Familial Mediterranean Fever & Other Autoinflammatory Diseases

International Online Meeting

FMF2021.org

Cerrahpasa Rheumatology Society 1983

ABSTRACT BOOK

SCIENTIFIC PROGRAM

May 17, 2021 (Monday)

Time Zone: (GMT+3)

17.00-17.15 **Welcome**

Huri Özdoğan

University of Istanbul-Cerrahpasa, Turkey

SESSION 1 **Crossing roads: *Genes, pandemias and disease***

Chairs

Eldad Ben-Chetrit — *Hadassah-Hebrew University, Israel*

Mehmet Tunca — *Dokuz Eylül University, Turkey*

Huri Özdoğan — *University of Istanbul-Cerrahpasa Turkey*

17.15-17.45 **From the footprints of MEFV and FMF**

Eldad Ben-Chetrit

Hadassah-Hebrew University, Israel

17.45-18.15 **Plague pandemias in FMF geography**

Nükhet Varlık

Department of History, Rutgers University – Newark, US

18.15-18.45 **The impact of Yersinia pestis in the evolution of FMF mutations**

Daniel Kastner

National Institutes of Health, USA

18.45-19:00 Discussion

19.00-19.30 **Covid-19, autoinflammation and FMF**

Ahmet Gül

University of İstanbul,Turkey

19.30-19.45 Discussion

19.45-20:00 **Oral Presantation**

No Protective or Ameliorative Effect of Regular Doses of Colchicine or Hydroxychloroquine Treatment on COVID-19 in Patients with Different Underlying Diseases: A Comparative Study with Household Contacts

Mert Öztaş

Clinical Features and the Course of COVID-19 in Patients with Familial Mediterranean Fever

Abdurrahman Tufan

May 18, 2021 (Tuesday)

Time Zone: (GMT+3)

SESSION 2 — **Changing concepts and needs in genetics of FMF**

Chairs

Seza Özen
Hacettepe University, Turkey

Marco Gattorno
G. Gaslini Institute for Children, Italy

17.00-17.30	**Update: Genetics of FMF, clinical vs genetic FMF** **Seza Özen** *Hacettepe University, Turkey*
17.30-18.00	**Current and future advances in genetic testing for FMF & other autoinflammatory diseases** **Ivona Aksentijevich** *National Institutes of Health, USA*
18.00-18.30	**Impact of rare variants in FMF and MEFV as a modifier gene** **Yael Shinar** Sheba Medical Center, Israel
18.30-18.50	Discussion

SESSION 3 — **The impact of epigenetics and environment in FMF**

Chairs

Isabelle Touitou
Université de Montpellier, France

Abdurrahman Tufan
Gazi University, Turkey

19.00-19.30	**Update: Epigenetics and FMF** **Eda Tahir Turanlı** *Istanbul Technical University, Turkey*
19.30-20.00	**Enviroment and microbiota in FMF** **Sophie Georgin-Lavialle** Sorbonne University, France
20.00-20.20	Discussion

May 19, 2021 (Wednesday)

Time Zone: (GMT+3)

SESSION 4 — **Changing concepts and needs in clinical aspects of FMF**

Chairs

Avi Livneh
Sheba Medical Center,Israel

Fatoş Önen
Dokuz Eylül University, Turkey

16.00-16.30 **Changing concepts and needs in FMF: from nosology to prognosis**
Ilan Ben-Zvi
Sheba Medical Center, Israel

16.30-17.00 **FMF and associated diseases: Ankylosing Spondylitis and beyond**
Servet Akar
Izmir Katip Celebi University, Turkey

17.00-17.20 Discussion

SESSION 5 — **Changing concepts and needs in pediatric FMF**

Chairs

Özgür Kasapçopur
University of Istanbul-Cerrahpaşa, Turkey

Fatoş Yalçınkaya
University of Ankara, Turkey

17.30-18.00 **Pediatric FMF, overlap with JIA and other autoinflammatory diseases**
Yosef Uziel
Tel-Aviv University, Israel

18:00-18:15 **Oral Presantation**

Evaluation of the Medical Conditions of First-degree Relatives of Patients with Familial Mediterranean Fever
Fatih Haslak

From mild to severe distinct faces of adenosine deaminase 2 deficiency in the single pediatric rheumatology center study
Betül Sözeri

18:15-18:30 Discussion

18.30-19.00 **Break**

19.00-19.30 **SATELLITE SYMPOSIUM - NOVARTIS**

Chairs **Huri Özdoğan*** **Serdal Uğurlu***

**University of Istanbul-Cerrahpasa, Turkey*

Long-term safety and efficacy of anti-IL-1b treatments from the window of CAPS

Helen Lachmann

University College London, England

SESSION 6 **Changing concepts and needs in the treatment of FMF**

Chairs **Helen Lachmann** University College London, England. **Serdal Uğurlu** *University of Istanbul-Cerrahpasa, Turkey*

19.30-20.00 **Colchicine treatment**

Eldad Ben-Chetrit

Hadassah-Hebrew University, Israel

20.00-20.30 **Alternative treatments**

Huri Özdoğan* **Serdal Uğurlu***

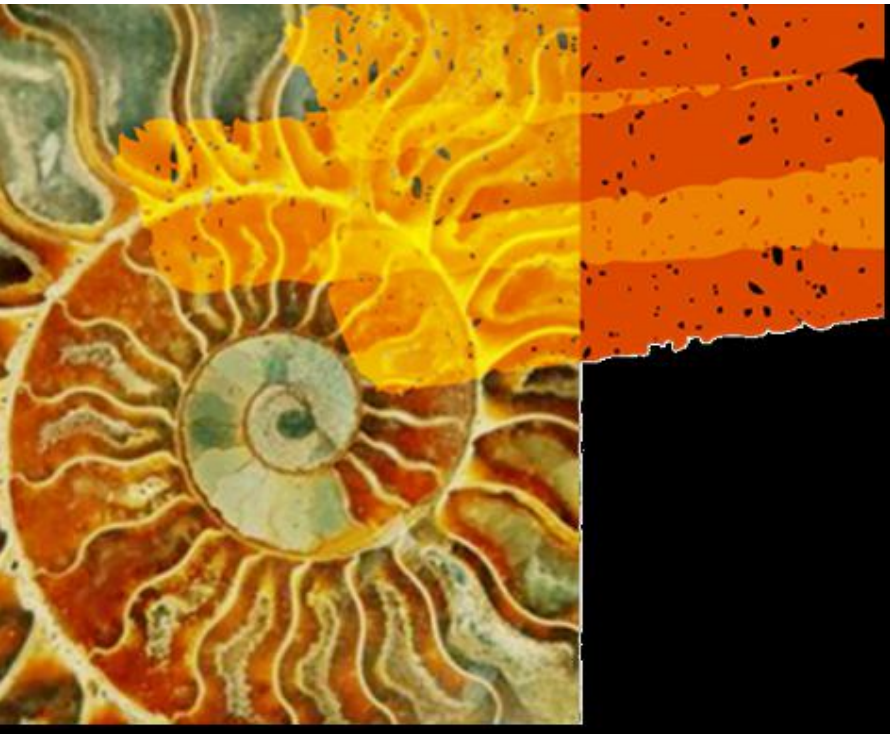
**University of Istanbul-Cerrahpaşa, Turkey*

20.30-20.50 Discussion

20.50-21.00 **Closing remarks**

Huri Özdoğan

University of Istanbul-Cerrahpaşa, Turkey



Oral Presentations

OP-01

Clinical Features and the Course of COVID-19 in Patients with Familial Mediterranean Fever

Aslihan Avanoglu Guler[1], Tuba Yuce Inel[2], Hazan Karadeniz[1], Reyhan Bilici Salman[1], Hasan Satiş[1], Hamit Kucuk[1], Mehmet Akif Ozturk[1], Berna Goker[1], Seminur Haznedaroglu[1], Ismail Sari[2], Timucin Kasifoglu[3], Abdurrahman Tufan[1]
[1]Rheumatology Department, Gazi University Faculty of Medicine Hospital, Ankara, Turkey
[2]Rheumatology Department, Dokuz Eylul University Faculty of Medicine Hospital, Izmir, Turkey
[3]Rheumatology Department, Eskisehir Osmangazi University Faculty of Medicine Hospital, Eskisehir, Turkey

Background: The novel coronavirus 2019 (COVID-19) has a wide range of clinical presentation from asymptomatic or mild viral infection to severe life-threating complications, including acute respiratory distress syndrome (ARDS), which develop as a result of immune system dysregulation, exaggerated immune response, and cytokine release syndrome. Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disorder characterized by dysfunction of the innate immune system and excessive production of proinflammatory cytokines, including interleukin (IL)-1β, IL-6, interferon-gamma, and tumor necrosis factor-alpha, all of which have increased in severe cases in COVID-19.
Objectives: The aim of this study is to report clinical characteristics and outcome of FMF patients with COVID-19.
Methods: This study included 48 consecutive FMF patients who were diagnosed COVID-19 by SARS-CoV-2 nucleic acid RT-PCR in nasopharyngeal swab or sputum, or symptoms and computed tomography findings suggestive for COVID-19. Data on demographic and clinicalcharacteristics of FMF disease, clinical course and outcome of COVID-19 were evaluated.
Results: The median age of patients was 35.5 (29-43.5) years, ranging from 18 to 87 years. The median disease duration of FMF was 10 (6-16) years. The most common presenting symptoms and signs of patients during attacks were peritonitis (85.5%), fever (81.3%), and pleuritis (48%). Twelve (25%) patients had amyloidosis. Comorbidities were present in half ofpatients with ankylosing spondylitis (21%) and hypertension (17%) being the most frequentlyseen. Two-third of patients (66%) were in remission for FMF. The median dosage of colchicine for FMF was 1.5 (IQR 1) mg/day. 90% of patients continued colchicine treatment for FMF during the COVID-19 course. The baseline characteristics and treatment modalities of patients were demonstrated in Table 1. Forty-six patients presented with at least one COVID-19 symptoms. Fever (73%), myalgia/arthralgia (69%), and cough (60%) were the mostcommon symptoms. 16 patients were admitted at hospital, 5 of them required oxygen therapy and 2 patients with amyloidosis developed ARDS and went to intensive care unit (ICU) for invasive mechanical ventilation (IMV). One patient who had been followed-up at ICU died.

