Objectives: Our study aimed to compare the accuracy of serum biomarkers for the diagnosis of MAS complicating s-JIA and to investigate the clinical significance of serum neopterin levels as an indicator of disease activity and diagnosis of MAS complicating s-JIA.

Methods: Serum cytokine levels (neopterin, IL-18, and CXCL9) and soluble tumor necrosis factor receptor type I (sTNFR-I) and II were determined by enzyme-linked immunosorbent assay in 78 patients with s-JIA, including 21 with MAS. The accuracy of these levels for the diagnosis of MAS were compared. Next, serum neopterin levels, in total 125 patients with s-JIA, including 30 with MAS, 15 with Epstein–Barr virus-induced hemophagocytic lymphohistiocytosis (EBV-HLH), and 15 with Kawasaki disease (KD), as well as 28 healthy controls (HCs) were analysed. Results were compared with the clinical features of MAS.

Results: Receiver operating characteristic curve analysis revealed area under the curve values and cut off values of neopterin, IL-18, CXCL9, sTNFR-II/I ratio and ferritin were 0.9465/19.5nmol/l, 0.8985/92920ng/ml, 0.9333/3130pg/ml, 0.9393/5.796 and 0.8671/2560ng/ml, respectively. Serum neopterin levels were significantly elevated in patients with MAS and EBV-HLH compared with those in patients with acute-phase s-JIA and KD. Serum neopterin levels profoundly and rapidly increased as MAS developed and correlated positively with disease activity.

Conclusion: Serum neopterin levels may be used as a promising indicator of disease activity in s-JIA and MAS and for evaluating it. It may also be a useful marker to diagnose the transition to MAS from acute-phase s-JIA.

REFERENCES:

Disclose of Interests: None declared


FAMILIAR MEDITERRANEAN FEVER (FMF): A SINGLE CENTER EXPERIENCE FROM TURKEY

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Background: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease mainly affecting ethnic groups living at Mediterranean region. Since the discovery of the Mediterranean Fever (MEFV) gene, molecular genetic testing has been used as a diagnostic adjunct especially in atypical cases (1, 2). Although substantial progress has been achieved about the etiopathogenetic mechanisms of FMF during the past 20 years, the diagnosis is still based on clinical criteria.

Objectives: To define best treatment approach in patients with TRAPS

Methods: The medical records of 1685 children diagnosed and followed up as FMF were reviewed retrospectively. All patients were evaluated for three diagnostic criteria.

Results: A total of 1685 children (839 girls, 846 boys) were involved to the study. Family history of FMF was positive in 46.1%. The mean standard deviation of current age, age at symptom onset, age at diagnosis were 13±5.4, 5.4±4.05, 7.9±4.1 years, respectively. Median (min-max) follow-up period was 3 (0.5-18) years. Among 1685 patients, 82.8% had 78.2% had abdominal pain, 36.1% had arthritis, 22.6% had chest pain and 16.6% had erysipeloid-like erythema. Three patients had biopsy proven amyloidosis. Concomitant disease was present in 140 (8.3%) patients. Most of them (40.7%) were diagnosed with juvenile idiopathic arthritis and FMF. Henoch-Schönlein vasculitis was observed in 35 (25%) patients. Median (min-max) PRAS score was 7 (3-13). Forty-four (26%) patients were unresponsive to adequate doses of colchicine. Among them, 16 (36.4%) were treated with anakinra and 28 (63.6%) received canakinumab. Children homozygous for M694V were found to have more severe course of disease and higher PRAS scores (P<0.001). Furthermore, 34 (77.3%) of colchicine resistant patients carried at least one M694V variant. When we applied the diagnostic criteria to our cohort, 99.5% met the Livneh criteria, 91.6% fulfilled the pediatric criteria and 82.9% satisfied the Tel-Hashomer criteria.

