Methods: Familial Mediterranean Fever (FMF) is characterised with recurrent inflammatory attacks with serosal inflammation. The clinical findings of FMF is performed in 83,657 patients. 716 patients had a value <30 IU/L without any assay >40 IU/L. Selected records were analysed to eliminate secondary causes of hypophosphatasia. A telephone questionnaire was conducted with included patients from the rheumatology and internal medicine departments. Results: In 2013, 288,851 PAL assays were performed in 1,240,44 patients. In 2013, 288,851 PAL assays were performed in 1,240,44 patients. 716 patients had a value <30 IU/L. Of these, 174 had 1 single dosage, 542 multiple dosages, of which 186 never had value >40. 31 patients were excluded due to secondary hypophosphatasemia: severe caloric restriction (n=10), massive surgery (n=6), cancer/hemopathy (n=8), high-dose corticosteroid therapy (n=3). 155 patients were selected; the prevalence of hypophosphatasemia in hospitals is therefore 0.124%. Hypophosphatasemia was noticed in the summary file. However, the existence of hypophosphatasemia should be systematically recorded in the general population. This biological anomaly is almost never recorded in the general population. Conclusions: The prevalence of hypophosphatasemia is higher in hospitals than in the general population. This biological anomaly is almost never recorded in the general population. This biological anomaly is almost never recorded in the general population.

Disclosure of Interest: None declared


THU0619

THE FREQUENCY OF EXON-10 MUTATIONS IN MEVF GENE IN “PROBABLE” DIAGNOSED FMF PATIENTS ACCORDING TO TEL HASHOMER CRITERIA

F. Cosan1, O. Sarı2, O.M. Gediz Tutok2. 1Department of Internal Medicine, Division of Rheumatology, Bahçeşehir University, Faculty of Medicine, Istanbul, Turkey

Background: Familial Mediterranean Fever (FMF) is characterised with recurrent inflammatory attacks with serosal inflammation. The clinical findings of FMF is seen in a large spectrum. Tel Hashomer criteria are widely used for classifying FMF. According this criteria set FMF is classified as ‘definite’ and ‘probable’ disease.

Objectives: We aimed in this study to investigate the frequency of exon-10 MEVF mutations in ‘probable’ FMF patients according to Tel Hashomer criteria.

Methods: The study group consisted of 117 patients (79 male, 38 female, median age 43.8 years). The 12 frequently seen mutations in Turkey analysed in all blood samples and compared with the previous reported ‘definite’ FMF data from Turkey.

Results: We found in probable FMF group single mutation in 36 patients (%30.8), two mutations in 56 patients (%47.9), 3 mutations in 5 patients (%4.3) and no mutations in 20 patients (%17.1). The distribution of exon 10 mutations showed single exon-10 mutation in 48 patients (%39.3) and two exon-10 mutations only in 23 patients (%18.7). The detailed distribution of MEVF mutations in ‘probable’ FMF group is shown in table 1.

Conclusion: We found decreased frequency of exon 10 mutations in the MEVF gene in ‘probable’ FMF group according to Tel-Hashomer criteria in comparison previous reported MEVF mutations data. The distribution of non-exon 10 mutations were similar in the definite FMF group. It is needed more clinical studies with large patient group for the clinical significance of non-exon 10 mutations in “probable” FMF patients.

Disclosure of Interest: None declared


THU0620

ON DEMAND USE OF ANAKINRA FOR THE ATTACKS OF FAMILIAL MEDITERRANEAN FEVER (FMF)

H. Babaguloglu1, O. Varan1, H. Kuck2, N. Atas2, H. Satis3, R.B. Salman1, M. A. Öztük1, B. Goker1, S. Haznedaroglu1, A. Tufan1. 1Department of Internal Medicine, Division of Rheumatology, Gazi University Hospital, Ankara; 2Department of Internal Medicine, Division of Rheumatology, Erzurum Research and Training Hospital, Erzurum, Turkey

Background: IL-1 blocking agents have been shown to be effective in the prevention of attacks in colchicine-resistant FMF (crFMF) patients by their regular use. However, their high cost, side effects and treatment incompliance limit their use which might be overwhelmed by on-demand use of them which has not been reported in FMF patients. Herein, we evaluated the efficacy of on demand use of anakinra in crFMF patients.

Methods: Data were derived from Gazi FMF cohort which was established in the year 2010. From that date patients with FMF who were diagnosed according to the Tel Hashomer criteria were registered. Co-morbidities, detailed attack characteristics, type, duration, severity, treatments, laboratory parameters and impact of FMF on their life in terms of quality of life and work productivity were recorded either by FMF diary or a mobile phone application (FMF AID) free to download from AppStore and Android market). A retrospective cohort analysis was made from records of patients who have ever been treated with IL-1 inhibitors.

