FRI0335 EARLIER ONSET AND BRAINSTEM INVOLVEMENT AS KEY FEATURES IN A BRAZILIAN NEURO-BEHÇET'S DISEASE COHORT

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Background: Behçet's disease (BD) is a multisystem disease in which central nervous system involvement – neuro-Behçet's disease (NBD) – may strike young patients with devastating consequences. In this regard, early diagnosis and treatment is essential to prevent injury.
Objectives: This study aimed to analyze NBD clinical features compared to non-neurological BD in order to distinguish disease patterns.
Methods: A retrospective study was performed in 101 BD outpatients from a single tertiary center followed between 2011 and 2016. BD diagnosis was based on the 2014 International Criteria for Behçet's Disease. Demographic, clinical and imaging features of 28 NBD patients were compared to 73 BD patients without neurological involvement.
Results: Earlier disease onset was found in NBD compared to BD (26.0±10.2 vs. 30.2±8.8 years, p=0.04). There were no differences between genders incidences, with a female predominance in both groups (64.3 vs. 72.6%, p>0.05). Over half of patients (53.6%) presented NBD as the first symptom and the mean time between diagnosis and NBD onset was 3.8±5.9 years. Uveitis was less frequent in NBD patients (25% vs. 47.9%, p=0.04), together with cutaneous disease (50% vs. 76.7%, p=0.01) and articular involvement (17.9% vs. 46.5%, p=0.01). Oral ulcers, genital ulcers, intestinal and vascular involvement frequencies were similar in both groups. Regarding NBD presentation, brainstem involvement was the most prevalent (67.9%), followed by central venous thrombosis (32.1%), aseptic meningitis (17.9%), stroke (3.6%) and peripheral neuropathy (3.6%). Most patients (82.1%) had a single neurological attack whereas relapsing disease was found in 18.5%.
Conclusions: Our study found an earlier disease onset in NBD patients and a lower frequency of ocular, cutaneous and articular involvement. Moreover, several patients may unfold the disease as NBD, with lack of other manifestations. In addition, brainstem lesions occurred in most patients. Recognizing these disease patterns might support to expedite NBD diagnosis.
Disclosure of Interest: None declared
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FRI0336 EFFICACY OF TOCILIZUMAB IN 31 PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is often a disease refractory to corticosteroids and, besides, the efficacy of immunosuppressive agents is not well established. In recent years, several case reports and small case series have shown efficacy with the use of tocilizumab (TCZ).
Objectives: Our aim was to assess in a clinical practise setting the short and long-term efficacy of TCZ in GCA patients with refractory disease and/or with unacceptable side effects due to corticosteroids.
Methods: Retrospective multicenter open-label study on 31 GCA patients treated with TCZ [intravenously at standard dose of 8 mg/kg/monthly (n=29), and subcutaneously at a dose of 162 mg/week (n=2)]. We assessed the efficacy on clinical and laboratory parameters, the reduction of the dose of corticosteroids, as well as the short and long-term side effects and the possibility of discontinuation or reduction of the dose of TCZ. Wilcoxon test was used to compare laboratory parameters across time.
Results: We included 31 patients (24 women/ 7 men), with a mean age of 73±9 years. The main clinical features at TCZ onset were: polymyalgia rheumatica (n=21), asthenia (n=8), headache (n=8), constitutional syndrome (n=11), jaw claudication (n=3), and visual loss (n=4). Besides corticosteroids and before TCZ onset, 26 patients had also received several conventional immunosuppressive and/or biologic drugs. Twenty-seven of 31 patients achieved a rapid and maintained clinical improvement after TCZ therapy (Table). After a median follow-up of 18 [interquartile range, 6–30] months we observe a reduction of the median of: a) CRP from 1.9 [1.1–3.7] to 0.1 [0.1–0.7] mg/dL; b) ESR from 44 [17–74] to 12 [4–16] mm/1st hour; and c) the dose of prednisone from 20 [10–45] to 2.5 [0–7.5] mg/day. In this follow-up period, the outcome of patients was as follows: a) discontinuation of TCZ (n=8) due to sustained remission; b) dose reduction due to improvement (n=5) or side effects (n=2); c) withdrawal of TCZ because of side effects (n=7); and d) the same dose that at onset (n=8). The reasons why TCZ had to be discontinued were: severe neutropenia; recurrent pneumonia; colon adenocarcinoma; cytomegalovirus infection; hypertensive crisis during infusion; myelodysplastic syndrome; and overall health deterioration. The latter patient died because of stroke. Another patient also died after the second TCZ infusion due to stroke in the context of an infective endocarditis.

