SAT0625

SARCOIDOSIS IS ASSOCIATED WITH AN INCREASED RISK OF GASTROINTESTINAL EVENTS: A POPULATION-BASED RETROSPECTIVE COHORT STUDY 1976–2013

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Background: An increased risk of gastrointestinal (GI) diseases has been observed in several chronic inflammatory disorders but the risk in patients with sarcoidosis is not known.

Objectives: This study was undertaken to characterise the risk of GI diseases in patients with sarcoidosis.

Methods: A population-based cohort of 345 incident cases of sarcoidosis among Olmsted County, Minnesota residents in 1976–2013 was identified from a comprehensive medical record-linkage system. Diagnosis was confirmed by individual medical record review. A cohort of 345 sex and age-matched comparators was also identified from the same underlying population. Medical records of both groups were reviewed for GI diseases. Cox models adjusted for age, sex and calendar year were used to compare the rate of development of GI diseases between the groups.

Results: GI events occurred in 101 cases and 63 comparators, corresponding to an adjusted hazard ratio (HR) of 1.90 (95% confidence interval [CI] 1.38–2.61). Patients with sarcoidosis had an increased risk for both upper (HR 1.90; 95% CI 1.27–2.83) and lower GI events (HR 1.97; 95% CI 1.27–3.05) relative to comparators. By disease type, patients with sarcoidosis had a significantly elevated risk of upper GI ulcer, upper GI haemorrhage and diverticulitis (**table 1**).

Comorbidity	Number of events prior to index date	p-value	Number of events after index date	Cumulative incidence at 10 years for non-sarcoidosis subjects (±SE)	Cumulative incidence at 10 years for sarcoidosis patients (±SE)	Hazard ratio (95% CI)	p-value
Upper GI diagnoses							
Upper ulcer	21/19	0.87	11/27	1.9 (0.2, 3.6)	4.5 (2.0, 6.8)	2.56 (1.27, 5.17)	0.009
Upper bleed	6/14	0.11	14/29	0.9 (0.0, 2.0)	4.4 (1.9, 6.9)	2.36 (1.24, 4.47)	0.009
Upper perforation	2/0	0.50	0/1	–	–	–	–
Upper obstruction	1/3	0.62	7/8	1.4 (0.0, 2.7)	0.3 (0.0, 0.9)	1.20 (0.43, 3.32)	0.72
Esophagitis	7/4	0.55	18/27	3.6 (1.4, 5.8)	5.4 (2.7, 8.1)	1.58 (0.87, 2.88)	0.13
Esophageal varices	0/3	0.25	1/6	0.0 (0.0, 0.0)	0.7 (0.0, 1.8)	6.51 (0.78, 54.16)	0.083
Lower GI diagnoses							
Lower ulcer	2/1	1.0	2/7	0.6 (0.0, 1.4)	1.4 (0.0, 2.8)	3.51 (0.73, 16.92)	0.12
Lower bleed	5/3	0.72	12/15	1.8 (0.2, 3.3)	2.9 (1.0, 4.8)	1.32 (0.62, 2.82)	0.48
Lower perforation	0/0	–	2/1	–	–	–	–
Lower obstruction	0/2	0.50	1/2	–	–	–	–
Diverticulitis	3/2	1.0	9/18	0.4 (0.0, 1.1)	2.3 (0.6, 4.0)	2.29 (1.03, 5.10)	0.043
Ischaemic colitis	2/0	0.50	3/7	0.0 (0.0, 0.0)	0.6 (0.0, 1.5)	2.38 (0.61, 9.26)	0.21
Infectious colitis	1/5	0.22	7/13	0.6 (0.0, 1.5)	2.9 (0.9, 4.9)	1.99 (0.79, 5.00)	0.14

Conclusions: Patients with sarcoidosis have a higher risk of both upper and lower GI events compared with subjects without sarcoidosis.

Disclosure of Interest: None declared

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SAT0626

ANAKINRA TREATMENT IN REFRACTORY CASES OF ADULT-ONSET STILL DISEASE: CASE SERIES

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Background: Despite methotrexate and steroid treatment, in cases of Adult-onset Still's disease (AOSD) it is usually difficult to maintain clinic stability. In refractory cases, Anakinra treatment has been reported to be efficacious.¹

Objectives: In this retrospective review, it is aimed to evaluate the AOSD cases treated with anakinra in our centre.

