diseases within this spectrum. We wanted to present a sibling pair who have been followed up as connective tissue disease patients since childhood, and subsequently diagnosed with Aicardi-Goutières syndrome(AGS) through genetic testing.

Case Presentation: The elder of the two siblings(46 years old), who presented with difficulty in walking, thickening of the skin, and auto-amputations of the fingers, was found to have symptoms starting from the neonatal period. The patient had been followed up as undifferentiated connective tissue disease for many years due to his complaints and autoantibodies. It was learned that the complaints of the younger sibling(32 years old) began at the age of two. The patient presented with difficulty in walking, wounds on the fingertips, and chilblains, and was followed up as mixed connective tissue disease due to the compatibility of his autoantibody profile. It was determined that the patients, who had received various treatments regulating autoimmunity for many years, did not have significant kidney or lung involvement. Genetic testing was conducted for the patients, and the results were found to be consistent with AGS. Upon reports of significant improvement in patients with chronic elevation of Type-1 interferon signaling with JAK-inhibition, the patients were started on JAK inhibitors as treatment.

Conclusion: Interferonopathies are highly rare diseases. Particularly in patients whose symptoms start in the neonatal period, differential diagnosis may involve congenital infections. Although there is not yet complete consensus on their treatment, JAK-inh appear to be beneficial.

Keywords: interferonopathy, jak-inhibitor

EP-07

RHEUMATOID ARTHRITIS REACTIVATED BY BILATERAL PLEURAL EFFUSION

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Introduction: 60% of RA patients have lung involvement can be encountered with various clinical pictures according to pleura, parenchyma and airway involvement(1,2).

Case: A 63-year-old female patient who was diagnosed with seropositive RA 2 years ago was admitted to our outpatient clinic with joint pain and dry eyes while taking Methotrexate (MTX) 15 mg/hf subcutaneous (sc) for a year. He did not have active arthritis. CCP>500, RF 121.7, ANA (-), ENA(-), CRP 2.06 mg/l, sedimentation 24/hr were detected in the tests. MTX 15mg/hf sc treatment was continued. While the patient was in MTX treatment a year later, he applied with complaints of fever, chills, chest pain. There was no active arthritis. Bilateral pleural effusion was detected in Thoracic Computed Tomography (CT). There was no parenchyma involvement. The patient's CRP was 159mg/l, sedimentation was 71mm/hr. In pleural fluid analysis; glucose was < 1mg/dl, protein was 62.1 g/dl, LDH 3808U/l, ARB (-). There was no reproduction in culture. PE in the patient was evaluated as lung involvement of RA. The patient's MTX treatment was discontinued and Leflunomide 20 mg/day and prednisolone 5 mg/day was started. Ten days later, CRP 2.11 mg/l, sedimentation 25/h and PA chest X-ray had a regression in pleural effusion.

Discussion: Pleural effusion may occur as a symptom of disease exacerbation or asymptomatic before the start of RA joint involvement or after diagnosis(3). We also evaluated our case as RA exacerbation, which is manifested pleural effusion while under MTX treatment. With the initiation of KS and replacement of DMARD, we saw a dramatic improvement in pleural effusion and acute phase indicators. It should not be forgotten that a patient with RA may have an exacerbation of the disease with pleural effusion without arthritis while under treatment.

Keywords: Pleural effusion, Rheumatoid Arthritis

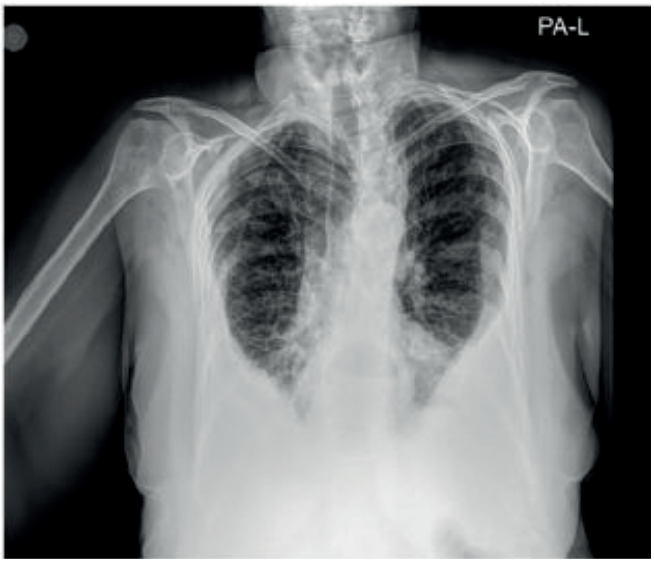

Figure 1. Bilateral pleural effüsion

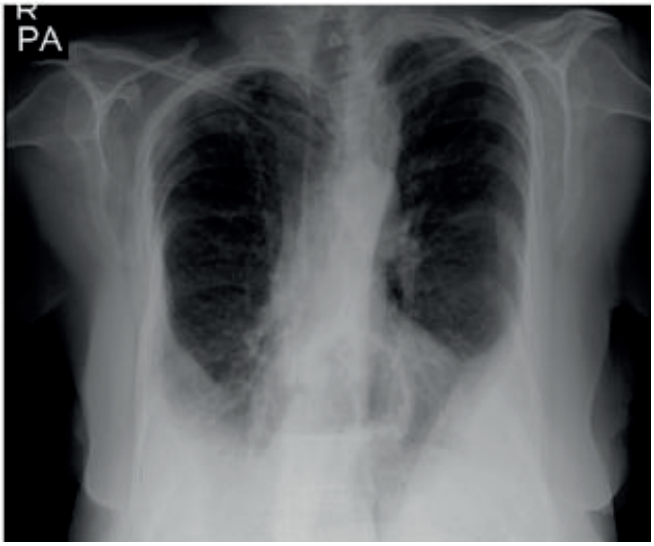

Figure 2. Regration of pleural effusion on 14 th. of treatment

EP-08

CASE REPORT: LATE ONSET BEHÇET'S DISEASE

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Behçet's disease (BD) is more commonly diagnosed between the second and fourth decades. Onset after 50 years of age is a rare condition. Here we will present a 60-year-old patient diagnosed with Behcet's disease.

60 year old man was admitted to the our clinic with with the symptom of bilateral tender red nodules on the anterior tibia. At the age of 57, he was diagnosed seronegative rheumatoid arthritis after oligoarthritis in the lower limbs and treated with methotreaxate and short-term steroids. He was complaining of recurrent mouth ulcerations. There were no genital ulsers or scar. There was no history of vascular involvement or uveitis. Crp was elevated, 31 mg/L (0-5 mg/L), at the admission. Serologic workup revealed negative rheumatoid factor (RF), anti-cyclic citrullinated protein (anti-CCP) antibodies, antinuclear antibodies (ANA) and antineutrophil cytoplasmic antibodies (ANCA). Serum Ace level was slightly increased(68 U/L, range:13-63.9), but there was no hilar lymphadenopathy or parenchymal involvement suggestive of sarcoidosis on thorax CT. As a result of the skin biopsy, neutrophil-rich perivascular dermatitis and panniculitis were considered. The skin pathergy test was conducted using 20G needle pricks and additional application of 23-valent polysaccharide pneumococcal vaccine, as a result pustular positive reaction was observed. With the history of oligoarthritis, recurrent mouth ulcerations, erythema nodosum and positive pathergy test patient diagnosed Behçet's Disease. The symptoms were releaved after the administration of colchicine, methylprednisolone, and azathioprine.

Although Behçet's disease generally affects young adults, it should be considered in the presence of clinical symptoms in older patients.

Keywords: Behçet's disease, eyrthema nodosum

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