lungs (spirography), kidneys (concentration function, glomerular filtration rate, daily microalbuminuria), lipid spectrum and blood coagulation. Deviations from standard age-gender normal values were taken into account. It was used statistical methods for identifying relationships (stepwise multiple regression). As the dependent value the number of detected changes in the state of internal organs and systems is taken. The independent variables included standard clinical and laboratory parameters, the age of the onset of JIA, the total duration of the disease, the characteristic of the articular syndrome, activity indicators (C-reactive protein, RF and ANA titers, JADAS27), as well as the term for the appointment of basic therapy relative to the debut of the disease, the nature of the dosage methotrexate (mg / m2 / week), the duration of its use at the time of examination.

Results: Based on the analysis and the obtained regression models for the formation of extra-articular lesions in children with various JIA options, it was found that the leading factors in the formation of comorbidity are the duration of the disease (p = 0.01), VAS results (including the child, parents and the physician) (p = 0.01), the dose of methotrexate (p = 0.01).

In the polyarticular variant, the body mass index (p = 0.02), erythrocyte content (p = 0.007) were significant for the formation of comorbid states and should be distinguished.

The overall duration of the disease (p = 0.02), the low age of initiation of therapy (p = 0.05), VAS of child (p = 0.003), CRP (p = 0.007), dose of methotrexate (p = 0.001) had the greatest significance level among the clinical and laboratory indicators included in the regression model of the formation of comorbidity with the oligoarticular variant.

A features of the prognostic model for the formation of organ lesions and metabolic disorders in uveitis-associated arthritis were GCS therapy presence (p <0.001), patient age (p <0.001), JADAS27 (p <0.001) and methotrexate dose (p <0.001).

Conclusion: Thus, in children with JIA, the formation of comorbid pathology is associated with a lower age of JIA debut in oligoarthritis and uveitis-associated arthritis, low body weight in poly- and oligoarticular JIA variants, an increase in the duration of the disease in the polyarticular variant, and the level of activity of the process, respectively, JADAS 27(p <0.01) and VAS. Prognostically unfavorable for the formation of pathological changes in the internal organs and homeostasis are anemia, high white blood cell count and ESR level.

Disclosure of Interests: None declared

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FRI0472 DIAGNOSIS AND MANAGEMENT OF ADENOSINE DEAMINASE 2 DEFICIENCY CHILDREN: THE EXPERIENCE FROM CHINA

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Background: Adenosine deaminase 2 deficiency (DADA2) is a rare antoinflammatory disease caused by mutations in ADA2 gene, few Chinese cases have been reported.

Objectives: To describe and compare the clinical features, genotypes, and treatments of Chinese DADA2 patients and foreign cases.

Methods: Primary immunodeficiency disease Panel or Whole Exome Sequencing was performed to suspected subjects, and assays for adenosine deaminase 2(ADA2) enzyme activity were also carried out to them and their parents. Case reports of Chinese and foreign patients with DADA2 were searched from PubMed and Chinese domestic databases.

Results: Seven unrelated DADA2 children from China were included in our study, 5 were identified at Peking union medical college hospital and 2 had been reported previously (1 on PubMed and 1 in Chinese literatures). 14 mutations in ADA2 were identified, and 9 of which have not been found in other countries. Four children receiving enzymatic analysis had lower ADA2 enzyme activity compared to their parents. Phenotypic manifestations included fever, skin symptoms, vasculitis, neurologic involvement, et al. The treatments varying from steroids, immunosuppressants, and tocilizumab, anti-TNF therapy and hematopoietic stem cell transplantation (HSCT) were effective depending on different phenotype and severity.

Conclusion: This study includes the biggest number of Chinese DADA2 patients at present. We recommend combination of enzymatic analysis with gene screening to confirm the diagnosis. Genotypes of patients from China were some different, the clinical manifestations were similar. We suggest anti-TNF therapy may not be necessary for mild case and HSCT should be considered even without hematological phenotype.

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Disclosure of Interests: None declared

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FRIDAY, 05 JUNE 2020

Other orphan diseases

FRI0473 ASSESSMENT OF FEMORAL VEIN WALL THICKNESS WITH DOPPLER US AS A DIAGNOSTIC TOOL FOR BEHCET'S DISEASE

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Background: Diagnosing Behcet's disease(BD) is a challenge, especially in countries with a low prevalence. International Study Group Criteria, accepted to as diagnostic, has low sensitivity, especially in early cases when major organ involvement such as uveitis or deep vein thrombosis(DVT) presents alone. We recently published a controlled study of assessing venous wall thickness(VWT) as a surrogate marker of venous disease in BD with ultrasound(US) and observed a very sensitive and specific VWT in male BD patients. The common femoral vein(CFV) thickness measurement, as the primary site of US with the cut-off values > 0.48-0.49 mm, had a high area under the receiver operating characteristic curve(>0.8) with sensitivity and specificity of around 80%(1).