Conclusions: Our FMF patients with COVID-19 have similar clinical features and outcomes as general population. Dysregulation of innate immune system in FMF might not be risk factors for COVID-19. Besides, colchicine and IL-1 inhibitors intake might have protective and preventive effects on COVID-19 progression.

Keywords: Familial Mediterranean Fever, COVID-19

Table 1 Baseline characteristics, treatment modalities and outcome of patients

Age years, median (IQR)	39.4 (15)
Gender (F/M)	25/23
FMF Disease duration, years, median (IQR)	10 (10)
Mutations*, n (%)	
Monoallelic mutation	6 (14)
Biallelic mutation	34 (81)
Homozygous M694V mutation	18 (43)
Heterozygous M694V mutation	15 (36)
Comorbidities, n (%)	24 (50)
FMF treatment	
Colchicine 1 mg/day, n (%)	17 (35.5)
Colchicine 1.5 mg/day, n (%)	18 (37.5)
Colchicine 2 mg/day, n (%)	13 (27)
Anakinra, n (%)	12 (25)
Canakinumab, n (%)	3 (6.3)
Positive SARS-Cov-2 RT-PCR, n (%)	42 (87.5)
Interstitial pneumonia in CT scan, n (%)	15 (31.3)
COVID-19 treatment, n (%)	46 (95.8)
Outpatient treatment, n (%)	32 (66.7)
Hospitalized, not required supplemental oxygen, n (%)	9 (18.8)
Hospitalized, required supplemental oxygen, n (%)	5 (10.4)
ICU, required IMV, n (%)	2 (4.2)
Outcome	
Recovered, n (%)	47 (98)
Deceased, n (%)	1 (2)
Complications, n (%)	3 (6.3)

**42 patients were included in the analysis*

OP-02

No Protective or Ameliorative Effect of Regular Doses of Colchicine or Hydroxychloroquine Treatment on COVID-19 in Patients with Different Underlying Diseases: A Comparative Study with Household Contacts

Mert Öztaş1, Murat Bektaş2, Ilker Karacan3, Numune Aliyeva2, Gulen Hatemi1, Sarvan Aghamuradov2, Murat Bolayirli4, Selma Sari2, Emire Seyahi1, Huri Ozdogan1, Ahmet Gul2, Serdal Ugurlu1
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2Istanbul University, Department of Medicine, Division of Rheumatology,Istanbul,Turkey
3Istanbul Medeniyet University, Science and Advanced Technology Research Center, Istanbul,Turkey
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Objectives. To investigate whether patients regularly using colchicine or hydroxychloroquine (HCQ) have an advantage of protection from COVID-19 or developing a less severe disease.

Methods. Patients who were taking colchicine or HCQ regularly for a rheumatic disease including Familial Mediterranean Fever, Behçet's syndrome, Systemic Lupus Erythematosus, Rheumatoid Arthritis and Sjogren's syndrome as well as their healthy household contacts as the control group were included into the study. The clinical data regarding COVID-19 were collected using a standard form, and serum samples were analyzed for anti-SARS-COV-2 nucleocapsid IgG. Patients and household controls were compared regarding the prevalence and severity of COVID-19.

Results. A total of 635 regular colchicine users with their 643 household contacts and 317 regular HCQ users with their 333 household contacts were analyzed. Anti-SARS-Cov2 IgG was positive in 43 regular colchicine users (6.8%) and 35 household contacts (5.4%, p=0.3). COVID-19 related symptoms were described by 29 (67.4%) of the patients and 17 (48.6%) household contacts (p=0.09), and hospital admission was observed in five (11.6%) and one (2.9%) of these subjects (p=0.1), respectively. Seropositive subjects were observed in 22 regular HCQ users (6.9%) and 24 household contacts (7.2%) (p=0.8). COVID-19-related symptoms occurred in 16 (72.7%) of the 22 patients and 12 (50%) of 24 household contacts (p=0.1). Three patients (13.6%) were admitted to hospital, while one household contact (4.2%) was hospitalized (p=0.2)

Conclusion. Being on a regular treatment of colchicine or HCQ was not resulted in the prevention of COVID-19 or amelioration of its manifestations.

Keywords: Covid-19, colchicine

Figure

Table 1. Demographic features and anti-SARS-COV-2 Nucleocapsid Ig G status of entire subjects.

	Colchicine			Hydroxychloroquine		
Characteristics	Patients (N=635)	Household contacts (N=643)	P value	Patients (N=317)	Household contacts (N=333)	P value
Age, mean ± SD years	39.1 ± 12.9	37 ± 15.8	0.01	48.3 ± 12.9	40.5 ± 16.8	0.001
Gender, n (%)						
Male	226 (25.6)	352 (54.7)	0.001	19 (6.0)	228 (68.5%)	0.001
Female	409 (64.4)	291 (45.3)		298 (94.0)	105 (31.5%)	
Mean colchicine dose, mg/day ± SD	1.5 ± 0.4	N/A	N/A	N/A	N/A	N/A
Mean duration of colchicine usage, years ± SD	11.3 ± 8.3	N/A	N/A	N/A	N/A	N/A
Mean HCQ dose, mg/day ± SD	N/A	N/A	N/A	263.4 ± 99.4	N/A	N/A
Mean duration of HCQ usage, years ± SD	N/A	N/A	N/A	9 ± 6.3	N/A	N/A
Positive antibody to SARS-COV-2, n (%)	43 (6.7)	35 (5.4)	0.3	22 (6.9)	22 (7.2%)	0.8
Symptomatic COVID-19 in seropositive cases, n(%)	29 (67.4)	17 (48.6)	0.09	16 (72.7)	12 (50.0%)	0.1
Hospital admission in seropositive cases, n (%)	5 (11.6)	1 (2.9)	0.1	3 (13.6%)	1 (4.2%)	0.2
Prior confirmed COVID-19 cases, n (%)	20 (2.8)	6 (0.9)	0.005	16 (5%)	5 (1.5%)	0.01
Positive antibody to SARS-COV-2 in prior confirmed cases, n (%)	17 (83.3)	5 (83.3)	0.9	13 (81.2%)	4 (80%)	0.9
Total hospital admission, n (%)	7* (1)	2** (0.003)	0.09	5 †	1	0.8

*Two Behcet' syndrome cases who did not seroconvert were hospitalized.
**One household contact of a Behcet' syndrome who did not seroconvert was hospitalized.
†One SS case who did not seroconvert was hospitalized.

Demographic features and anti-SARS-COV-2 Nucleocapsid Ig G status of entire subjects.

OP-03

Evaluation of the Medical Conditions of First-degree Relatives of Patients with Familial Mediterranean Fever

Sema Yildirim, Fatih Haslak, Mehmet Yildiz, Ayten Aliyeva, Oya Koker, Amra Adrovic, Sezgin Sahin, Kenan Barut, Ozgur Kasapcopur
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Introduction: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease. It was recently shown that the most common additional two diseases were juvenile idiopathic arthritis (JIA) and immunoglobulin (Ig) A vasculitis in children with FMF. Furthermore, it was demonstrated in the studies involving all age groups that the frequencies of spondyloarthropathies, Behçet disease, Sjögren disease, polyarteritis nodosa (PAN), inflammatory bowel diseases, multiple sclerosis (MS), and psoriasis were increased in patients with FMF.
Aim: Given the strong genetic background of FMF, the diseases that have been previously demonstrated as co-exists in children with FMF should also be investigated in the other family members. Therefore, we aimed to examine the diseases of first-degree relatives (FDRs) of our pediatric patients with FMF in the present study.
Materials-Method: In total, 449 patients with FMF and 147 patients with JIA who are being followed up at Istanbul University-Cerrahpasa Department of Pediatric Rheumatology and 93 healthy controls were interviewed between March 2019- November 2019 during routine outpatient visits. The medical conditions of their FDRs were asked. Among the FDRs of index cases, those with FMF were excluded from the study.
Results: The mean age of healthy children (n=93), patients with FMF (n=449), and patients with JIA (n=147) were 7.7 ± 4.6 years, 12.6 ± 4.8 years, and 11.6 ± 5.2 years, respectively. A total of 3071 FDRs (FMF:1975, JIA: 690, Healthy Children: 406) were included in the study. While the most common medical conditions reported among the FDRs of the patients with FMF were asthma (n=90, 4.5%), tonsillectomy history (n=66, 3.3%) and type 2 diabetes (n=59, 2.98%), the most common medical conditions detected among the FDRs of the patients with JIA were type 2 diabetes (n=17, 2.4%), asthma (n=15, 2.1%) and tonsillectomy history (n=13, 1.8%). Among the FDRs of the healthy children, asthma (n=15, 3.69%), tonsillectomy history (n=12, 2.95%), and type 2 diabetes (n=6, 1.47%) were the most commonly detected ones. The frequencies of acute rheumatic fever (ARF), asthma, allergic rhinitis, and appendectomy history were significantly higher among the FDRs of the patients with FMF compared to other FDRs (all <0.05) (Table 1).
Discussion: This is the first study evaluating the FDRs of patients with FMF. ARF, asthma, allergic rhinitis, and appendectomy history were found to be significantly more frequent in FDRs of the patients with FMF compared to the FDRs of healthy children and the patients with JIA.

Keywords: familial Mediterranean fever

Table 1: The comparison of the diseases reported among the 1st degree relatives of the participants between the groups.

