Objectives: To identify predictors of relapse of IgG4-RD after induction therapy.

Methods: We retrospectively reviewed 57 patients diagnosed with IgG4-RD and treated with GC in our hospital between January 2004 and November 2018. Clinical features at baseline, including organ involvement and blood markers (total hemolytic complement [CH50], its fractions [C3 and C4], IgG4, IgG, IgE, anti-nuclear antibody, rheumatoid factor, C-reactive protein, soluble interleukin-2 receptor, eosinophil), were collected. We divided patients into 2 groups on the basis of clinical features and examined whether they relapsed. In this study, hypocomplementemia was defined as decreased serum C3, C4, or CH50 less than the lower limit of normal. A relapse was defined as any new or worsened state of disease activity that required an escalation in treatment (immunosuppressants and/or GC). The follow-up period was defined as 182 days.

Results: Forty-three men and 14 women (mean age 68.1 ± 10.9 years) were included. Both serum IgG4 and IgG were measured at baseline in all patients (mean IgG4 798.8 ± 873.1 mg/dL and mean IgG 2874.0 ± 1934.1 mg/dL, respectively). All of the serum C3, C4, and CH50 were measured at baseline in 34/57 patients (mean C3 75.7 ± 33.3 mg/dL; mean C4 14.6 ± 11.5 mg/dL; and mean CH50 37.0 ± 23.1 U/mL). Fifteen patients had at least one episode of hypocomplementemia, and 19 patients did not. Most patients had multiple organ lesions. The details of dominant lesions were as follows: Dacryoadenitis and/or sialadenitis (Mikulicz disease), 36/57 patients (63.2%); biliary or pancreatic lesion, 29/57 patients (50.9%); periorbital fibrosis, 22/57 (38.6%); and renal lesion 16/57 (28.1%). All patients were given prednisolone and gradually reduced (mean induction dose 31.7 ± 9.8 mg/day). No patients received immunosuppressant as induction therapy. During the follow-up period, 6 patients relapsed, and the dose of prednisolone was increased immediately. Relapsed lesions were as follows: Mikulicz disease, 3/6 patients (50.0%); biliary or pancreatic lesion, 1/6 (16.7%); periorbital fibrosis 1/6 (16.7%); and pulmonary lesion 1/6 (16.7%). Patients with hypocomplementemia had significantly shorter relapse-free survival than those without (p=0.039, Figure 1). Patients with decreased serum C4 or CH50 (less than the lower limit of normal) also had significantly shorter relapse-free survival than those without, but those with decreased serum C3 did not.

Conclusion: Hypocomplementemia at baseline in patients with decreased serum C4 or CH50 may predict relapse of IgG4-RD after prednisolone therapy.

REFERENCES:

Disclosure of Interests: None declared

THU0593

CLINICAL AND GENETIC FEATURES OF CHINESE ADULT PATIENTS WITH TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME

Mengzhu Zhao, Yi Luo, Min Shen, Di Wu, Wen Zhang, Xiaofeng Zeng. Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education, Beijing, China

Background: Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) is an autosomal dominant autoinflammatory disease, associated with the mutation of tumor necrosis receptor superfamily member 1A (TNFRSF1A) gene, located on chromosome 12p13. TRAPS is usually diagnosed during pediatric age. However, adult-onset disease or diagnosis during adulthood has been occasionally described. Moreover, TRAPS has been hardly reported in the Chinese population. Herein, we aimed to characterize the clinical and genetic features of Chinese adult patients with TRAPS.

Objectives: Adult patients (≥16 years) suspected monogenic autoinflammatory diseases during the period April 2015 to October 2018, at the adult autoinflammatory disease center, Department of Rheumatology, Peking Union Medical College Hospital (PUMCH).

Methods: Clinical data were evaluated. Gene sequencing was performed in each patient to support the diagnosis and exclude other monogenic autoinflammatory diseases. Finally we compared the data with those from Japan and Europe.

