One of our patients reported that her psoriatic lesions got worse on anakinra. Forty one patients reported no adverse events during the treatment.

Conclusions: Anakinra was effective in controlling the symptoms in colchicine-resistant FMF cases. It was also effective in FMF related amyloidosis. The major cause of treatment termination was injection site reactions. Anakinra seems to be an effective alternative in patients who have insufficient response to colchicine.

Disclosure of Interest: None declared

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THU0612 BONE SARCOIDOSIS: A RETROSPECTIVE MULTICENTER STUDY OF 27 CASES

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Background: Studies on bone involvement of sarcoidosis (BS) are scarce.

Objectives: To analyse in depth main features, treatments and follow up of patients presenting a BS.

Methods: Among 926 patients with a proved sarcoidosis from four tertiary hospitals in Paris (France) seen between 2000 and 2015, all cases of BS were retrospectively analysed for demography, clinical features, biological tests and imaging results. Inclusion criteria were a) a bone biopsy with epithelioid granuloma and no casein necrosis, or b) radiological evidence of BS, after exclusion of other diagnoses.

Results: 27 out 926 (2.9%) sarcoidosis patients fulfilled inclusion criteria for BS. Most patients were caucasian (56%), M/F sex ratio 1.5, 30% were active smokers, mean age at sarcoidosis diagnosis was 39±12 years and at BS diagnosis 43 ±11 years. Extra-osseous involvement of sarcoidosis was found in lymph nodes (93%), lungs (78%), skin (52%), CNS (33%), ENT (33%), and heart (19%). BS was symptomatic in 15/27 (56%) patients i.e. bone pain (15/15), local inflammation (5/15), bone deformation (3/15), arthritis (4/15), and myalgia (5/15). BS was never the revealing symptom of sarcoidosis. BS was more frequently symptomatic when it was a Perthes-Jüngling osteitis and an appendicular skeleton involvement.

On imaging exams, BS lesions were found at the spine skeleton alone (14/27, 52%), appendicular skeleton alone (10/27, 37%) or both (3/27, 11%). BS lesions had an aspect of pseudo-metastasis (59%), micro-cysts (Perthes-Jüngling, 37%) or Paget disease (4%). Bone lesion was unique in 22% and 26% of patients had more than 10 lesions. When a bone biopsy was done it always confirmed the diagnosis (n=9); in all other cases extra-osseous biopsies confirmed the diagnosis of sarcoidosis.

Nine patients received a treatment for BS, i.e. prednisone (n=8, 0.25–1 mg/kg/day), hydroxychloroquine (n=8), and methotrexate (n=5). Response to treatment was complete (n=3), partial (n=4) or nul (n=2). Of note, 21 out of 27 patients received an immunosuppressant for a severe form of systemic sarcoidosis (n=11) or for a steroid-sparing effect (n=10). A relapse of BS was noted in 13 patients, with a mean number of relapse of 2.¹⁻²⁴ After a mean follow up of 49 months, BS was in complete remission (8/27, 30%), partial remission (16/27, 59%) or remained active (3/27, 11%).

Conclusions: Bone involvement remains a rare manifestation of sarcoidosis. It was symptomatic in 56% of patients, mainly when Perthes-Jüngling osteitis and appendicular skeleton involvement were present. Extra-osseous involvement of sarcoidosis were always present at the time of BS diagnosis. Treatment remains difficult with frequent relapses.

Disclosure of Interest: None declared

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THU0613 THE FREQUENCY AND CHARACTERISTICS OF HEADACHE IN BEHCET'S DISEASE AND ITS EVALUATION BY TRANSCRANIAL DOPPLER ULTRASONOGRAPHY

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Background: Behcet's disease (BD) is a multisystem vasculitic disease and the most often neurologic manifestation of BD is headache. Transcranial Doppler ultrasonography (TCD) is a test which used for evaluating the changes in blood flow velocity developed against visual stimulation. It is not well known TCD findings in BD patients who suffered from headache.

Objectives: To evaluate the frequency and the types of headache and to investigate cerebral reactivity by TCD in BD patients.

Methods: 113 patients with BD diagnosed based on diagnostic criteria of BD by ISG and 40 healthy individuals were included in the study. The patients with BD

who had neurological involvement were not included to the study. Headache type was specified by a specialist neurologist according to International classification of headache disorders society criteria. TCD was applied to 62 patients with BD and 40 healthy individuals. TCD results were evaluated by a specialist neurologist.

