Table 1. Treatment of 10 patients with rheumatic IMIDs and JAK-2 (V16F) mutation.

Cases, n	Underlying Disease	Age/Sex	Treatment	Clinical Evo
4	RA	67/M 87/F 93/M 82/M	NSAIDs PDN/MTX PDN/MTX HCQ	Improveme Improveme Improveme Improveme
3	PMR	68/M 89/M 82/M	PDN PDN PDN	Improveme Improveme Improveme
1	APS	76/F	Acenocumarol	No Improv
1	SS	78/F	HCQ	Improveme

Abbreviation: ANA: anakinra, BARI: baricitinib, NSAIDs: Non-Steroidal Anti-inflammatory Drugs, PDN: prdnisone, RA: Rheumatoid arthritis, SS: Sjögren syndrome, PMR: polymyalgia rheumatica.

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AB1321 THE DIAGNOSTIC DELAY IN PATIENTS WITH SCHNITZLER SYNDROME: A CASE SERIES

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Background: Schnitzler syndrome is a rare syndrome associated with recurrent whealing and monoclonal gammopathy. Since its first description in 1972 by the French dermatologist Prof. Liliane Schnitzler, around 500 cases have been described in Europe. The diagnostic delay in Schnitzler syndrome of 5 years was previously reported [Lipsker et al, 2001]. Despite a growing clinical experience [de Koning et al, 2014], Schnitzler syndrome presents a diagnostic challenge in clinical practice. The variation in the diagnostic delay in Europe is a subject of an ongoing systematic review by our multidisciplinary team.

Objectives: In this work, we would like to analyze a diagnostic delay in the patients with Schnitzler syndrome followed up at tertiary clinical and research setting.

Methods: We present the data from the patients with Schnitzler syndrome that have been under our care by a multidisciplinary team over a period from 2015 to 2021. All patients were analyzed for the age of disease onset and a diagnostic delay for Schnitzler syndrome.

Results: There are currently 14 patients with Schnitzler syndrome under our care. Of these, there were eight men and six women. The median age at the disease onset was 50.5 years, with the range from 25 to 79 years. The median diagnostic delay in our patient series was 3 years, ranging from 1 to 22 years. Noteworthy, in three patients the diagnostic delay for Schnitzler syndrome was over 5 years [6, 12 and 22 years]. Nine patients were treated with IL-1 inhibitors (iIL-1) (canakinumab and anakinra).

Conclusion: Our analysis suggest that the diagnostic delay remains considerable even 50 years after the initial description of this syndrome. Our data on the diagnostic delay in Schnitzler syndrome is in keeping with the clinical experience in most countries with over 5 published cases, including France, Germany, Spain, Portugal and Italy. An early recognition of Schnitzler syndrome is crucial for prompt treatment targeting IL-1. The rarity of this syndrome and a wide range of initial signs and symptoms in these patients delay the correct diagnosis and a start of the biological therapy in these patients. An increased awareness of Schnitzler syndrome may reduce the diagnostic delay in these patients. A multidisciplinary approach is essential for an early diagnosis of Schnitzler syndrome.

REFERENCES:

[1] Lipsker D *et al.* The Schnitzler Syndrome. Four new cases and review of the literature. *Medicine.* 2001; 80:37-44.

[2] de Koning HD. Schniztler's syndrome: lessons from 281 cases. *Clin Transl Allergy.* 2014; 4:41.

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AB1322 APPENDICITIS STILL A MISDIAGNOSIS FOR FMF PATIENTS

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Background: Familial Mediterranean Fever(FMF) is an autoinflammatory disease characterized by recurrent polyserositis attacks. Attacks typically consist of fever and/or abdominal pain and/or chest pain and/or arthritis. The disease is caused by mutations in the MEFV gene. Abdominal pain during the attacks is frequently misdiagnosed as acute abdomen and these patients go undersurgical intervention is not uncommon [1].

Objectives: Severe abdominal pain during FMF attacks is frequently misdiagnosed as acute abdomen and patients receive surgical intervention. In this study, we aim to compare the clinical and genetic characteristics of FMF patients with appendectomies to those without appendectomies.

Methods: We reviewed 176 patients with FMF who went under appendectomy. We randomly matched these patients with 176 FMF patients without appendectomy for comparison. We compared clinical manifestations, MEFV mutations, and treatment modalities.