Conclusion: This is the largest pediatric cohort studied and presented since now. We believe that the large number of our cohort is convincing at the point of discussing phenotype-genotype relations. We confirmed that carrying M694V mutation is associated with increased disease severity. On the other hand, we compared two adult and one pediatric validated diagnostic criteria at a largest group of children with FMF.

REFERENCES:

Disclosure of Interests: None declared


LONG-TERM OUTCOMES AND TREATMENT EFFICACY IN PATIENTS WITH TNF RECEPTOR-ASSOCIATED AUTOINFLAMMATORY SYNDROME (TRAPS): A SERIES OF 290 CASES FROM THE EUROFEVER/EUROTURAS INTERNATIONAL REGISTRY

Riccardo Papa1, Thirusha Lane2, Taryn Youngstem2, Tamer Rezk2, Chinalampia Papadopoulou3, Nicolina Ruptero1, Paul Brogan3, Philip N. Hawkins2, Patricia Woo3, Marco Gattorno1, Helen J. Lachmann1,1IRCCS Istituto Giannina Gaslini, Clinica Pediatrica e Reumatologia, Genova, Italy; 2Division of Medicine, Royal Free Campus, University College London, National Amyloidosis Centre, LONDON, United Kingdom; 3UCL Great Ormond Street Institute of Child Health, Department of Infection, Inflammation and Rheumatology, LONDON, United Kingdom.

Background: Tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) is one of the best known monogenic auto-inflammatory disorder resulting from an autosomal dominant variation in the TNF super family receptor 1A (TNFRSF1A) gene.

Objectives: To define best treatment approach in patients with TRAPS and effect on long-term outcomes.

Methods: We reviewed all data on patients with TNFRSF1A variants enrolled in the Eurofever/Euroturas international registry.

Results: On 290 patients were available. Patients with R92Q, P46L or intronic variants (49%) displayed milder disease than 147 patients with mutations affecting other coding regions, with less frequent abdominal pain and skin rashes (P<0.01), higher efficacy rate of colchicine as main or intronic variants (49%) displayed milder disease than 147 patients with mutations affecting other coding regions, with less frequent abdominal pain and skin rashes (P<0.01), higher efficacy rate of colchicine as main-
May some of the MEFV gene variants cause PFAPA syndrome like symptoms? Mehmet Yildiz, Amra Adrovic, İpek Ulkersoy, Neslihan Gucuyener, Oya Kokar, Sezgin Sahin, Kenan Barut, Ozgur Kasapcoglu. Cerrahpasa Medical School, Istanbul University Cerrahpasa, Department of Pediatric Rheumatology, Istanbul, Turkey

Background: PFAPA syndrome is characterized by periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis. As diagnosis usually depends on clinical diagnostic criteria, sometimes it can be difficult to distinguish this clinical entity from the other periodic fever syndromes, especially in regions endemic for FMF.

Objectives: The objective of the study is to evaluate the PFAPA patients MEFV gene variation frequencies (if it was performed) and relations between detected variants and clinical manifestations in pediatric PFAPA patients.

Methods: Nine hundred and thirty-seven patients that were recorded to our database as PFAPA syndrome were evaluated. Patients were: R202Q heterozygotes (25.9%), M694V heterozygotes (29.2%), R177P heterozygotes (13.4%), P369S heterozygotes (9.8%) and V726A heterozygotes (8.6%), respectively. 145 of 345 detected mutations were located in exon 2, 40 of them were located in exon 10 and 14.9 of them were located in exon 3 of the MEFV gene. Patients were divided into five groups according to their mutations' localization and groups were compared according to clinical features. There were significant differences between groups according to presence of pharyngitis, arthralgia, abdominal pain, myalgia and tonsillitis history (Table 1).

Table 1. Comparison of patients according to their mutations' location and clinical features.