Results: Headache was determined in 89 (78.8%) patients with BD. It was statistically significant compared to HC group (60%, p<0.03). 48 of 89 BD patients had tension type of headache and 33 of them had migrainous type. No significant difference was found between BD patients and HC group in terms of cerebral reactivity by TCD. Low pulsatility index for both the right side and the left side were noted in BD patients suffering from headache compared to BD patients not having headache (p<0.006, p<0.003). No significant differences were found between tension type and migrainous type of headache in terms of TCD parameters.

Conclusions: Headache is common in BD patients, but cerebral reactivity is maintained.

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THU0614 INTERSTITIAL LUNG DISEASE IN PATIENTS WITH ANTISYNTHEASE SYNDROME AND ANTI-RO52 ANTIBODIES POSITIVE

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Background: Antisynthetase syndrome (ASS) is characterised by the presence of myositis, arthritis, interstitial lung disease (ILD), fever, Raynaud's phenomenon and mechanical's hand, in the presence of antisynthetase autoantibodies (AA), the most frequent being anti-Jo1, anti-PL7 and anti-PL12. An association between ASS and anti-Ro52 with increased ILD has been described and it is believed that the presence of both antibodies is accompanied by a more severe ILD.

Objectives: To describe the clinical and analytical characteristics of a cohort of patients with ASS. To analyse the lung involvement in this type of patient and to determine the possible relationship between the different subtypes of ILD and the presence of anti-Ro52.

Methods: Retrospective descriptive study of patients treated in our Hospital (2006–2017), with AA and at least 2 clinical characteristics. The data was obtained through the review of medical records.

Variables analysed: age, sex, age, smoking, clinical presentation, diagnosis of ASS, associated neoplasia and paraneoplastic syndrome (PS) (neoplasia 3 years before or after the diagnosis of ASS), muscle enzymes (CK and aldolase), autoimmunity, glucocorticoids (GC), immunosuppressants (IS), diagnosis of ILD, HRCT pattern (High Resolution Computed Tomography) and respiratory function tests (RFT) at the beginning of ILD.

Results: We included 27 patients (20 women), mean age 61±13 years. 7.4% smokers and 18.5% ex-smokers. 88.8% were anti-Jo1, 7.4% anti-PL12 and 3.7% anti-PL7. Anti-Ro52 present in 18 patients. The most common clinical presentation: ILD 88% (59% had Ro52), followed by myositis 85% (40% are dermatomyositis), arthritis 81%, mechanic's hand 51%, fever 37% and Raynaud's phenomenon 25%. The classic triad (arthritis, myositis, ILD) was present in 16 patients. Three patients presented neoplasia in the course of the disease, being identified as PS. Elevation of CK in 70% and aldolase in 74%. 96% of patients have been treated with GC and IS.

The HRCT patterns were: non-specific interstitial pneumonia (NSIP) (66%), usual interstitial pneumonia (UIP) (29%), organised cryptogenic pneumonia (OP) (4%), baseline RFT were performed in 19 patients. Diagnosis of ASS and ILD, both entities appear at the same time in 6 patients, in 3 patients the ILD appears before and in 14 after. In these, the median duration (range) of the ASS until the diagnosis of ILD was 1 year (0–1).

There is no relationship between the HRCT and anti-Ro52 patterns (chi-square considering the exact distribution p=0.892), nor between the ILD and anti-Ro52 (Fisher exact test p=0.999).

Conclusions: Our results, in general, agree with what is published in the literature. Three patients have an uncommon presentation of ASS, with a diagnosis of ILD prior to myopathy (in most of the published cases, myositis precedes or coincides with the onset of IDL), and it is important to include ASS in the differential diagnosis of ILD. In our cohort, the association between ILD and anti-Ro52 has not been demonstrated, nor among the different subtypes of ILD to Ro52. Therefore, prospective studies with a greater number of patients are necessary to define Ro52's role in the development of ILD in ASS.

Disclosure of Interest: None declared

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THU0615 IMMUNE RELATED ADVERSE EVENTS (IRAEs) ASSOCIATED WITH CHECKPOINT INHIBITORS: 12 CASES FROM A SINGLE CENTRE

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Background: Immune checkpoint inhibitors (ICI) have made a significant impact on the treatment of many advanced malignancies. There is little data on the rheumatologic complications of these treatments.

Objectives: We describe 12 cases of rheumatologic IRAEs following ICI treatment to further characterise the spectrum of disease and treatment responses.

Methods: We report patients evaluated in a general Rheumatology outpatient clinic from 2014 to 2017. Cases were defined as those with new rheumatologic symptoms following treatment with an ICI. Alternative explanations for the presenting syndrome were excluded clinically. Clinical data was extracted by retrospective chart review.

