Rheumatoid arthritis - comorbidity and clinical aspects

FRI0022

EVALUATION OF DYSFUNCTIONAL HIGH-DENSITY LIPOPROTEIN LEVELS WITH MYELOPEROXIDASE/PARAOXONASE1 RATIO IN RHEUMATOID ARTHRITIS

ALISIK Tugba¹, Murat Alisik², Baris Nacir¹, Figen Ayhan¹, Hakan Genç¹, Ozcan Erel³. ¹Ankara Training and Research Hospital, Physical Medicine and Rehabilitation, Ankara, Turkey; ²Polatli State Hospital, Medical Biochemistry, Ankara, Turkey; ³Yildirim Beyazıt University, Medical Biochemistry, Ankara, Turkey

Background: Rheumatoid arthritis (RA) is a chronic, systemic and autoimmune disease with inflammatory arthritis. Atherosclerosis and cardiovascular diseases are common in RA patients. Although chronic systemic inflammation in RA patients is considered to be the main cause of this condition, the relationship between systemic inflammation and vascular pathophysiology is not clear [1]. While high-density lipoprotein (HDL) is known to be a negative risk factor for atherosclerosis by reverse cholesterol transport, recent studies show that HDL can be pro-atherogen (dysfunctional, inflammatory) by losing this characteristic in cases of inflammation and oxidative stress. Myeloperoxidase (MPO)/paraoxonase 1 (PON1) ratio is a valuable marker that can be routinely used as an indicator of dysfunctional HDL. PON1 is a lipoprotein-derived enzyme which provides antioxidant properties of HDL. Although MPO is a bactericidal enzyme derived from granular leukocytes, it causes oxidative modification of circulating lipoproteins [2].

Objectives: The aim of this study is to evaluate the levels of dysfunctional HDL in RA patients and to explore the relationship between dysfunctional HDL and coronary artery disease (CAD) in RA patients.

Methods: Sixty seven healthy individuals and 130 RA patients without diabetes mellitus, hypertension and hyperlipidemia were included to study. Blood samples taken from patients and healthy volunteers were centrifuged to separate serum and these serum samples were stored at -80 °C until the study day. Total cholesterol (TC), triglyceride (TG), HDL, Low-density lipoprotein cholesterol (LDL), MPO and PON1 levels were measured. The MPO/PON1 ratio was calculated as a dysfunctional HDL marker. Cardiology notes of the patients were examined to detect patients who also have CAD.

Results: The mean age of the patient and control groups were 54.6 ± 11.3 and 52.0 ± 10.0, respectively (p:0.107). The mean DAS28 score of the patients was 2.77 ± 0.96. There were no significant differences between two groups in TC, TG, HDL and LDL (p> 0.05). MPO, PON1 and dysfunctional HDL levels were significantly higher in the RA group compared to control group (p <0.001, p <0.023, and p <0.001; respectively).

Dysfunctional HDL levels were higher in 44 RA patients with CAD compared to 86 RA patients without CAD (p = 0.002). 58 patients with active RA had higher dysfunctional HDL levels compared to 72 patients with remission (p = 0.002). There was a positive correlation between DAS28 scores and dysfunctional HDL levels (rho: 0.357, p < 0.001).

Conclusion: Our study shows that, although there is no abnormality in lipid profile parameters, dysfunctional HDL levels were higher in patients with active disease than patients with RA in remission and RA patient with CAD than without CADs. This condition could be associated with CAD in RA patients. Disturbance as a result of inflammation on HDL functions such as inhibition of LDL oxidation and reverse cholesterol transport, could be the cause of CAD in RA patients. As a result screening of conventional cardiovascular risk factors in RA patients with normal lipid panel might be inadequate. Therefore as an additional parameter, dysfunctional HDL are promising to evaluate cardiovascular risk of RA patients.

