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AB0984 **TOCILIZUMAB MONOTHERAPY FOR POLYMYALGIA RHEUMATICA ~ RESULTS OF 52-WEEK TREATMENT OF A PROSPECTIVE, SINGLE-CENTER, OPEN, SINGLE-ARM TRIAL**

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Background: Polymyalgia rheumatic (PMR) is a chronic inflammatory rheumatic disease in the elderly people. Glucocorticoid (GC) is still definitely a mainstay for the treatment of PMR, but long-term GC therapy is a major risk factor of osteoporotic fractures, diabetes, hyperlipidemia, cardio-cerebral vascular events, glaucoma, etc. So GC-free treatment strategies for PMR are necessary for some patients with PMR. IL-6 is involved in the pathogenesis of PMR and quite a few case reports have already shown the efficacy of tocilizumab (TCZ) in PMR patients and some of them received TCZ monotherapy without GC.

Objectives: To assess the efficacy and safety of TCZ monotherapy for PMR

Methods: Thirteen PMR patients (male 3, female 10) who had been diagnosed by 2012 ACR/EULAR classification criteria from Jan 2013 to Feb 2015 were enrolled in our study (IRB application No. 638, UMIN registration No. 000008812) after obtaining the written informed consent. TCZ (8 mg/kg) was administered biweekly for the first 2 months (5 infusions) and every 4 weeks thereafter for 40 weeks (total 48 weeks). ESR, CRP, patient's global health assessed by visual analog scale (VAS), PMR activity score were evaluated every 4 week prospectively and were evaluated at week 52. Remission was defined as PMR activity score less than 1.5.

Results: Baseline patients' characteristics revealed various kinds of comorbidities in 11 patients; hypertension in 7, hyperlipidemia in 5, diabetes mellitus in 3, osteoporotic vertebral fractures in 2, history of angina pectoris in 1, history of brain infarction in 1, history of hematemesis due to NSAID ulcer in 1 and glaucoma in one patient. Nine patients could complete this 52-week trial and could achieve remission at week 52. Two patients discontinued TCZ because of no response at week 6 (No.1) and week 16 (No. 8) respectively. One patient (No.2), who were in clinical remission of PMR, dropped out from this study due to pemphigoid at week 50 and received GC therapy. Patient No. 12 abandoned TCZ at week 12 because of lung infiltrates although she was treated successfully with TCZ monotherapy, and she had been in remission without any treatment until week 52. The other 3 drop-out patients could obtain remission with GC therapy at week 52. There were no serious adverse events during 52-week treatment period.

Conclusions: TCZ mono-therapy was effective in most (9 out of 13) PMR patients although response was not so rapid as compared to GC. TCZ mono-therapy may be a good alternative therapy instead of GC for elderly patients with various comorbidities.

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AB0985 **METHOTREXATE AS INDUCTION OF REMISSION THERAPY FOR LOCALIZED MANIFESTATIONS OF IGG4-RELATED DISEASE**

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Background: Medium to high dose glucocorticoids represents the treatment of choice for inducing remission in IgG4-related disease (IgG4-RD) patients¹. However, clinicians might prefer alternative equally effective drugs in clinical settings where long-term corticosteroids treatment is contraindicated, such as diabetes or osteoporosis. We recently reported the efficacy of methotrexate in maintaining glucocorticoids induced IgG4-RD remission².

Objectives: To evaluate the efficacy of methotrexate as induction of remission therapy in selected cases of mild and localized IgG4-RD complicated by clinical scenarios that might advise against corticosteroids treatment.

Methods: Five patients with active untreated IgG4-RD were started on oral or subcutaneous methotrexate (up to 15–20 mg/week). Efficacy of methotrexate in inducing remission was assessed at 6 months by 18F-FDG PET/CT scan and by measuring the IgG4-RD Responder Index (RI)³ and circulating plasmablasts⁴. Partial response (PR) corresponded to an improvement of the IgG4-RD RI >2 points. Complete response (CR) corresponded to an IgG4-RD RI score <3.

