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Background: Immune checkpoint inhibitors (ICI) have changed the treatment landscape of many cancer types, but are also associated with development of immune-related adverse events, including *de novo* sarcoid like reactions. However, little is known about the use of ICI therapy in patients with preexisting sarcoidosis as patients with preexisting autoimmune diseases have been systematically excluded from clinical trials of ICI therapy due to concerns of heightened toxicities. Emerging research suggests that ICI therapy can be considered in some patients with autoimmune diseases.¹

Objectives: To determine the risk of sarcoidosis exacerbation or flare in patients with preexisting sarcoidosis receiving ICI therapy.

Methods: We conducted a retrospective cohort study of patients seen at The University of Texas MD Anderson Cancer Center between 2016-2019. Patients were included in the cohort if they received one of 7 ICI therapies (ipilimumab, nivolumab, pembrolizumab, durvalumab, avelumab, atezolizumab, or cemiplimab) and had an International Classification of Disease version 10 code of sarcoidosis (D86.*), prior to the ICI initiation, with diagnosis confirmed in medical record by treating physicians. A sarcoidosis diagnosis was considered "possible" if the medical record documented a history of sarcoidosis, "probable" if a history of biopsy proven sarcoidosis was mentioned, and "definitive" if histological evidence was available. Frequency of flares and outcomes of patients after receiving ICI were collected.

Results: During the study timeframe a total of 32 patients with preexisting sarcoidosis received ICI therapy. Nine patients (28%) had a definitive diagnosis of sarcoidosis, 12 (37%) had a probable diagnosis and 11 (35%) had a possible diagnosis of sarcoidosis. The mean time between diagnosis of sarcoidosis and initiation of ICI therapy was 13 years (range: <1 to 51 years). Twenty-seven patients (84%) received monotherapy and five patients (16%) received combination or sequential ICI therapy. Of the 32 patients, one patient with a 20-year remote history of sarcoidosis, never treated, developed a clinically symptomatic exacerbation of sarcoidosis one month after the initial dose of atezolizumab, with increased hilar nodules on imaging, skin nodules, arthritis and uveitis. Biopsy of a lymph node showed non-necrotizing granulomas, and biopsy of the skin panniculitis. The patient also developed colitis thought to be an immune-related adverse event. Atezolizumab was discontinued after 3 doses. Patient was treated with prednisone and azathioprine.

Conclusion: Patients with a remote history of stable sarcoidosis at the time of ICI therapy infrequently develop a flare of their sarcoidosis. The risk of flares in patients with active sarcoidosis requiring immunosuppression at the time of ICI initiation is unknown.

References:

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SAT0537 ANALYSIS OF ADULTS PATIENTS WITH NOD2-ASSOCIATED AUTOINFLAMMATORY DISEASE

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Background: More than 100 mutations of the NOD2 gene have been described, some of which have been related to diseases such as Crohn's disease, Blau syndrome, early-onset sarcoidosis and NOD2-associated autoinflammatory disease (NAID), the latter of polygenic character. The inflammatory disease associated with a NOD 2 gene is characterized by periodic fever, dermatitis, polyarthritis, gastrointestinal symptoms and symptoms similar to those of the dry syndrome and currently associated with the NOD2 variants.

Objectives: Describe the clinical characteristics and genetic variants of a cohort of patients in adulthood with autoinflammatory disease associated with the NOD2 gene with follow-up in a third level hospital in southern Spain

Methods: Retrospective descriptive study of patients in adulthood with diagnostic suspicion of autoinflammatory disease and with genetic mutation in NOD2 gene. Patients with follow-up from 2013 to the present and in which another diagnosis of autoimmune disease (inflammatory bowel disease, sarcoidosis, etc.) were excluded. Data were obtained by review of medical records.

Results: 17 patients with alterations in the NOD2 gene were included. 14 cases (76.4%) were women. The mean age at diagnosis was 34.3 years (± 13.2). In the 17 patients, 19 mutations were found at the level of the NOD2 gene, the most

frequent was with 9 cases (47.3%) the mutation in exon 4 (R702W), followed by mutation in exon 11 (1007finsC) with 5 cases (26.3%) and mutation in exon 4 (P268S) with 3 cases (15.4%). Other mutations obtained were mutation in exon 4 (R311w), mutation in exon 6 (M863V) and mutation in exon 11 (G908R) with a single case in each of them. In 6 cases (35.3%) there were first-degree relatives with a similar clinic, although not in all cases they were studied. Regarding the clinical manifestations, joint involvement (arthralgia and / or arthritis) with 12 cases (70.6%) was the most frequent followed by rash skin involvement with 10 cases (58.9%) and nonspecific abdominal pain with 9 cases (52.3%). Other less frequent manifestations were evening predominance fever and the elevation of acute phase reactants (CRP and ESR) with 8 cases (47.1%), oral thrush present in 5 patients (27.8%) and diarrhea with 4 cases (23.5%).