	FMF† (n=1975)	JIA‡ (n=690)	Healthy Control (n=406)	p value
Henoch-Schönlein Purpura	1 (0.05)	1 (0.14)	0 (0)	0.98
Behçet's Disease	11 (0.5)	0 (0)	2 (0.49)	0.11
Juvenile Idiopathic Arthritis	5 (0.25)	1 (0.14)	0 (0)	0.54
Rheumatoid Arthritis	23 (1.1)	7 (1)	0 (0)	0.09
Ankylosing Arthritis	5 (0.25)	4 (0.5)	2 (0.49)	0.41
Systemic Lupus Erythamatosus	1 (0.05)	0 (0)	0 (0)	0.64
Acute Rheumatic Fever	22 (1.1)	1 (0.14)	1 (0.24)	**0.01**
PFAPA syndrome††	2 (0.1)	0 (0)	0 (0)	0.57
Crohn Disease	1 (0.05)	0 (0)	0 (0)	0.75
Ulcerative Colitis	2 (0.1)	0 (0)	1 (0.24)	0.45
Celiac Disease	1 (0.05)	0 (0)	1 (0.24)	0.27
Autoimmune Hepatitis	0 (0)	1 (0.14)	0 (0)	0.17
Uveitis	7 (0.35)	0 (0)	0 (0)	0.20
Psoriasis	14 (0.7)	1 (0.14)	2 (0.49)	0.22
Multiple Sclerosis	2 (0.1)	1 (0.14)	1 (0.24)	0.59
Type 2 Diabetes	59 (2.98)	17 (2.4)	6 (1.47)	0.22
Asthma	90 (4.5)	15 (2.1)	15 (3.69)	**0.02**
Atopic Dermatitis	43 (2.1)	12 (1.7)	3 (0.73)	0.14
Allergic Rhinitis	35 (1.7)	4 (0.5)	1 (0.24)	**0.008**
Hypothyroidism	50 (2.5)	13 (1.8)	6 (1.47)	0.32
Hyperthyroidism	11 (0.5)	4 (0.5)	1 (0.24)	0.86
Food Allergy	1 (0.05)	1 (0.14)	0 (0)	0.58
Tonsillectomy	66 (3.3)	13 (1.8)	12 (2.95)	0.15
Adenoidectomy	34 (1.7)	12 (1.7)	5 (1.23)	0.76
Appendectomy	50 (2.5)	3 (0.4)	1 (0.24)	**0.000**
Scleroderma	1 (0.05)	0 (0)	0 (0)	1.00
Sjogren disease	1 (0.05)	0 (0)	0 (0)	1.00
Drug Allergy	2 (0.1)	0 (0)	0 (0)	0.71
Urticaria	2 (0.1)	1 (0.14)	0 (0)	1.00
Fibromyalgia	2 (0.1)	0 (0)	0 (0)	0.71
Cystic fibrosis	1 (0.05)	0 (0)	0 (0)	1.00
Thrombophilia	2 (0.1)	0 (0)	0 (0)	1.00
Ectodermal dysplasia	1 (0.05)	0 (0)	0 (0)	0.75
Sarcoidosis	1 (0.05)	1 (0.14)	0 (0)	0.58
Adrenal Insufficiency	0 (0)	1 (0.14)	0 (0)	0.35
Hemolytic Anemia	0 (0)	1 (0.14)	0 (0)	0.35
Amyloidosis	1 (0.05)	0 (0)	0 (0)	1.00
Cataract	0 (0)	1 (0.14)	0 (0)	0.35
Osteogenesis Imperfecta	0 (0)	1 (0.14)	0 (0)	0.35
Trisomy 18	0 (0)	1 (0.14)	0 (0)	0.35
Thalassemia	2 (0.1)	2 (0.28)	0 (0)	0.30
Goiter	13 (0.65)	2 (0.28)	1 (0.24)	0.48
Hodgkin Lymphoma	0 (0)	1 (0.14)	0 (0)	0.35
Acute Myeloid Leukemia	0 (0)	1 (0.14)	0 (0)	0.35
Myocarditis	0 (0)	1 (0.14)	0 (0)	0.35
Breast cancer	0 (0)	1 (0.14)	0 (0)	0.35
Epilepsy	3 (0.15)	1 (0.14)	0 (0)	0.85
Gut disease	1 (0.05)	0 (0)	1 (0.24)	0.29
Neuroblastoma	0 (0)	0 (0)	2 (0.49)	0.13
Vitiligo	0 (0)	0 (0)	1 (0.24)	**0.01**
Nephrolithiasis	0 (0)	0 (0)	1 (0.24)	0.13
Hirschsprung disease	0 (0)	0 (0)	1 (0.24)	0.13
Hypertension	0 (0)	0 (0)	1 (0.24)	0.13
Lymphedema	1 (0.05)	0 (0)	0 (0)	1.00
Brain tumor	1 (0.05)	0 (0)	0 (0)	1.00
Spastic paraplegia	1 (0.05)	0 (0)	0 (0)	1.00
Migraine	1 (0.05)	0 (0)	0 (0)	1.00
Precocious puberty	1 (0.05)	0 (0)	0 (0)	1.00
Gastritis	1 (0.05)	0 (0)	0 (0)	1.00
Colonic polyps	1 (0.05)	0 (0)	0 (0)	1.00

†Familial Mediterranean Fever, ‡Juvenile Idiopathic Arthritis, ††Periodic fever, aphthous stomatitis, pharyngitis, adenitis syndrome

The comparison of the diseases reported among the 1st degree relatives of the participants between the groups.

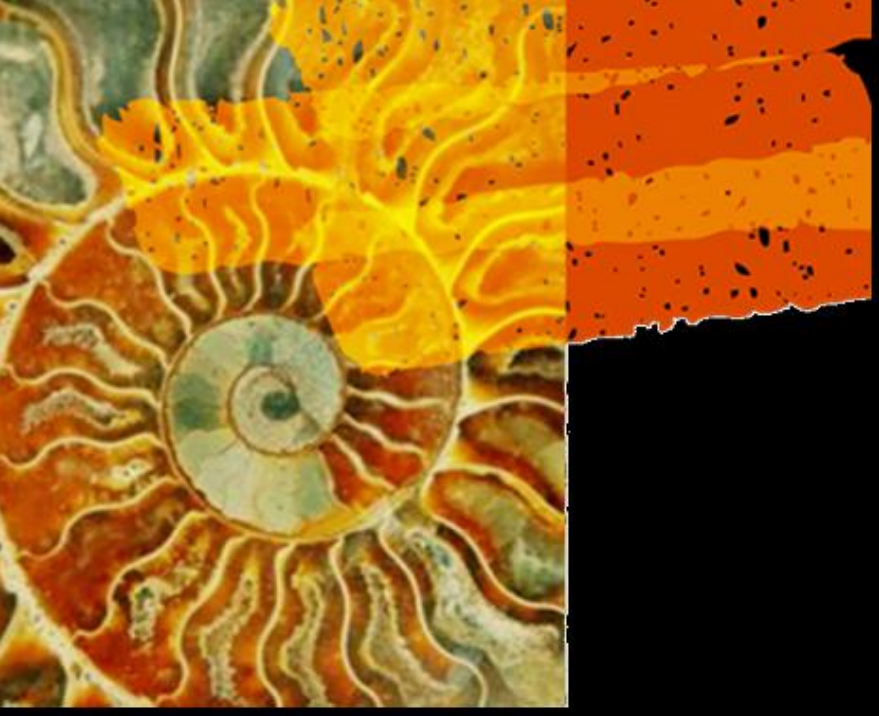
OP-04

From mild to severe distinct faces of adenosine deaminase 2 deficiency in the singlepediatric rheumatology center study

Betul Sozeri, Ferhat Demir
Sağlık Bilimleri Üniversitesi, Ümraniye Eğitim Araştırma Hastanesi, Pediatric Rheumatology

Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive disorder characterized by poliarteritis nodosa-like symptoms, fever, livedoid racemose, early-onset stroke and mild immunodeficiency. The loss-of-function mutations in CECR1 gene which encodes the enzymatic protein adenosine deaminase 2 (ADA2) associated with the DADA2. DADA2 is present with a spectrum of vascular and inflammatory phenotypes with highly varied clinical expression. The patients can present with isolated constitutional symptoms, arthralgia, myalgia, and/or livedoid rash. The severe phenotype of the disease is emerge as early-onset stroke, bone morrow suppression, neutropenia, liver failure and/or neurologic disorders It is currently not well understood what cause the variability in the severity of clinical phenotype.
We aim to describe the clinical characteristics, genotype and treatment of patients diagnosed with DADA2 in our clinic.
All the patients diagnosed and followed up in Department of Pediatric Rheumatology, Umraniye Training and Research Hospital, Istanbul, Turkey, between 2016 and 2020. All symptomatic patients suspected with DADA2 were analyze by genetic test and ADA-2 enzyme activity, also relatives of index cases were also screened. ADA-2 enzyme activity was evaluated at Duke University Medical Center.
Results: We diagnosed 10 patients with DADA2, 5 of them had mild phenotype or asymptomatic, or they were relatives of index cases, and 5 of the patients had severe phenotype. Three of the patients were girls and seven were boysThe age of the patients at diagnosis was in the range of 2–28 years. The age of the patients at disease onset was also in the range of 2 months–14 years. Six of the patients were index cases and the other four were their relatives. Homozygous mutations in CECR1 were shown in all subjects.The frequency of phenotypic manifestations of the patients were seen as follow respectively; fever 80%, livedoid rash 70%, digital ulsers and/or amputations 20%, neurologic involvement 50%, gastrointestinal involvement 20%, hematological involvement 40%, and immunodeficiency 30%.The initial diagnosis of index cases were as follows; two classic PAN, one cutaneos PAN, one Behçet's disease and two Diamond Blackfan syndrome. The activity of ADA2 was evaluated and clearly diminished in all patients (0-12.1 mU/g protein). 6 of the 10 patients were treated with anti-tumor necrosis factor therapy.Two patients were awaiting bone marrow transplantation.
Conclusions: The clinical manifestations of DADA2 vary from mild skin involvement to severe multisystemic vasculitis. It is suggesting that both residual ADA2 activity levels and gene mutation are important in clinical phenotype.