	Baseline	Month 6	Month 12	Month 18	Month 24
Clinical improvement, % (n)		100** (27/27)	95** (20/21)	85** (11/13)	100** (11/11)
Laboratory markers, median [IQR]					
ESR (mm/1st/h)	44 [17-74]** (28)	6 [2-11]** (24)	7.5 [3-23]** (18)	9.5 [2-19]* (12)	6 [2-14]** (10)
CRP (mg/dl)	1.9 [1.1-3.7]** (31)	0.1 [0.1-0.7]** (27)	0.2 [0.1-0.7]** (19)	0.1 [0.1-0.5]* (13)	0.2 [0.1-0.4]** (11)
Dose of corticosteroids, median [IQR]	20 [10-45]** (31)	5 [5-9]** (29)	3.75 [0-5]** (21)	2.5 [0-5]** (13)	2.5 [0-5]** (11)

The number of patients with available data is shown in parentheses
* p <0.05 ** p <0.01 (Wilcoxon test).

Conclusions: TCZ therapy leads to a rapid and maintained improvement in patients with refractory GCA and/or with unacceptable side effects related to corticosteroids. However, the risk of neutropenia and infection should be kept in mind when using this biologic agent in patients with GCA.
Disclosure of Interest: None declared
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FRI0337 ANCA PATTERN IN GRANULOMATOSIS WITH POLYANGITIS AND MICROPOLYANGITIS. A RETROSPECTIVE ANALYSIS ON A MULTICENTRIC INCEPTION COHORT

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Background: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are multi-systemic diseases associated with anti-neutrophil cytoplasmic antibody (ANCA) often characterized by overlapping clinical manifestations. Recently ANCA pattern has been reported to define different clinical manifestations and long-term outcomes1.
Objectives: To analyze how ANCA could influence clinical manifestations and long-term outcomes in ANCA-associated vasculitis (AAV) patients, previously classified as GPA or MPA, from three different referral centers of Northern Italy.
Methods: Clinical manifestations and long-term outcomes of GPA and MPA patients were retrospectively collected. We considered clinical (including BVASv3 and VDI), radiological and histological data at diagnosis, relapse and mortality rates at the last follow-up. The complete cohort was splitted into three groups based on ANCA (anti-myeloperoxidase (MPO), anti-proteinase 3 (PR3), and ANCA negative) for statistical analysis.
Results: We included 171 patients, 90 (52.6%) anti-PR3 positive, 52 (30.4%) anti-MPO positive and 25 (14.6%) ANCA negative. Patients were mainly middle aged (52.5±15.9 years), Caucasian (98.2%) and both sexes were equally represented (Female 53.2%).
Anti-MPO positive patients were older (65 [52.5–69.7] years) at disease onset (p<0.001), affected by more comorbidities (p=0.045). They presented more frequently renal involvement (p<0.001) with higher creatinine levels at diagnosis (0.98 [0.75–1.92] mg/dL, p<0.001) (Fig. 1), systemic symptoms (p=0.039) but lower frequency of upper airways involvement (p=0.005).
Anti-PR3 positive scored higher BVASv3 at onset (p<0.001) and presented more upper airways involvement (p=0.033), lung nodules (p=0.002) and skin purpura (p=0.016).
ANCA negative showed a longer diagnostic latency (8.5 [3.5–49] months, p<0.0001), they presented with a higher VDI at diagnosis (1 [0–2.7], p<0.0001)

