FRI0205

CLINICAL FEATURES OF MONONEURITIS MULTIPLEX ASSOCIATED WITH ANCA-ASSOCIATED VASCULITIS

S. Hama¹, Y. Hayashi¹, K. Izumi¹, M. Higashida-Konishi¹, M. Ushikubo¹, K. Akiya¹, Y. Okano¹, H. Oshima¹. ¹National Hospital Organization Tokyo Medical Center, Connective Tissue Diseases, Tokyo, Japan

Background: ANCA-associated vasculitis sometimes presents mononeuritis multiplex which worsens the prognosis and activity of daily living in patients.

Objectives: This study aimed to determine the clinical feature of mononeuritis multiplex associated with AAV.

Methods: Consecutive patients with AAV who visited Tokyo Medical Center between April 2006 and December 2019 were included in this study. We examined the following clinical features: prevalence of neuropathy, age of onset, sex, the worst blood test values before the initial therapy (white blood cell count (WBC), eosinophil count (Eo), MPO-ANCA, PR3-ANCA, and C-reactive protein (CRP) levels), manual muscle testing (MMT) score of 20 muscles (Max 100 points), and time (days) from the initial symptoms to the initial induction therapies.

Results: A total of 89 patients with AAV were identified. Among them, 19 patients had eosinophilic granulomatosis with polyangiitis (EGPA) (8 males and 11 females, mean age 63.3 ± 2.7), 9 patients had granulomatosis with polyangiitis (GPA) (0 males, 9 females, mean age 75.6 ± 3.9), and 61 patients had microscopic polyangiitis (MPA) (17 males, 44 females, mean age 78.2 ± 1.5). Of the 89 AAV patients, 26 had sensory neuropathy (15/19 EGPA (78.9%), 11/61 MPA (18.0%), and 0/9 GPA (0%)). Motor neuropathy was observed in 19 patients (EGPA 14/19 (73.7%), MPA 5/61 (8.2%), GPA 0/9 (0%)). 15 patients had both sensory and motor neuropathies (EGPA 12/19 (63.2%), MPA 3/61 (4.9%), GPA 0 (0%)). In patients with both sensory and motor neuropathy, sensory impairment preceded in all cases. Among patients with neuropathy, the time from initial symptoms to initial induction therapy in patients with and without motor neuropathy was 34 ± 10.1 days and 30 ± 10.8 days ($p = 0.776$), respectively. Also, when comparing those who were treated within 7 days from the onset of movement disorders with those who were treated later, MMT score two weeks after the start of treatment were 92.15 ± 1.47 vs. 91.25 ± 2.65 ($p = 0.77$).

Between the patients with EGPA with and without sensory neuropathy, there were no significant differences in the following: highest WBC (19620.0 ± 2082.6 vs. 19350.0 ± 4033.5 cells/uL ($p = 0.953$)), highest Eo (10790.6 ± 1774.8 vs. 12440.8 ± 3436.9 cells/uL ($p = 0.6750$)), and highest CRP levels (4.467 ± 0.96 vs. 2.70 ± 1.85 mg/dL ($p = 0.41$)) before the initial therapy. On the other hand, comparing the EGPA patients with and without motor neuron disorder, CRP levels were significantly higher in those with motor impairment than those without ($WBC 20978.6 \pm 2049.8$ vs. 15600.0 ± 3429.9 cells/uL ($p = 0.20$); $Eo 12213.4 \pm 1775.5$ vs. 8127.0 ± 2971.0 cells/uL ($p = 0.25$); $CRP 5.13 \pm 0.89$ vs. 1.20 ± 1.48 mg/dL ($p = 0.04$)). And in patients with motor neuropathy, the decrease in MMT score was significantly correlated with the worst levels of CRP ($p = 0.001$) while the decrease was not correlated with the other blood tests. ANCA levels were not associated with sensory or motor neuropathy. In similar analyses of patients with MPA and GPA, there were no significant findings.

Conclusion: Worst CRP levels before the initial therapy can be a poor prognosis factor for motor neuropathy in patients with EGPA. Therefore, EGPA patients with high CRP levels need to be paid more attention to because of possible development of motor neuropathy.

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FRI0206

THE RELEVANCE OF SERUM IGA LEVEL MEASUREMENT IN ADULT IGA VASCULITIS

A. Hocevar^{1,2}, M. Tomsic^{1,2}, V. Jurcic³, K. Perdan-Pirkmajer^{1,2}, Z. Rotar¹ on behalf of -. ¹University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia; ²Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia; ³Faculty of Medicine, University of Ljubljana, Institute of Pathology, Ljubljana, Slovenia

Background:

Objectives: To evaluate the role of serum IgA level as a biomarker in adult IgA vasculitis (IgAV).