Results: During the study period, 8 patients with TRAPS were diagnosed and follow-up. The ratio of male to female was 3:1. The median age of disease onset was 4 (0.5–38.5), and adult-onset was observed in 2 (25%) patients. The median time of diagnosis delay was 17.8 (1.5–50.5) years. There were seven Chinese Han and one Manchu patients. One patient had a family history of TRAPS. The most frequent symptom was fever (8, 100%). The attacks of 5 (62.5%) patients lasted more than 1 week, and the intervals of 7 (87.5%) patients were longer than 2 weeks. Skin involvement occurred in 6 (75%) patients, with maculopapular mentioned in 6 and erythema annulare presented in 3. Four (50%) patients had arthralgia, while one had polyarthralgia. 4 (50%) patients complained respectively of myalgia or headache. 4 (50%) patients experienced abdominal pain and one (12.5%) had vomiting. One (12.5%) patient had periodical edema, while 3 (37.5%) had conjunctivitis. Up to 5 (62.5%) patients got nonspecific pharyngitis. No patient suffered from chest pain or amyloidosis. Eight gene variants were detected in TNFRSF1A gene. Heterozygous gene variants were found in 7 Chinese Han patients, and homozgyous (c.769-23T>C, IVS8) happened to the Manchu patient. The variants included C58 (exon 2), G65E (exon 3), F89L (exon 3), C99G (exon 3), V202G (exon 6), c.769-23T>C (IVS8), S290I (exon 9) and m.1735A>G (non-coding region). NSAIDs were given to 2 patients, glucocorticoid or immunosuppressive agents given to 3 patients respectively, and etanercept to 5 patients. A complete response was found in all the 5 patients received etanercept. The effectiveness of other drugs were 50% in NSAIDs, 66.7% in glucocorticoid and immunosuppressive agents.

Conclusion: This is the first and largest case series of TRAPS in Chinese adult patients. It highlights the importance of screening TNFRSF1A gene in patients with unexplained periodic fever syndrome. Four novel TNFRSF1A variants, S290I, F89L, V202G and m.1735A>G in non-coding region, have been identified. The atypical clinical manifestations of our patients compared to those from Europe might be related to their low-penetrance TNFRSF1A variants. Further studies are needed to explore the more accurate phenotypes and genotypes of the Chinese patients with TRAPS.
Diagnostics and imaging procedures

THU0594

CLINICAL VERSUS IMAGING REMISSION IN JUVENILE IDIOPATHIC ARTHRITIS (JIA): PRELIMINARY RESULTS OF THE REMECO STUDY

Marta Mazzoni1,2, Silvia Merlo1, Angela Pistorio3, Stefania Viola3, Alessandro Consolaro1,2, Angelo Ravelli1,2, Clara Malattia1,2, 1Università degli studi di Genova, Genova, Italy; 2IRCCS Istituto Giannina Gaslini, Clinica Pediatrica e Reumatologia, Genova, Italy; 3IRCCS Istituto Giannina Gaslini, Epidemiologia e Biostatistica, Genova, Italy.

Background: remission is becoming a realistic target in JIA, but clinical remission (CR) may not accurately reflect real absence of synovitis. It would be desirable to have instruments to predict the risk of relapse in patients in CR in order to establish the most appropriate therapeutic strategy. Despite in RA the role of imaging to predict disease flare is established, this field has remained almost unexplored in JIA.

Objectives: 1) to investigate the prevalence of musculoskeletal ultrasound (MSUS)-detected subclinical synovitis in JIA patients in CR; 2) to establish which and how many joints should be scanned to reliably assess remission; 3) to evaluate the persistence of subclinical synovitis over the time; 4) to investigate whether subclinical synovitis entails a risk of disease flare; 5) MSUS data will be integrated with serum levels of inflammatory biomarkers to develop a multidimensional measure of remission.

Methods: it is a longitudinal prospective 4 years study started on November 2017. So far we have enrolled 99 consecutive JIA patients who met the Wallace criteria for CR. For each patient 46 joints were scanned for synovial hyperplasia/joint effusion and PD signal, all graded semiquantitatively on a 0–3 scale independently by 2 expert ultrasonographers. Subclinical synovitis was defined when total synovitis score for each joint was ≥2. MSUS was performed at baseline and at 6 months follow up visit. At inclusion serum assays have been stored to determine levels of inflammatory biomarkers (S100A8/A9-A12, bFGF, IL-6, IL-10, CXCL9-10, VEGF, YKL40). A flare of synovitis was defined as a recurrence of clinically active arthritis.

