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FRI0486 POTENTIAL PREDICTORS OF VISCERAL INVOLVEMENT IN ADULT IGA VASCULITIS

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Background: Predictors of severity of visceral involvement in acute adult IgA vasculitis (IgAV) are poorly recognised.
Objectives: The aim of our study was to evaluate the role of smoking and extension of skin lesions on the visceral manifestations of acute adult IgA vasculitis.
Methods: We analysed medical records of adult, histologically proven IgAV cases, diagnosed at our secondary/tertiary rheumatology centre between 1 January 2010 and 31 December 2017. Purpura was defined as generalised when skin lesions extended above the waistline. Gastrointestinal (GI) disease was considered severe in case of bloody diarrhoea, ileus or bowel perforation. Renal disease was defined as severe when nephritic syndrome with acute renal failure or nephrotic syndrome developed.
Results: During the study period we identified 230 incident IgAV cases (57.8% males, median (IQR) age 64.8 (45.6–77.3) years). Ninety-eight (42.6%) patients were smokers (56 past and 42 current). Skin, joint, GI, renal and involvement were present in 230 (generalised purpura in 114 (49.6%), necrotizing in 108 (47.0%)), 93 (40.4%), 70 (30.4%; severe in 17) and 102 (44.3%; severe in 27) patients, respectively. Smoking was associated with renal disease (RR 1.3 (95% CI 1.0–1.8)) and its severity (RR 3.2 (95%CI 1.5–7.0)), but not with GI involvement or its severity. Generalised purpura was associated with GI involvement (RR 2.9 (95%CI 1.8–4.7) and its severity (RR 3.3 (95%CI 1.1–9.8)), as well as with renal involvement (RR 1.4 (95%CI 1.0–1.9)). Data of combined influence of smoking and purpura extension on visceral involvement are presented in table 1. The risk of severe renal involvement in IgAV was the highest in ever-smoker with generalised purpura (RR 8.1 (95%CI 1.9–34.7) in comparison to IgAV non-smoker with localised purpura).
Table 1 The influence of smoking and purpura extension on visceral involvement in IgAV

Visceral involvement	Nonsmokers with localized purpura	Ever-smokers with localized purpura	Nonsmokers with generalized purpura	Ever-smokers with generalized purpura
Number of cases	69	47	63	51
GI (%)	13.0	19.1	47.6	43.1
Severe GI (%)	2.9	4.3	11.1	11.8
Renal (%)	30.4	46.8	47.6	56.9
Severe renal (%)	2.9	14.9	9.5	23.5

Legend: GI gastrointestinal; severe GI involvement: bloody diarrhea or ileus or bowel perforation; severe renal involvement: nephritic syndrome with acute renal failure or nephrotic syndrome;

Conclusions: Smoking and generalised purpura were associated with visceral involvement in adult IgAV.
Disclosure of Interest: None declared
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FRI0487 SERUM INTERLEUKIN-6 LEVELS IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS

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Background: The deregulated overproduction of interleukin (IL)−6 has been implicated in several inflammatory and antibody-mediated autoimmune diseases.
Objectives: To investigate serum IL-6 levels (sIL-6) during active disease, remission, and relapse in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), and to explore the association of changes in sIL-6 with repopulation of blood B cells and disease relapse.
Methods: sIL-6 levels (explanatory variable) were measured longitudinally over 18 months in 78 patients with AAV enrolled in a prospective, double-blinded, randomised, control trial comparing treatment with rituximab (RTX) (n=45) or cyclophosphamide (CYC)/azathioprine (AZA) (n=33). Outcome variables included baseline clinical features, ANCA type and titers, disease activity (status of active disease versus complete remission (CR)), time to B cell repopulation, relapse and severe relapse.
Results: Baseline sIL6 levels were detectable (>0.49 pg/ml) in 81% of patients. At baseline, **s**IL-6 positively correlated with proteinase (PR3)-ANCA levels (r_s=0.36, p<0.01), but not with myeloperoxidase (MPO)-ANCA levels (r_s=−0.17, p=0.47). Higher baseline sIL-6 levels were associated with the presence of fever, pulmonary nodules/cavities, PR3-ANCA, and absence of renal involvement (p<0.05 for all comparisons).
The median sIL-6 level was higher at baseline and promptly declined with induction therapy at following time-points (baseline, median [25%>75% IQR], 2.66 [0.76–20.98]; month 6th, 0.49 [0.49–1.16]; p<0.01) in a similar fashion in both treatment arms.
An increase in sIL-6 during clinical remission was a predictor for subsequent severe relapse in RTX-treated patients (Hazard Ratio (HR) 7.24, p=0.01), but not in CYC/AZA-treated patients (HR 0.62, p=0.50).
In RTX-treated B cell depleted patients (CD19 +B cell/microliter<10), the rise of sIL-6 levels did not precede B cell reappearance, regardless of whether a cut-off of ≥10 CD19+B cell/microliter (HR=0.97; p=0.97) or of ≥69 CD19+B cell/microliter (HR=1.50; p=0.41) was considered. Eighty percent of the patients who subsequently had a severe relapse in the RTX arm had B cell redetection before or at the time of the IL-6 increase, with a mean time between the redetection of B cells and sIL-6 increase of 55 days (25%>75%IQR: 0–184.25; range 0–210 days).
Conclusions: At baseline, sIL-6 correlates with PR3-ANCA titers and associates with the presence of fever and pulmonary nodules/cavities. A rise in sIL-6 levels after complete remission is associated with subsequent severe relapse only in RTX-treated patients. The observed discrepancies between treatments deserve confirmation and further study.