Methods: This prospective study included large cohort of histologically proven adult IgAV cases diagnosed between January 2013 and December 2019 at our secondary/tertiary rheumatology centre. All patients underwent a detailed clinical evaluation and laboratory workup. Patients were then stratified based on baseline serum IgA level into two groups (elevated serum IgA vs. normal serum IgA), and clinical features were compared between the two groups. Next we used multivariable logistic regression analysis to determine factors predicting gastrointestinal (GI) or renal involvement in adult IgAV.

Results: During the 84-month observation period, we identified 227 incipient adult IgAV cases (60.6% males, median (interquartile range) age 64 (47–76) years, 44 (19.4%) current smokers). One hundred and eleven (48.9%) patients had elevated serum IgA level at baseline, the rest had normal IgA level. None of the patients had subnormal serum IgA level. Skin involvement, constitutional symptoms, arthritis, GI tract and renal involvement developed in 227 (100%), 32 (14.1%), 30 (13.2%), 62 (27.3%), and 93 (41.0%) patients, respectively. Patients with elevated serum IgA less frequently developed constitutional symptoms ($p = 0.036$) and GI tract involvement ($p = 0.017$), but had more commonly renal involvement ($p < 0.001$), compared to those with normal serum IgA. Results of univariate analysis are shown in Table 1. In the multivariable logistic regression model, elevated serum IgA level persisted as a factor associated with lower risk of GI tract involvement (OR 0.47 (95%CI 0.23–0.95), and a higher risk of renal involvement (OR 2.71 (95%CI 1.48–4.96). The other factors associated with risk of GI and renal involvement are presented in Table 2.

Table 1. Clinical characteristic of IgAV patients with and without elevated serum IgA

Characteristic	All IgAV	Elevated s+++IgA	Normal sIgA	p value
Number of patients (%)	227	111 (48.9)	116 (51.1)	–
Males (%)	60.8	67.6	54.3	0.043
Age (years)*	64 (47-76)	58 (37-74)	66 (55-77)	0.289
Prior infection (%)	32.2	26.1	37.9	0.065
Constitutional symptoms (%)	14.1	9.0	19.0	0.036
Generalized purpura* (%)	52.0	55.0	49.1	0.426
Necrotic purpura (%)	46.3	53.2	39.7	0.046
Arthritis (%)	13.2	9.0	17.2	0.079
GI involvement (%)	27.3	19.8	34.5	0.017
Renal involvement (%)	41.0	53.2	29.3	<0.001

Legend: # median (IQR); GI gastrointestinal; * above the waistline;

Table 2. Risk factors of GI and renal involvement, multiple logistic regression

Characteristic	GI involvement OR (95%CI)	Renal involvement OR (95%CI)
Age	0.98 (0.96-1.0)	1.02 (1.00-1.04)
Current smoking	–	3.32 (1.56-7.07)
Generalized purpura*	5.86 (2.82-12.16)	2.03 (1.13-3.66)
↑ serum IgA	0.47 (0.23-0.95)	2.71 (1.48-4.96)
NLR >3.5	3.37 (1.59-7.12)	2.24 (1.19-4.23)

Legend: * purpura above the waistline; NLR neutrophil to lymphocyte ratio

Conclusion: Serum IgA level might be a useful biomarker in IgA vasculitis, identifying patients at risk for visceral (GI and renal) involvement.

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FRI0207

CANCER INCIDENCE AND FEATURES IN ADULT VASCULITIS PATIENTS

R. C. Kardaş¹, E. C. Bolek², B. Y. Aktaş³, S. Kılıçkap⁴, O. Karadağ². ¹Hacettepe Üniversitesi Tıp Fakültesi, Department of Internal Medicine, Ankara, Turkey; ²Hacettepe Üniversitesi Tıp Fakültesi, Department of Rheumatology, Ankara, Turkey; ³Hacettepe University Oncology Hospital, Department of Oncology, Ankara, Turkey; ⁴Hacettepe University Oncology Hospital, Department of Preventive Oncology, Ankara, Turkey

Background: Vasculitis, like other diseases with chronic inflammation, may be associated with increased cancer risk; possibly due to the inflammation triggering and advancing the neoplastic process. (1-3).

Objectives: The primary objective of this study was to determine the incidence of cancer cases among systemic vasculitis cases followed in a university hospital clinic. Secondary objective was to analyze the relationship between the vasculitis and cancer subtypes and their demographical and clinical features.

Methods: In this study, adult vasculitis patients followed at Hacettepe University Cancer Research, Diagnosis and Treatment Center (HUVAM) between October 2014 and May 2019 were reviewed for neoplastic development and cancer features. Standardized cancer incidence rate was calculated using the online International Agency for Research on Cancer GLOBOCAN database and the population data for Turkey published by Turkish Statistical Institute.

Results: Among 684 patients with a mean age of 46.4 ± 16.9 years and a median follow up duration of 29 months, 38 patients (5.6%) developed cancer. Colon (5 cases, 13%) and lung (4 cases, 11%) were the most commonly seen types of cancer. Among the patients with cancer, giant cell arteritis was the most common type of vasculitis (8 cases, 11%; Table 1). There was no statistically significant association between different cancer and vasculitis subtypes; however, there was increased trend for association between lung cancer and giant cell arteritis (data not shown).