REFERENCES:

- [1] Bag-Ozbek, A. and J.T. Giles, Inflammation, adiposity, and atherogenic dyslipidemia in rheumatoid arthritis: is there a paradoxical relationship? *Curr Allergy Asthma Rep*, 2015. 15(2): p. 497.
- [2] Haraguchi, Y., et al., Serum myeloperoxidase/paraoxonase 1 ratio as potential indicator of dysfunctional high-density lipoprotein and risk stratification in coronary artery disease. *Atherosclerosis*, 2014. 234(2): p. 288-294.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.7811

FRI0023

CARDIOVASCULAR RISK AND VITAMIN D DEFICIENCY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THERAPY WITH TNF-ALPHA INHIBITORS

Daniela Anghel¹, Livia Otlocan², Maria Magdalena Negru², Raluca Bursuc¹, Anca Manolache¹, Elena Busuioc¹, Valeriu Smedescu¹, Adrian Anghel¹, Florentina Cristina Plesa¹, Ciprian Jurcut¹. ¹Dr. Carol Davila' Central Military Emergency University Hospital, Internal Medicine, Bucharest, Romania; ²Stanta Maria' Clinical Hospital, Internal Medicine and Rheumatology, Bucharest, Romania

Background: Cardiovascular disease is the main cause of mortality and morbidity in patients with rheumatoid arthritis (RA). Correlation between vitamin D deficiency and atherosclerosis in patients with rheumatoid arthritis is a subject of medical interest.

Objectives: We studied the correlation between vitamin D deficiency, body mass index (BMI) and carotid intima-media thickness (CIMT) in patients with rheumatoid arthritis with anti tumor necrosis factor-alpha (TNF-α) therapy.

Methods: Our study included 75 RA patients with anti-TNF-alpha therapy (Adalimumab, Infliximab, Etanercept) and 30 RA patients with DMARDs (Methotrexate/Leflunomide). The patients were diagnosed with RA according to ACR/EULAR (2010) classification **criteria**.

CIMT was measured using high-resolution Doppler ultrasonography. CIMT ≥ 0.9 mm is considered as a marker of atherosclerosis. Vitamin D deficiency was defined as serum 25-OH-vitamin D level <20 ng/mL. Other parameters included are age, body mass index (BMI=18.5-24.9kg/m²- normal weight; BMI≥25kg/m²- overweight) and disease activity (DAS28<2.6: remission; DAS28=2.6-3.2: low disease activity, DAS28=3.2-5.1: moderate disease activity; DAS28>5.1: high disease activity).

Patients with current use of vitamin D supplements were excluded.

Results: The anti-TNF group included 29 patients with Adalimumab (38.7%), 25 with Etanercept (33.3%) and 21 patients in treatment with Infliximab (28%). Their mean age was 52.0 years.

We evaluated patients at baseline and after 12 months with treatment.

In anti-TNF group we found 9 patients (12%) with normal BMI and normal vitamin D level correlated with high CIMT (p=0.001), 21 patients (28%) with overweight and normal vitamin D level correlated with high CIMT (p=0.003), and 31 patients (41.3%) with overweight and low vitamin D level correlated with high CIMT (p=0.001). 14 patients (18.7%) with normal vitamin D level and normal weight (9) or overweight (5) were correlated with normal CIMT (p=0.01).

In DMARDs group we followed the same correlation. Patients with normal BMI and normal vitamin D level had a low correlation with CIMT increase (p=0.01). Patients with overweight and low vitamin D level had a significant correlation with CIMT increase (p=0.003) than group with anti-TNF-alpha therapy.

After 12 months of therapy, patients treated with Adalimumab had lower CIMT levels than patients treated with Etanercept.

Conclusion: Rheumatoid arthritis patients treated with TNF inhibitors and with vitamin D deficiency but with normal BMI have been correlated with lower increase of CIMT than patients with DMARDs therapy. Normal vitamin D level was associated with low increase of CIMT in these patients. Deficiency of Vitamin D associated with overweight are risk factors for carotid atherosclerosis in patients with RA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.5535

FRI0024

AA AMYLOIDOSIS AND LUNG DISEASES IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 147 PATIENTS

Ágnes Apáthy^{1,2}, Miklós Bély³. ¹St. Margaret Clinic Budapest, Department of Rheumatology, Budapest, Hungary; ²St. Margaret Clinic, Budapest, Department of Rheumatology, Budapest, Hungary; ³Hospital of the Order of the Brothers Saint John of God in Budapest, Department of Pathology, Budapest, Hungary

Background: Systemic AA amyloidosis (AAa) is one of the most important complications of rheumatoid arthritis (RA) [1].

A wide spectrum of lung diseases may complicate RA or associate with RA [2-4].

Objectives: The aim of this study was to determine the influence of AAa on lung diseases related or not related to RA.

Methods: We studied 161 random autopsy patients with RA [1]. RA was confirmed clinically according to the criteria of the ARA [5]. Tissue samples of the lungs were available for histological evaluation of 147 patients.

