AB0993

COMORBIDITIES IN FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is a periodic fever syndrome, characterized by recurrent episodes of fever and serosal inflammation accompanied with high acute phase reactants. The analysis of possible comorbidities is important to understand the impact of these conditions on clinical care and whether they share a common etiological pathway.

Objectives: We aimed to evaluate the comorbidities associated with FMF patients in a large genetically diagnosed cohort.

Methods: We retrospectively evaluated the medical records of FMF patients who were followed up at Department of Pediatric Rheumatology in Hacettepe University between 2000 and 2015. This study was approved by the Research Ethics Committee and was conducted in accordance with the Declaration of Helsinki. The diagnosis of FMF was made according to Tel Hashomer diagnosis criteria for patients who applied prior to April 2009 and to the Turkish FMF pediatric diagnosis criteria after April 2009. The FMF patients who had homozygous or compound heterozygous mutations were included in the study. Comorbidities associated with FMF were divided into three groups; associated with increased inflammation, associated with FMF and incidental.

Results: A total of 1999 patients were enrolled in the study. Of all 1999 FMF patients, 636 were children (31.8%), 1029 were males (51.4%), with a mean age of 31.60±16.01 years. The mean follow up time was 4.50 ±3.99 years (median:3.84 range from 0.21-29.4 years). 880 of 1999 (44%) FMF patients had homozygous MEFV gene mutation, the most common mutation was M694V homozygous. The remaining were compound heterozygous. 656 patients (32.8%) had one or more than one comorbidity associated with FMF. Ankylosing spondylitis was the most common comorbidity associated with increased inflammation while the most common comorbidity in FMF related comorbidities was renal amyloidosis. The frequency of ankylosing spondylitis, henoch schonlein purpura, juvenile idiopathic arthritis, polyarteritis nodosa (PAN), multiple sclerosis (MS) and Behçet's disease were increased in patients with FMF when compared to those in the literature. Systemic lupus erythematosus was observed less frequently in the patients with FMF than in the population. While the increase in the frequency of MS was 3.3 times, the frequency of PAN was increased 110 times.

Conclusion: This study shows that FMF is a hereditary disease associated with significant comorbidity. We also confirm that inflammatory and rheumatic diseases are more common in FMF.

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VITAMIN D STATUS IN CHILDREN WITH JIA DEPENDING ON THE SEASON

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Background: Plenty of studies demonstrated the relationship between vitamin D and Juvenile idiopathic arthritis (JIA) disease activity [1,2]. Others reported no relationship between 25(OH)D and disease activity [3,4]. The main source of vitamin D is endogenous vitamin D synthesis induced by sunlight exposure.

Objectives: The aim of this study was to examine the status of vitamin D in children with JIA depending on the peculiarities of the disease and the season.

Methods: 92 patients with JIA were examined. The median age of them was 10.5±1.7 years, from 1.8 to 17.6 years (55 female, 37 male). The serum level of vitamin D was measured through blood test by chemiluminescence method. The relationship between the level of vitamin D and disease activity was analyzed based on juvenile arthritis disease activity score (JADAS27).

Results: The average level of vitamin D was 22,75±1,97ng/ml (corresponded to an insufficient level). It was not found relationship between the frequency of vitamin D deficiency and gender. Vitamin D status changed throughout the year from lowest value 19,52±1,61 ng/ml (in May) till the greatest value 29,62±2,49 ng/ml (in September). Significantly higher level of vitamin D was in September compared to most months (January, p=0,04; February, p=0,04; March, p=0,01; April, p=0,02; May, p=0,01; October, p=0,03; November, p=0,03; December, p=0,01).

The geographical location of Kharkiv (Ukraine) is at 50° latitude. It was proved that UVB radiation above the 33° latitude is not intense enough for the synthesis of vitamin D during the whole year [5].

At the same time there was no significant relationship between the low level of vitamin D in serum and disease activity.

Conclusion: A decrease of vitamin D status were observed throughout the year. Despite the fact that in September was the highest level of vitamin D, the normal concentration was not reached. Seasons should be taken into account, but patients with JIA need supplementation of vitamin D all around the year.