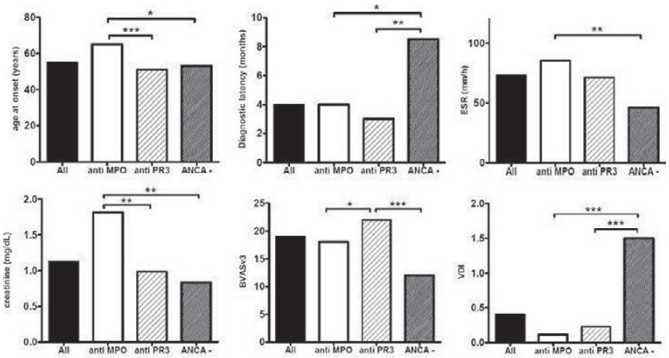

Figure 1: Post hoc analysis results. *Significance level: * p=0,05-0,01; ** p=0,01-0,001; *** p<0,001.*
ESR: erythrocyte sedimentation rate; BVASv3: Birmingham Vasculitis Activity Score version 3; VDI: Vasculitis Damage Index (VDI)

and the highest frequencies of sinuses (p=0.031), laryngeal (p=0.026) and CNS (p=0.020) involvement.
Long-term outcomes were available only in 113 patients. A low long-term mortality rate (8, 7.1% deaths) was noted (mean follow-up of 66.6±30.6 months), significantly higher in anti-MPO positive patients 7 (21.9%) when compared to anti-PR3 positive 1 (1.6%) and ANCA negative 0 (0%) ($p<0.001$). Nevertheless, the highest number of relapses/years were associated with anti-PR3 positivity (0.7±1.3 vs 0.1±0.3 in anti-MPO and 0.4±0.7 in ANCA negative, p=0.012). At multivariate analysis, anti-PR3 pattern resulted an independent predictive factor of relapses (p=0.0036, OR 5.8, IC95%: 1.1–29).
Conclusions: Our study confirms the hypothesis that each ANCA pattern could define a specific disease subset with different clinical manifestations and outcomes in AAV. Furthermore, in our cohort we observed a lower rate of recurrence and a better long term survival (92.9%) than in literature.
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FRI0338 THERAPEUTIC CONFORMITY TO GUIDELINES AND DRUG-APPROVAL IN ADAMANTIADES-BEHCET'S DISEASE: A RETROSPECTIVE ANALYSIS OF A MIDDLE-EUROPEAN COHORT

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Background: Adamantiades-Behcet's disease (ABD) is a chronic systemic vasculitic disease. Because of multiorgan involvement with diagnostic and therapeutic challenges for physicians, treatment decisions can be very difficult.
Objectives: To retrospectively assess the use of medication for ABD-therapy in view of 1.) current guidelines and 2.) approval by authorities in a Middle-European tertiary care center.
Methods: Data between 1997 and 2016 from a Middle-European ABD-cohort were retrospectively analysed. First, medical treatment was evaluated for conformity with the EULAR-recommendations for ABD-management and the anti-TNF therapy recommendations by Sfikakis et al. (1,2). Second, medical treatment was evaluated for use according to indications approved by authorities. Therefore official prescribing informations of the Bundesamt für Sicherheit im Gesundheitswesen (BASG)/European Medicines Agency (EMA), exemplary for Europe, and the Food and Drug Administration (FDA), exemplary for the USA, were screened (3–5). The study was approved by the local ethics committee.
Results: A total of 174 medical interventions were identified in 76 patients. Until 2008, treatment of ABD was based only on few clinical trials. According to EULAR-recommendations 93,7% were considered as being treated appropriately, including 55.2% of therapeutic approaches exactly matching the recommendations. 88.9% of TNF-inhibitors were indicated according to the anti-TNF-therapy recommendations (n=8/9). Out of 27 used drugs only prednisolone was approved by BASG/EMA- and FDA-authorities for a general indication including ABD, and cyclosporin A had the specific BASG/EMA-indication for ABD-uveitis. Another 12 medications had the indications for different symptoms of ABD, and thirteen medications were not authority-approved for any ABD-treatment.
Conclusions: Approvals by BASG/EMA- and FDA-authorities are often missing the indication of ABD. Therefore physicians not only face the complexity of ABD as a rare multiorgan disease, but also have to treat their ABD-patients with unapproved drugs. We propose that medications recommended by international guidelines for the management of rare diseases should be recognized by BASG/EMA- and FDA-authorities, even in case of low evidence.
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FRI0339 B CELL REPOPULATION KINETICS AFTER RITUXIMAB TREATMENT IN ANCA-ASSOCIATED VASCULITIDES COMPARED TO RHEUMATOID ARTHRITIS, AND CONNECTIVE TISSUE DISEASES: A LONGITUDINAL OBSERVATIONAL STUDY ON 120 PATIENTS