Results: All patients were males with a mean age of 67 years (range 53–78). Two had pancreatic involvement; one had lymph node enlargement; one had pancreatic and lymph node involvement; one had pancreatic, aortic, submandibular gland and lymph node involvement. Patients with pancreatic involvement presented with increased serum amylases or abdominal discomfort; none had obstructive jaundice; all had overt diabetes. The mean IgG4-RD RI, serum IgG4 concentration and plasmablasts counts at baseline were 8 (6–15), 483 mg/dL (136–983) and 3336/mL (330–9330/mL), respectively. All patients had increased 18F-FDG uptake on PET/CT scan within the affected organs. After 6 months of methotrexate, Patients 1, 2, and 3 were on CR with improved or normalized PET/CT findings, serum IgG4 and plasmablasts levels. Patient 5 achieved PR, showing improved 18F-FDG-PET/CT findings, normal plasmablasts level, but stable serum IgG4 concentration; after 10 months of methotrexate, persistence of disease activity prompted the introduction of glucocorticoids. Methotrexate was stopped in Patient 4 after 5 months because of nausea and vomiting; at 6 months he showed persistently increased plasmablasts count and 18F-FDG uptake on PET/CT, thus requiring a rescue therapy with glucocorticoids. (Table 1)

Patient #1 (M, 78)			Patient #2 (M, 67)		Patient #3 (M, 70)	
Type 1 AIP, aortic, submandibular gland, lymph node involvement			Type 1 AIP		Type 1 AIP, lymph node involvement	
	Pre-Treatment	6 months (MTX 20 mg/week)	Pre-Treatment	6 months (MTX 15 mg/week)	Pre-Treatment	6 months (MTX 15 mg/week)
IgG4-RD RI	15	2 (CR)	6	2 (CR)	9	1 (CR)
IgG4 (mg/dL)	498	313	586	324	221	157
PBs/mL	2520	250	940	470	3560	130
18F-FDG-PET/CT	Increased FDG activity in all affected organs except pancreas	Decreased FDG activity in submandibular glands; negative in all the other organs	Increased FDG activity in pancreatic head and tail	Partial reduction in pancreatic FDG activity	Increased FDG activity in pancreas and hilar lymph nodes	Negative in all the involved organs

Patient #4 (M, 61)			Patient #5 (M, 53)	
Type 1 AIP			Lymph node involvement	
	Pre-Treatment	6 months (MTX 15 mg/week)	Pre-Treatment	6 months (MTX 20 mg/week)
IgG4-RD RI	6	NA	6	3 (PR)
IgG4 (mg/dL)	136	NA	973	819
PBs/mL	330	880	9330	0
18F-FDG-PET/CT	Increased FDG activity in pancreatic head and body	Markedly increased FDG activity in pancreatic head and body	Increased nodal FDG activity	Decreased nodal FDG activity, but not dimensional reduction of the lymph nodes

Abbreviations: M, male; AIP, autoimmune pancreatitis; MTX, methotrexate; PDN, prednisone; IgG4-RD RI, IgG4-related disease responder index; PBs, plasmablasts; 18F-FDG, fluorodeoxyglucose; PET/CT, positron emission tomography/CT scan; CR, complete response; PR, partial response; NA, not available.

Conclusions: In localized forms of IgG4-RD with mild manifestations, methotrexate represents a promising alternative strategy for inducing disease remission, especially in the presence of contraindications to glucocorticoids.

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AB0986 **FAMILY MEDITERRANEAN FEVER GENE MUTATIONS: A POORLY STUDIED CAUSE OF INTERMITTENT HYDRARTHROSIS**

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Background: Familial Mediterranean Fever (FMF) is an inherited autoinflammatory disorder caused by mutations in the MEFV gene encoding pyrin, characterized by recurrent episodes of fever and serositis. Some patients with FMF present incomplete penetrance of the disease and may manifest only as intermittent arthritis.

Objectives: Characterization of musculoskeletal clinical manifestations in patients with mutations of the MEFV gene in our hospital.