The prevalence of **AAa** and of distinctly different forms of multifocal inflammation, such as purulent bronchitis and bronchiolitis (**purBr**) or bronchopneumonia (**BrPn**), infarct with pneumonia (**InfPn**), occlusive pneumonia (**OcclPn** – focal pneumonia caused by compressive peribronchial nodular lymphoid hyperplasia or bronchial blockage by a necrotic nodule) were examined. In addition, rheumatoid pneumonia (**RhPn**), furthermore interstitial pneumonia (**IPn**) [1-4] were determined at autopsy and confirmed in a detailed review of extensive histological material.

The possible role of **AAa** on the prevalence of **purBr** or **BrPn**, **InfPn**, **OcclPn**, **RhPn** and **IPn** was analyzed with Pearson's chi-squared (χ^2) test.

Results: **AAa** complicated **RA** in **34 (23.13%)** of 147 patients. Pulmonary blood vessels of different caliber and various tissue structures of the lungs were involved in **25 (73.53%)** of 34 cases; the lungs were not involved by **AAa** in **9 (26.47%)** of 34 cases.

purBr or **BrPn** were associated with **RA** in **19 (21.1%)**, **InfPn** in **5 (3.4%)**, **OcclPn** in **2 (1.4%)**, **RhPn** in **3 (2.1%)** of 147 patients (only the fatal cases were considered). **IPn** – characterized by interstitial cellular infiltration with or without edema, fibrinoid deposition, with or without fibrosis, and with or without corresponding pleuritis was present in **35 (23.8%)** of 147 patients; **IPn** alone was not fatal in our cohort and contributed to the death only in association with cardiac, circulatory or cardio-respiratory insufficiency.

Pulmonary amyloid A deposition (**n=25**) was associated with **purBr** or **BrPn** in **1 (5.26%)** of 19, **InfPn** in **1 (20.0%)** of 5, **OcclPn** in **2 (100.0%)** of 2, **RhPn** in **none (0.0%)** of 3, **IPn** in **12 (34.29%)** of 35 patients.

The relationship between pulmonary **AAa** and **purBr** or **BrPn** ($\chi^2=1.2836$, $p<0.25$), **InfPn** ($\chi^2=0.1800$, $p<0.67$) or **RhPn** ($\chi^2=0.00025$, $p<0.98$) was not significant. There was a **significant and positive correlation** between pulmonary **AAa** and **OcclPn** ($\chi^2=4.8313$, $p<0.02$) or between **AAa** and **IPn** ($\chi^2=9.7106$, $p<0.0018$).

Conclusion: The main complications of **RA**, such as **AAa**, may influence the prevalence, clinical course and symptoms of associated diseases and vice versa. Knowledge of these relationships is important to estimate the relative danger they potentially represent.

The **significant correlation** between **AAa** and **OcclPn** or **IPn** suggests a positive influence of pulmonary amyloid A deposition on **OcclPn** or **IPn**. The statistically not significant correlations suggest that **purBr** or **BrPn**, **InfPn** and **RhPn** are independent entities which are not influenced by **AAa**.

REFERENCES:

- [1] Bély M, Apáthy Ágnes: Clinical pathology of rheumatoid arthritis. pp 1-440, Akadémiai Kiadó, Budapest 2012 <http://www.akkrt.hu>
- [2] Wright GP, Heard BE: The lungs in rheumatoid arthritis. In Symmers *Systemic pathology*, ch. 7, pp 370-371, Churchill Livingstone, Edinburgh, London, New York 1976
- [3] Bély M, Apáthy Á: *Acta Morphologica Hungarica*, 1991, 39: 117-156.
- [4] Bély M: *Zentralblatt für allgemeine Pathologie und pathologische Anatomie*, 1988, 134: 647-664.
- [5] Arnett FC, et al: *Arthritis Rheum.* 1988; 3:315-24, DOI: 10.1002/art.1780310302

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.1018

FR10025

DOES COMORBIDITY IMPACT ON THE ACTIVITY AND MANAGEMENT OF RHEUMATOID ARTHRITIS?

Aida Babaeva¹, Elena Kalinina¹, Maxim Zvonorenko¹, Karina Solodenkova².

¹Volgograd State Medical University, Volgograd, Russian Federation; ²I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

Background: Patients with rheumatoid arthritis (RA) are in increased risk of developing comorbid conditions. Recent data suggest the relationship between severity of RA and concomitant diseases [1, 2]. Drug therapy is considered as impotent risk factor for numerous comorbidities. On the other hand comorbidity can impact negatively on the RA course and on the pts management [3].