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Background: B cell depletion with rituximab (RTX) is approved for treatment of rheumatoid arthritis (RA) and ANCA-associated vasculitides (AAV). Recently, RTX has been shown to be effective in AAV maintenance therapy, but an optimal RTX treatment schedule is unknown and the time to B cell repopulation after RTX has not been studied.
Objectives: To compare kinetics of B cell repopulation after RTX treatment in AAV, RA and connective tissue diseases (CTD) to improve the design of RTX-retreatment schedules in AAV and other autoimmune diseases.
Methods: Retrospective single-center analysis of patients with AAV, RA or CTD treated with RTX and a follow-up of >9 months were included. B-cell-repopulation was defined as a peripheral B-cell count >0.5% and >5/μl. Prolonged B cell depletion was defined by a B cell repopulation starting later than 12 months after RTX treatment.
Results: 120 patients were included in the study. Sixty-six patients had AAV with 55 classified as granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) and 11 as eosinophilic granulomatosis with polyangiitis (EGPA). Thirty-five patients had RA and 19 were treated with RTX because of CTD. There were no significant differences between the groups regarding age and sex. Most patients were treated with RTX 1000mg twice, two weeks apart. Cumulative CYC doses were higher in patients with AAV or CTD than in RA patients. In RA and CTD we observed a B-cell repopulation in all patients (100%) while only 33 AAV patients (50%) had started B-cell repopulation ($p<0.0001$). 93% of the RA and 88% of the CTD patients showed a normal repopulation within the first 12 months after RTX compared to only 10% in GPA and 0% in EGPA ($p<0.0001$). Mean time to repopulation was significantly longer in GPA/MPA (21 months) and in EGPA (20 months) compared to RA (8.5 months) and CTD (8.7 months). Median time of persistent depletion was 26 months in GPA/MPA, 21 months in EGPA compared to 9 months in RA and 8 months in CTD ($p<0.0001$). In 25 AAV patients B cell depletion persisted longer than 24 months (mean time 4.4±18.1 years). In ten of 55 GPA/MPA patients B-cells were still depleted 4 years, in six patients even after more than 5 years after only one RTX treatment cycle. One patient had a complete B cell depletion even 8 years after the second RTX treatment. Immunoglobulin production was affected by RTX-treatment with a significant decrease in IgG, IgA and IgM compared to baseline values in GPA/MPA, but not in RA or CTD. In EGPA only IgM declined significantly. Significantly more patients with GPA/MPA and EGPA developed a hypogammaglobulinemia (IgG<7g/L, IgM<0.4g/L). In some AAV patients hypogammaglobulinemia became clinically relevant and required IVIG treatment.
Conclusions: In contrast to RA and CTD, in AAV RTX induces long-lasting depletion of B cells that is associated with decreased antibody production. This observation points towards potential defects in the B cell compartment in AAV and has important implications for the design of maintenance treatment schedules using RTX.
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FRI0340 B-CELL ACTIVATING FACTOR AS A BIOMARKER OF ACTIVITY OF SYSTEMIC NECROTIZING VASCULITIS (SNV)

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Background: Non-specific marker of inflammation such as C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) have limited value in assessment of vasculitis activity. Normal ESR values do not exclude the diagnosis of active vasculitis, and its increase may be due to concomitant infection.
Objectives: To evaluate the levels of B-cell activating factor and ESR in pts with different activity of SNV.
Methods: The serum levels of B-cell activating factor (BAFF) and ESR were measured in 48 pts with SNV (granulomatosis with polyangiitis – 22, eosinophilic granulomatosis with polyangiitis – 9, microscopic polyangiitis – 6, polyarteritis nodosa – 11). The 48 pts included 18 male and 30 female with median age 49; 24 were positive for cytoplasmic antineutrophil cytoplasmic antibodies and 11 for perinuclear antineutrophil cytoplasmic antibodies. At screening, 9 pts were without any treatment, 26 pts were receiving glucocorticoids (GCs) and 13 pts were receiving some cytotoxic agents and GCs. Clinical activities of pts were calculated by the Birmingham Vasculitis Activity Score (BVAS). All pts were divided into 3 groups according to the value of BVAS: group 1 (BVAS≤11; n=12), group 2 (BVAS =12–23; n=23) and group 3 (BVAS≥24; n=13). The outcomes of this study were the differences in marker levels between groups estimated by analysis of the absolute changes in marker levels and the areas under receiver operating characteristic (ROC) curves.