THU0582

THE TNF RECEPTOR-ASSOCIATED PERIODIC SYNDROME (TRAPS): CLINICAL AND GENETIC CHARACTERIZATION OF A COHORT OF ADULTS DIAGNOSED OF TRAPS SYNDROME

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Background: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is a disease that is included within of hereditary syndromes of periodic fever. It presents an autosomal dominant pattern of inheritance. It's due to mutations of TNFRSF1A gene. It is usually present in childhood although it can also appear in adulthood and it tends to cause high levels of acute phase reactants, fever, musculoskeletal symptoms (myalgias, arthralgias, arthritis), rash, abdominal pain, etc

Objectives: To describe the clinical characteristics and genetic variants of patients diagnosed with TRAPS syndrome in a cohort of patients with autoinflammatory syndromes with follow-up in a tertiary hospital from 2013 to the present

Methods: Retrospective descriptive study of adult patients diagnosed with autoinflammatory syndrome since 2013 (year of introduction of genetic tests in the hospital laboratory) until now. The data was obtained from the review of medical records. All patients with mutations in TNFRSF1A gene and clinically compatible with this diagnosis were reviewed

Results: Of a total of 44 adult patients diagnosed with hereditary syndromes of periodic fever (FMF, TRAPS, cryopyrinopathies, HIDS) and compatible genetic mutations (excluding polymorphisms), 13 (29.5%) presented mutations in the TNFRSF1A gene. Of those 13 patients, 9 (69.2%) were women. The most frequent mutations were the mutation in heterozygosis in exon 4 (p.R92Q) with 12 cases (92.3%) and one case (7.6%) with mutation in heterozygosis in exon 3 (p.P46L). The mean age at diagnosis was 27.92 years (IR 12-55 years). 5 patients showed simultaneous genetic variants in other genes related to autoinflammatory syndromes. Signs and/or symptoms were myalgia and elevation of acute-phase reactants with 12 patients (86%) followed by fever and joint symptoms (arthralgias and/or arthritis) with 11 patients (79%) were the most frequent. 2 patients (14%) had conjunctivitis. 9 patients (64%) presented cutaneous involvement. 2 cases (14%) presented lymphadenopathy. Regarding treatment, 5 patients (36%) had received treatment with biological therapy (anti-IL-1 or anti-TNF) and another 5 patients (36%) had used colchicine. The corticoids were used in 6 patients (43%)

Conclusion: The TRAPS syndrome is a clinical entity to consider when making a differential diagnosis in patients with suspected autoinflammatory syndrome, that present fever, acute phase reactants elevation, arthromyalgia and its confirmation diagnosis is with genetic test

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.7036

THU0583

EXPERIENCE OF ANAKINRA AND CANAKINUMAB IN PATIENTS WITH COLCHICINE-RESISTANT FAMILIAL MEDITERRANEAN FEVER AND COMPLICATED WITH AMYLOIDOSIS

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Background: Familial Mediterranean Fever (FMF) is a hereditary auto-inflammatory disease characterized by recurrent fever and serosal inflammation (1). The goal of FMF treatment is to prevent the attacks and to minimize subclinical inflammation between attacks, and in attacks-free period. Colchicine is a major drug that sine qua non in the treatment of FMF. However, anti-interleukin-1 agents are recommended in colchicine resistant and/or intolerant FMF patients (2).

Objectives: The aim of this study is to evaluate the efficacy of anti-interleukin-1 (anti-IL-1) agents in 54 FMF patients with resistant/intolerant to colchicine or complicated with amyloidosis.

Methods: Between January 2014 and December 2018, fifty four patients who were diagnosed as FMF according to the criteria of Tel-Hashomer that following-up at Sivas Cumhuriyet University Medical Faculty, Rheumatology-Internal Medicine Department were included in to the study.

Results: 25 (46.3%) male and 29 (53.7%) female were included in the study. The median age of the patients was 29 (min:17-max: 60) years and the median age at diagnosis was 18 (min: 3-max: 46) years. Anakinra was used in 34 (63%) FMF patients (100 mg/day), and

canakinumab was used in 20 (37%) patients (150mg/8weeks). 37 cases were resistant to colchicine, 8 were intolerant to colchicine, 9 (20%) cases were complicated with amyloidosis. 8 patients had renal transplantation. MEFV gene mutations are shown in Table 1. Median duration of anti-IL-1 agent use was 12 months (min:2-max40). 5 patients were resistant to anakinra, 4 patients had side effects which anakinra related. After a median follow up 12 months overall clinical response was%95 (frequency of attacks <1/6months). Median proteinuria decreased from 3850 mg/day to median 1600 mg/day (p= 0.04) (Table 2). IL-6 treatment was started in 3 patients because of ineffectiveness of canakinumab. One pregnant patient was followed up with anakinra during pregnancy and there were no problems.

