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SAT0265

RISK FACTORS FOR INFECTIOUS COMPLICATIONS FOLLOWING RITUXIMAB TREATMENT – MULTICENTER POLISH EXPERIENCE

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Background: Rituximab (RTX) is a B cell depleting monoclonal antibody with proven efficacy in the treatment of ANCA-associated vasculitis (AAV). The infectious complications occur in 15-25%.

Objectives: We aimed to assess the frequency and risk factors of infections in patients with AAV receiving RTX among Polish patients.

Methods: 7 tertiary referral centers experienced in the treatment of vasculitis completed a questionnaire regarding AAV patients treated with RTX.

Results: Among 49 patients included in the analysis (47 with GPA, 2 with MPA; 36/73% men; mean age at diagnosis 42.45±14.9 yrs., mean age on RTX initiation 46.14±14.72 yrs.) at least one infection occurred in 20 patients (40.82%) after mean time of 16.65±16.01 weeks since the administration of RTX. Patients were followed for a mean time of 26.88±21.94 months. There were no differences in the incidence of infectious complications by gender, age, BMI, smoking status, severity of the disease, activity of the disease (BVAS), time from diagnosis to RTX initiation, carriage of staphylococcus aureus in the upper respiratory tract, total dose of CYC before RTX treatment. We didn't observe severe hypogammaglobulinemia or neutropenia after RTX treatment. 40% of the observed infections occurred during the first month, 35% between second and sixth month of follow-up, while 25% were observed between 6 and 12 months after the RTX initiation. Of the 20 patients who developed infection, 12 (24.5%) had further infections. Antibiotic prophylaxis with trimethoprim-sulfamethoxazole was administered in 40 out of 49 (81.63%). Upper respiratory tract infection was the most common infectious complication (n=11), followed by lower respiratory tract (n=4), soft tissues (n=4) and urinary tract infections (n=4), lacrimal gland abscess (n=2) and abdomen (n=1). In cases with a positive microbial result Staphylococcus aureus (n=4), Klebsiella pneumoniae (n=2), Pseudomonas aeruginosa (n=1), Candida (n=1) and others (n=6) were identified. No fatalities were recorded and only 3 patients had severe infection with the necessity of prolonged treatment.

Conclusion: Despite the high number of infections in our group treated with RTX, most of them were not severe. Upper respiratory tract was the most common site of infection.

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SAT0266

FAMILIAR AGGREGATION OF LONGEVITY IN GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA

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Background: The long-term mortality in giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) is unexpectedly decreased (1,2,3,4) or at least not increased regardless increased mortality risk factors that these diseases share with other systemic inflammatory disorders.

Objectives: We aimed to test the hypothesis on aggregation of increased longevity in families of PMR/GCA patients because the family members of long-lived subjects have a survival advantage.

Methods: After questioning our patients we compared age of death of 358 parents of 179 PMR and GCA patients with corresponding data retrieved from 506 parents of 235 randomly collected age and sex matched controls.

Results: We found the number of nonagenarian (≥90 year old) mothers of PMR/GCA patients significantly higher vs controls. Both nonagenarian parents were found in 6 patients (3.35%) and in none of the controls. Decreased number of nonagenarian fathers of our patients remains unexplained.

Conclusion: Confirming our findings in a wider studies would imply a need of including some genetic or behavioural factors to explain PMR/GCA survival advantage.

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Table 1. Number of nonagenarians (≥90 years olds) in parents of PMR/GCA patients

	Parents age	PMR/GCA (N=179)	Controls (N=253)	OR	95%CI	p
Mothers	<90	148 (82.68%)	243 (96.05%)			
	≥90	31 (17.32%)	10 (3.95%)	2.34	1.11-11.95	<0.0005
Fathers	<90	161 (89.94%)	203 (80.24%)	0.45	0.24-0.83	0.0064
	≥90	18 (10.06%)	50 (19.76%)			
One of parents	<90	136 (75.98%)	193 (76.28%)	1.02	0.63-1.63	0.9412
	≥90	43 (24.02%)	60 (23.72%)			
Both parents	<90	173 (96.65%)	253 (100.00%)	8.77	2.26-405.10	0.003
	≥90	6 (3.35%)	0 (0%)			
Mothers of female patients	<90	105 (84%)	149 (97%)	7.1	2.27-29.19	0.0001
	≥90	20 (16%)	4 (3%)			
Mothers of male patients	<90	43 (80)	94 (94%)	4.01	1.25-13.97	0.0066
	≥90	11 (20%)	6 (6%)			

N - number of all parents

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SAT0267

ROLE OF AGGRESSIVE IMMUNOSUPPRESSION ON SUBGLOTTIC STENOSIS IN GRANULOMATOSIS WITH POLYANGIITIS: RETROSPECTIVE ANALYSIS OF A MONOCENTRIC COHORT

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Background: Subglottic stenosis (SGS) is defined as airway narrowing below the vocal cords and is a common and potentially life-threatening manifestation of Granulomatosis with Polyangiitis (GPA), with an estimated prevalence of 16-23% (1). Balloon catheter dilation is effective in GPA-related SGS, but relapses are frequent. Little is known about the role of immunosuppression in this setting.

Objectives: to analyse the clinical characteristics of a monocentric GPA cohort, describe phenotype differences among patients with and without SGS and investigate the role of surgical and medical treatments on relapse risk and general outcome.