Keywords: DADA2, pediatric rheumatology



Video Presentations

VP-01

Chronic Arthritis of Familial Mediterranean Fever: Clinical Characteristics and Treatment

Aslihan Avanoglu Guler[1], Cagatay Coskun[2], Salih Ünal[3], Hazan Karadeniz[1], Reyhan Bilici Salman[1], Hasan Satis[1], Derya Yildirim[1], Hamit Kucuk[1], Seminur Haznedaroglu[1], Berna Goker[1], Mehmet Akif Ozturk[1], Abdurrahman Tufan[1]
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Introduction
Familial Mediterranean fever (FMF) is the most common hereditary periodic fever syndrome, characterized by recurrent attacks of fever, peritonitis, pleuritis, erysipeloid erythema and arthritis. Although FMF arthritis is largely self-limited that resolves in a few days, some patients suffer from chronic arthritis which is poorly characterized. Herein, we aim to investigate demographic, genetic, clinical and treatment features of FMF patients with chronic arthritis.
Methods
Data is derived from the Gazi FMF cohort which was established in 2010. Data of adult patients with FMF who were diagnosed according to the Tel Hashomer criteria were registered with regular intervals. A retrospective cohort analysis was made from records of patients. Comorbidities, detailed characteristics of attacks, genetic analyzes, presence of HLA-B27, type and location of chronic arthritis, treatments, and response to treatments were retrieved from database.
Results
We have identified 41 (22 males and 19 female) patients who had chronic arthritis. The mean age of study population was 37±11 years and 22 (53.6%) were male. The most common MEFV variant was M694V, observed in 36 (88%) patients (27 were homozygous). HLA B27 was evaluated in 27 patients, which was positive in 6 patients. Twenty-two (53.6%) patients had fulfilled ASAS criteria of spondyloarthritis. With regard to other inflammatory co-morbidities 2 patients had Crohn colitis, 2 had psoriasis and 1 had hidradenitis. Two patients with chronic arthritis are diagnosed with JIA in their childhood period. FMF attacks of patients were fever (%82.9), peritonitis (%80.5), pleuritis (%56.1). In 8 patients (%19.5), chronic arthritis was the sole manifestation of disease without other disease manifestations. Median age at onset of arthritis was 18 years (min:3 - max:43). Eight patients (19.5%) had monoarthritis and 33 patients (80.5%) had oligoarthritis. Any patients found to have polyarthritis. The most common arthritis locations were knees (56.1%) followed by hips (36.6%) and ankles (36.6%). Chronic arthritis was treated with methotrexate (n=9), sulfasalazine (n=19), interleukin (IL)-1 antagonists (n=26), tumor necrosis factor antagonists (n=24) and IL-6 antagonist (n=2). Despite treatments 15 patients has deforming arthritis and 6 required joint prosthesis.
Conclusion
Chronic arthritis is a rare complication of FMF. Most commonly affected joints were knees, hips and ankles. Despite advanced treatments prognosis is poor in chronic arthritis which can be improved by early identification and prompt treatment of condition.
Keywords: Familial Mediterranean Fever, Chronic Arthritis

VP-02

Retrospective Evaluation of Pediatric Behçet Patients: A Single Center Experience

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Introduction
Behçet's Disease (BD) is a multisystem disease, initially described by Hulusi Behçet in 1937. It is characterized with recurrent oral and/or genital aphtous ulcerations accompanied by ocular, cutaneous, musculoskeletal, gastrointestinal and neurologic findings. In the nomenclature of the Chapel Hill Consensus Conference, BD is defined as a variable vessel vasculitis that can affect any size of vessels. Athough the etiology of the disease is not known clearly, the pathogenesis involves both the innate and the adaptive immune system. This suggests to be involved in the spectrum of autoinflammatory diseases.
Methods
A total of 32 pediatric patients diagnosed as BD according to the criteria of the International Behçet Study Group and followed up in the Pediatric Rheumatology Clinic of Ondokuz Mayıs University Faculty of Medicine between 2016-2020 were retrospectively analyzed. Demographic, clinical and laboratory findings, and treatment approaches of the patients were evaluated.
Results
Of the patients, 53.1% were female (n: 17) and 46.9% were male (n: 15). Family members of 10 patients (31.2%) had a diagnosis of BD. Only 7 patients (21.8%) had pathergy test positivity. MEFV gene mutation was examined in 19 patients. Genetic analysis of 6 patients was wild type, 4 patients were found to have homozygous or compound heterozygous MEFV gene mutations, and 9 patients had heterozygous MEFV gene mutations. All patients had a history of recurrent oral aphthae and 22 patients (68.7%) had genital ulcers. Eight (25%) patients had neurological symptoms including papilledema, diplopia and nystagmus. Ten patients (31.2%) presented with vascular lesions causing thrombosis and ischemia (8 patients had sinus vein thrombosis, one patient had portal vein thrombosis, one patient had recurrent peripheral deep vein thrombosis). Fifteen patients (46.8%) had abdominal pain and gastrointestinal symptoms similar to inflammatory bowel disease. Colchicine treatment was given to all patients. Azathioprine in 21 patients, anti-TNF therapy in 11 patients, varying doses of steroid therapy in 10 patients, and cyclosporine treatment in 3 patients were added as additional drugs. In 4 patients, active disease continues despite anti-TNF therapy. Eighteen patients (56.2%) were in complete remission, 10 patients (31.2%) were in partial remission, One patient with complete remission is accompanied by sequelaes of bilateral optic atrophy and blindness developed due to sinus vein thrombosis and increased intracranial pressure.
Conclusion

It is important to initiate steroids, steroid sparing immunosuppressive therapies and anti-TNF treatments in refractory cases in the early period of BD.

Keywords: Pediatric, Behçet

VP-03

Is Exon 2 Associated with FMF or a New Disease?

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Background/Purpose: In Familial Mediterranean Fever (FMF), patients having exon 10 mutations, specifically M694V, M680I, and V726A are more common and their disease profiles tend to complicate more. Other mutations, especially the ones in exon 2, can be defined as benign polymorphisms due to being rare. The objective of this study was to understand the clinical nature of patients having mutations of E148Q and R202Q in exon 2 as well as how these mutations affect their complaints and treatment response.

Methods: In this study, we reported patients with FMF diagnosis according to Tel Hashomer criteria, who had mutations of E148Q, R202Q or both. These patients were a randomized subset of the ones followed in our outpatient rheumatology clinic. Clinical features of these patients were collected from their files. In terms of symptoms abdominal pain, chest pain, fever, arthritis, arthralgia, myalgia, erysipelas-like rash were noted. In terms of complications, renal FMF-related systemic AA Amyloidosis was noted. Also, we checked the family history of FMF. These patients were compared with the control group of patients having M694V mutation.

Results: The clinical symptoms of the patients are summarized in Table 1. One of the primary outcomes of this study was the treatment response. 98% of the patients were treated with colchicine. Fifty-two patients (91%) in the control group and 33 patients (78%) in the exon 2 group responded to colchicine. Colchicine response was 100% in the R202Q group, 68% in the E148Q group, and 80% in the mixed exon 2 group. Family history was positive in 9 patients (36%) of E148Q group, in 1 patient (8%) of R202Q group, in 1 patient (20%) in mixed exon 2 group which equals a total of 11 patients (26%). In the control group, 39 patients (68%) had an FMF diagnosis in their family. Amyloidosis was reported in one patient with E148Q mutation, one patient with R202Q mutation, two patients with M694V mutation.

Conclusion: In conclusion, in comparison with M694V patients, patients with exon 2 mutations, tend to have more atypical symptoms of FMF such as chest pain, arthralgia, and myalgia. The presentation of these symptoms is milder than the typical symptoms of FMF. The fact of low colchicine response in exon 2 patients cannot be overlooked as well. Therefore, exon 2 mutations can be evaluated as a separate clinical entity; in fact, these cases should also be further searched for a potential autoinflammatory disorder.

Keywords: exon 2 and FMF

Clinical symptoms of patients with different exon mutations

	E148Q (3H+22h)* (n:25)	R202Q (0H+12h)(n:12)	Mixed E148Q +R202Q (0H+5h) (n:5)	Total of Exon 2 patients (3H+39h) (n:42)	Control M694V (20H+37h) (n:57)
Abdominal Pain	15 (%60)	10 (%83)	3 (%60)	28 (%66)	51 (%89)
Fever	12 (%48)	8 (%66)	3 (%60)	23 (%54)	44 (%77)
Chest Pain	10 (%40)	2 (%16)	2 (%40)	14 (%33)	13 (%22)
Arthritis	8 (%32)	0	1 (%20)	9 (%21)	20 (%35)
Arthralgia	21 (%84)	6 (%50)	4 (%80)	31 (%73)	25 (%43)
Myalgia	10 (%40)	0	0	10 (%23)	3 (%5)
Erysipelas-like rash	3 (%12)	1 (%8)	0	4 (%9)	3 (%5)

** H:homozygous h:heterozygous*

VP-04

Increased inattention/hyperactivity in children and adolescents with familial Mediterrenean fever

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Objective: Although familial Mediterranean fever (FMF) progresses with attacks, its subclinical inflammation may continue in attack-free periods. To date, increased inflammatory cytokines have been reported in many psychiatric diseases. In this study, we aimed to evaluate the psychological symptoms, especially inattention/hyperactivity, in children and adolescents with FMF.
Materials-Methods: The study included 272 children and adolescents with FMF and 250

healthy peers as a control group. The Strengths and Difficulties Questionnaire-Parent Form was used to assess emotion, behavior and peer related problems, as well as inattention/hyperactivity and prosocial behavior in participants.
Results: The mean age of the patients was 12.35, ± 2.65 years, and the mean age of the control group was 12.08, ± 2.67. In total, 51% (n = 139) of patients with FMF and 56% (n = 140) of the control group were females. The age and gender of the children were similar across groups (p=0.265 for age; p=0.262 for gender). The emotional and behavioral problem subscale scores of patients with FMF were significantly higher than those of healthy controls. The inattention/hyperactivity scores of patients with FMF were also significantly higher than those of the control group (3.99 ± 2.34 vs 2.93± 2.26, p <0.001). The psychological scale comparisons of the patient and control groups are given in Table 1 in detail. When patients with FMF were compared according to the presence of attacks in the last year, presence of exertional leg pain as well as their mutation types, no differences were found in terms of inattention/hyperactivity scores. However, patients whose FMF symptoms started before 8 years of age had significantly higher inattention/hyperactivity scores than those whose symptoms begun after 8 years of age (4.15 ± 2.39 vs 3.03 ± 1.75; p =0.006)
Conclusion: This research demonstrated that FMF patients had increased inattention/hyperactivity, similar across all ages and genders, which was unaffected by FMF-related variables, except for age of onset. The FMF-inattention/hyperactivity relationship may be due to a common etiology in which proinflammatory cytokines play a role.