Objectives: In this study, we aimed to investigate the diagnostic performance of CVF thickness measurement in BD including females comparing with multiple control disease groups.

Methods: One hundred-ten patients with BD, 47 healthy controls(HC), 21 patients with systemic vasculitides, 28 patients with venous insufficiency,29 patients with antiphospholipid syndrome (APS) having DVT history, were included the study. Bilateral CFV thickness was measured with US by an experienced radiologist blinded to cases(Figure 1).

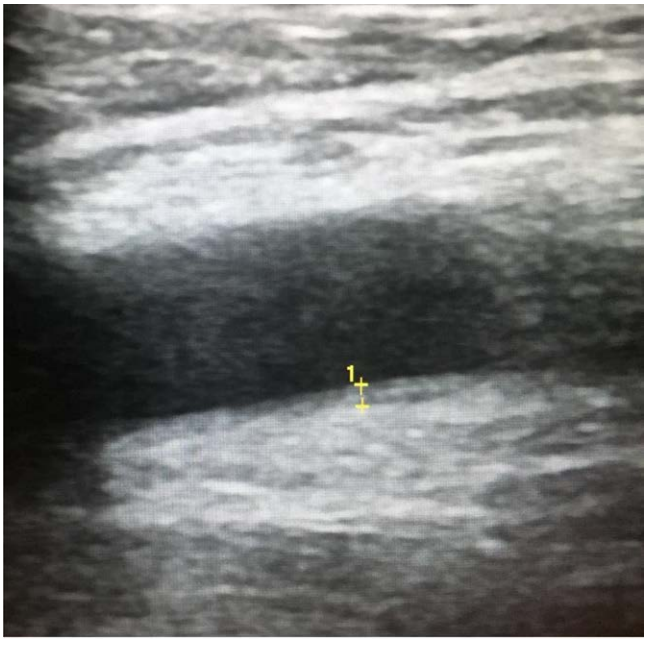

Figure 1. Measurement of common femoral vein thickness

Results: Bilateral CFV thickness was significantly higher in BD compared to all comparative groups (p<0.001 for all)(Table 1,Figure 2). No correlations were present between CFV thickness and both BSAS and CRP levels (p>0.05 for all). In only 2 (8%) patients with venous insufficiency and 2 (10%) patients with systemic vasculitis, bilateral CVF thickness was higher than the cut- off values. Interestingly, APS was the only control group with positivity, in 12 (41%) patients with APS, bilateral CFV thickness was higher than the cut-offs. There was no difference between male vs female BD patients regarding CFV thickness (right CFV:0.78 mm vs 0.79 mm,p=0.96, left CFV:0.78 vs 0.8, p=0.80). Although a higher CVF thickness tendency was observed in VBD, no statistically significant difference was present between BD patients with (n=40) and without (n=58) vascular involvement (right CFV:0.82±0.3 mm vs 0.75±0.3 mm, p=0.122, left CFV:0.84 ± 0.3 vs 0.76±0.3, p=0.165).

Table 1. Venous Wall Measurements of Lower Extremity in Study Groups

	Behcet's Disease (n=110)	Healthy Controls (n=47)	Systemic Vasculitis (n=21)	Venous Insufficiency (n=28)	Anti-phospholipid Syndrome with DVT (n=29)
Age (years)	33.5 ± 6	30.1 ± 5	33.3 ± 7	36.7 ± 6	38.3± 9
Gender, male n (%)	89 (81)	40 (85)	12 (57)	13 (46)	9 (31)
Body Mass Index, kg/m2	25.5 ± 4	24 ± 2	23.8 ± 3.5	27.7 ± 4	27.2 ± 7
Right CFV Thickness (mm)	0.79 ± 0.3	0.34 ± 0.1	0.34 ± 0.15	0.38± 0.1	0.48 ± 0.15
Left CFV Thickness (mm)	0.78 ± 0.3	0.3 ± 0.1	0.36 ± 0.14	0.38 ± 0.2	0.48 ± 0.15

CFV: Common Femoral vein, DVT:Deep Venous Thrombosis

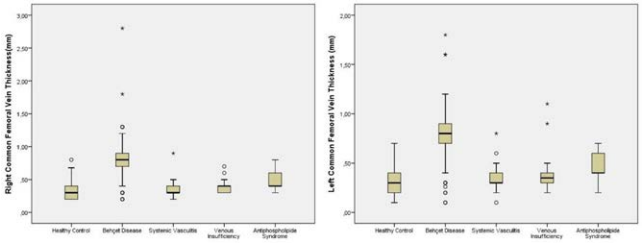

Figure 2. Distribution of common femoral vein thickness in study groups

Conclusion: Increased CFV thickness is present in BD patients,independent of vascular involvement.We also found that CFV thickness is a distinctive feature of BD, rarely present in other inflammatory/vascular diseases such as ankylosing spondylitis (previously shown),systemic vasculitides and venous insufficiency(except APS with DVT).CFV thicknesses are easily and reliably measured by Doppler US. We, therefore, suggest that assessment of CFV can be a diagnostic tool for BD with a good sensitivity and specificity to differentiate BD from similar disorders.