Conclusion: Anti-interleukin-1 agents can be used effectively and safely in the treatment of FMF patients. These agents are especially effective in the treatment of proteinuria due to amyloidosis. Large and long-lasting follow-up studies are needed to evaluate long-term effects of these drugs.

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Table 1. MEFV mutations in FMF patients

MEFV Mutations	n
M694V homozygus	20 (37%)
M694V heterozygous	8 (15%)
Compound mutation	14 (26%)
Other mutation	8 (15%)
No mutation	4 (8%)

Table 2. Laboratory Findings of the FMF patients treated with anti-IL-1 agents

	Pre-treatment (median)	Post-Treatment (median)	p
Number of attacks	>2/6month	<1/6month	p<0.05
ESR mm/h	33	8	p<0.05
CRP mg/dl	43	4.3	p<0.05
Proteinuria mg/day	3856	1600	p<0.05

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.4760

THU0584

RHEUMATOLOGICAL IMMUNE-RELATED ADVERSE EVENTS ASSOCIATED WITH IMMUNOTHERAPY IN SOLID ORGAN TUMOR. STUDY OF 102 CASES FROM A REFERRAL SINGLE CENTER FOR LAST 4 YEARS

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Background: Immune checkpoint blockade therapy (ICBT) currently is one of the most used therapies against cancer. The activation of the immune system can lead to different immune-related adverse events (irAEs), being the rheumatological side effects among the most common.

Objectives: Our aim was to assess the rheumatological irAEs in patients who received immunotherapy.

Methods: We set up an observational study of patients treated with Nivolumab and Pembrolizumab (anti-PD1), Atezolizumab (anti-PD-L1) and Ipilimumab (antiCTLA-4) for solid organ tumors. All these patients were followed in a single reference University Hospital from March-2015 up to December-2018. The main outcome was to determinate the incidence of rheumatological irAEs.

Results: We studied 102 patients (63♂/39♀) with a mean age of 60.6 ±9.7 with different solid organ tumors. Only 7 patients (6.8%) had a previous diagnosis of an immune-mediated disease: psoriasis (n=2), psoriatic arthritis (1), systemic lupus erythematosus (1), spondyloarthritis (1), rheumatoid arthritis (1) and skin lupus (1).

Rheumatological side effects were observed in 15 patients (14.7%): inflammatory arthralgia (8), arthritis (6), myositis (2) and aortitis (1). The time of appearance of the rheumatological irAEs was of 6.36 months (± 5.81). From the 7 patients with previous diagnosis of an immune-mediated disease, only 1 patient with psoriasis suffered a worsening of skin symptoms and another one with psoriatic arthritis had a monoarthritis episode.

Among the 14 patients who suffered from arthralgia/arthritis, the most frequent pattern was oligoarticular (40%), followed by poly (30%) and monoarticular (30%). The most affected joint was the knee ($n=4$), followed by wrist (3), hands (3), ankle (2), shoulder (2) and foot (1).

Apart from the articular disease, 2 patients suffered from myositis in lower limbs, with weakness of legs and arthralgia in their knees. A patient was diagnosed of aortitis through a PET, although the patient did not have any symptom.

Immunology tests with RF, ACCP and ANA were done in 8 out of the 15 patients with musculoskeletal irAEs, being negative in all cases.

Interviewing 40 of the patients who received ICBT, 7 of them (17.5%) referred xerophthalmia. 6 of them (15%) had a positive Schirmer test, and 3 (7.5%) had a reduced tear break-up time. None patient met Sjögren criteria.

In 6 out of the 15 patients with rheumatological irAEs (all of them with arthralgia/arthritis) the ICBT was removed, temporary in all cases, and could be reintroduced after a mean of 33 ± 18.9 days. 6 patients were treated with NSAIDs and 5 with oral prednisone (2 of them also required intra-articular corticoids).

Conclusion: Rheumatological irAEs are common in clinical practice. Arthralgia-Arthritis and dry-syndrome are the most frequent adverse events.