Keywords: Attention Deficit Hyperactivity Disorder, Familial Mediterranean Fever

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Comparison of SDQ scale scores in patient and control groups

	Patients (n=272)	Controls (n=250)	p
SDQ- total score	11.82 ± 5.71	8.97 ± 5.54	<0.001
SDQ- emotional problems	3.22 ± 2.42	1.97 ± 2.09	<0.001
SDQ- conduct problems	1.93 ± 1.69	1.34 ± 1.57	<0.001
SDQ- hyperactivity/inattention	3.99 ± 2.34	2.93 ± 2.26	<0.001
SDQ- peer problems	2.67 ± 1.57	2.73 ± 1.87	0.914
SDQ- prosocial behavior	8.10 ± 1.93	7.98 ± 2.21	0.858

mean ± SD SDQ, Strenghts and Difficulties Questionarie

VP-05

A Case of Amyloidosis due to DADA2 and HA20

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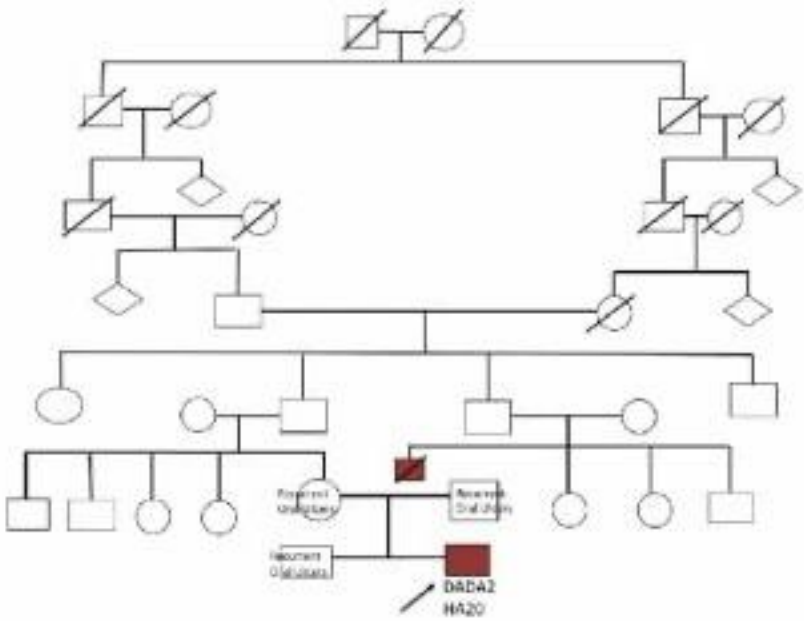
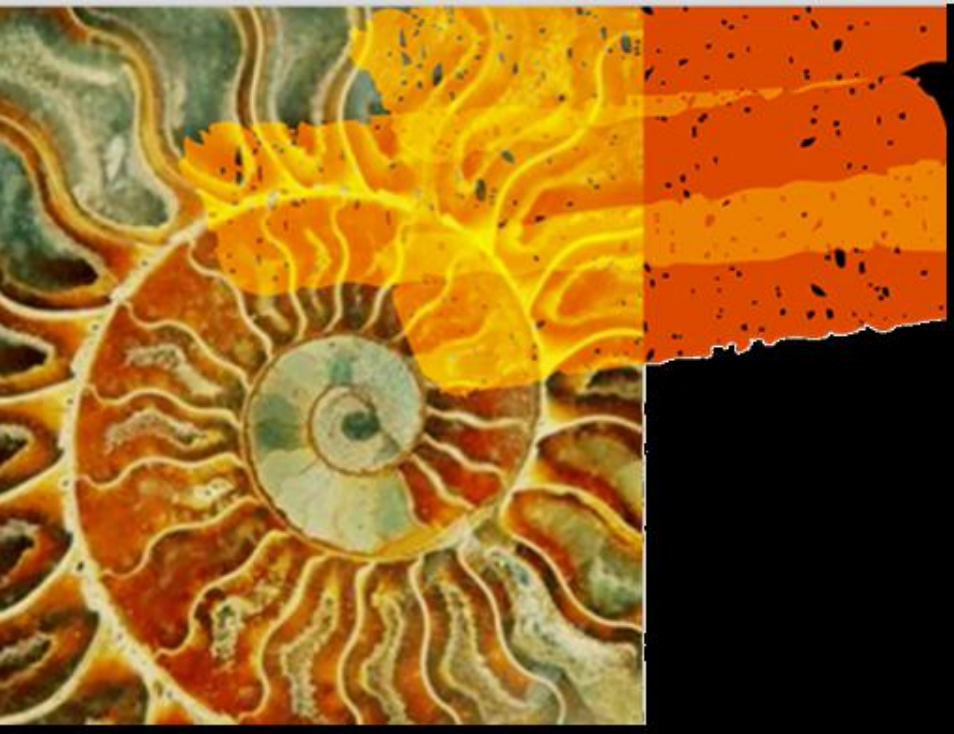
Adenosine Deaminase 2 Deficiency (DADA2) and Haploinsufficiency of A20 (HA20) are two recently described monogenic autoinflammatory diseases (AID). Uncontrolled inflammatory response has been associated with an increased risk of AA amyloidosis in other AID, but there are only two reported patients with DADA2-related amyloidosis so far.

Case:
A 20-year-old male patient, born to consanguineous parents (Fig.1), applied to our hospital with fever and abdominal pain in June 2014. Peritonitis, hepatomegaly and a palpable non-tender mass in the right axillary cavity were detected along with leukocytosis, high acute phase reactants (APR), and nephrotic range proteinuria. CT angiography revealed multiple thrombotic microaneurysms in celiac, splenic, superior, and inferior mesenteric and bilateral renal arteries; and MRI showed an aneurysm in anterior communicating artery. Hepatitis serology was normal.
He had been diagnosed with polyarteritis nodosa, and prednisolone and azathioprine were started. Renal histopathology confirmed the AA amyloidosis. Genetic analysis revealed no pathogenic MEFV variant. Colchicine and anakinra 100 mg/day were added to his treatment. He experienced 1-2 abdominal episodes annually between 2014-2019 with normal APR between attacks.
In March 2019, he was admitted to the hospital because of abdominal pain, high APR and iron deficiency anemia. No gross pathology was observed in endoscopic examination of gastrointestinal tract, but histopathological investigation of gastric mucosa and terminal ileum showed AA amyloidosis. Multiple aneurysms were detected in renal arteries with angiography.
Deep sequencing of the targeted genes revealed homozygous p.Pro251Leu in ADA2 gene and heterozygous p.Thr647Pro in TNFAIP3 gene, confirming the molecular diagnosis of DADA2 and HA20. The patient described oral recurrent aphthous ulcers starting from childhood, but he had no uveitis or genital ulcers. His mother and brother also had recurrent oral aphthous ulcers. Genetic analyses showed heterozygous p.Pro251Leu variant in ADA2 gene in his mother, and heterozygous p.Gln703Lys variant in NLRP3 gene as well as heterozygous p.Thr647Pro TNFAIP3 variant and heterozygous p.Pro251Leu ADA2 in his brother.
An improvement was observed within 2 weeks after switching his anakinra to adalimumab 40 mg every other week. At his last visit in February 2021, the patient had no complaints with normal APR, and urinalysis analysis showed 200 mg/day proteinuria, which was regressed from 3 g/day.
Discussion:
This is the first case with variants associated with both DADA2 and HA20, who also developed AA amyloidosis. Clical findings were mainly compatible with DADA2, but combination of ADA2 and TNFAIP3 gene variants may have further increased the risk of the amyloidosis.

Keywords: Adenosine Deaminase 2 Deficiency (DADA2), Haploinsufficiency of A20 (HA20)

Figure1: Pedigree of family





Poster Presentations

PS-01

Colchicine response in Juvenile Idiopathic Arthritis case with MEFV gene mutation

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Introduction: Familial Mediterranean Fever (FMF) is the most common autosomal recessive autoinflammatory disease characterized by recurrent acute inflammation attacks. Mutations in MEFV gene are responsible for the occurrence of the disease. Here, we will discuss Juvenile Idiopathic Arthritis (JIA) case that responded to colchicine treatment.
Case: A fifteen-year-old woman presented with pain in the shoulders, swelling in the right hand and ankles, fingers, pain, and limitation of movement. Findings consistent with arthritis were detected in the physical examination; RF and anti-CCP were measured 49 IU / ml, 228 U / ml respectively. She was diagnosed with JIA and treated with methotrexate 20 mg / week tb, sulfasalazine 2 * 500 mg tb, hydroxychloroquine 2 * 200 mg tb, prednisolone 1 * 5 mg tb. Physical examination of the patient, whose joint complaints continued despite the treatment, was compatible with arthritis in bilateral wrists and ankles, proximal interphalangeal joints of the hand, C-reactive protein (CRP) was measured as 12 mg / dl and sedimentation was 35 mm / hour. Sulfasalazine and hydroxychloroquine were discontinued, certolizumab 200 mg / 2 week sc treatment was added to methotrexate and prednisolone. CRP was measured as 11 mg / dl and sedimentation was 30 mm / hour in the patient whose arthritis did not regress in the left ankle; Certolizumab was discontinued and tocilizumab 600 mg / month iv treatment was started. Patient's arthralgia continued in the shoulders, fingers and ankles, and CRP was measured 29 mg / dl and sedimentation was 29 mm / hour. When the patient with persistent acute phase elevation was questioned, we learned that she had abdominal pain that recurred several times a year and lasted for approximately 12 hours, and that his cousin developed kidney failure at a young age; MEFV gene mutation was sent to elucidate possible FMF etiology.. Patient had M680I heterozygous mutation and colchicine dispert 3 * 0.5 mg tb was started. The patient's joint complaints regressed; CRP was 0.29 mg / dl and sedimentation was 9 mm / hour.
Discussion: FMF is a disease with recurrent attacks of acute inflammation. In the presence of other accompanying rheumatological diseases, FMF clinical findings can often be overlooked. Turks are among the ethnic groups where FMF is common. Therefore, in patients with unexplained acute phase elevation, it would be useful to question the patient for FMF and to analyze MEFV gene mutation when clinical findings support it.