Objectives: The aim of our study was to evaluate the prevalence of concomitant conditions in RA pts, to compare the RA activity and management in relation with comorbidities.

Methods: 168 pts with established and longstanding RA were observed at in-patient clinic for RA clinical assessment and revealing concomitant diseases (cardiovascular, gastrointestinal, liver, pulmonary, endocrine, blood). The activity of disease according to DAS28-ESR index in RA subgroups with different comorbidities was compared. The spectrum and used doses of anti-rheumatic medications (DMARD, biologics, GC) in these subgroups was analyzed in term to assess the RA rational treatment.

Results: The majority (88.1%) of observed RA pts had concomitant condition. The most frequent associated diseases were: cardiovascular (AH, IHD, HF, AF) in 86.9% and gastrointestinal (gastritis, duodenitis, gastroduodenal ulcer, colitis) in 64.3% less common comorbidities were anemia (30.9%), liver and kidney abnormalities (hepatomegaly, steatohepatitis, CKD, pyelonephritis) in 25% and 12.5% respectively, endocrine (type 2 diabetes mellitus, thyroid disorders) in 16.7%. Multimorbidity determined as combination of different system disorders in the setting of RA was detected in 54.8% of RA pts. We found out significant difference in RA activity on the basis of DAS28 between RA subgroup without concomitant conditions (the 1st) on the one hand and RA subgroups with comorbidities (the 2nd) ($t1=2.76$, $p<0.01$) or multimorbidities ($t2=3.73$, $p<0.01$) on the other hand (tab.1).

Index	RA without comorbidities (1 st group)	RA with comorbidities (2 nd group)	RA with multimorbidities (3 ^d group)
DAS 28	4.20 ±0.31	5.09±0.09	5.44±0.12

In RA with comorbidities/multimorbidities the mean doses of MTX and SSZ were lower than in RA without comorbidities, while the dose of GC and frequency of GC use was significantly higher in the 2nd and 3^d groups ($\chi^2=4.25$, 4.41 respectively). 55% of pts from the 1st group and only 19.6% of total amount of pts from the 2nd and 3^d groups were treated with biologics ($\chi^2=5.67$).

Conclusion: Obtained data suggest that comorbidities have a negative impact on the severity of RA and can interfere in the implementation of T2T strategy in daily clinical practice.

REFERENCES:

- [1] Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). *Ann Rheum Dis* (2014) 73(1):62–8. doi:10.1136/annrheumdis-2013-204223
- [2] Radner H. Multimorbidity in rheumatic conditions. *Wien Klin Wochenschr* (2016) 128(21–22):786–90. doi:10.1007/s00508-016-1090-x
- [3] Radner H, Yoshida K, Frits M, Iannaccone C, Shadick NA, Weinblatt M, et al. The impact of multimorbidity status on treatment response in rheumatoid arthritis patients initiating disease-modifying anti-rheumatic drugs. *Rheumatology (Oxford)* (2015) 54(11):2076–84. doi:10.1093/rheumatology/kev239

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.7351

FR10026

SYSTEMIC, RENAL AND CARDIAC AA AMYLOIDOSIS IN RHEUMATOID ARTHRITIS – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS

Miklós Bély¹, Ágnes Apáthy². ¹Hospital of the Order of the Brothers Saint John of God in Budapest, Department of Pathology, Budapest, Hungary; ²St. Margaret Clinic, Budapest, Department of Rheumatology, Budapest, Hungary

Objectives: The aim of our study was to determine the incidence of systemic **AA** amyloidosis (**sAAa**) in **RA**, to appraise the prevalence and severity of amyloid A deposits in different tissue structures of the kidneys and heart, to outline the development of renal and cardiac **AA** amyloidosis (**rAAa** and **cAAa**), and to estimate the role of **rAAa** and **cAAa** in mortality.

Methods: One hundred sixty one (161) non-selected autopsy patients with rheumatoid arthritis (**RA**) were studied. **RA** was confirmed clinically according to the criteria of the **ACR** [1]. **sAAa** was specified histologically, based on evaluation of 5 organs (heart, lung, liver, kidney and pancreas). Amyloid A deposition was diagnosed histologically according to Romhányi by a modified (more sensitive) Congo red staining [2]. Amyloid