Conclusion: The autoinflammatory disease associated with the NOD2 gene is an entity that can occur in adulthood and that can occur in a similar way to other auto-inflammatory diseases of a monogenic nature and in which the joint, cutaneous and abdominal involvement may predominate. We must maintain a high degree of suspicion and always include inflammatory bowel diseases in the differential diagnosis.

Disclosure of Interests: None declared

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SAT0538 CLINICAL PROFILE OF AUTOIMMUNE UVEITIS NOT ASSOCIATED WITH HLA B27: A RETROSPECTIVE SINGLE CENTER STUDY

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Background: Autoimmune uveitis is frequently referred to a rheumatologist for evaluation & treatment. While clinical characteristics of HLA B27 associated uveitis are well documented, scanty information is available on non HLA-B27 associated autoimmune uveitis. We have described the clinical characteristics of our patients of non-B27 uveitis and compare the same with patients of Asian Indian HLAB27 uveitis.

Objectives: To describe and compare the clinical characteristics of non HLA-B27 associated autoimmune uveitis.

Methods: Retrospective review of records from hospital's electronic medical record database and included all cases of autoimmune uveitis that were referred to rheumatology from January 2017 and December 2018. Among these, those who did not have HLA B tissue typing record or were HLAB27 positive; were excluded. Pertinent details like age, sex, no. of episodes, unilateral or bilateral, location of uveitis (anterior, posterior or pan uveitis, association of synechiae & vasculitis), baseline CRP & ESR levels along with the HLA B profile(SSP-PCR) & nature of treatment received (systemic steroids, DMARD initiation) were collected. For comparison, clinical features of a HLA B27+ve uveitis series from the same ethnic Asian-Indian population were used¹. Subgroup analysis was also done between the common non B27 HLA genotypes. Descriptive statistics were summarized using mean & percentage. Chi square & Fischer's test was used to compare the groups and subgroups.

Results: Out of total 210 patients screened, 17 cases were HLA B27 negative on HLA B tissue typing. The key demographic and clinical features of our patients of autoimmune uveitis not associated with HLA B27 in comparison with the B27 +ve uveitis group are given in table 1.

Table 1 Comparison of clinical features of our patients versus B27 +ve uveitis

	Non HLA B27 Autoimmune Uveitis (N=17)	Ninan et al (N=25)	P value
Age (years) at disease onset			
16-35	4	15	
More than 35	13	7	0.009
Onset not known	0	3	
Sex			
Male	6	21	0.002
Female	11	4	
Region of uveitis			
anterior	9	24	0.001
posterior & pan-uveitis	8	1	
Biochemical parameters			
CRP (mg/L)	6.45 ± 8.39	N.A	-
ESR (mm/hr)	24.75 ± 18.80	N.A	
Associated complications			
synechiae formation	4 of 17	4 of 25	0.69
retinal vasculitis	4 of 17	0 of 17	-

Recurrent uveitis was seen in 11 out of 17 patients in our patients as compared to 15 out of 22 (p 0.81) in HLA B27 +ve patients.

HLA B7 and HLA B35 were the most frequent genotypes (figure 1). Sub group analysis showed that 87.5% of patients with a component of posterior uveitis were HLA B7 or HLA B35 positive. It was noted none of 5 cases of HLA B35 +ve uveitis needed second line DMARD initiation after a tapering course of systemic steroids. There was no other significant difference in the clinical or treatment parameters noted in the subgroup analysis between the HLA genotypes.

Conclusion: Autoimmune uveitis not associated with HLA B27 tends to have older age of onset, female predominance, more common involvement of posterior uvea and association of vasculitis than HLAB27 autoimmune uveitis. Among non HLA B27 uveitis, HLA B07 and HLA B35 are the most common serotypes in our Asian south Indian group. Therapeutic stratification for a delayed initiation of second line DMARD therapy needs to be studied further particularly in HLA B35 +ve uveitis.

References:

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SAT0539 MUCKLE-WELLS SYNDROME IN RHEUMATOLOGY PRACTICE, FAMILY CASES: FEDERAL CENTER EXPERIENCE.

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Background: Muckle-Wells syndrome (MWS) is a monogenic autoinflammatory disease caused by a NLRP3 gene mutation. It is the most common variant of cryopyrin-associated periodic syndromes (CAPS) and can be observed in rheumatology practice. It manifests itself in fever, urticaria-like rash, arthralgias/arthritis, conjunctivitis/uveitis, sensorineural hearing loss, acute-phase markers (ESR, CRP). The disease's onset usually takes place in infancy. There are examples of family cases. Targeted therapy: interleukin-1 inhibitors (anakinra, canakinumab).

Objectives: to provide characteristics of MWS patients, family cases in the rheumatology practice of the Federal Rheumatology Center in Russia.