Methods: Fourteen AOSD patients (11 female, 3 male) who were being followed in our outpatient clinic were reviewed retrospectively. The demographic characteristics, pre- and post-treatment clinical findings were reported.

Results: The mean follow-up period of the patient population was 33.5±30.07 months (mean ±SD). Initial prednisolone dose was 37.3 mg/day. Except for one, all of our patients were exposed to methotrexate before being treated with anakinra. This patient was being treated with cyclosporine instead, since she had concomitant Macrophage Activation Syndrome. The other medications, the patients were previously treated with, were Etanercept (n=2), Tocilizumab (n=3), Infliximab (n=1) and Adalimumab (n=1).

All patients were on 100 mgs of Anakinra, daily, except for the one treated with 200 mg/day. The mean duration of Anakinra therapy was 11.4 months. Among 7 patients in whom anakinra therapy was terminated, 1 had drug induced urticaria, 1 was primary irresponsive, 4 were secondary irresponsive and the other had severe pneumonia. Primary irresponsiveness is the lack of response to the therapy since the drug was first introduced, whereas in secondary irresponsiveness the case responds to the medication for a while and starts to flare again after asymptomatic-free period on the medication. Among 14, 7 of our patients are still on 100 mg/d Anakinra.

The mean level of C reactive protein (CRP) measures was reduced from 64.38 ±61.95 mg/L to 34.3±24.3 mg/L with Anakinra therapy (p=0.003). Similarly, mean Erythrocyte Sedimentation Rate (ESR) was dropped to 33±22 mm/h from 59 ±35 mm/h by the help of the therapy (p<0.001). Among patients who primarily responded Anakinra therapy the mean Ferritin measures dropped to 427.25 ng/ml from 910 ng/ml (p=0.006). On the other hand, the Ferritin level was not significantly reduced in patients who did not respond Anakinra. The mean Patient reported Global Visual Analogue Scale (PG-VAS) score was also decreased to 3.83±4.7 from 9.5±0.07 following the therapy (p<0.001). Unfortunately, one of our 7 patients who were followed in remission under Anakinra died of an unknown etiology.

Conclusions: Adult-onset Still's disease is a challenging disorder, lacking a sufficient long-time clinical control. In order to obtain a full remission, various efforts have been spent so far. One of these approaches is to treat refractory cases with Anakinra, an IL-1 blocking agent. According to our clinical experience we state that, anakinra has a relatively high efficacy in controlling refractory cases.

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SAT0627

FABRY DISEASE: DIAGNOSTIC ERRORS IN RHEUMATOLOGY PRACTICE

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Background: Fabry disease (FD) is a rare X-linked storage disease resulting from the deficient activity of the lysosomal α-galactosidase A (AGAL) and leading to a progressive accumulation of glycosphingolipids in a wide range of cell types throughout the body, including kidney, heart and nervous system. Certain manifestations of FD can mimic those of rheumatic diseases.

Objectives: To evaluate the occurrence and the possible causes of diagnostic errors in patients with FD in rheumatology practice.

Methods: We retrospectively studied the medical records of 82 adult patients with definite FD (low or absent AGAL activity, pathogenic mutation in the GLA gene, typical clinical symptoms in patient and/or his relatives, results of kidney biopsy). There were 55 males and 27 females aged of 18 to 69 years (median 38²⁹, 48⁴⁸ years).

Results: Seventy two of 82 patients (87.8%) had a history of classic phenotype of FD from childhood or adolescence. The typical manifestations included neuropathic pain that was related to heat and fever (65/82; 79%), angiokeratoma (37/

82; 45%), anhidrosis/hypohidrosis (44/82; 53.6%), and cornea verticillata (40/62; 64.5%). However, there was a significant delay to diagnosis of up to 51 years (median 18⁹; 27 years). Moreover, diagnosis was established by nationwide screening in dialysis units in 22/82 (26.8%) patients or by family screening in 34/82 (41.4%) patients. At the time of diagnosis, patients usually presented with a clinical picture of systemic disease with mild to moderate proteinuria with or without impairment of kidney function (70/82; 85.4%), left ventricular hypertrophy (56/82; 68.3%), white matter lesions on brain MRI (38/72; 52.8%), and/or a history of stroke (15/82; 18.3%). Twenty six of 82 patients (31.7%) previously had at least one diagnosis of rheumatic disease (Table 1). The common causes for referral to rheumatologist were skin rash and neuropathic pain. In 6 of 26 patients (23.1%), the latter was initially misdiagnosed as joint pain. The possible causes of diagnostic errors included also 'genuine' arthralgia (6/26; 23.1%), episodes of unexplained fever (13/26; 50%), Raynaud phenomenon (2/26; 7.7%), and the laboratory markers of inflammation (11/26; 42.3%).