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FRI0488 INSUFFICIENT IMMUNOSUPPRESSIVE USE IS THE LEADING CAUSE OF VASCULAR RELAPSES IN BEHCET'S DISEASE

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Background: Vascular involvement is observed in up to 40% in Behcet Disease (BD) patients, as an important cause of mortality and morbidity, especially for males (Kural-Syahi E et al,1984).
Objectives: Purpose of this study is to describe clinical-demographic properties, treatments and prognosis of vascular BD patients in a tertiary rheumatology clinic.
Methods: BD patients fullfilling ISG 1990 criteria are recruited from the multi-disciplinary Behcet's Clinic in Marmara University, Istanbul for this retrospective study. All data is collected from patient files (ISG for BD,1990).
Results: Mean age of BD patients (M/F:102/22) was 29.3±7.3 years at diagnosis and 32.4±9.5 years old during first vascular event. Median follow up was $47^{17–71}$ months. Mean age of female patients was significantly older during first vascular event (table 1). 73.2% of vascular involvement was venous, mostly deep vein trombosis (table 2). 32% (n=40) of patients presented first with a vascular event and diagnosed as BD. Twenty (16%) patients were diagnosed with a median of $12^{1–120}$ months after the first vascular event. 15 (6.5%) patients were using immunsupressive (IS- mainly azatiopirin) drugs either for resistant mucocutaneous symptoms or major other organ involvement during the first vascular event.
Vascular relaps rate was 40.7% and it was similar between sexes (F: 33.3% vs M: 42.2%, p=0.6). After the first vascular event, 96 (85.7%) patients had been treated with ISs and 58.9% used anticoagulants. Median IS and anticoagulant usage duration was 25.5 (5–48) and 2 (0–12) months respectively. Relaps rate was higher in patients who had stopped ISs (87.5% vs 32.3%). IS treatment duration

was shorter at relapsing patients (44 vs 64 months, p=0.001). Smoking rate was higher at male patients but no association was observed with vascular relapses.

Abstract FRI0488 – Table 1. Clinic and demographic features of Behcet's Disease patients

		Female (n=22)	Male (n=102)	p
Mean age at first vascular event		37±12.6	31.5±8.5	0.019
Mean age at BD diagnosis		30.5±9.5	29.1±7.5	0.467
Smoking	Yes	4 (%33.3)	32 (%68.1)	0.018
	No	8 (%66.7)	15 (%31.9)	
Patergy	Positive	12 (%66.7)	54 (%62.8)	0.99
	Negative	6 (%33.3)	32 (%37.2)	
Number of vascular event/s	1	14 (%63.6)	55 (%54.5)	
	2	6 (%27.3)	39 (%38.5)	
	3 or more	2 (%9.1)	7 (%7)	

Abstract FRI0488 – Table 2. Type and charateristics of vascular involvment

Venous n=134 (%73.2)	Ekxtremties	106 (% 79.1)	Arteries n=44 (%23.5)	Pulmoner Trombus	36 (% 81.8)
	Cerebral	16 (% 12)		Aneurysme (2 coronary, 2 pulmoner, 2 aorta)	6 (% 13.6)
	Others (SVC, IVC, renal, retinal)	12 (8.9		PAT+PAA	2 (% 4.6)

IVC: inferior vena cava, PAA: pulmoner arter aneurysmeı, PAT: pulmoner arter trombus, SVC: superior vena cava

Conclusions: Our results show that female BD patients have a vascular event at a later age compared to males, but the course of vascular disease is not influenced with gender. Early termination of immunosupressive treatments seems to be the most important cause of vascular relapses

Disclosure of Interest: None declared

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FRI0489 UTILITY OF APREMILAST IN REFRACTORY ORAL AND/OR GENITAL ULCERS IN BEHÇET'S DISEASE

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Background: Behçet´s disease (BD) is characterised by recurrent oral and/or genital ulcers accompanied by ocular, cutaneous, articular, gastrointestinal, and/or neurologic manifestations. Oral and/or genital aphthous ulcers are often refractory to conventional treatment. Apremilast is an orally-active small molecule which inhibits phosphodiesterase-4 (PDE-4) that modulates some inflammatory pathways.