Results: A total of 60 patients were treated with anakinra in our cohort and 15 patients were identified who were received on demand anakinra protocol. Rationale for on demand use of anakinra was prominent prodrome or trigger for attacks and patients’ personal claim. Six patients were switched from regular use and 9 directly started as on demand use. All were using background colchicine in maximum tolerated doses. None of patients had evidence of persistently elevated acute phase reactants or proteinuria. The median duration of on demand anakinra use was 6 (min 3- max 36) months. Pre-and post-on demand anakinra periods were compared (table 1). Patient reported attack severity (p=0.002), duration (p=0.001), absence/employed (p=0.001) and presenteeism (p=0.002) were significantly
improved but C-reactive protein (CRP) remained in the same levels. On demand anakinra prevented progression of prodromes to full-blown attacks which was demonstrated by decrease in the rate of attack/prodrome ratio (p=0.002). On demand anakinra can be continued in 10 subjects on long-term but continuous treatment was required in 5 subjects.

### Abstract THU0620 – Table 1. Comparison of attack characteristics before and after on demand anakinra protocol

<table>
<thead>
<tr>
<th></th>
<th>Colchicine period</th>
<th>Colchicine plus On-Demand Anakinra period</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attack severity, VAS</td>
<td>10 (2)</td>
<td>6 (3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Duration, days</td>
<td>3 (2)</td>
<td>1.5 (1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Frequency*, number</td>
<td>4 (1.5)</td>
<td>1.5 (1.75)</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>5.1 (6.1)</td>
<td>4.1 (5.9)</td>
<td>0.58</td>
</tr>
<tr>
<td>AIDAI</td>
<td>18 (22.5)</td>
<td>4 (5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Attack/prodrom ratio</td>
<td>1</td>
<td>0.6 (0.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>(n=10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absorbtionis, days</td>
<td>7 (8)</td>
<td>2 (2.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Presenteisms, days</td>
<td>9 (7.5)</td>
<td>2.5 (3)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Attack frequency and work productivity parameters are adjusted for 3 months intervals. VAS: visual analogue scale, CRP: C-reactive protein, AIDAI: autoinflammatory disease activity index

**Conclusions:** On demand anakinra significantly improved FMF attacks which suggest this approach would be of benefit in daily practice in selected patients.

**Disclosure of Interest:** None declared

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### THU0621

**PERSISTENT PRURITIC SKIN LESIONS WITH DYSKERATOTIC CELLS IN UPPER LAYER OF EPIDERMIS ARE SPECIFIC AND ASSOCIATED WITH HIGH LEVELS OF SERUM IL-18 IN ADULT-ONSET STILL’S DISEASE**

H. Nishikawa1, Y. Taniguchi1, N. Maeda-Aoyama1, K. Nakajima1, S. Inotani1, Y. Shimamura1, K. Inoue1, K. Ari1, S. Sano1, Y. Terada1, D. Nephrology and Rheumatology, 2. Dermatology, Koichi Medical School Hospital, Nankoku, 3. Internal Medicine, Koichi Red Cross Hospital, Koichi, Japan

**Background:** Adult-onset Still’s disease (AOSD) is an acute and systemic inflammatory disorder that is characterised by high spiking fever, evanescant rash, arthralgia/arthritis and hyperferritinemia. However, recent reports showed that not only typical evanescent salmon-coloured rash but also atypical skin lesions, persistent pruritic papules and plaques, could be associated with AOSD.

**Objectives:** To assess the clinical significance of dyskeratotic cells (DCs) in skin lesions of AOSD.

**Methods:** We assessed histology of skin lesions including persistent pruritic skin lesions in Japanese patients with AOSD (n=15). Moreover, we compared histology of AOSD with dermatomyositis (DM) (n=6), drug eruptions (DE) (n=7), and graft versus host disease (GVHD) (n=6).

**Results:** AOSD with persistent pruritic skin lesion (n=10) histologically showed DCs only in upper layer of epidermis and horny layer without inflammatory cells infiltrations, indicating dyskeratosis. AOSD with evanescant rash (n=5) histologically showed no DCs. DCs were positive by ssDNA staining, suggesting apoptotic cells. Serum IL-18 showed significantly higher in AOSD patients with dyskeratosis (n=10) than without dyskeratosis (n=5). In contrast to AOSD with DCs, the histology of DM, DE and GVHD demonstrated that DCs existed in all layers of epidermis with inflammatory cells infiltrations.

**Conclusions:** Persistent pruritic skin lesions in AOSD are specific by prominent epidermal apoptosis involving the upper layers of epidermis. Moreover, hyper IL-18 might be related with dyskeratosis.