Results: 99 patients (79.8% F; median age 11.3 y; median disease duration 5.3 y; median CR duration 1.6 y) were included. Thirty-eight (38.4%) patients had persistent oligoarthritis; 34/99 (34.3%) extended oligoarthritis; 22/99 (22.2%) polyarthritis; 5/99 (5.1%) systemic arthritis. Fifty-nine/99 (59.6%) patients were in CR on medication. Subclinical synovitis was detected in 54/99 (54.5%; 95% CI: 45.2–65.5%) patients, PD signal in 7/99 (7.1%; 95% CI: 2.9–14%) patients. Subclinical synovitis was found more frequently in the ankle (31/54 (57.4%) patients) and wrist joints [17/54 (31.5%) patients]. No patients had subclinical synovitis in the hip. A 14-joint reduced count including bilateral knee, ankle (tibiotaral, subtalar and talonavicular joints), wrist (radiocarpal and intercarpal joints) and elbow joints, detected 92.6% of children with subclinical synovitis. Patients who relapsed were a small percentage, but to extend follow up is crucial to test predictive value of MSUS. Imaging findings will be combined with serum biomarkers leading to the construction of a predictive model.

Conclusion: our preliminary results confirm the discrepancy between clinical and imaging remission and that clinical evaluation may not sensitive to detect an inflammation-free state. Bilateral US assessment of the elbow, wrist, knee and ankle joints is reliable to detect subclinical synovitis. So far, patients who have relapsed are a small percentage, but to extend follow up is crucial to test predictive value of MSUS. Imaging findings will be combined with serum biomarkers leading to the construction of a predictive model.

REFERENCES:


Disclosure of Interests: Marta Mazzoni: None declared, Silvia Merlo: None declared, Angela Pistorio: None declared, Stefania Viola: None declared, Angela Ravelli: None declared, Clara Malattia: None declared.

DEVELOPMENT OF AN AUTOMATED SEGMENTATION ALGORITHM TO IDENTIFY BONES OF THE HAND

Adwaye Rambojun1, William Tillett2,3, Neil Campbell4, Tony Shardlow1.  

Background: The evaluation of structural damage with plain radiography is important to clinicians and patients. Standard scoring methods include the Sharp-van der Heijde (SVdH) and Ratingen methods [1] however these systems are time-consuming. Therefore, it is difficult to perform large cohort studies. We set out to develop an automated algorithm to identify bones on plain radiographs as a step towards developing automated quantification of structural damage for use on large datasets.

Objectives: To develop a novel algorithm to segment outlines of finger bones in hand radiographs.

Methods: 101 hand radiographs were gathered from the Bath longitudinal cohort (UK). All patients fulfilled the CASPAR criteria for Psoriatic Arthritis (PSA). None of the patients had damage on SVdH and Ratingen scoring (blinded). The metacarpal (MC), proximal phalanx (PP), middle phalanx (MP), and distal phalanx (DP) in the right index finger were delineated by a rheumatologist. These outlines were used to build a statistical model of the shape using a Gaussian Process Latent Variable Model (GPLVM) [2]. Bones are segmented by matching the shape on a radiograph to the statistical model.

Results: The performance of the matching algorithm was compared with a traditional algorithm (snakes) using the Adjusted Rand Score (ARND). The ARND score measures the similarity of the segmentation with the ground truth. A perfect segmentation has a score close to 1. The metacarpal (MC), proximal phalanx (PP), middle phalanx (MP), and distal phalanx (DP) in the right index finger were delineated by a rheumatologist. These outlines were used to build a statistical model of the shape using a Gaussian Process Latent Variable Model (GPLVM) [2]. Bones are segmented by matching the shape on a radiograph to the statistical model.

Conclusion: We report a reliable algorithm for the identification of metacarpal, proximal, middle and distal phalanx bones of the hand. Future work will focus on using the output of the segmentation algorithm to track damage progression over time.

REFERENCES:

Table 1. Adjusted RAND scores for comparing our algorithm to a traditional one (snakes)

<table>
<thead>
<tr>
<th>Bone</th>
<th>Snakes</th>
<th>Johnsson</th>
<th>Shape matching</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>MP</td>
<td>0.70</td>
<td>0.95</td>
</tr>
<tr>
<td>Case 2</td>
<td>MP</td>
<td>0.89</td>
<td>0.96</td>
</tr>
<tr>
<td>Case 3</td>
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<td>0.82</td>
<td>0.96</td>
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<tr>
<td>Case 4</td>
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<td>Case 5</td>
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<td>0.53</td>
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<td>Case 6</td>
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<td>0.87</td>
<td>0.97</td>
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<tr>
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<tr>
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</tr>
<tr>
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<td>0.75</td>
<td>0.95</td>
</tr>
<tr>
<td>Case 3</td>
<td>MP</td>
<td>0.75</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Key: Adjusted Rand Score (ARND) score measures the similarity of the segmentation with the ground truth. A perfect segmentation has a score close to 1. Metacarpal (MC), proximal phalanx (PP), middle phalanx (MP), and distal phalanx (DP)