Results: This case series includes 12 patients (6 female, 6 male) with a mean age at IRAE onset of 63.9 years (range 33–79). Multiple cancers were represented including melanoma (n=9), Hodgkin's lymphoma (n=1), squamous cell lung cancer (n=1), and adenocarcinoma of the lung (n=1). 5/12 patients received Nivolumab, 8/12 received Pembrolizumab, and 2/9 received Ipilimumab. ICI exposure was associated with various rheumatologic IRAEs including PMR-like syndrome (n=4), symmetric polyarthritis (n=6), psoriatic arthritis (n=1), oligoarthritis (n=1), and erythema nodosum (n=1). Other IRAEs were also noted including vitiligo (n=1), pulmonary capillaritis (n=1), ulcerative colitis flare (n=1), inflammatory seborrheic keratosis and psoriasis (n=1). The mean time of onset of the IRAE from the first exposure to an ICI was 6.8 months (range 0–21 months). In 7 cases, rheumatologic symptoms worsened with each ICI dose. Laboratory investigations demonstrated elevated CRP in 7 cases (mean 75.6; range 3.7–290.1), RF positivity in 2 cases, weak positive ANAs in 4 cases (1:80), SSA positivity in 2 cases, and a single case where a pre-existing anti-CCP antibody was identified. Steroids were used in 11 cases at a mean starting dose of 36 mg (range 10–50 mg) by mouth daily for an average duration of 6.1 months (range 1–12 months). Other DMARDs were necessary in some cases (Hydroxychloroquine n=1; Methotrexate n=5). While 6 patients experienced rapid improvement, 4 experienced gradual improvement. Most patients achieved partial resolution of symptoms (n=6) while only 4 achieved complete resolution. Tumour response was observed in all 12 patients.

Conclusions: This case series of IRAEs associated with ICI treatment suggest that symmetric polyarthritis and PMR-like syndromes are the most common rheumatologic IRAEs, although the spectrum is broad. IRAEs seem to develop around 6 months after first exposure, worsen with ongoing doses of ICI administration, and respond to treatment with corticosteroids. Treatment doses and duration were higher than expected for phenotype, with few patients achieving significant improvement with short courses. Those with IRAEs tend to have good tumour response, despite concurrent use of immunosuppressants. MTX and HCQ appear to be safe and effective, but more experience with these and other DMARDs/biologics is required in these patients.

Disclosure of Interest: None declared

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THU0616 ELEVATED THYROID STIMULATING HORMONE AS A POTENTIAL BIOMARKER FOR RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS FOLLOWING PD-1 INHIBITOR THERAPY

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Background: Programmed cell death protein (PD-1) inhibitor immunotherapy is being increasingly used in oncology, but may cause immune-related adverse events (irAEs) resembling classical rheumatic and non-rheumatic autoimmune diseases. While oncological response to therapy has been associated with the development of rheumatic irAEs, no biomarker to predict the development of rheumatic irAEs has yet been identified. Thyroid stimulating hormone (TSH) is readily available in clinical practice and is frequently tested prior to the administration of PD-1 inhibitors to screen for existing thyroid disease.

Objectives: To investigate whether thyroid stimulating hormone, or changes to it, are associated with the development of immune-related adverse events (irAEs) following PD-1 inhibitor therapy for cancer.

Methods: This was a retrospective chart review of all patients at a single centre who had a TSH level performed in the institutional laboratory prior to the patient being dispensed nivolumab or pembrolizumab before January 1, 2017, with follow-up until July 1, 2017. TSH levels before and during PD-1 inhibitor therapy were recorded. Patients with any diagnosis of a rheumatic irAE or any non-

cutaneous irAE were identified. Linear regression was performed to determine the relationship between TSH and the development of irAEs. Youden's index was used to derive the optimal cut-off point. Recursive partitioning methods with imbalanced prior probabilities were used to create a decision tree model.