**Disclosure of Interest:** None declared

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### THU0622

**HISTOPATHOLOGY AND EXPRESSIONS OF CHEMOKINES, CXCL10, CXCL13, AND CXCR3, AND AN ENDODGENOUS LIGAND S100A8/A9 IN LYMPH NODES OF PATIENTS WITH ADULT-ONSET STILL’S DISEASE**

H. A. Kim1, J.H. Han2, 1. Department of Rheumatology, 2. Department of Pathology, Ajou University School of Medicine, Suwon, Korea, Republic of Ireland

**Background:** Adult-onset still’s disease (AOSD) is a rare systemic inflammatory disease with several symptoms, such as a persistent high spiking fever, typical rash, and lymphadenopathy. Endogenous factors related to interleukin (IL)–1, such as S100A8/A9 and several chemokines including CXCL10, CXCL13 and CXCR3, could play a potential role in the pathogenesis of AOSD.

**Objectives:** We aimed to find out typical histopathologic features, expressed pattern of chemokines in lymph nodes (LN) of AOSD patients.

**Methods:** Formalin-fixed paraffin-embedded excisional LN tissues from 48 AOSD patients and 6 nonspecific reactive hyperplasia were histologically reviewed. The immunohistochemical stain for CXCL10, CXCL13, CXCR3 and S100A8/A9 were done. The clinical and laboratory data of the patients who underwent LN biopsies were reviewed.

**Results:** The LN specimens were categorised according to four distinctive patterns: follicular (n=2, 4.2%), paracortical (n=19, 39.6%), diffuse (n=9, 18.8%), and interstitial hyperplasia (n=11, 22.9%). The expression of chemokines and S100A8/A9 were higher than that of nonspecific reactive hyperplasia. The expression of chemokines and S100A8/A9 were higher than that of nonspecific reactive hyperplasia.

**Conclusions:** Histopathologic findings of LN in AOSD patients are diverse enough to be included various differential diagnosis. Because the several chemokines and S100A8/A9 were more expressed in AOSD patients than those of reactive hyperplasia, they may serve as a pathogenesis of AOSD.

**Disclosure of Interest:** None declared

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### THU0623

**SERUM IGG4 LEVELS AT DIAGNOSIS CAN PREDICT THE OUTCOMES OF UNTREATED PATIENTS WITH IGG4-RELATED DISEASE: A RETROSPECTIVE STUDY**

M. Mushimizu, N. Suzuki, M. Yoshida, A. Takeji, T. Matsunaga, T. Toshima, S. Hara, K. Itô, H. Fuji, K. Yamada, M. Kawano, Division of Rheumatology, Kanazawa University Hospital, Kanazawa, Japan

**Background:** IgG4-related disease (IgG4-RD) is a recently recognised systemic fibro-inflammatory disorder that can affect many organs. In IgG4-RD, spontaneous, or at least temporary, remissions without treatment have been reported, and watchful waiting may be appropriate in certain patients with asymptomatic and inactive disease. However, the outcomes of patients with IgG4-RD who do not undergo treatment are still unclear.

**Objectives:** This study aimed to clarify the outcomes of untreated patients with IgG4-RD and the factors related to the outcomes.

**Methods:** We retrospectively reviewed the medical records of 107 patients with IgG4-RD, who were followed up for more than 6 months, at a single centre in Japan. Among them, 27 patients were followed up without treatment after the initial diagnosis. We compared the clinical features of these 27 patients with those of the 80 patients who underwent treatment. The outcomes of untreated patients were investigated, and logistic regression analysis was performed to assess factors related to the outcomes. Deterioration of IgG4-RD was defined as symptomatic, radiological, or functional exacerbation of the organ involved or new organ involvement.

**Results:** The patients comprised 73 men and 34 women (mean age 65.7 years). The follow-up periods were 7–252 (mean, 84.1) months, and the serum IgG4 levels at diagnosis were 10.7–3610 (mean, 706) mg/dL. The 27 untreated patients had significantly fewer affected organs (1.9±1.2 vs 3.0±1.6, p=0.001), lower IgG4-RD responder index (10.8±5.1 vs 13.8±6.8, p=0.048), and lower frequency of ophthalmic and renal parenchymal lesions (25.9% vs 53.8%, p=0.015, and 3.7% vs 26.3%, p=0.012, respectively) than did the 80 patients who underwent treatment. Of these 27 patients, 8 experienced deterioration of IgG4-RD 3–232 months (mean, 62.8) after the diagnosis. New organ involvement was observed in all 8 patients, 2 of whom concurrently suffered exacerbation of the organs involved. In age- and sex-adjusted logistic regression analysis, serum IgG4 elevation (per 100 mg/dL, odds ratio 1.194, 95% confidence interval 1.017–1.402, p=0.030) was the only significant factor related to deterioration of disease in untreated patients with IgG4-RD.

**Conclusions:** The present study suggests that serum IgG4 levels may be useful to predict the outcomes of untreated patients with IgG4-RD, who tend to have fewer affected organs and lower IgG4-RD responder index.

**References:**


**Disclosure of Interest:** None declared

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