<table>
<thead>
<tr>
<th>Exon 2</th>
<th>Exon 3</th>
<th>Exon 10</th>
<th>No Mutation</th>
<th>MEFV study not performed</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngitis</td>
<td>Yes</td>
<td>21</td>
<td>9 (40.9)</td>
<td>45</td>
<td>28 (87.5)</td>
</tr>
<tr>
<td>No</td>
<td>(87.5)</td>
<td>13</td>
<td>(80.4)</td>
<td>4 (12.5)</td>
<td>24 (12.5)</td>
</tr>
<tr>
<td>Cervical</td>
<td>Yes</td>
<td>10</td>
<td>8 (36.4)</td>
<td>21</td>
<td>14 (56.6)</td>
</tr>
<tr>
<td>No</td>
<td>(58.3)</td>
<td>14</td>
<td>(63.6)</td>
<td>35</td>
<td>(62.5)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>Yes</td>
<td>0</td>
<td>0 (0)</td>
<td>14</td>
<td>7 (29.2)</td>
</tr>
<tr>
<td>No</td>
<td>(70.8)</td>
<td>10</td>
<td>(48.2)</td>
<td>29</td>
<td>(63.6)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>Yes</td>
<td>17</td>
<td>12</td>
<td>27</td>
<td>16 (50)</td>
</tr>
<tr>
<td>No</td>
<td>(70.6)</td>
<td>14</td>
<td>(54.5)</td>
<td>29</td>
<td>(83.9)</td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>Yes</td>
<td>14</td>
<td>5 (22.7)</td>
<td>21</td>
<td>14 (47)</td>
</tr>
<tr>
<td>No</td>
<td>(58.3)</td>
<td>17</td>
<td>(38.9)</td>
<td>47</td>
<td>(86.6)</td>
</tr>
</tbody>
</table>

Conclusion: In this study, we reported increased frequency of MEFV mutations in a large PFAPA patients cohort. Frequency differences of clinical features between groups suggest that some of the MEFV gene mutations may modify phenotype of PFAPA syndrome. Furthermore, underlying MEFV gene mutations possibly lead to PFAPA like clinical presentation in FMF patients. Another remarkable finding of this study is the relatively high P369S mutation rates in patients with PFAPA syndrome.

REFERENCES:

Disclosure of Interests: None declared


FR0539

WNT6 MUTATION CAUSES AN EARLY ONSET GRANULOMATOSUS INTESTINAL DISEASE WITH RECURRENT HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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Background: Use of NGS in patients with unclassifiable disease lies a possible approach to the identification of novel disease causing genes. Objectives: We report a patient with an early onset inflammatory bowel disease with granulomatous lesions and recurrent HLH episodes carrying a missense mutation in the WNT6 gene.

Methods: A triad based Whole Exome Sequencing (WES) approach was used. Cytokine levels were measured by multiplex assay and by specific ELISAs.

Results: Ten years old Caucasian boy affected by early onset pan-colitis from 9 months of age. Since the disease onset the patient is on glucocorticoid treatment with amino acidic enteral nutrition and oligo antigenic diet. Because of recurrent disease relapses at any attempt of glucocorticoid withdrawal, azathioprine and cyclosporine treatments were also added. At 2 years of age he received total colectomy with ileostomy.


FR0538

MAY SOME OF THE MEFV GENE VARIANTS CAUSE PFAPA SYNDROME LIKE SYMPTOMS?


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This funding has been reimbursed for the research activities of the hospital in a fully independent manner, without any commitment with third parties. Consultant: For: Received honoraria for consultancies or speaker bureaus (< 10,000 USD each) from the following pharmaceutical companies in the past 3 years: Abylny, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi-Servier, Seringe, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (<10,000 USD each) from each pharmaceutical company in the past 3 years: Abylny, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Seringle, Sobi and Takeda., Paul Brogan Grant/research support from: SOBI, Neslihan Gucuyener: Grant/research support from: The Gaslini Hospital, where NR works as consultant for: Novartis, Taryn Youngstein: None declared, Tamer Rezk: None declared, Vincenzo Tumiati: None declared, Wadad Frangos: None declared, Zoro Tudor: None declared