Results: There were 213 episodes of therapy which met criteria, of which a non-cutaneous irAE occurred in 62 episodes (29.1%), thyroid irAEs occurred in 22 episodes (10.3%) and rheumatic irAEs were diagnosed in 16 episodes (7.5%). Even when corrected for duration of exposure to PD-1 inhibitor therapy, elevated TSH levels (>4.2 mU/L) were statistically significantly associated with the development of rheumatic irAEs (adjusted OR 6.08, 1.53–24.22), and this was not weakened by excluding patients who went on to develop thyroid irAEs. There was no significant association between elevated TSH levels and the development of any non-cutaneous irAE. Change in TSH levels with PD-1 inhibitor therapy was also not associated with the development of non-cutaneous irAEs or rheumatic irAEs specifically. Using a TSH level >2.4 to predict rheumatic irAEs led to a positive predictive value of 25% and a negative predictive value of 93% in our cohort. A decision tree model to predict rheumatic irAEs combining a pre-PD-1 inhibitor TSH level >2.4 and an oncological response to therapy led to a positive predictive value of 50% and a negative predictive value of 94% in our cohort.

Conclusions: Elevated TSH levels may be a potential biomarker for the development of rheumatic irAEs. In particular, a pre-PD-1 inhibitor TSH level of >2.4 mU/L, in combination with oncological response to therapy, may identify patients at risk of rheumatic irAEs. Associations observed in this cohort should be examined in larger cohorts to determine the clinical utility of TSH in predicting rheumatic irAEs.

Disclosure of Interest: None declared

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THU0617 IS THE NUMBER OF IGG4+ PLASMA CELLS SEEN BY IMMUNOSTAINING USEFUL BEYOND ITS DIAGNOSTIC UTILITY IN IGG4-RELATED DISEASE?

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Background: The histopathological findings in IgG4-related disease (IgG4-RD) includes the presence of marked IgG4 + plasma cell infiltration seen by immunostaining and it has been used in clinical practice only as a diagnostic tool. Whether the number of IgG4 + plasma cells in tissue is associated with any clinical or serological feature of the disease has not been previously evaluated.

Objectives: To evaluate if the number of IgG4 + plasma cell infiltration is associated with any clinical or serological outcome.

Methods: We included 30 patients with biopsy proven IgG4-RD according to the Comprehensive Diagnostic Criteria for IgG4-RD who regularly attended a tertiary referral centre in Mexico City (2000–2017). We collected demographics, clinical (organ involvement, relapses and the disease activity assessed by the IgG4-RD Responder Index [IgG4-RD RI] at baseline) as well as baseline laboratory data (C3, C4, total eosinophil count, IgG4 levels). Patients were divided in three groups according to the number of IgG4 + plasma cells seen by immunostaining as follows: <50 IgG4 + plasma cells/HPF, 50–100 IgG4 + plasma cells/HPF, and >100 IgG4 + plasma cells/HPF.

Results: We included 30 patients, 17 (56.6%) women, mean age 53±13.9 years and median disease duration 13 months. The biopsies were from the following tissues: lacrimal gland (n=6), pancreas (n=5), orbit (n=4), kidney (n=4), lymph node (n=3), mediastinum (n=2), salivary gland (n=2) and other tissues (n=4). Eleven patients (36.6%) had <50 IgG4 + plasma cells/HPF, 9 patients (30%) 50–100 IgG4 + plasma cells/HPF and 10 (33.3%) patients >100 IgG4 + plasma cells/HPF. We did not find any difference regarding age, gender, time of follow up, number of involved organs and relapses. The median basal IgG4-RD RI was 9, 6 and 15, for the <50 IgG4 + plasma cells/HPF, 50–100 IgG4 + plasma cells/HPF, and >100 IgG4 + plasma cells/HPF groups respectively, however, they did not reach statistical significance. The group with >100 IgG4 + plasma cells/HPF had more frequently lymphadenopathy when compared with the other groups (36.4%, 66.7% and 80%, p=0.02; respectively) while the proportion of involvement of the other anatomic sites were similar. We found a statistical difference in serum C3 levels (99.5 mg/dl, 159 mg/dl, 78.5 mg/dl, p=0.04) and a tendency for serum C4 levels (20 mg/dl, 27 mg/dl, and 6 mg/dl, p=0.08) among the groups, whereas the levels of serum IgG4 (60.8 mg/dl, 196 mg/dl, 245 mg/dl, p=0.35) and the eosinophil count (284/mm³, 189/mm³, 283/mm³, p=0.46) were similar. The C3 and C4 serum levels negatively correlated with the basal IgG4-RD RI (τ = -0.48, p=0.005 and τ = -0.58, p=0.001).

Conclusions: Our results show that the number of IgG4 + plasma cells seen by immunostaining in IgG4-RD may be of value in identifying a subset of patients with hypocomplementemia, lymphadenopathy and probably higher basal disease activity. The finding of an association between hypocomplementemia and higher tissue infiltration by IgG4 + plasma cells expands the evidence that complement activation may contribute to the pathogenesis of IgG4-RD.