Methods: We retrospectively reviewed clinical records of patients with mutations detected in the Family Mediterranean Fever MEFV gene in our hospital from January 1, 2008 to October 1, 2016. We collected parameters such as age at diagnosis, age of onset of the symptoms, sex, affected joints, other extra-articular manifestations and type of MEFV gene mutation.

Abstract AB0986 – Table 1

Patient	Sex	Diagnostic age	Onset age	Arthritis	Location	Other musculoskeletal manifestations	Extra-articular manifestations	MEFV Mutation	Homo/ Heterocytosis
1	M	47	40	Yes	Knee	No	No	p Glu148Gln	Heterocytosis
2	M	14	13	Yes	Knee	No	No	R202Q	Homocytosis
3	M	22	22	No		No	Lymphocytic myocarditis	p Glu148Gln	Heterocytosis
4	M	52	47	No		Arthralgias	Abdominal pain. Pleuritis	R202Q	Heterocytosis
5	M	39	20	Yes	PIPs	Arthralgias	Abdominal pain	R202Q	Heterocytosis
6	M	61	54	No		Tendinopathy	Recurrent pericarditis	R202Q	Homocytosis
7	M	17	16	No		No	Abdominal pain	R202Q	Heterocytosis

Results: Seven patients with MEFV gene mutations were reviewed, all of them were women, ranging in age from 14 to 61 years old. Two of them had *recurrent knee monoarthritis*, one had a history of *arthritis* in the hands and *erratic arthralgias*, one had *erratic arthralgias* and two had no musculoskeletal manifestations. The 2 patients with intermittent hydrarthrosis responded satisfactorily to *colchicine*, but not the other patients with other musculoskeletal manifestations.

Conclusions: Genetic testing of the common mutations of the MEFV gene should be considered in patients with *recurrent episodes of monoarthritis* without justifying cause (palindromic rheumatism, intermittent hydrarthrosis, etc.)

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AB0988 BEHÇET'S DISEASE IN A DEFINED AREA OF NORTHWESTERN SPAIN

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Background: Behçet's disease (BD) is a multisystemic inflammatory chronic disease. There is a wide variation in the clinical features of BD among geographical groups.

Objectives: To determine the demographic and clinical characteristics of BD in a defined area of northwestern Spain (Vigo).

Methods: Patients with BD (International Criteria BD) and seen in the University Hospital of Vigo in Spain, from 1994 to 2016, were retrospectively enrolled. Demographic, clinical, treatment and evolution data were recorded and analyzed using SPSS 22.0.

Results: Our patients were 26 male and 25 female. The mean age at the onset of the disease was 33±11.95 years (11–62). Oral and genital ulcers were seen in 100% and 84.3% respectively and skin lesions in 88.2%. Ocular involvement occurred in 35.3%, neurological disease in 39.2% and gastrointestinal involvement in 29.4% (the area worst affected was colon and small bowel). Vascular disease was present in 33.3%. See table 1. Pathergy test was performed in 18 patients (35.29%) and 10 (55.5%) were positives. HLA B51 was studied in only 13 patients (25.5%) and 8 (61.5%) were positives. 62.7% of patients had no cardiovascular risk factors (CVRF), 27.4% were smokers, 7.8% were hypertensive and 3.9% were hyperlipidemic and diabetic respectively. CVRF were not related to thrombotic events ($p>0.05$). In regard to gender influence, only pseudofolliculitis was significantly more frequent in men ($p<0.001$). There was a trend for increased prevalence of ocular disease and elevated erythrocyte sedimentation rate/serum C-reactive protein in men, and anemia in women, which, however, did not reach statistical significance. Treatment consisted of corticosteroids (92.2%), colchicine (68.6%) and another immunosuppressive agent (35.3%). During the disease course 78.4% of the patients had an outbreak, 45.1% initiated or changed to immunosuppressive agent and 19.6% used biological drugs. Most of our patients (92.1%) were admitted to hospital and these constitute an evident bias. Two patients died during the followup period, but only one in relation of BD (upper gastrointestinal bleeding and seizures).

Conclusions: Our series has some particular aspects especially the high frequency of gastrointestinal lesions and neurologic involvement. CVRF do not seem to play a role in the development of thrombotic events. Our results confirm the ethnic and geographic variation of BD expression.