Results: In this study, 176 patients with FMF went under appendectomy. Only 2 of these appendectomies were performed after FMF diagnosis. In the appendectomy group fever(84% vs 68%), abdominal pain(91% vs 79%), pathogenic exon 10 mutations(65% vs 59%), lower leg pain(0.5% vs 0%) and orchitis(0.5% vs 0%) were more common but only the abdominal pain and fever was statistically significant. In the control group chest pain(18% vs 19%), arthralgia(46% vs 53%), arthritis(29% vs 37%), anti IL-1 usage(3% vs 5%), amyloidosis (0% vs 3%) and erysipelas(1% vs 3%) were more common but none of them were statistically significant. Myalgia(3%) was the same in both groups[Table 1]. Median diagnostic delay was 8(IQR 2-15) years in the appendectomy group and 3.5(IQR1-10) years in the control group.

Table 1. Characteristics of the patients

	No Of Patients(%) Appendicitis	No Of Patients(%) Control Group	P value
Patients	176(100)	176(100)	
Fever	148(84)	120(68)	0.0007
Abdominal Pain	160(91)	139(79)	0.0029
Chest Pain	32(18)	33(19)	1
Arthralgia	81(46)	94(53)	0.20
Arthritis	51(29)	65(37)	0.12
Myalgia	5(3)	5(3)	1
Erysipelas	2(1)	5(3)	0.45
Lower Leg Pain	1(0.5)	0(0)	-
Orchitis	1(0.5)	0(0)	-
Anti IL-1 usage	6(3)	9(5)	0.6
Amyloidosis	0(0)	6(3)	-
Diagnostic Delay	8.5(IQR2-15) years	3.5(IQR1-10) years	0.0002
Pathogenic Exon 10 Mutations	114(65)	103(59)	0.27
Appendectomy Before FMF diagnosis	174(99)	0(0)	

Conclusion: Even after the discovery of colchicine and identification of the MEFV gene diagnosis of FMF remains a challenge. Previous studies reported a median diagnostic delay of 8.2-11 years. In these studies, 28%-32% of the patients went under abdominal surgical intervention before the diagnosis of the FMF[2,3]. The most common symptoms of FMF(fever and abdominal pain) are also the most common symptoms of acute abdomen. Thus distinguishing between FMF and acute abdomen in undiagnosed FMF patients represents an understated problem. These patients have a longer diagnostic delay[8(IQR 2-15) vs 3.5(IQR1-10) years], worse control of attacks, poorer quality of life. In our study, most of the appendectomies were unnecessary in the FMF patients. Thus we recommend investigating the patient for FMF if the evidence of the acute abdomen does not expand beyond the symptoms.

REFERENCES:

[1] Ozdogan H, Ugurlu S. Familial Mediterranean Fever. Presse Med. 2019 Feb;48(1 Pt 2):e61-e76.

[2] Erdogan M, Ugurlu S, Ozdogan H, Seyahi E. Familial Mediterranean fever: misdiagnosis and diagnostic delay in Turkey. Clin Exp Rheumatol. 2019 Nov-Dec;37 Suppl 121(6):119-124.

[3] Hageman IMG, Visser H, Veenstra J, Baas F, Siegert CEH. Familial Mediterranean Fever (FMF): a single centre retrospective study in Amsterdam.

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AB1323 THE MYSTERY OF FAMILIAL MEDITERRANEAN FEVER: IS THERE ANY FACTOR TRIGGERING THE ATTACKS?

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory disease characterized by recurrent episodes of fever and serositis. Although it is known that the attack frequency differs among patients carrying different mutant genotypes [1], whether physical and environmental factors play a role in triggering attacks or whether they have an influence on timing of attacks remains to be elucidated.
Objectives: We aimed to identify different conditions causing flare-ups in FMF course and to investigate if there is a significant difference between patients carrying distinct mutations, regarding the distribution of the factors mentioned.
Methods: Two hundred patients were randomly selected among individuals who were routinely followed-up with FMF diagnosis in our centre. Individuals carrying only a variant of unknown significance or polymorphism such as R202Q, according to Infevers database, were excluded in order to gather a cohort consisting of patients with definite FMF. An inquiry was made based upon triggering factors determined by the patients themselves. The patients were classified into subgroups by their sex and mutation genotype. Since M694V variant is responsible for pronounced FMF course [2], we sorted the patients according to their status for M694V mutant allele. Group A included patients carrying M694V homozygously. Group B included patients carrying at least one M694V mutant allele whereas Group C consisted of patients who were non-M694V carriers. Chi-square test was performed to assess distribution of the trigger factors in terms of establishing its significance.
Results: Detailed distribution of trigger factors is shown in Table 1. 144 out of 200 patients described a culprit condition. Patients usually stated more than one factor, however some patients reported only one. The most-reported trigger factors by the cohort are summarized as following: 76 emotional stress (38%), 60 menstruation (30%), 40 cold exposure (20%), 34 fatigue (17%), 13 seasonal changes (6.5%). The distribution of trigger factors between Group A, B, and C were non-significant (p=0.88).