Abstract SAT0627 – Table 1. 'Rheumatic' diagnoses in Fabry patients

Misdiagnoses	Number of patients
Vasculitis*	6 (7.3%)
Arthritis**	5 (6.1%)
Osler-Weber-Rendu disease	4 (4.9%)
Rheumatic fever	4 (4.9%)
Systemic lupus erythematosus	3 (3.7%)
Familial Mediterranean fever	1 (1.2%)

Note: *Vasculitides included IgA-vasculitis, Behcet disease, etc. **Arthritides included rheumatoid arthritis, juvenile rheumatoid arthritis and osteoarthritis.

Conclusions: Practicing rheumatologists should be aware of FD, given a high occurrence of diagnostic errors. The clues to correct diagnosis include a history of typical symptoms (i.e. neuropathic pain, angiokeratoma, hypohidrosis) from childhood or adolescence and/or the presence of typical manifestations in family members. Notably, FD can initially present as an autoinflammatory disorder with episodes of joint pain and unexplained fever associated with the laboratory markers of inflammation.

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SAT0628 A RETROSPECTIVE OBSERVATIONAL STUDY OF AZATHIOPRINE MAINTENANCE THERAPY ON BEHCET'S DISEASE WITH VASCULAR INVOLVEMENT

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Background: Vascular disease which has potential to involve both arteries and veins of all size is one of the major causes of mortality and morbidity in Behçet's disease (BD). There is no controlled studies for the immunosuppressive (IS) therapy in vascular involvement of BD. For the induction and/or maintenance therapy, azathioprine (AZA) is widely used as a corticosteroid tapering IS agent in vascular BD although there are many different clinical presentation.

Objectives: The purpose of this study to investigate relapse rate and the clinical factors affecting it during AZA maintenance therapy.

Methods: Consecutive BD patients with a documentation for arterial or venous involvement were evaluated from two rheumatology centre between January-September 2017. Patients who have been treated for at least 3 months after the complete or partial remission were included to study. The baseline clinical and laboratory findings, treatment protocol, first vascular relapse time and adverse events were obtained medical records. Long-term outcome and factor associated with vascular relapse were assessed.

Results: Totally 78 patients were included to the study and majority of them [59 (%75.6)] was male. The mean age $\pm$ SD of the patients was 37.5 $\pm$ 9 years. Clinical characteristics of patients are seen in table 1. The median duration of maintenance therapy with AZA was 25 (min 3- max 144) months and the mean dose $\pm$ SD of AZA was found as 1.7 $\pm$ 0.3 mg/kg/day. AZA was withdrawn in 4 (% 5.1) patients because of adverse events. Twenty patients (%25.6) were receiving anti-coagulant therapy. Vascular relapse was observed in 14 (%17.9) patients. In relapsing group, arterial involvement and uveitis was higher statistically (p=0.014 and 0.045 respectively). In regression analysis, arterial involvement was independent risk factor for relapse (p=0.016). The percentage of relapses

was calculated as 39 (7/18) in patient subgroup with arterial involvement. Relapse free survival rates according to involving vessel were seen in figure 1.

Abstract SAT0628 – Table 1. Clinical characteristics of vascular Behçet's Disease (n=78)

The mean age $\pm$ SD	37.5 $\pm$ 9.2
Male gender n (%)	59 (76)
Genital ulcer n (%)	49 (63)
Skin lesions n (%)	44 (57)
Patherji positivity n (%)	29 (38)
Uveitis n (%)	17 (22)
Musculoskeletal involvement n (%)	15 (20)
CNS involvement n (%)	1 (1.2)
GIS involvement n (%)	1 (1.2)
Venous involvement n (%)	67 (86)
Arterial involvement n (%)	18 (24)

SD: Standart deviation, CNS: Central nervous system, GIS: Gastrointestinal system

Abstract SAT0628 – Figure 1. Relapse free survival rates according to involving vessels in patients with Behçet's disease (BD) by using Kaplan-Meier method (BDVI: Behçet's disease with venous involvement, BDAl: Behçet's disease with arterial involvement, p=0.001 by log-rank test).