Objectives: Our aim was to assess the efficacy of apremilast in BD patients with oral and/or genital ulcers refractory to conventional treatment.

Methods: Retrospective national multicenter open-label study on 19 BD patients treated with apremilast at standard dose of 30 mg twice daily. The main outcome was achievement of oral ulcers remission.

Results: We included 19 patients (14 women and 5 men) with a mean age of 43.6 ±14.8 years. Before apremilast, all patients had also received several systemic conventional drugs: oral corticosteroids (n=18), colchicine (n=19), NSAIDs (n=10), methotrexate (n=10), azathioprine (n=10), cyclosporine (n=6), infliximab (n=3), adalimumab (n=5), dapsone (n=3), etanercept (n=1), mycophenolate mofetil (n=1), tocilizumab (n=1). The main clinical symptoms for starting apremilast were oral aphthous ulcers (n=19) and genital ulcers (n=14). Other manifestations present at apremilast onset were arthralgia/arthritis (n=6), folliculitis/pseudofolliculitis (n=6), asthenia (n=5), furunculosis (n=1), erythema nodosum (n=1), erythematosus and scaly skin lesions (n=1), psoriasis (n=1), deep venous thrombosis (n=2) and ileitis (n=1). Table 1 shows the evolution of the patients. After a median follow-up of 6 [interquartile range, 5–10] months, most of the patients experienced clinical improvement. In this period of time, 11 patients developed any side-effect: dyspepsia (n=5), nauseas (n=4), diarrhoea (n=4), abdominal pain (n=4), headache (n=3), loss of appetite (n=3), weight loss (n=1) and halitosis (n=1). Three patients had to reduce the dose to 30 mg/day. Apremilast was discontinued in 4 patients: because of not obtaining the expected improvement (n=2), due to desire of pregnancy (n=1) and due to development of neurological involvement (n=1).

Abstract FRI0489 – Table 1

	Basal n= 19	Week 1-2 n= 19	Week 4 n= 19	Month 3 n= 18	Month 6 n= 11
Resolution of main symptom, oral and/or genital ulcers n, (%)					
Complete		7/19 (36.8)	12/19 (63.1)	13/18 (72.2)	7/11 (63.6)
Partial		8/19 (42.1)	4/19 (21.0)	1/18 (5.5)	3/11 (27.3)
Resolution of other symptoms n, (%)					
Complete		5/13 (38.5)	6/13 (46.1)	6/12 (50.0)	5/7 (71.4)
Partial		1/13 (7.7)	2/13 (15.4)	4/12 (33.3)	2/7 (28.6)
Dose of prednisone (mg/day), median [IQR]	7.5 [0-12.5]	6.2 [0-10]	6.2 [0-10]	3.7 [0-5]	2.5 [0-4.4]*

*p <0.05

Conclusions: Apremilast leads to a rapid and maintained improvement in many patients with refractory mucocutaneous ulcers of BD. Even in patients refractory to several systemic drugs including biologic therapy. However, the development of adverse digestive effects is frequent.

Disclosure of Interest: None declared

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FRI0490 MORTALITY AND EARLY SEVERE INFECTION IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: The introduction of treatment regimens comprising of cyclophosphamide or rituximab combined with corticosteroids has brought about dramatic improvements in the prognosis of ANCA-associated vasculitis.[1] Severe infectious events, especially in the early phase of treatment, associated with risk of death have been reported in the past several studies.[2,3]

Objectives: We retrospectively investigated the association between mortality and early severe infection in patients with antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV), and we also attempted to identify the potential predictors for early severe infection.

Methods: We recruited 182 consecutive hospitalised patients newly diagnosed with AAV at our hospital, from January 2000 to June 2017, in this retrospective cohort study. All cause mortality, relapse, and severe infections within six months after starting treatment (early severe infection) were analysed.

Results: The mean age was 70 years at diagnosis, and the classification according to the Chapel Hill Conference definition were microscopic polyangiitis (MPA) in 82 patients (45.1%), granulomatosis with polyangiitis (GPA) in 36 patients (19.8%), eosinophilic granulomatosis with polyangiitis (EGPA) in 24 patients (13.2%), and renal-limited vasculitis in 32 patients (17.6%).[4] Median follow up was 158 weeks (range 0–182 w). Using Cox regression analysis, elderly onset (age ≥75 years) AAV (p=0.027) and early severe infection (p≤0.001) were independent predictors of all cause mortality (table 1).

Early severe infection tended to increase among patients who received immunosuppressive therapy of a corticosteroid combined with cyclophosphamide or rituximab (conventional treatment), and this trend was significant in non-severe (BVAS <20) AAV patients (p=0.030) (table 2). Treatment response rate (p=0.058)