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Disclosure of Interests: None declared

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FRI0474 IMMUNE CHECKPOINT INHIBITOR-INDUCED MUSCULOSKELETAL MANIFESTATIONS. A SYSTEMATIC REVIEW

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Background: Immune checkpoint inhibitors (ICI) are potent anti-cancer drugs that associate with a wide range of immune related adverse events (Ir-AE), including musculoskeletal manifestations.

Objectives: We performed a systematic literature review of ICI-induced musculoskeletal manifestations aiming at exploring the following: 1) the prevalence of these manifestations and the time from first ICI administration to symptom onset, 2) the main clinical phenotypes and the type of treatment required to control symptoms (steroids/DMARDs), 3) the type of ICI (CTLA-4 vs PD-1/PD-L1 inhibitors) mostly associated with Ir-AE, 4) the percentage of patients with positive auto-antibodies and family history of autoimmune disease, 5) the percentage of patients requiring permanent ICI discontinuation due to musculoskeletal Ir-AE, 6) the association between musculoskeletal Ir-AE and oncologic response and 7) the risk of flare in patients with pre-existing autoimmune disease (PAD).

Methods: An electronic (PubMed) search was performed aiming at identifying all studies reporting musculoskeletal Ir-AE.

Results: We identified 3 prospective studies, 17 retrospective studies and 4 case series reporting 363 patients in total. Combined data from all 3 prospective studies provide a prevalence rate of 6.13%. Most patients were males (59.68%) and the vast majority (73%) were on programmed death-1 (PD-1)/programmed death ligand-1 (PD-L1) inhibitors. Most studies report a median time of ≤ 12 weeks from first ICI administration to symptom onset. The main clinical phenotypes reported were: a) inflammatory arthritis (57.57%), b) myositis (14.04%) and c) polymyalgia rheumatica (PMR) (12.12%). A total of 256 patients required steroids (70.52%) and 67 patients (18.45%) were treated with DMARDs. From the 363 patients reported in total, 265 (73%) were treated with PD-1/PD-L1 inhibitors in sharp contrast to only 11 (3.03%) with CTLA4 inhibitors with the rest patients receiving combination immunotherapy Positive auto-antibodies and family history of any autoimmune disease were present in 18.48% and 19.04% of cases, respectively. Only a few patients (19%) had to discontinue treatment due to musculoskeletal Ir-AE. Two prospective studies show that significantly more patients with musculoskeletal Ir-AE exhibit a favorable oncologic response compared to patients not exhibiting such manifestations whereas retrospective studies show that 77.22% of patients with musculoskeletal Ir-AE have a good tumor response.

Conclusion: One out of 15 patients treated with ICI will develop musculoskeletal Ir-AE; in most cases the severity of these manifestations is mild/moderate and usually ICI is continued. Rheumatologists should familiarize themselves with this new clinical entity and develop relevant therapeutic algorithms.

Disclosure of Interests: None declared

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FRI0475 STEROID SPARING AGENTS IN POLYMYALGIA RHEUMATICA: A SYSTEMATIC REVIEW

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Background: Polymyalgia rheumatica (PMR) is the commonest chronic inflammatory musculoskeletal disease of the elderly. The mainstay of treatment for PMR is long term systemic glucocorticoid (GC), which is associated with significant systemic toxicity. There is a need for steroid sparing drugs in PMR to reduce GC cumulative dose and GC induced adverse effects.(1)

Objectives: To evaluate the role of steroid sparing agents in PMR.

Primary outcomes:

1. Steroid sparing effect of the intervention, measured by difference in cumulative glucocorticoid dose
2. Percentage of patients in remission.

Secondary outcomes:

1. Mean reduction of CRP/ESR
2. Adverse event/toxicity the drugs being compared—measured as number of patients with adverse events in the compared groups
3. Percentage of patients with relapse during study period
4. Mortality

Methods: Electronic databases including Medline, Embase and Cochrane databases (CENTRAL) were searched since inception for prospective randomized control trials comparing disease modifying anti rheumatic drugs (DMARDs) and biologics with systemic GC in PMR, published in English with more than 20 patients and a minimum study duration of 24 weeks. As different classification criteria for PMR exist, studies were included if they used any accepted classification criteria for PMR. Case series, case reports, retrospective, non-randomized trials, abstracts, systematic reviews and non English language trials were not included. Patients with Giant cell arteritis (GCA) were excluded. Risk of bias and quality was assessed using the Cochrane tool.

The studies were assessed for cumulative GC dose, proportion of patients in remission, proportion of patients with relapse, reduction in inflammatory markers, adverse events and mortality.

Results: 5 studies were selected for final review-- 3 studies involving Methotrexate, one study on azathioprine, one on Infliximab. The study on Azathioprine