REFERENCES

- [1] Szymańska-Kaluza J, Biernacka-Zielińska M, Stańczyk J, Smolewska E. Vitamin D level in children with juvenile idiopathic arthritis and its correlation with clinical picture of the disease. *Reumatologia*. 2013;51:271–6. doi: 10.5114/reum.2013.37250.
- [2] Çomak E, Doğan ÇS, Uslu-gökçeoğlu A, Akbaş H, Özdem S. Association between vitamin D deficiency and disease activity in juvenile idiopathic arthritis. *Türk J Pediatr*. 2014;56:626–631.
- [3] Dağdeviren-çakır A, Arvas A, Barut K, Gür E, Kasapçopur Ö. Serum vitamin D levels during activation and remission periods of patients with juvenile idiopathic arthritis and familial Mediterranean fever. *Türk J Pediatr*. 2016;58:125–31. doi: 10.24953/turkjped.2016.02.001.
- [4] Bouaddi I, Rostom S, El Badri D, Hassani A, Chkirate B, Abouqal R, et al. Vitamin D concentrations and disease activity in Moroccan children with juvenile idiopathic arthritis. *BMC Musculoskelet Disord*. 2014;15:115. doi: 10.1186/1471-2474-15-115.
- [5] Wacker M, Holick MF. Sunlight and vitamin D: a global perspective for health. *Dermatoendocrinol*. 2013;5:51–108. doi: 10.4161/derm.24494.

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EXPLORING UVEITIS IN EARLY ONSET ANA POSITIVE JIA

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Background: Juvenile idiopathic arthritis (JIA) is the most frequent childhood systemic disease affiliated with uveitis, where uveitis occurs in 10-13% of the patients, frequently causing long lasting consequences when unrecognized, untimely or incorrectly treated.

Objectives: To explore correlations between age, gender, ANA, RF titer in patients with JIA, occurrence of ocular manifestations and its complications. To examine similarities and differences between patients with different subtypes of JIA and uveitis.

Methods: The retrospective study included 31 children treated for JIA and uveitis in the period 2009-2017 at the Department of Paediatrics, UHC Zagreb. The SUN working group classification and grading system were used to evaluate ocular manifestations. Data analysis was executed using R programming language.

Results: We followed 31 patients (81% female) suffering from JIA with ocular manifestations. Median age at JIA onset in girls was 2.5 (1-14) years and in boys 8.6 (1-14.5) years, while girls had median age 4.25 (1-14) years at first ocular manifestation and boys 8.25 (4 -13.5) years. All patients were RF negative. 61% of patients was ANA positive, out of

which 88% had onset of JIA before the age of 6 (all girls). Complete remission of uveitis was achieved in two patients treated with topical corticosteroids, with non-steroid anti-inflammatory medication and methotrexate used in one of the patients. Inactive uveitis was most frequently achieved with a combined therapy which included biologics. A patient suffering from uveitis and JIA was found to be significantly more likely to suffer from oligoarthritic subtype (64.5%, CI 45.4-80.8%, $p<0.001$). We determined that a positive ANA titer occurred statistically significantly more frequent in females (OR inf., CI 3.18-inf., $p=0.001$). No significant statistical difference in ANA titer was found between groups of patients who were diagnosed with rheumatologic or ocular disease before and after the age of 6 (OR 1.85, CI 0.12-29.57, $p=0.6111$) nor between different subtypes of JIA. There was no difference in time passed between the occurrence of rheumatologic and ocular manifestations (median difference =1.75 years, $W=131$, $p=0.2597$), nor between ANA titer (OR 0.57, CI 0.09-3.12, $p=0.4775$) between groups with and without ocular complications. Patients who first presented with ocular manifestations did not have a greater likelihood to develop ocular complications (OR 5.59, CI 0.51-299.98, $p=0.175$).

Conclusion: A group of female patients suffering from RF negative subtypes of JIA and uveitis, with onset occurring before the age of 6 and positive ANA was prominent. These patients were traditionally classified as different subtypes of JIA, but together, they are best described as "early onset ANA positive JIA", concurring the need for reclassification of JIA. Limited by a small number of patients, this was partly confirmed with significant statistical findings, a recurrent positive ANA titer in females with JIA and uveitis and a more frequent occurrence of uveitis in oligoarthritis. The occurrence of ocular complications was not dependent upon ANA titer, nor upon the time difference between rheumatic and ocular symptoms or their order of appearance.

REFERENCE

- [1] Martini A., Ravelli A., Avcin T. et al. Toward New Classification Criteria for Juvenile Idiopathic Arthritis: First Steps, Pediatric Rheumatology International Trials Organization International Consensus. *J Rheumatol.* 2018;Oct 1.

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APPLICATION OF YAMAGUCHI CRITERIA FOR CLASSIFICATION OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: The ILAR criteria require the presence of arthritis to classify a patient as having sJIA. The sJIA patients prior to the onset of arthritis (suspected sJIA) appeared clinically similar to patients fulfilling the ILAR criteria for sJIA.