Table 1. The distribution of triggering factors in subgroups.

Group	Total (%)	Reported trigger factor (%)	Menstruation (%)	Emotional stress (%)	Cold exposure (%)	Fatigue (%)	Seasonal changes (%)	Others (%)
Female	123	97 (78.8)	60 (48.8)	47 (38.2)	24 (19.5)	19 (15.4)	7 (5.7)	6 (4.9)
Male	77	47 (61)	-	29 (37.7)	16 (20.8)	15 (19.5)	6 (7.8)	7 (9.1)
Group A	61	44 (72.1)	14 (23)	24 (39.3)	13 (21.3)	12 (19.7)	4 (6.6)	6 (9.8)
Group B	165	120 (72.7)	49 (29.7)	66 (40)	34 (20.6)	29 (17.6)	13 (7.9)	11 (6.6)
Group C	35	24 (68.6)	11 (31.4)	10 (28.6)	6 (17.1)	5 (14.3)	0	1 (2.8)

Group A: M694V homozygous patients, Group B: patients with at least one M694V allele, Group C: non-M694V carriers

Conclusion: We concluded that trigger factors did not vary between distinct mutant genotypes. Although emotional stress is the most reported trigger factor by the participants, one should bear in mind that emotional stress influences most chronic diseases negatively. We also observed that menstruation overtly triggers an FMF attack. Additionally, cold exposure should be considered as a notable trigger factor. It is still unclear what triggers an FMF attack in 28% of the patients, remains a mystery.
REFERENCES:
[1] Grossman C, Kassel Y, Livneh A, Ben-Zvi I. Familial Mediterranean fever (FMF) phenotype in patients homozygous to the MEFV M694V mutation. Eur J Med Genet. 2019 Jun;62(6):103532. doi: 10.1016/j.ejmg.2018.08.013.
[2] Egeli BH, Ugurlu S. Familial Mediterranean Fever: Clinical State Of The Art. QJM. 2020 Oct 20:hcaa291. doi: 10.1093/qjmed/hcaa291.
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AB1324 DIFFERENCES IN PERIPHERAL BLOOD B-CELL SUBSETS IN PATIENTS WITH IGG4-RELATED DISEASE, PRIMARY SJOGREN'S SYNDROME AND HEALTHY DONORS

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Background: The level of circulating plasmablasts has been proposed as a good marker for diagnosing and monitoring IgG4-related disease (IgG4-RD) independent of serum IgG4 level [1]. However elevated plasmablasts can be seen in other rheumatologic conditions.
Objectives: To compare B-cell subsets in peripheral blood of IgG4-RD, Sjogren's syndrome (SjS) patients (pts) and healthy controls.
Methods: Twelve pts with clinically active IgG4-RD (7F/5M, mean age 50,25 years (range 33-62), 20 active SjS pts (19F/1M, mean age 42 years (range 32-54 years); median disease duration 3 (2-10) years; ESSDAI score ≥5 in 6 pts,) and 20 healthy donors were included. SS was diagnosed based on the ACR-EULAR 2016 criteria. IgG4-RD was diagnosed according to comprehensive diagnostic criteria (H. Umehara, 2011). CD19+ B cells, memory B-cells (CD19+CD27+), non-switched memory B-cells (CD19+IgD+CD27+), switched memory B-cells (CD19+IgD-CD27+), naïve (CD19+IgD+CD27-), double negative (CD19+IgD-CD27-), transitional (CD19+IgD+CD10+CD38+) B-cells, plasmablasts (CD19+CD38+++IgD-CD27+), and plasma cells (CD19+CD38+) were analyzed by multicolor flow cytometry using cytometer Navios (Beckman Coulter, USA). The nonparametric Mann-Whitney test was used for statistical analysis. Data were shown as median (Me) with an interquartile range of 25 - 75 percentile. The differences were considered statistically significant when p <0.05. Statistica 10 for Windows (StatSoft Inc., USA) package was used for statistical data processing.
Results: There were no significant differences in the number of all studied B-cell subsets between pts with IgG4-RD and with SjS. But absolute numbers of plasmablasts, memory B-cells cells and transitional B-cells in IgG4-RD were significantly higher than in healthy donors: 4.5[1;9.8] $x10^3$/μl vs. 0.2 [0.09;0.4] $x10^3$/μl; 41 [33.5;57.5] $x10^3$/μl vs. 2.5 [1;6.3]; 12 [6.5;21] $x10^3$/μl vs. 0.1 [0;0.23] $x10^3$/μl respectively, p<0.05 for all cases.