Conclusions: According to our study, AZA is seen as safe in maintenance therapy of BD with vascular involvement, however it can be said that the relapse rate is not favourable especially in patients with arterial involvement. Vascular involvement is considered as related to endotel inflammation resulting BD activity and the effect of anti-coagulant therapy is still controversial. TNF inhibitors or other immunosuppressant may be alternative to AZA for maintenance therapy with the support of randomized-controlled studies.

Disclosure of Interest: None declared

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SAT0629 IGG4 RELATED CASTLEMAN'S DISEASE OR "SECONDARY" IGG4 RELATED DISEASE OF MULTICENTER CASTLEMAN'S DISEASE?

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Background: It's widely accepted that a diagnosis of IgG4-related disease (IgG4-RD) can be made under a premise of rule out a series of disease including Castleman's disease (CD). Clinically, the two diseases may share similar clinical manifestations, such as multiple organ involvement. Pathologically, in some cases with CD, IgG4 positive plasma cell infiltrations are also evident. Otherwise, IgG4-RD may pathologically exhibits CD-like feature.¹⁻³

Objectives: When the histopathology coincides with the diagnosis of both IgG4-RD and CD, it is hard to depart the two disease entity utterly. It's unknown whether it is IgG4 related CD or "secondary" IgG4-RD of multicentric CD, here we call it IgG4-CD provisionally. To our knowledge, no comparative study of IgG4-CD and IgG4-RD has yet been published. In this study, we aim to review the clinical feature of IgG4-CD.

Methods: This study is based on a retrospective analysis of a prospectively acquired database. IgG4-CD were defined histopathologically in patients who fulfilled the diagnosis of both IgG4-RD and CD. Forty five definite IgG4-RD patients were recruited as control. Clinical features including organ involvement, serum IgG4, IgG, IgE, ESR and CRP levels of all the participants were collected and analysed statistically.

Results: Fifteen patients (2.8%) out of 534 patients with IgG4-RD in China's largest prospective IgG4-RD and Mimicry cohort fulfilled the definition of IgG4-CD. There were 14 males and 1 female, mean age was 47±18 years, and the median disease duration before diagnosis was 12 (1–132) months. Eight patients have allergic history. IgG4-CD patients had more lymph node involvement (100% vs 57.8%, $p<0.01$), while IgG4-RD patients had more submandibular (33.3% vs 77.1%, $p<0.01$) and parotid gland (13.3% vs 40.9%, $p<0.05$) affected. IgG4-CD patients had significantly higher levels of ESR (mm/h), CRP (mg/L), IgG (g/L), IgG1 (g/L), IgG3(g/L), IgG4(mg/dL), and IgE (g/L) [76.50 (5.00–129.00) vs 17.00 (2.00–89.00), 5.39 (0.54–134.00) vs 1.6 (0.08–113.74), 35.28 (9.76–69.00) vs 19.36 (7.46–61.00), 11.2 (6.84–41.00) vs 8.07 (4.08–16.70), 1.55 (0.19–3.20) vs 0.53 (0.09–2.00), 1590.00 (133.00–6420.00) vs 1070.00 (152.0–6100.00), 807.5 (215.00–2967.00) vs 214.00 (20.40–2437.00), respectively. $p<0.05$). Except for one patient refused to receive drug therapy untreated, the remaining patients with IgG4-CD all received glucocorticoid (GC) treatment. Patients with multi-organ involvement or in severe inflammatory condition were treated with both GC and immunosuppressive agents, those who with active disease but resistant to above regimen accepted biologics such as rituximab. All patients with IgG4-CD exhibited favourable outcomes.

Conclusions: Both IgG4-RD and CD can involve multiple organs. There are a small group of patients who had clinical and pathological characteristics of both CD and IgG4-RD showed better clinical outcome. Long-term prognosis of these patients, the relationship of CD and IgG4-RD are waiting to be further elucidated.

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Diagnostics and imaging procedures

SAT0630

AGREEMENT BETWEEN PATIENT-REPORTED SWOLLEN AND TENDER JOINTS, CLINICAL EXAMINATION AND SYNOVITIS DETECTED BY ULTRASONOGRAPHY IN RHEUMATOID ARTHRITIS PATIENTS AT THE TIME OF PATIENT-REPORTED FLARE

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Background: In Rheumatoid Arthritis (RA), patient-reported tender joints (PrTJ) correlate better with clinical examination than patient-reported swollen joints (PrSJ).¹ Clinical examination has inferior sensitivity to detect synovitis compared to ultrasonography (US).² However, data is sparse about these findings at the time of patient-reported flare (PRFI).

Objectives: To investigate agreement between PrSJ, PrTJ, clinically detected swollen and tender joints (cSJ and cTJ), and inflammation by Colour Doppler (CD) US in RA patients at the time of PRFI.

Methods: 80 consecutive rheumatoid-factor and/or anti-cyclic citrullinated peptide antibody positive RA patients with DAS28-CRP<3.2 and no swollen joints at baseline were during a one-year follow-up period requested to contact the hospital in case of a hand flare according to patients' perspective. At the flare visit, patients indicated PrSJ and PrTJ, and underwent examination for cSJ and cTJ, and US of

bilateral wrists (wrist joints and six extensor tendon compartments), 1–5 metacarpophalangeal joints (MCP) and 1–5 proximal interphalangeal joints (PIP). CD synovitis and tenosynovitis were graded 0–3 according to EULAR/OMERACT scoring system³ and joints and tendon sheaths with CD ≥ 1 were considered positive. Percentage agreement and Cohen's kappa were calculated between PrSJ, PrTJ, cSJ, cTJ and CD in joints and tendon sheaths.

Results: Thirty-six percent (29/80) of the RA patients reported a hand flare (69% female, mean age 65 years, median DAS28-CRP 1.8, at baseline). At flare, mean (±SD) number of PrSJ, cSJ, PrTJ, cTJ and CD positive joints were 2.7 (2.86), 1.5 (1.02), 4 (3.04), 4 (3.46) and 1.8 (1.31), respectively. For swelling, there was slightly superior agreement with CD for cSJ than for PrSJ, except for wrist tenosynovitis where patients agreed more frequently with CD than clinical examination did (table 1). Highest percentage agreement was seen for PIP, followed by MCP. Agreement, as assessed by kappa, was poor to fair, ranging from –0.009 to 0.33. Swelling in MCP and PIP joints, by patients and clinicians, and swelling in the wrist by clinician showed better agreement with CD than tenderness did.

Abstract SAT0630 – Table 1. Concordance between patient-reported and clinically examined swollen and tender joints versus CD at the time of patient-reported flare

Joint	No of joints examined	Comparison between	+/+	+/–	–/+	–/–	% agreement
Wrist	n=58	Clinical swelling vs CD synovitis	6	10	11	31	64
		Clinical swelling vs CD tenosynovitis	4	12	4	38	72
		Patient-reported swelling vs CD synovitis	5	13	12	28	57
		Patient-reported swelling vs CD tenosynovitis	6	12	2	38	76
		Clinical tenderness vs CD synovitis	5	11	12	30	60
		Clinical tenderness vs CD tenosynovitis	4	12	4	38	72
		Patient-reported tenderness vs CD synovitis	5	11	12	30	60
		Patient-reported tenderness vs CD tenosynovitis	5	11	3	39	76
MCP	n=290	Clinical swelling vs CD synovitis	0	18	27	245	85
		Patient-reported swelling vs CD synovitis	3	34	24	229	80
		Clinical tenderness vs CD synovitis	7	47	20	216	77
		Patient-reported tenderness vs CD synovitis	4	45	23	218	77
PIP	n=290	Clinical swelling vs CD synovitis	0	8	9	273	94
		Patient-reported swelling vs CD synovitis	0	19	9	262	90
		Clinical tenderness vs CD synovitis	3	30	6	251	88
		Patient-reported tenderness vs CD synovitis	1	38	8	243	84

CD: Colour Doppler; MCP: metacarpophalangeal joint; PIP: proximal interphalangeal joint.

Conclusions: Thirty-six percent of the RA patients reported flares in the hand during one year follow-up. Numbers of joints affected by swelling, tenderness or positive CD sign were low. Limited concordance between US, patient-reports and clinical examination suggests that these domains reflect different and potentially complementary aspects of inflammation in patient-reported flare.

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