Disclosure of Interests: Lara Sánchez Bilbao: None declared, Iñigo González-Mazón: None declared, Rosalía Demetrio-Pablo: None declared, José Luis Martín-Varillas: None declared, Marina Delgado Ruiz: None declared, Isabel Bernat Piña: None declared, Belén Atienza-Mateo: None declared, Monica Calderón-Goercke: None declared, D. Prieto-Peña: None declared, Almudena García Castaño: None declared, Miguel A González-Gay Grant/research support from: Prof. MA Gonzalez-Gay received grants/research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker's bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Ricardo Blanco Grant/research support from: Abbvie, MSD, and Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen

DOI: 10.1136/annrheumdis-2019-eular.7386

THU0585

LYMPHADENOPATHY IN IGG4-RELATED DISEASE IS ASSOCIATED WITH DISEASE ACTIVITY AND EOSINOPHILIA

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Background: IgG4-related disease (IgG4-RD) is an immune-mediated systemic disease characterized by the enlargement of multiple organs. IgG4-RD frequently involves the pancreas, lacrimal glands, salivary glands, bile duct, kidneys, lungs, and retroperitoneum, but can potentially affect any organs. Lymphadenopathy is often seen in patients with IgG4-RD along with other organ involvements, but the significance of the exist of lymphadenopathy in IgG4-RD is unclear.

Objectives: The aim of this study is to clarify the characteristics of patients with IgG4-RD who have lymphadenopathy.

Methods: We conducted cluster analysis with clinical data in consecutive 85 patients with untreated active IgG4-RD in our institute. We divided the patients into two groups who had lymphadenopathy or not (lymph group and non-lymph group), and compared clinical characteristics between the two groups. We counted the areas of swollen lymph nodes and performed correlation analysis with clinical characteristics. We also comprehensively screened serum protein concentrations in IgG4-RD patients ($n=15$) and healthy controls ($n=5$) by using high-throughput proteomic analysis, and differentially expressed proteins were extracted. We compared the concentrations of serum proteins which were extracted between lymph group and non-lymph group.

Results: Among 85 patients with IgG4-RD, 44 (52%) were male. Median age was 63 years old. Forty-seven (55%) patients were lymph group. Cluster analysis revealed that lymphadenopathy was in a cluster with serum IgG4, IgG4/IgG, IgG4-RD responder index (IgG4-RD RI), soluble interleukin-2 receptor (sIL-2R), eosinophilia, erythrocyte sedimentation rate (ESR), lung involvement, hemoglobin, albumin, C3 and C4. In lymph group, serum IgG4, IgG4/IgG, IgG4-RD RI, eosinophilia, sIL-2R and ESR were significantly higher than non-lymph group (Figure). Spearman's correlation analysis revealed that areas of the swollen lymph nodes were positively correlated with serum IgG4, IgG4/IgG, sIL-2R, eosinophilia. Proteomics analysis revealed that 68 proteins were significantly higher in IgG4-RD ($p<0.05$). Among them, proteins related to adhesion of immune cells, fibrosis, formation of lymph node and eosinophil activation such as integrin $\alpha 1\beta 1$, CCL18, CCL19 and eotaxin3 were higher in lymph group ($p=0.03$, $p=0.03$, $p=0.06$ and $p=0.06$, respectively).

Conclusion: Lymphadenopathy in IgG4-RD is associated with disease activity and eosinophilia. Proteomics analysis can provide some clues for elucidating the significance of lymphadenopathy in IgG4-RD.

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Disclosure of Interests: Satoshi Takanashi: None declared, Jun Kikuchi: None declared, Takanori Sasaki: None declared, Mitsuhiro Akiyama: None declared, Yuko Kaneko Grant/research support from: Abbvie, Eisai, Speakers bureau: AbbVie, Astellas, Ayumi, Bristol-Myers Squibb, Chugai, Eisai, Eli Lilly, Janssen, Kissei, Pfizer, Sanofi, Takeda, Tanabe-Mitsubishi, UCB, Hidekata Yasuoka: None declared, Katsuya Suzuki: None declared, Kunio Sugahara: None declared, Tsutomu Takeuchi Grant/research support from: Astellas Pharma Inc, Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Takeda Pharmaceutical Co., Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Eisai Co., Ltd., AYUMI Pharmaceutical Corporation, Nipponkayaku Co. Ltd., Novartis Pharma K.K., Grant/research support from: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Grant/research support from: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Abbvie GK, Nipponkayaku Co.Ltd, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Taiho Pharmaceutical Co. Ltd., Chugai Pharmaceutical Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., GlaxoSmithKline K.K., UCB Japan Co. Ltd., Consultant for: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen,