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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.
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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.
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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

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Group 1 and Group 2. Chest pain (p=0.005), myalgia (p<0.001), and erysipelas-like erythema (p=0.041) were more common in Group 2 than Group 1. Patients with positive family history were more frequent in Group 2 than Group 1 (p=0.046).

Table 1.

	Group 1 (2000-2010, n=1151)	Group 2 (2011-2021, n=821)	p
Female/Male, n	704/447	522/299	0.275
Age at onset, median (IQR) years	13 (7-21)	18 (12-26)	**<0.001**
Delay in diagnosis, median (IQR) years	4 (1-11)	5,5(2-15)	**<0.001**
Attack duration, median (IQR) years	3(2-4)	3(2-4)	0.325
Presence of at least one M694V mutation (%)	526(46%)	390(60%)	**<0.001**
Presence of abdominal pain in the initial attack (%)	936(81%)	669(81%)	0.926
Presence of fever in the initial attack (%)	855(74%)	592(72%)	0.281
Presence of chest pain in the initial attack (%)	218(19%)	199(24%)	**0.005**
Presence of arthritis in the initial attack (%)	330(29%)	215(26%)	0.224
Presence of arthralgia in the initial attack (%)	213(19%)	170(21%)	0.223
Presence of myalgia in the initial attack (%)	45(4%)	65(8%)	**<0.001**
Presence of erysipelas like erythema in the initial attack (%)	31(3%)	36(4%)	**0.041**
Presence of positive family history (%)	652(57%)	502(61%)	**0.046**

Conclusion: There was some increase in the diagnostic delay in 2011-2021 compared to 2000-2010. This may be partly due to the later onset of symptoms in patients diagnosed in 2011-2021, which could have led the physicians to consider other differential diagnoses. Nevertheless, diagnostic delay in FMF still seems a prevalent problem that should be addressed to prevent excess morbidity and mortality.

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AB1326 EFFICACY AND SECURITY OF TNF-A INHIBITORS BIOSIMILARS IN NON INFECTIOUS UVEITIS

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Background: Biological drugs have become established as an effective therapeutic alternative to non infectious uveitis refractory to the usual treatment. In that sense, expiry of patents for tumor necrosis factor (TNF-a inhibitors) has allowed the development of biosimilars such as Infliximab and Adalimumab; both originals with years of experience in such pathology but with barely no evidence in real life case series of its biosimilars.

Objectives: To analyze the effectiveness and security of biosimilars of Infliximab and Adalimumab used in uveitis in a third level hospital.

Methods: Descriptive study based on a retrospective cohort of 40 patients suffering of non infectious uveitis who have received biological treatment with Infliximab and Adalimumab collected over the last 20 years (2000-2021), taking into account the complete substitution of the original for the biosimilar in our hospital in February 2015 and March 2019, respectively. The number of outbreaks during both the years before and after the start of the biological therapy, as well as the number of outbreaks during the year following the switch from the original to the biosimilar, have been analyzed. In that regard, we have studied variables such as visual acuity, presence of macular edema, vitritis and retinal vasculitis, as well as the need for systemic corticosteroids treatment. We have registered minor and major side effects associated with the treatment and the cases that have required a change of drug.

Results: The average duration of the immunosuppressive therapy previous to the introduction of the biological therapy was 3,15 years with an average frequency of 2,25 outbreaks during the previous years of the start of the biological therapy. Subsequently, 30 patients received treatment with Adalimumab and 10 with Infliximab showing an average of 0,35+- 0,73 outbreaks during the following year of its start. The switch from the original drug to the biosimilar was subsequently performed in 27 patients (25 for Adalimumab and 2 for Infliximab) with an average of 0,2 +-0,5 and 0,12+-0,44 outbreaks during the 12 months following the switch. Most of them (87%) stayed with the concomitant immunosuppressive treatment, being the Methotrexate the most frequently used (55%). No major side effect has been registered during the biological therapy; however a 25% of the patients showed minor side effects, mostly infections. In 11 cases (27,5%) the biosimilar drug had to be switched, in 7 cases due to inefficiency and 4 to poor tolerance, all of them corresponding to Adalimumab biosimilar. In 5 of those cases the switch was back to the original biological therapy while in the 5 remaining it was to Infliximab biosimilar (4) and Tocilizumab. Two cases of suspension of Adalimumab biosimilar due to disease remission should be highlighted.

Conclusion: According to our experience, the use of biosimilars of Infliximab and Adalimumab in non infectious uveitis is safe. The switch to biosimilars could be considered a feasible therapeutic choice in regards to keeping its effectiveness in patients previously treated with the original drug, even though studies featuring longer follow-up time and more population would be needed.

Table 1.

BASAL CHARACTERISTICS	
AGE, mean (SD)	36,8 (24)
Male n (%), Female n (%)	23 (57,5%), 17 (42,5%)
UVEITIS	
Primary n (%)	20 (50%)
Secundary n(%)	20 (50%)
***Systemic disease association**	JIA (30%); Behcet (15%); AS (10%); Others (45%)
Anterior Uveitis n (%)	22 (55%)
Posterior Uveitis n(%)	9 (22,5%)
Panuveitis n(%)	9 (22,5%)
Acute Uveitis n(%)	14 (35%)
Chronic Uveitis n(%)	26 (65%)
Bilateral Uveitis n(%)	28 (70%)
Unilateral Uveitis n(%)	12 (30%)
ANA	
Not Performed n(%)	1 (2,5%)
Negative n(%)	32 (80%)
Positive n(%)	7 (17,5%)
HLA	B27 4(10%), B51 7 (17,5%), negative 26 (65%)

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AB1327 PREVALENCE OF IMMUNORELATED MUSCULOSKELETAL ADVERSE EFFECTS IN PATIENTS WITH LUNG CANCER OR MELANOMA TREATED WITH IMMUNO-CHECKPOINT INHIBITORS

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Background: mmunotherapy in the field of medical oncology, consisting of inhibiting key immune checkpoints, is revolutionising the way patients with these pathologies are treated, being mainly used in skin and lung tumours. These molecules are aimed at controlling T-cell activation by interacting with cytotoxic T-lymphocyte antigen 4 (CTLA-4) protein (Ipilimumab); by acting on the programmed cell death receptor (PD-1) (Pembrolizumad, Nivolumab); or by binding to programmed cell death ligand 1 (PDL-1) such as Atezolizumad or durvalumad. Despite the improvement in survival in the management of cancers with poor prognosis, this type of therapy is characterised by a series of side effects, including dermatological, gastrointestinal, endocrine, rheumatological and other effects. In this study, we focused mainly on rheumatological adverse effects, ranging from mechanical and/or inflammatory musculoskeletal involvement to dry syndrome, vasculitis, polymyalgia rheumatica, inflammatory myopathy, among others.

Aims: To assess the prevalence of immuno-related adverse effects (Eair) in cancer patients with lung cancer or melanoma treated with immunotherapy targeting check-ponits, such as anti-CTLA-4, anti-PD-1, anti-PDL-1.

Objectives: To assess the prevalence of immuno-related adverse effects (Eair) in cancer patients with lung cancer or melanoma treated with immunotherapy targeting check-ponits, such as anti-CTLA-4, anti-PD-1, anti-PDL-1.

Methods: Observational study of a series of 115 patients diagnosed with lung cancer or melanoma, in treatment with checkpoint inhibitors (nivolumab, pembrolixumab, durvalumab, atezolizumab), from 2016 to 2021 at the Hospital Universitario Clínico San Cecilio. Patients who developed some type of rheumatological symptomatology after the start of immunotherapy were included. The clinical history of these patients was reviewed to confirm or rule out these adverse effects. The following musculoskeletal Eair were included: arthralgias, arthritis, generalised musculoskeletal pain, myalgias, osteoporosis and/or osteopenia. In the Eair registry, the following entities were not included: polymyalgia rheumatica, vasculitis and myositis.

Results: Out of a total of 115 patients who received immunotherapy, with age, type of tumour and treatment received (Table 1); 24 developed non-specific arthromyalgia, low back pain and/or neck pain, with no previous history of interest, and clearly related to the immunotherapy treatment. Five of the patients developed active arthritis with visible swelling; only one of them had previous RA with treatment, the others had no PA of interest. Of the patients with rheumatological involvement, x had underlying PsA, x had a family history of immune-mediated disease. Of the total patients, 2 had a gout flare-up (one of them with a previous diagnosis).

Conclusion: The most frequent rheumatological adverse effects related to immunotherapy are non-specific arthromyalgias considered to be grade 1 or 2 in severity, for which patients do not require specific treatment or suspension of treatment doses. However, several of the patients did develop active arthritis, requiring corticosteroid treatment and in some cases, the suspension of at least one treatment session. In our study, there is no clear relationship between one immunosuppressive drug or another for the development of Eair.

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