SAT0534

RITUXIMAB FOR REFRACTORY IDIOPATHIC RETROPERITONEAL FIBROSIS: A SINGLE TERTIARY CENTER EXPERIENCE

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Background: Idiopathic retroperitoneal fibrosis (RPF) is a progressive disorder of the retroperitoneum which is often idiopathic. Although prednisolone is the mainstay approach to treating RPF, the remission rates range between 75% to 95% (1-2).

Objectives: Here, we report the outcomes and steroid-sparing effect of Rituximab (Rtx) therapy in 14 patients with RPF.

Methods: This retrospective study was conducted at a tertiary rheumatology center. Patients were diagnosed with RPF and had at least a course of 0.5-1 mg/kg prednisolone treatment previously. These patients were switched to Rtx due to inadequate response or side effects while on prednisone, tamoxifen, azathioprine or cyclophosphamide therapy. Patients were treated with Rtx in order to be included in this study. Involvement and activation of RPF was shown via PET-CT either before or at least 6 months after the therapy. Daily prednisolone dose was noted before rituximab initiation and 6 months after the therapy. All of the patients reported, except two, were followed for at least 6 months after the Rtx treatment. The final disease status of the three patients were not included in the study.

Results: Fourteen patients (7F) received at least 2 cycles (1 gr for each) of Rtx. The age of diagnosis was 54.3 ± 11.0 years, follow-up duration was 46.0 ± 37.2 months. The previous treatments, number of the cycles of Rtx and final disease status were shown in the Table. The Control PET-CT revealed metabolic and radiologic remission in 3 patients. In 6 patients, the disease remained stable. In 2 patients there was disease progression hence they were treated with the second course of Rtx. One of the two patients had the progression two years after the first cycle but then, was lost to follow-up. The mean prednisolone dose decreased from 15.5 ± 12.4 mg to 2.2 ± 2.2 mg/day after 6 months of Rtx initiation. Final prednisolone dose was 2.6 ± 5.5 mg/day (Figure). Rtx treatment was ceased in 6 patients with sustained remission.

Conclusion: The present study shows that Rtx could be a therapeutic option after glucocorticoid or DMARD failure. The steroid sparing effect of Rtx is essential and further prospective studies are needed to assess the Rtx efficacy more objectively in RPF treatment.

Table. Characteristics and final disease status of the patients

Number	Age of Rituximab Initiation	Sex	Previous Treatments	Number of Rituximab Cycle(s)	Final Pet-CT
1	49	M	Pred, Mtx	1	Stable disease
2	54	M	Pred, Mtx	1	Stable disease
3	46	F	Pred, Aza, Tmx, Mmf	2	Progression
4	40	M	Pred, Aza, Mtx	4	Remission
5	63	F	Pred, Tmx	10	Stable disease
6	47	F	Pred, Mtx	2	Stable disease
7	30	F	Pred	1	Stable disease
8	52	M	Pred, Aza	2	Progression
9	54	M	Pred	1	N/A
10	59	M	Pred, Aza, Mtx	1	N/A
11	30	F	Pred, Mtx	6	Remission
12	40	F	Pred, Aza, Tmx; Cyc	3	Stable disease
13	50	M	Pred	2	N/A
14	45	F	Pred, Aza	3	Remission

Pred: Prednisolone,

Tmx: Tamoxifen, Mtx: Methotrexate, Cyc: cyclophosphamide

Aza: Azathioprine,

Figure: Corticosteroids sparing effects of Rituximab

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SAT0535

CLINICAL COURSE IN PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF) IN A MULTIDISCIPLINARY CONSULTATION.

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Background: A proportion of patients with Interstitial Lung Disease (ILD) show autoimmune characteristics but do not completely meet the classification criteria for a definitive connective tissue disease. In order to unify the nomenclature and criteria to define this condition, the classification of patients with Interstitial Pneumonia with Autoimmune Features (IPAF) has recently been adopted (Fisher, et al).

Objectives: To describe the sociodemographic, clinical, functional characteristics and therapeutic management of IPAF patients in clinical practice and to evaluate the incidence rate of functional respiratory impairment over time.

Methods: A longitudinal observational study was performed. Patients with IPAF classification criteria (Fischer et al) were included from the time of ILD diagnosis (Feb 2017 to Sept 2018) and followed until loss of follow-up or end of the study (Oct 2019), in a multidisciplinary team, carried by a pneumologist and a rheumatologist in a Tertiary Hospital in Madrid. Main outcome: relative functional respiratory impairment: defined as decline in percent predicted forced vital capacity (FVC%) of $\geq 5\%$ compared to the previous visit. Respiratory function was measured at baseline and every 6 months. Covariates: a) sociodemographic, b) clinical, c) radiological pattern (non-specific interstitial pneumonia [NSIP]; usual interstitial pneumonia [UIP], others); d) FVC%, DLCO%; e) laboratory tests; f) therapy used (glucocorticosteroids, disease modifying antirheumatic drugs [DMARDs] and Biologic Agents). Statistical analysis: description of the sociodemographic, clinical, radiological, functional and treatment characteristics of the patients. Survival techniques were used to estimate the incidence rate (IR) of relative functional respiratory impairment, expressed per 100 patient-semester with their respective confidence interval [95 % CI].

Results: 17 patients were included with a mean follow-up of 3 ± 1.5 years, 70.6% were women with a mean age of 65 ± 10 years. The most frequent IPAF classification criteria were: a) clinical: arthritis (50%), Raynaud's phenomenon (33%) and mechanical hands (17%); b) serological: 65% had ANA $\geq 1/360$; 31% FR > 40 ; 30% Anti-Ro positive; c) morphologic: 59% presented NSIP pattern and 29.4% was UIP. The baseline median FVC% and DLCO% were 89 [83-107.7] and 63 [50-79.8] respectively. During the study period, 94% received treatment: 87.5% glucocorticosteroids, 68.5% mycophenolate, 56% azathioprine, 18.7% cyclophosphamide iv and 33% antifibrotics. During the follow-up (104.6 patient - semester), 15 patients presented relative functional respiratory impairment, with an IR of 23.8 [16.1-35.3]. After 14 months from IPAF diagnosis 50% of the patients had relative functional respiratory impairment. At the end of the follow-up, 50% showed a worsening of the DLCO%.

Conclusion: IPAF patients are mostly women in their sixties. The most frequent clinical criteria are arthritis and Raynaud's phenomenon and the serological were FR and ANAs. The most frequent radiological pattern was NSIP. The therapeutic management is mainly with glucocorticosteroids, mycophenolate and azathioprine. At the beginning, patients have a slightly diminished lung function. These patients have significant functional impairment over time that will impact in their prognosis. Longitudinal and multicenter studies are necessary to advance in the knowledge and management of these patients.

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SAT0536

IMMUNE CHECKPOINT INHIBITOR THERAPY IN PATIENTS WITH PREEXISTING SARCOIDOSIS

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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 ($\pm$ 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.