Objectives: Children with sJIA may have a delayed onset of arthritis and it fail to fulfill the ILAR criteria for sJIA. This study was undertaken to determine whether the Yamaguchi criteria is useful in classification of child with sJIA particularly in pre-arthritis phase of illness.

Methods: Retrospective chart review all patients with a diagnosis of sJIA in Hallym University Medical Center from Feb. 2002 through April 2016.

Results: Total 73 patients were diagnosed by ILAR classification criteria. 38 boys and 35 girls formed the study cohort. There are only 20 patients who are fulfilled of ILAR criteria in sJIA.

Characteristics sJIA (n=20) suspected (n=53) Total (n=73)

Evanescent Rash 19 24

Sore throat 1 5

Lymphadenopathy 2 11

Hepatomegaly 1 11

Splenomegaly 4 10

37 patients were diagnosed with suspected sJIA due to have not an arthritis. 36 patients were presented the arthritis at the onset of sJIA. The Yamaguchi criteria was fulfilled in a higher number of patients in the study (n=44) as compared to the ILAR criteria (n=20). Among the

patients with the absence of arthritis (n=37), 25 patients fulfilled the Yamaguchi criteria. (67.5%).

ILAR criteria Yamaguchi criteria

Yamaguchi criteria fulfilled 16 28

Yamaguchi criteria not fulfilled 4 25

Total cohort 20 53

Conclusion: Overall the Yamaguchi criteria was fulfilled in a higher number of patients in the study (60.2%) as compared to the ILAR criteria (27.3%). The failure of ILAR criteria was mainly due to the absence of arthritis. The Yamaguchi criteria is more helpful to diagnosis of sJIA. The Yamaguchi criteria may be useful on early diagnosis and treatment for patient with delayed onset arthritis at onset of disease.

REFERENCE

- [1] Kumar S., Junhraman D.S. and Jajam L. et al: Application of the Yamaguchi criteria for classification of "suspected" systemic juvenile idiopathic arthritis (sJIA). *Pediatric Rheumatology* 2012, 10:40.

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MATCHED CONTROLLED SURVEILLANCE OF TOCILIZUMAB TREATMENT FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS—AN INTERIM ANALYSIS

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Background: Tocilizumab (TOC) is approved for treatment of polyarticular juvenile idiopathic arthritis (poly-JIA). Real world data are limited.

Objectives: Long-term surveillance of patients newly initiating tocilizumab treatment for at least five years compared to a cohort of patients newly initiating a comparator biologic using the BIKER-registry.

Methods: Baseline demographics, clinical characteristics and disease activity parameters as well as efficacy and safety parameters were compared between patients using TOC and a control cohort using alternative biologics. The cohorts were matched for region and date of therapy start. Efficacy outcome variables were JADAS10 and joint counts. Functional status was determined with the Childhood Health Assessment Questionnaire disability-index (CHAQ-DI). Safety assessments were based on adverse events (AE) reports.

Results: Patients starting on TOC had a longer disease duration (5.2y vs. 2.9 y; $p=0.0001$) and had TOC significantly more often as second line biologic than patients in the comparator group (80% vs 14%, $p<0.0001$). No differences could be observed regarding disease activity parameters (JADAS 10 14.7 +/- 6.4 vs 15.8 +/- 6.0) or disability (CHAQ DI 0.65 +/- 0.63 vs 0.66 +/- 0.66) at baseline. Patients treated with TOC showed a substantial response to treatment with a significant reduction in JADAS 10 from 14.7 to 5.4 ($p<0.0001$). After 6 months of TOC treatment, 40% of patients had reached JADAS minimal disease activity (MDA), 22% of patients had reached JADAS remission. Tolerability was comparable between the two cohorts, with 31 in the TOC versus 34 patients in the control cohort experiencing AE; serious AE (SAE) were documented in 3 patients in the TOC and one patient in the control cohort. The SAE in the TOC cohort were medication intoxication with suicidal intent, JIA flare, gastrointestinal infection and abdominal pain in 1 patient each. In the control cohort there were JIA flare in 2 patients and gastrointestinal infection in 1 patient. No significant differences regarding infectious AEs, cytopenias or elevated transaminases were observed. No other AE were reported more than once; no deaths occurred.

Conclusion: Comparability of efficacy was limited due to the fact that patients in the TOC cohort had longer disease duration and were more often second line biologic users. Tolerability was comparable in both cohorts. Long-term observation is ongoing.