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AB0989 RHEUMATOLOGIC COMPLICATIONS OF THALASSEMIA: SHOULD RHEUMATOLOGISTS JOIN THE MANAGEMENT TEAM?

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Background: Beta-thalassemia major is accompanied by progressive multiple organ systems involvement due to the disease pathophysiology as well as iron overload from blood transfusions on a regular basis. Rheumatologists are not frequently involved in the multidisciplinary management of the disease, in which rheumatologic complications are relatively common.

AB0987 THE RELATIONSHIP BETWEEN ANTI-INTERLEUKIN-1 THERAPIES AND MEFV GENE MUTATIONS IN FAMILIAL MEDITERRANEAN FEVER PATIENTS: A SINGLE CENTER EXPERIENCE

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Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease characterizing recurrent self-limiting attacks of inflammation mainly placed in serosal surfaces of the body with fever (1). Colchicine is an important weapon of the humanity in FMF treatment yet. However, the puzzle of inflammation was solved, and so, inflammasome complex and interleukin-1 were discovered. Eventually, new era started with anti-interleukin-1 agents in colchicine resistant and/or intolerant FMF patients (2).

Objectives: The aim of this study is to evaluate the effectiveness of anti-interleukin-1 (anti-IL-1) agents on the characteristics of attacks, the adverse effects associated with anti-IL-1 treatment, and relation between therapy and MEFV gene mutations in 23 FMF patients with resistant and/or intolerant to colchicine.

Methods: Between January 2015 and December 2016, twenty-three-FMF patients that following-up at Cumhuriyet University Medical Faculty Rheumatology-Internal Medicine Department were included in to the study. Anakinra (69,6%), and canakinumab (30,4%) were used in 23 FMF patients. 20 cases were resistant to colchicine, 3 were intolerant to colchicine.

Results: The median age of the patients was 28 years, (18–54) and the median age at diagnosis was 20 years (3–50). Of the FMF patients, nine (39.1%) were female and fourteen (60.9%) were male. The distribution of MEFV gene mutation frequencies in the FMF patients was no mutation in one (4.3%) patient, M694V heterozygous in nine (39.1%), M694V homozygous in 7 (30.4%), E148Q heterozygous in one (4.3%), and compound heterozygous mutation in 3. (13%) patients. 16 patients used anakinra (100mg/day) for 6 months (median) and 7 used canakinumab (150mg/2 months) for 3 months (median). Four of 7 patients were resistant to anakinra. After a median follow up 6 months overall clinical response [no attack (18 patients) or decreased frequency of attacks (5 patients)] was %100. In an FMF patient with no mutation, his brother and mother had FMF with no mutations on MEFV gene. We achieved good clinical and laboratory responses in the patient by canakinumab.

Conclusions: Anti-IL-1 agents can be got involved in a new place safely and effectively in FMF patients along with colchicine. In addition, whole gene analysis should be done in refractory FMF patients with no mutations in order to could investigate new mutations, epigenetic mechanisms or other unexplained reasons.

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Abstract AB0988 – Table 1. Clinical manifestation of our BD patients

Skin lesions 41/55 (88.2%)	Ocular disease 18/51 (35.3%)	Neurologic disease 20/51 (39.2%)	Vascular disease 17/51 (33.3%)	Gastrointestinal involvement 15/51 (29.4%)
Pseudofolliculitis 58.8%	Uveitis 23.5%	Aseptic meningitis 11.7%	Venous thrombosis 21.6%	Pain 11.7%
Erythema nodosum 39.2%	Retinal vasculitis 5.9%	Seizures 7.8%	Arterial thrombosis 7.8%	Bleeding 9.8%
Leukocytoclastic vasculitis 5.9%	Episcleritis 3.9%	Cerebral venous thrombosis 5.9%	Mixed thrombosis 2%	Diarrhea 5.9%
	Vascular occlusion 2%	White matter lesions 5.9%	Aneurysm 2%	Fever 2%
		Stroke 3.9%		
		Paresthesias 3.9%		
		Others 5.9%		