Table 1. Peripheral blood B-cell subsets in patients with SS and healthy donors.

B-cell subsets, Abs. $x10^3$/μl	IgG4-RD	SjS	HD	P<0.05
B lymphocyte	166 [109.3;251.3]	164.5 [109.3;236.3]	150 [95;200]	
plasmablasts	4.5 [1;9.8]	2 [1;3.5]	0.2 [0.09;0.4]	*
transitional B-cells	12 [6.5;21]	8.5 [4;32.5]	0.1 [0;0.23]	*
switched cells	24.5 [20;41.8]	18.5 [11;29.8]	20 [9.75;40]	
non-switched cells	16.5 [10.5;21]	7 [3.75;15.5]	10 [4.75;20]	
memory B-cells	41 [33.5;57.5]	26 [14.8;40.8]	2.5 [1;6.3]	*
naïve B-cells	122 [63.3;176.5]	107.5 [49.5;193.8]	100 [57.5;100]	
double negative	13.5 [8.8;17]	10.5 [5.3;22.3]	20 [9.75;22.5]	

HD healthy donors
* IgG4-RD and HD groups compared, p<0.05

Conclusion: Immunophenotyping showed disturbed homeostasis of the B-cells subpopulations in IgG4-RD pts with a significant increase in plasmablasts compared to HD, but there were no differences between IgG4-RD and SjS pts. Further research is needed to evaluate the diagnostic utility of circulating plasmablasts in IgG4-RD.
REFERENCES:
[1] Wallace ZS, Mattoo H, Carruthers M, Mahajan VS, Della Torre E, Lee H, Kulikova M, Deshpande V, Pillai S, Stone JH. Plasmablasts as a biomarker for IgG4-related disease, independent of serum IgG4 concentrations. Ann Rheum Dis 2015 Jan;74(1):190-5.
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AB1325 DIAGNOSTIC DELAY IN FAMILIAL MEDITERRANEAN FEVER: IS IT STILL A PROBLEM?

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Background: Familial Mediterranean fever (FMF) is a rare hereditary autoinflammatory disease with disease onset in childhood in most cases. Although autoinflammatory disease awareness is increasing among physicians, delayed diagnosis is still prevalent as a cause of greater morbidity[1].
Objectives: We aimed to study the characteristics of FMF patients diagnosed between 2000-2010 and 2011-2021 and to see if there was a difference in diagnostic delay.
Methods: We retrospectively evaluated the medical records of the FMF patients followed up in our rheumatology clinic that were diagnosed between 2000-2021 and split them into two groups according to the year they received their diagnosis. There were 1151 patients diagnosed between 2000-2010 (Group 1) and 821 patients diagnosed between 2011-2021 (Group 2). The data studied included gender, age of onset, diagnostic delay, attack characteristics, MEFV mutation, and family history.
Results: The median current age of patients in Group 1 is 37 years (IQR:30-46) and the median current age of the patients in Group 2 is 36 years (IQR:29-44). The female to male ratio was 1.57 in Group 1 and 1.75 in Group 2, with no significant difference between the groups. Group 2 had later disease onset (p<0.001) and later diagnosis (p<0.001) than Group 1 as shown in the Table 1. The proportion of patients with at least one M694V mutation was higher in Group 2 (p<0.001). The attack durations did not vary between the groups. There was no significant difference in the prevalence of abdominal pain, fever, arthritis, and arthralgia between