Keywords: Familial Mediterranean Fever, Juvenile Idiopathic Arthritis

PS-02

Yao syndrome with myastenia gravis

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İzmir Bozyaka Eğitim Araştırma Hastanesi

Introduction: YAO syndrome was first reported in 2011 as NOD2-associated autoinflammatory disease. Patients have periodic recurrent attacks with fever, dermatitits, oligo-poliarthrytis, distal lower extremity swelling, abdominal pain, diarrhea, pleuritis, pericarditis and sicca-like symptoms (1). In this case report we discuss a patient with YAO syndrome with myastenia gravis.
Case: 32 year old female referred to our clinic with swelling and pain in her hands and feet. Patient has fever, dermatitis,poliarthritis and abdominal pain attacks for 6 years. She was started colchicine and prednisolone considering FMF/CAPS 3 years ago. 2 years ago she referred to neurologist with new onset weakness in proximal limb muscles, ptosis and diplopia worsens with exercise. She was well responded to pridostigmin and diagnosed as myastenia gravis. After 1 year of treatment she was brought to the emergency room with disphagia and dispnea. High dose prednisone and IVIG started for myasthenic crisis.
In her physical examination she has arthritis in both wrists,2rd-3th MCPs - PIP joints and bilateral ankle joints with dorsal non-pitting eudema. Her fever was 37.8 C degrees. She hadn't dermatitis and abdominal pain since she was started prednisone and colchicine. RF, CCP and ANA tests were negative. Tests for autoinflammatory diseases showed no mutations in MEFV, NLRP3, TNFRSF1A,IL 1, IL 10, genes. But NOD2 IVS8+158 found heterozygous positive. Patient diagnosed as Yao syndrome started sulphasalasine (up to 2000 mg). After one month of treatment arthritis and swelling began to resolve.
Discussion: YAO syndrome is a polygenic SAID, and the presence of specific NOD2 variants confers susceptibility to the disease(2). In a large cohort study of the 143 patients, NAID was sporadic in 93% of cases. Oligopolyarthritis was characteristic distal lower extremity swelling. Associated NOD2 variants were primarily IVS8+158 or compound IVS8+158 and R702W.Treatment with glucocorticoids and sulfasalazine found effective in most YAOS patients, canakinumab also have some benefits in resistant cases(3).
Myasthenia gravis asscociated with many autoimmune disorders but there is no known relationship with autoinflammatory diseases. This is the first case that Yao syndrome concomittant with myastenia gravis.
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Keywords: Yao syndrome, myastenia gravis

PS-03

Successful treatment with anti-interleukin 1 agents of Familial Mediterranean fever associated with optic neuritis

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Introduction:
Familial mediterranean fever (FMF) is an inherited periodic auto-inflammatory disease characterized by recurrent attacks of fever, synovitis and serositis (kaynak). Neurological manifestations of FMF are extremely rare (kaynak). Here in, we present a case diagnosed with optic neuritis associated with FMF and try to promote awareness as a type of neurologic involvement in FMF.
Case presentation:
A 51 year-old-male patient with a previous history of optic neuritis presented neurology department with sudden loos of vision. Two months before admission, he had a loss of vision in the left eye, pulse methylprednisolone was given for three times with the diagnosis of optic neuritis and the patient's vision had improved significantly.
On admission, neuro-ophthalmological examination revealed that optic disc was swollen and loss of altitudinal vision in the right eye. On his laboratory examination, blood cell count 10,800/mm3(referance range4,3-10,3), platelets 341,000/mm3(referance range 156-343.000), hemoglobin 13,6g/dl(referance range 13,6-17,2) and biochemical parameters including vitamin B12 were within normal limits. Erythrocyte edimentation rate (ESR) was elevated at 36 mm/hour (referance range 0-20), C-reactive protein (CRP) at 4.18 mg/ml (referance range 0-0.8). Visual evoked potential (VEP) showed bilateral significant prolongation. Brain stem auditory evoked potential (BAEP) was normal. An orbital magnetic resonance imaging (MRI) was performed and showed enhancement of the right optic nerve. Cranial MRG revealed no pathology. Cerebrospinal fluid (CSF) investigations including protein, glucose, viral markers, IgG index and oligoclonal band were normal. Neuromyelitis optica (NMO) antibody was normal. The patients had been diagnosed with optic neuritis. The patient was received initial pulse methylprednisolone, followed with plasma exchange (PLEX) therapy. The ophthalmologic examination was performed with VEP/BAEP and reported parsiel responce.
Then, the patient was referred to our rheumatology department for evaluation of possible rheumatologic dieseases. The detailed questioning of the patient revealed that he had episodic attacks of fever, abdominal pain and arthritis since 20 years. The patient had been diagnosed with FMF with heterozygous mutation on M694V. Colchicine was started and dosage was increased up to 2mg/day. On colchicine treatment, he had a flare of serositis and optic neuritis and anankira was added to his therapy.
Conclusion:
Here, we report a patient who had developed recurrent attacks of optic neuritis concurrently with his FMF episodes. Since early treatment is essential to avoid irreversible complications, the clinicians should be aware of FMF as a potential cause for acute optic neuritis.

Keywords: familial Mediterranean fever, optic neuritis anti interleukin-1 agents

PS-04

Scalp edema in a patient with FMF and HSP coexistence

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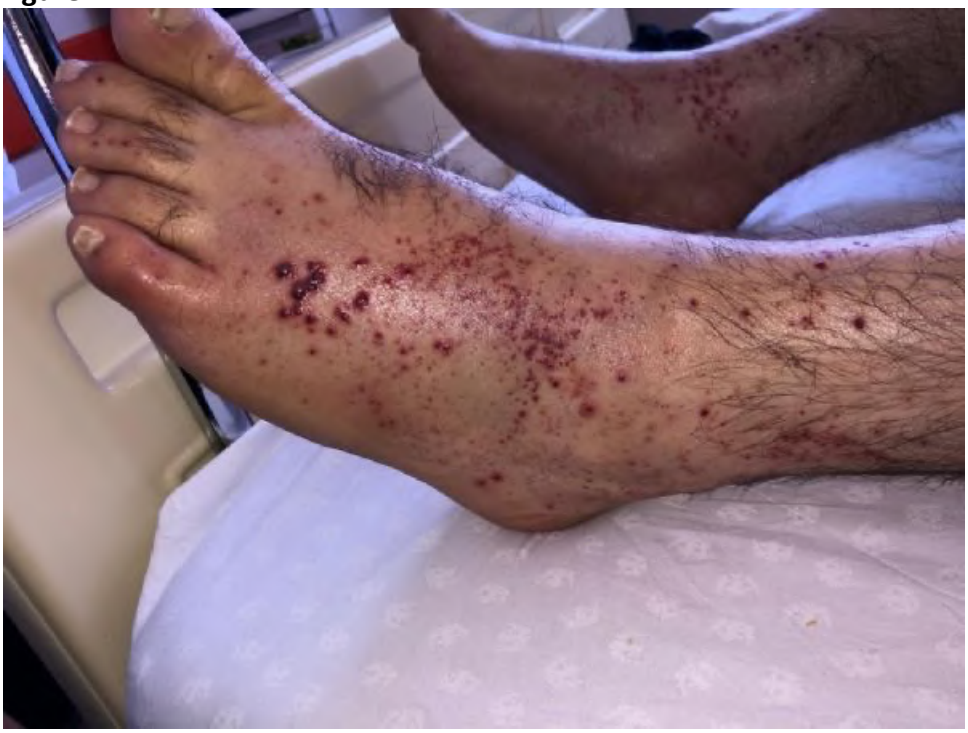
İNTRODUCTİON
Familial Mediterranean fever(FMF) is the most common periodic fever syndrome with anautosomal recessive inheritance pattern characterized by recurrent episodes of polyserositisand fever. Henoch-Schönlein purpura(HSP) is the most common vasculitis in childhood; It is a systemic disease that can affect many organs, especially the skin, joints, kidneys and GIS. HSP prevalence of FMF patients, 2,7% is detected in Turkey. In this case, we presented scalp edema that developed in a patient with FMF and HSP coexistence.
CASE
A 45-year-old male patient with FMF for 15 years and a compound heterozygous mutagen M680I-M694V used antibiotics for a 1-week sore throat. Subsequently, petechial rashes on both legs below the knee and in the hip, swelling, pain, and limitation of movement occurred in the left knee and both wrists. The patient, who applied to the outpatient clinic with these complaints, was considered for leukocytoclastic vasculitis (Figure1). Skin biopsy result was compatible with leukocytoclastic vasculitis. In the laboratory tests of the patient, leukocyte: 11.6 Hgb:10.5 plt:492000 creatinine:0.54 mg/dl, ALT:175nIU, albumin:3.1g/dl, sedimentation: 75 mm/hour, CRP: 58 mg/L was determined. A diffuse symmetrical increase in thickness, starting from the traits and continuing along the proximal jejunal segments, reaching 11 mm in diameter at the thickest part, was detected on abdominal CT performed due to nausea, abdominal pain, and hematochezia. Besides, there is a diffuse symmetrical wall thickness increase of up to 5 mm in an ileal segment of approximately 10 cm in the right quadrant of the abdomen. Vasculitis? reported as. In colonoscopy, including the terminal ileum and whole colon mucosa were covered with patches of pronounced mucosal hyperemia and finger-pressure-like appearance, as well as diffuse active red blood in the entire colon and terminal ileum. Pathology results came as extensive bleeding areas at the mucosal level (Vasculitis?). With these findings, the patient was diagnosed with HSP. Brain CT taken due to local soft tissue swelling that developed suddenly without a history of trauma in the temporal region was reported as soft tissue thickening in the left parietotemporal region, compatible with edema reaching 9 mm in the widest part of the skull (Figure2). Prednisolone 1 mg / kg / day was given. The patient, who had a clinical response to steroids, was followed up in the outpatient clinic.
DİSCUSSİON
During the course of FMF, HSP is more common than the general population. While scalp edema is more common in childhood, it is rarely seen in adulthood.

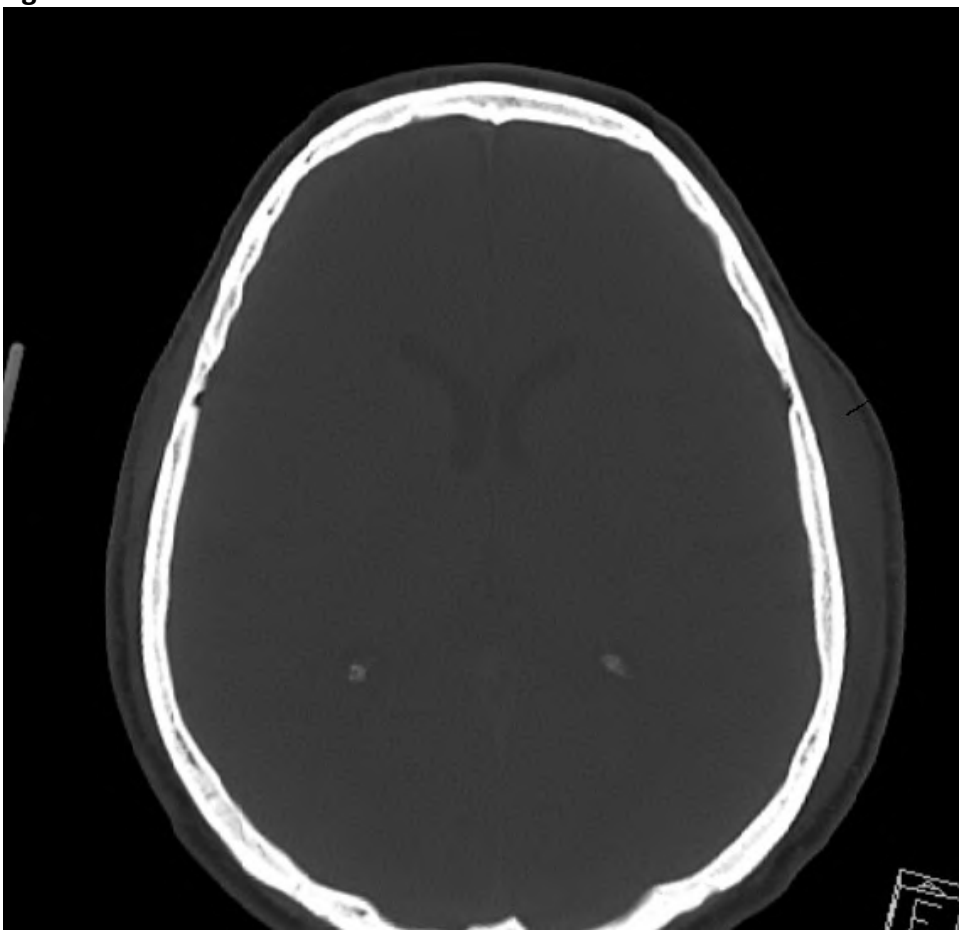
Keywords: Familial Mediterranean fever, Henoch-Schönlein purpura

figure 1



Leukocytoclastic vasculitis on the foot and legs

figure 2



Scalp edema on the cranial tomography

Tables

Table 1. The distribution of medicines used in our patients		
Biologic agents	36	33,3
Canakinumab	2	1,9
Tocilizumab	5	4,6
Anti-TNF*	30	27,8
Etanercept	10	9,3
Infliximab	8	7,4
Golimumab	1	0,9
Adalimumab	15	13,9
Other DMARDs		
Methotrexate	42	38,9
Salazopyrine	6	5,6
systemic steroid	11	10,2
Azathioprine	4	3,7
Hydroxy chloroquine	1	0,9
Colchicine	9	8,3
* Some patients used more than one type of anti-TNF because of drug changes during the pandemic period.		

Table 2. The frequency of symptoms related to COVID 19 in patients with JIA		
	n=12	%
Fatigue	8	67
Cough	7	58
Haedache	7	58
Myalgia	6	50
Loss of taste	4	33
Loss of smell	4	33
Fever	4	33
Chest pain	2	17
Dyspnoea	2	17
Abdominal pain	2	17
Diarrhea	1	8
Sore throat	1	8

PS-05

Is Anakinra an option in a patient with kidney transplant?

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Objective: Autoinflammatory diseases are the common name given to a group of diseases that occurs with recurrent episodes of fever, polyserositis, and rash. In this case, we aimed to present a case of renal transplant who was considered to have autoinflammatory disease and was used interleukin-1 (IL-1) receptor antagonist Anakinra.
Case: A 40-year-old female patient underwent hemodialysis for 3 years due to renal failure due to hypertension. Renal transplant was performed from her mother in 2008 and she was followed up without any problems. Although she had taken 15 mg of mycophenolate mofetil, tacrolimus, prednisolone (PRD), she was referred to the rheumatology due to the development of arthritis in his wrists and knees and fever, which occurred approximately every 3 weeks for the last 6 months. In October 2014, it was learned that there was swelling in the ankle, and gout with high uric acid levels was considered. She was followed up with allopurinol. Hydroxychloroquine was given when the arthritis recurred. After this date, it was observed that he was admitted to the emergency department many times with episodes of fever, arthritis (small joints of the hand, knee and ankle) and rash. Infective endocarditis, tuberculosis, lymphoma and other malignancies were investigated. No vegetation was detected in echocardiography. Neck, thoraco-abdomino-pelvic computed tomography was normal. The blood, urine and throat cultures were negative. Despite 15-mg PRD in August 2016, there was arthritis and fever in the hands and ankles.
Laboratory Findings: Sedimentation: 102/h CRP: 23.5 mg / dl (0-0.5 mg / dl), creatinine: 0.9, ALT: 10, leukocyte: 23800, Hgb: 9.3 Plt: 271000, ANA: Negative, ANA profile negative, PPD: 0 mm (2 times), protein electrophoresis normal, MEFV gene mutation negative, brucella and Q fever negative, procalcitonin: negative, ferritin: 1664 (previously viewed 1444), serum Amyloid A: 174 (<6.8 mg / L), TIT: Protein-negative WBC: 0 RBC: 0 detected.
Autoinflammatory disease was considered in the patient who had recurrent attacks of fever, arthritis and rash, whose attacks spontaneously regressed in 3 days, and who had high ferritin, anakinra 100 mg sc 1x1 treatment was started. The patient, whose follow-up does not have fever and arthritis, continues to be followed up without episodes.
Conclusion: Since the discontinuation of anti-IL-1 treatment during and after renal transplantation maycause disease activation in most patients, there are cases in the literature who are followed up without any problem during and after the operation.

Keywords: Anakinra, renal transplant

PS-06

Protracted Febrile Myalgia in Children With Unexplained Generalized Myalgia

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Hereditary periodic fever syndromes are a group of monogenic disorders that occur with serous inflammation and recurrent fever. Familial Mediterranean fever (FMF) is the prototype of periodic fever syndromes and is caused by mutations in the MEFV gene. FMF often presents with attacks in the form of fever, abdominal pain, chest pain, erysipelas-like erythema. Protracted febrile myalgia is a rare symptom of FMF, characterized by prolonged fever and severe myalgia and etiopathogenesis is not clearly known. Although acute phase reactants are increased, creatine kinase (CK) values are within the normal range.
In this study, we aimed to share the clinical, laboratory and imaging findings of our four patients we followed up for protracted febrile myalgia.
Two of our patients were females and two males. On admission to the hospital, there were complaints of fever and myalgia lasting more than ten days. Additionally, three of our patients had athralgia. On physical examinations, there was widespread muscle sensitivity and we did not find any loss of muscle strength. In all our patients, c-reactive protein and sedimentation values were high, and CK values were in the normal range. Magnetic resonance imaging (MRI) of our two patients revealed signal changes in muscle fibers consistent with myositis. Viral serologies, brucella agglutination tests and serologies, borrelia burgdorferi serologies were found to be negative in the tests performed for etiology. No evidence of malignancy was observed in the bone marrow aspiration evaluations of our patients. We excluded possible metabolic, infectious and malignant etiologies with biochemistry, culture, serology and bone marrow aspiration studies. Heterozygous mutation was present in the MEFV gene screening panel of our three patients. MEFV gene screening result of a patient with clinical findings compatible with FMF and high serum amyloid A values is followed up. While two of the patients had a known diagnosis of FMF, we found protracted febrile miyalgia as the first finding in the other two. The symptoms of our two cases regressed with colchicine and non-steroidal anti-inflammatory treatments. We responded to steroid treatment in one of our cases, while another was unresponsive to steroid treatment and his symptoms regressed with anakinra treatment.
Protracted febrile myalgia should be kept in mind in cases of prolonged fever and generalized myalgia. The first sign of FMF may be protracted febrile myalgia. Anakinra treatment is an alternative in patients with steroid-unresponsive symptoms.

Keywords: FMF, protracted febrile myalgia

PS-07

AA amyloidosis of uncertain etiology: treatment challenges

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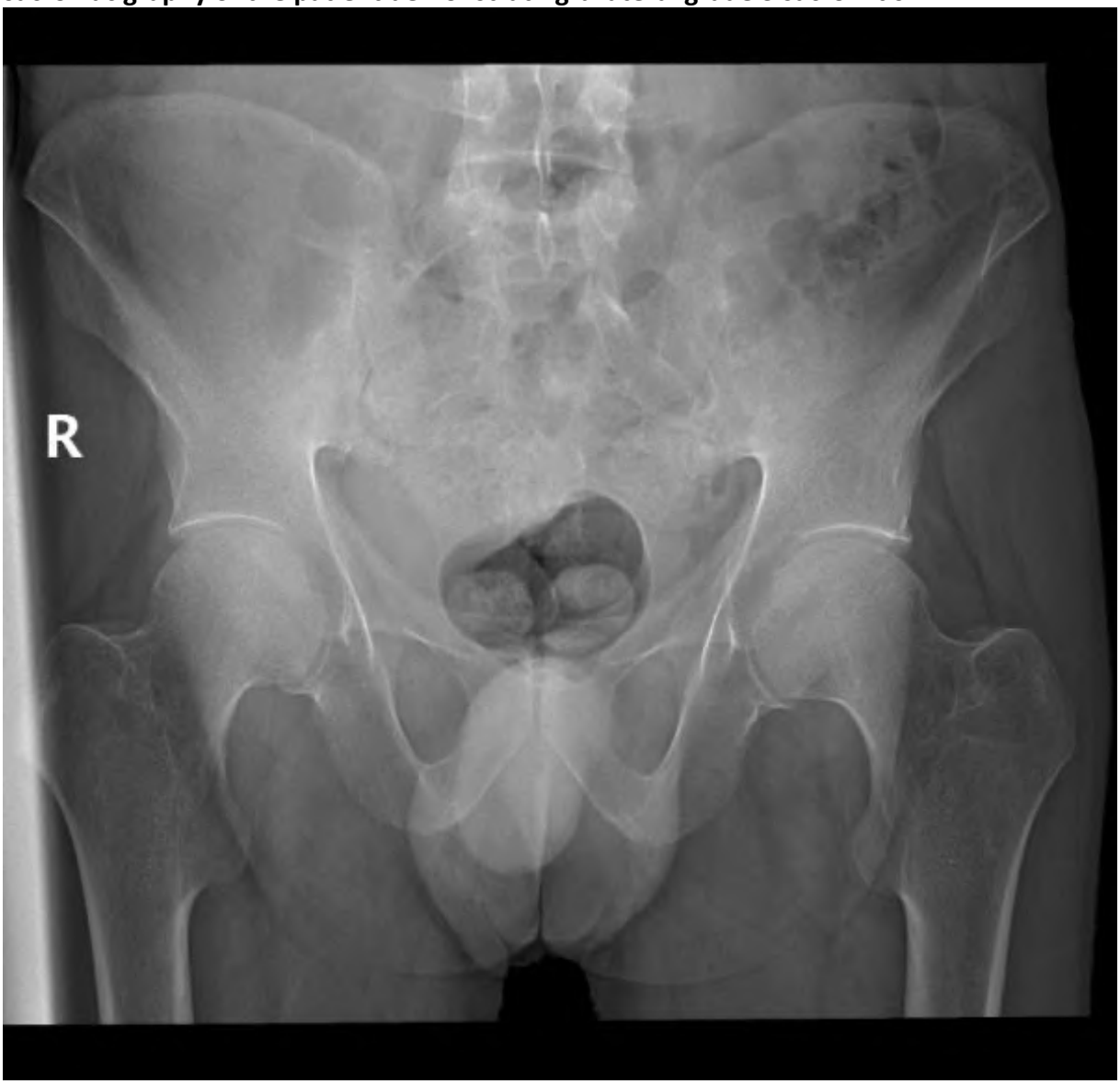
Background: There is no standardized treatment for AA amyloidosis of uncertain etiology.
Case presentations: Case 1. A 22-year-old Caucasian male was evaluated because of massive gastrointestinal hemorrhage due to AA amyloidosis of the intestinal wall. History revealed no finding suggestive of an inflammatory disease. No family history of any inflammatory disease was also present. The gene panel revealed no mutations regarding the periodic fever syndromes that consisted of MEFV, MVK, NLRP3, NLRP12, TNFRSF1A, TNFRSF11A, LPIN2, PSTPIP1, CECR1, and NOD2. At the time of diagnosis, the patient had nephrotic proteinuria and restrictive cardiomyopathy suggestive of systemic AA amyloidosis. Serum creatinine and transaminases were normal. He had anemia (Hb: 10.1 g/dL), leukocytosis (WBC: 11.400/µL), thombocytosis (564.000/µL) and high acute phase reactants (ESR: mm/h, CRP: 49.5 mg/L) and serum amyloid A (40 mg/L). A trial of anakinra (100 mg/day s.c.) resulted in no improvement after 6 weeks but after canakinumab 150 mg/month i.v. proteinuria decreased from 6.5 to 1.5 gr/day and the acute phase reactants and serum amyloid A were normalized. The patient is still followed up under canakinumab 150 mg/2 months.
Case 2. A 60-year-old female was evaluated because of AA amyloidosis (of the lypmph nodes) of uncertain etiology. She had no finding suggestive of any rheumatic/inflammatory/neoplastic/infectious disease. The gene panel revealed no mutations regarding the periodic fever syndromes that consisted of MEFV, MVK, NLRP3, NLRP12, TNFRSF1A, TNFRSF11A, LPIN2, PSTPIP1, CECR1, and NOD2. Acute phase reactants and serum amyloid A were normal with normal urinary protein excretion. Treatment with sequential anakinra and canakinumab resulted in stabilization but no improvement. After a follow-up of 15 months under anti-IL1 agents, tocilizumab was started because of arthropathy but had no effect on the disease progression.
Conclusions: Treatment with anti-IL1 and -IL6 agents should be studied in AA amyoidosis of uncertain etiology.

Keywords: amyloid, secondary

sacroiliac graphy of the patient demonstrating bilateral grade 3 sacroiliitis



PS-08

Coexistence of Vasculitis and Familial Mediterranean fever

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Objective: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease affecting mainly the ethnic groups of the Mediterranean basin. It has been reported that it can coexist with various systemic inflammatory diseases. The relation between FMF and vasculitis has long been debated. The present study aimed to obtain information on vasculitis that can accompany FMF and to evaluate the relations
Materials-Methods:
Twenty two adult patients with FMF coexisted with vasculitis were recruited from the Department of Rheumatology between between January 2018- 2021 April in the study.

Familial Mediterranean Fever diagnosed according to Tel Hashomer criteria. Epidemiologic, clinical, laboratory, and radiologic findings were obtained retrospectively by examining patient records.
Results: In the present study, FMF coexisted with patients with Behçet's disease (BD) in 12, Henoch – Schoenlein Purpura in 5, leukocytoclastic vasculitis in 2, Takayasu arteritis in 1, eosinophilic granulomatous polyangiitis in 1, polyarteritis nodosa in 1 patients. Of these 12 were female (54.5 %) and 10 male (45.5%). The mean age of the patients was 44.3 (20-62). Eıghteen patients with comorbid vasculitis underwent M694V analysis In these patients, the most common mutation was M694V (in exon 10) homozygote which was found in 8 (36.4%) patients. M694V heterozygote was found in 4 (18.2%), compound heterozygote in 3 (1.6 %), normal mutation in 2 (9%), others in 2 (9%) patients. Eleven patients with comorbid BD underwent HLA-B51 analysis, with positive results in 4 patients.
Conclusions: The risk of vasculitis development seems to be increased in FMF patients. MEFV gene mutations associated with FMF may contribute to the development of vasculitis in some FMF patients. The associations may be just coincidental or an extension of the underlying common pathology. Further studies are required to determine pathogenic pathways between FMF and vasculitis

Keywords: Familial Mediterranean Fever; Vasculitis: MEFV mutation

PS-09

Familial Mediterranean Fever Patients may have Unmet Needs for the Treatments of Enthesitis

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Objectives: Enthesitis is one of the common chronic musculoskeletal findings of familial Mediterranean fever (FMF). It is not accepted as main treatment targets and this findings usually underestimated by the clinicans. Herein, we assessed the effectiveness of FMF treatments on enthesitis in FMF patients.

Material-Methods: We have included 218 FMF patients to the study. We retrospectively compared the FMF attacks' frequency, duration and intensity (FMF attack VAS score) and levels of enthesitis VAS scores between pre-treatment stage and while patients were on treatment at the last visit.

Results: 52 (23.9%) of the patients had complaints compatible with enthesitis. All patients were on colchicine treatment. Furthermore, only three patients were using Il-1 blockers during the study. Frequebcy, duration and intensity of the FMF attacks decreased significantly with treatment. Moreover, enthesis VAS scores (p=0.17) were improved with treatment non-significantly.

Conclusion: FMF treatments had somewhat favourable effect on enthesitis in FMF patients. However, the response rates would be inadequate. Therefore, there would be unmet need for treatment of enthesitis in FMF patients.

Keywords: Familial Mediterranean fever, enthesitis

	Pre-treatment	Treatment	p
Attack frequency (per year)	19.4±16.6	2.8±4.5	<0.001
Attack duration (day)	3.6±2.2	1.3±1.6	<0.001
VAS attack score (0-100)	90.2±14.3	29.0±32.5	<0.001
VAS enthesitis score (0-100)	51.5±34.9	43.1±27.5	0.17

Familial Mediterranean Fever
&
Other Autoinflammatory Diseases

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