Methods: Biopsy-proven patients with SGS were identified by review of medical charts among a cohort of patients with GPA, classified according to the algorithm of the European Medicine Agency (2). The clinical characteristics

of patients with SGS were retrospectively collected over a median follow-up time of 15.9 years and compared to those of patients without SGS.

Results: Fourteen patients with SGS-GPA were identified, with a female to male ratio of 1:1 and a prevalence of 29.2% among the cohort. The mean $\pm$ SD age at GPA onset was 30.8 ± 14.4 years, with a mean time from GPA diagnosis to SGS onset of 4.7 ± 4.2 years. ANCA were positive in 78.6% (54.0% anti-PR3, 18.1% anti-MPO and 27.9% IFI only). The mean Birmingham Vasculitis Activity Score (BVAS) at onset was 10.0 ± 5.6 . The main clinical manifestations associated with SGS were crusty rhinitis (100%), sinusitis (78%), pulmonary disease (72.7%), otitis/mastoiditis (50%), glomerulonephritis (42.9%), orbital pseudotumor (28.6%). Six patients (42.9%) received medical treatment only, other six (42.9%) had one to three balloon dilations and two (14.2%) underwent four or more procedures. Eight patients had no SGS relapse (maximum one dilation) and they all received immunosuppression with rituximab (RTX), cyclophosphamide (CYC) or azathioprine (AZA). All patients who received no immunosuppression, methotrexate (MTX) or mycophenolate (MMF) had at least one relapse. Patients treated with MTX or MMF had a mean relapse-free survival of 13.1 months, which was comparable to the one of patients not receiving medical treatment (40.2 months; $p=NS$) and shorter than the one of patients receiving CYC or RTX (153.2 months; $p=0.032$). CYC use also inversely correlated with the number of surgical procedures ($r=-0.691$, $p=0.006$). Compared to patients without SGS (31 consecutive patients with at least 4 years of follow-up), patients with SGS-GPA had an earlier disease onset (mean age 30.8 vs 50.4 years; $p<0.001$), but with lower BVAS (mean 10.0 vs 15.3; $p=0.013$) and showed a higher prevalence of crusty rhinitis (100% vs 67.7%; $p=0.019$). No difference was observed in damage accrual over time between the two groups.

Conclusion: Subglottic stenosis is highly prevalent in patients with GPA and may define a milder disease subset occurring more frequently in younger patients. MTX and MMF might be insufficient to prevent SGS relapses requiring balloon dilation. Aggressive immunosuppression (CYC or RTX) might have a non-redundant role in this setting and reduce the risk of relapses.

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SAT0268 COMPLEMENT ACTIVATION VIA ALTERNATIVE PATHWAY IN ANCA-ASSOCIATED VASCULITIS

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Background: There is increasing evidence that the complement system, in particular the alternative pathway, plays a crucial role in the pathogenesis of ANCA-associated vasculitis (AAV) [1]. Efficacy of C5a receptor antagonists indicates that chemoattraction mediated by C5a plays a key role in the inflammatory process observed in AAV [2]. Another promising research object are regulatory proteins such as factor B [3].

Objectives: To study complement activation via the alternative pathway in patients with active ANCA-associated vasculitis.

Methods: 59 patients with newly diagnosed ($n=35$) or relapsing GPA or MPA ($n=24$) were enrolled in this prospective study. Median BVAS v.3 at the time of AAV onset was 16.5 (9.5; 20). In 28 patients activation of complement was reassessed

during sustained remission (BVAS v.3 = 0) after a median of 16 months. Thirty six age- and gender-matched healthy volunteers comprised the control group. Levels of complement components (C3, C5, C3a, C5a, vitronectin, factor B and factor P) were measured by ELISA (Cloud Inc.). Data were not normally distributed, therefore, values are given as medians and IQRs and nonparametric statistical tests were used.

Results: The concentrations of C5, C3, vitronectin and CFB were significantly higher in patients with active AAV than control group. There were no significant differences in the levels of factor P in patients with active AAV and control group (388000 (371960; 417150)) vs 416000 (400200; 437000), ng/ml, $p>0.05$ (Fig. 1).

Fig 1. Concentration of complement components in patients with active AAV and healthy controls (* $p<0.05$)

Serum level of C5a and C3a were higher in patients with active AAV than in healthy controls (22.9 (14.4; 33.0) vs 3.0 (0.35; 6.73), ng/ml, $p<0.001$; 21436 (11395; 21436) vs 1224.5 (798.5; 1947.7), ng/ml, $p<0.001$). Patients with active AAV had significantly higher MAC levels than healthy controls (24646 (15342; 46681) vs 3305.5 (2780.2; 3777.5), mAU/ml, $p<0.001$).

The levels of complement components were similar in PR3-ANCA and MPO-ANCA disease, and severe and non-severe AAV. C5a/C5 and C3a/C3 ratios were not influenced by disease activity, severity or ANCA type.

After immunosuppressive treatment concentrations of C5, C3, and their activated products, C5a, C3a significantly decreased (Fig. 2). However, concentrations of regulatory proteins such as factor B, factor P and vitronectin were unaffected. Interestingly, that there was no significant difference in MAC levels before and after immunosuppressive treatment (24646 (15342; 46681) vs 20057.4 (19709.3; 41477.6), mAU/ml, $p=0.925$).

Fig 2. Concentration of complement components in patients with active disease and remission (* $p<0.001$)

Conclusion: The complement system plays an important role in AAV. While treatment affects some component, some remain unchanged and are not dependent on AAV severity or ANCA serotype.