Table 1. Distribution of patients and number of cancer in each vasculitis subgroup

Type of vasculitis	Total	With cancer	
	N	N	%**
Takayasu arteritis	123	4	3%
Granulomatous polyangiitis	100	4	4%
Giant cell arteritis	71	8	11%
Vasculitis limited to skin	62	4	6%
IgG4-related disease	41	1	2%
Polyarteritis nodosa	34	1	3%
Vasculitis secondary to CTD	32	2	6%
Eosinophilic granulomatous polyangiitis	32	2	6%
IgA vasculitis	30	2	7%
Renal limited AAV	17	4	24%
Buerger disease	17	1	6%
Isolated aortitis	13	1	8%
Microscopic polyangiitis	10	1	10%
Cryoglobulinemic vasculitis	8	2	25%
Drug-induced Vasculitis	1	1	100

Compared to the general population in Turkey, cancer incidence was four times higher (SIR: 4.1, 95% CI: 2.9–5.5, $P < 0.001$). Patients whom both the vasculitis and cancer diagnosis was within the same year, had a higher ratio of male patients (87%, $P = 0.01$), had a higher rate of smoking (77%, $P < 0.001$) and had a worse rate of survival (median survival: 54 months, 95% CI: <1 month–125.9 months, $P = 0.005$). There was no association between cyclophosphamide (CYC) use and cancer development, with a low cumulative CYC dose among cancer patients (median: 2 g).

Conclusion: The increase in the cancer incidence may indeed be due to chronic inflammation; however, VDI and BVAS scores during the last visit (median: <0.1) indicate that non-inflammatory factor may play a role as the inflammatory damage caused by vasculitis in these patients seem to be low. Similar to other recent cohorts in the literature, there was no association between CYC usage and cancer development.

In conclusion, compared to the general population, cancer incidence is significantly higher in patients with vasculitis and the timing of diagnosis between vasculitis and cancer may be associated with different clinical features.

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FRI0208

CORRELATIONS BETWEEN NEUTROPHIL-TO-LYMPHOCYTE RATIO AND TH17/TREG IMMUNE BALANCE IN PATIENTS WITH BEHCET'S DISEASE

Y. Liu¹, R. Su², X. Zheng², X. Li², C. Wang². ¹The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China; ²The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China

Background: Behcet's disease (BD) is a systemic perivascularitis where mucocutaneous manifestations are well known to show neutrophilic dermatosis denoted by significant neutrophil infiltration^[1]. The neutrophil-to-lymphocyte ratio has been proved as an inflammatory biomarkers in BD^[2]. At present, the Th17/Treg immune imbalance may be the involved factors in the pathway of BD^[3]. However, the correlations between the number of neutrophil, the number of lymphocyte, the neutrophil-to-lymphocyte ratio (NLR) and Th17/Treg immune imbalance remain unclear.

Objectives: The aim of this study was to examine correlations between the number of neutrophil, the number of lymphocyte, the neutrophil-to-lymphocyte ratio and Th17/Treg immune balance in patients with BD.

Methods: The study included 59 BD patients and 66 healthy controls. The absolute counts of lymphocyte subsets and CD4⁺T cell subsets were detected by flow cytometry for all participants. The neutrophil and lymphocyte were measured by routine blood test for all BD patients. To calculate the NLR, the ratio of absolute neutrophil count to absolute lymphocyte count was obtained. The Mann-Whitney U test was used to compare continuous measures. Correlations between the number of neutrophil, the number of lymphocyte, the NLR and Th17/Treg immune balance were assessed by Spearman's rank correlation tests.

Results: (1) Compared to healthy controls, the absolute counts of NK cells were decreased ($P = 0.047$), the absolute counts of B cells were increased ($P = 0.021$), the absolute counts of CD4⁺T cells were also increased ($P = 0.035$), the absolute counts of Th1 and Th17 cells were significantly increased ($P < 0.005$), the absolute counts of Th2 and Treg cells were decreased ($P < 0.05$), the ratio of Th1/Th2 and Th17/Treg were increased ($P < 0.001$) in BD group. (2) The numbers of neutrophil were positively correlated with Th17/Treg ($r = 0.344, P = 0.008$); The NLR was positively correlated with Th17/Treg ($r = 0.291, P = 0.026$).

Conclusion: Our research shows that T cell homeostasis perturbation, especially Th17 expansion, Treg insufficiency and Th17/Treg immune imbalance, is the cornerstone of BD pathogenesis. Except neutrophil, these findings suggest that imbalance Th17/Treg may be dominant in the pathogenesis of BD. The NLR was positively correlated with Th17/Treg. Further studies are required to evaluate these preliminary findings in different patient populations and also examine the possible molecular mechanisms behind our observations.

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Figure 1. The absolute counts of lymphocyte subsets in BD patients and healthy controls. Data are expressed as means $\pm$ SD.