Methods: in a 10-year period (2009 to 2019), MWS was diagnosed in 42 outpatient and inpatient patients, among them were 24 children, 18 adults, and 9 family cases. All of them underwent a standard rheumatology examination, including a ECR, CRP, ophthalmologist examination, and an audiogram. A molecular genetic test of the NLRP3 gene was carried out for all patients, the diagnosis was confirmed in all of them.

Results: Out of 18 adult patients aged between 19 and 59 years, women were prevalent (16 to 2), the onset age was 0 to 53 years, in 88.9% cases the onset took place before a patient was 18 years old. When diagnosed, the disease duration varied from 6 to 46 years. Most patients demonstrated fever, urticaria-like rash, arthralgias/arthritis, which were observed in 16 patients (88.9%), conjunctivitis were observed in 15 patients (83.3%), sensorineural hearing loss – in 8 patients (44.4%), abdominal pain, nausea, vomiting – in 4 patients, headache, dizziness – in 6 patients. There also were rare manifestations, such as: recurrent oral ulcers (8), genital ulcers (3), erythema nodosum (3), sore throat and raids on the tonsils (PFAPA-like phenotype) was observed in 2 patients. In 3 patients manifestations were triggered by cold temperature. All patients had an increased ESR and C-reactive protein concentration. Eight family cases of MWS were identified (in total 26 family members aged between 2.5 and 62 years) with a number of affected in one family ranging from 2 to 6 people of different age (8 children, 18 adults, out of which 20 were female, and 6 were male). Most patients had fever

(17), urticaria-like rash (18), conjunctivitis (12), oral ulcers (7), articular syndrome (14), sensorineural hearing loss (5), and 2 patients died of renal insufficiency (probably due to amyloidosis of the kidneys). The heterozygous mutations in NLRP3 have been identified in pts: T348M (3 families), R262W (2 families), A439V (1), V198M (1), Pro294Ser (1). Ten patients received canakinumab for a period of 6 months to 6.5 years, and 5 patients received anakinra before canakinumab.

Conclusion: MWS is an orphan autoinflammatory disease, however it sometimes can be observed in rheumatology practice. It is very important to acquire family medical history to identify affected family members and prescribe therapy in a timely manner. IL-1 inhibitors are an effective and safe treatment option for MWS patients.

Disclosure of Interests: None declared

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SAT0540 ONE-YEAR OUTCOMES AFTER RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS FROM CHECKPOINT INHIBITORS

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Background: Description and initial management of rheumatic immune-related adverse-events (irAEs) from cancer immunotherapies have been reported by several groups but to date, few studies have evaluated the long-term outcomes and management of rheumatic irAEs (1).

Objectives: To describe the long-term management and assess the one-year outcomes of patients who experienced rheumatic immune-related adverse events (irAEs) due to immune checkpoint inhibitors (ICI).

Methods: This was a single-centre prospective observational study including patients referred for musculoskeletal symptoms while treated with ICI. After baseline rheumatological evaluation defining the clinical entity presented, follow-up visits were organised according to the type and severity of irAE. At one year, persistence of irAE, ongoing treatment, as well as cancer outcomes were assessed.

Results: 63 patients were included between September 2015 and June 2018. 24 patients (38%) presented with non-inflammatory musculoskeletal conditions managed with short-term symptomatic treatment and did not require specific follow-up. 39 patients (62%) experienced inflammatory manifestations, mimicking either rheumatoid arthritis (RA, n=19), polymyalgia rheumatica (PMR, n=16), psoriatic arthritis (PsA, n=3) and one flare of a preexisting axial spondyloarthritis. Overall, 32 patients (82%) received systemic glucocorticoids, with a median rheumatic dosage of 15mg/day (range: 5-60mg/day). None of the patients had to permanently discontinue ICI therapy for rheumatic irAE. 20 patients (67%) were still receiving glucocorticoids at one year, with a median dosage of 5mg/day (range: 2-20mg/day). Glucocorticoids were more frequently discontinued for patients with RA-like condition (44%) than PMR-like condition (23%), but no other predictive factor of glucocorticoids withdrawal could be identified. At one year, overall survival and progression-free survival were comparable between patients who were still receiving glucocorticoids for rheumatic irAE and patients who have discontinued. Eight patients required csDMARDs.

Conclusion: At one year, a majority of patients required long-term low-dose glucocorticoids for chronic rheumatic irAE, which seems not altering oncological control.

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SAT0541 THE SEVERITY OF FMF MAY BE ASSOCIATED WITH CO-MORBIDITIES

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Background: Familial Mediterranean fever (FMF) is an auto inflammatory disease with recurrent attacks of serositis. Frequent attacks and disease related sequels may be associated with co-morbidities in FMF patients.

Objectives: One of the tools for evaluating the FMF severity is the international severity scoring system for FMF (ISSF) ¹. This score includes disease related sequels, acute phase measurements, attack features and exertional leg pain.