References:

Table. Case control studies

Region (Year)	Diagnosis	TB with MTX	TB without MTX	Odds Ratio
Mexico (1999)	Mixed (4 RA)	1/6	5/75	2.76
Japan (2004)	RA	3/47	17/154	0.56
Canada (2009)	RA	29/483	21/1046	3.12
Brazil (2010)	Lupus	2/3	1/57	112
Taiwan (2012)	Psoriasis	33/144	464/2341	1.2
Taiwan (2015)	JIA	4/357	4/1026	2.90
South Africa (2017)	RA	0/134	0/18	NA

JIA=juvenile idiopathic arthritis

Acknowledgments: Funded by the International League Against Rheumatism and McGill University Global Health Scholar Awards

Disclosure of Interests: Anna Davidson: None declared, Alize Gunay: None declared, Ines Colmegna: None declared, Diane Lacaille: None declared, Hal Loewen: None declared, Michele Meltzer: None declared, Rosie Scuccimari: None declared, Yewondwossen Mengistu: None declared, Sasha Bernatsky: None declared, Carol Hitchon Grant/research support from: UCB Canada; Pfizer Canada

DOI: 10.1136/annrheumdis-2020-eular.1544

FRI0065

CLINICAL FEATURES OF METHOTREXATE ASSOCIATED LYMPHOPROLIFERATIVE DISORDER IN RHEUMATOID ARTHRITIS PATIENTS AND INFLUENCE OF CD8 POSITIVE LYMPHOCYTE INFILTRATION

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Background: Lymphoproliferative disorders (LPD) that develop in rheumatoid arthritis (RA) patients treated with MTX (MTX-LPD) is one of the important complications for RA patients. We have previously epidemiologically demonstrated an association between MTX and the development of LPD in RA patients¹⁾. MTX-LPD has varied pathologies including various clinical symptom and histological finding. Therefore, we need more information about MTX-LPD. In addition, it is one of the characteristics for MTX-LPD that spontaneous regression (SR) after MTX discontinuation. However, the mechanism of SR is not clarified.

Objectives: We collect the information such as clinical symptom and histological finding of MTX-LPD with RA patients, and clarify the clinical features of MTX-LPD. In addition, we investigated the difference between SR cases and cases that treated with chemotherapy after MTX discontinuation (CTx cases).

Methods: We enrolled 90 MTX-LPD patients from Kagawa Prefecture, Japan between June 2005 and December 2019. Patients were diagnosed according to American College of Rheumatology (ACR) 1987 classification criteria or ACR/European League Against Rheumatism (EULAR) 2010 classification criteria, and treated with disease modifying antirheumatic drugs (DMARDs) including MTX. We collected as follow information; age, gender, duration of RA, laboratory data (lymphocyte counts and sIL-2R) and treatment of MTX-LPD. In addition, we divided 16 MTX-LPD cases diagnosed histologically into two groups (SR:CTx group; n=10:6), and analyzed the histological findings (CD4, CD8, CD163 and CD47) using the staining in immunohistochemistry (IHC) between the two groups. Each positive cell analyzed using virtual viewer soft ImageScope.

Results: Characteristics of 90 MTX-LPD patients are as follow; mean age 66.5±11.2 years, 63 female, duration of RA 18.5±19.4 years. 65 patients (72.2%) were spontaneously improved by discontinuing MTX. 58 patients (64.4%) were proven MTX-LPD histologically. In these patients, diffuse large B-cell lymphoma (DLBCL) was the most frequent histological type of MTX-LPD (56.9%). Infiltration of CD8 positive lymphocyte in the lesion was significant less in the SR cases than in the CTx cases (Figure 1). However, CD4, CD163 and CD47 positive cells had no significant difference between two groups.

Conclusion: We revealed clinical features of MTX-LPD with RA patients. In addition, CD8 positive lymphocytes are involved in tumor immunity. In this study, we suggested that the extent of CD8 positive lymphocyte infiltration may predict SR of MTX-LPD. Further study is necessary on revealing the mechanism of SR in MTX-LPD.

References:

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.5309

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Figure 1. CD8 positive lymphocytes in the specimen of lesion using the staining in immunohistochemistry (IHC) between SR and CTxgroup.

FRI0066

SUBCLINICAL CORONARY CALCIFICATION ASSOCIATED WITH LONG-TERM CARDIOVASCULAR OUTCOMES IN RHEUMATOID ARTHRITIS

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Background: Large, multicenter studies established the strong prognostic value of coronary artery calcium (CAC) scoring in asymptomatic individuals. Increasing CAC score is an independent predictor of worsening cardiovascular disease event risk in general patients. The prognostic significance of higher CAC score strata in the long-term cardiovascular risk in rheumatoid arthritis (RA) is unknown.

Objectives: To evaluate the long-term cardiovascular event risk across CAC strata in a prospective, single center cohort of established RA patients without symptoms or prior diagnosis of cardiovascular disease.

Methods: One hundred-fifty patients underwent computed tomography angiography for coronary atherosclerosis evaluation. CAC score was measured according to Agatston. CVD events were prospectively recorded, including cardiac death, myocardial infarction, unstable angina, revascularization, stroke, claudication, and heart failure hospitalization over 6.0±2.4 years of follow-up. Unadjusted, robust Cox proportional hazards regression models evaluated CVD event risk across higher CAC strata (CAC=1-99, CAC=100-399 and CAC≥400) compared to CAC=0. Additional multivariable robust Cox regression models with time-varying covariates evaluated the impact of log transformed CAC or different CAC thresholds (CAC>0 vs. CAC=0, CAC≥100 vs. CAC<100 and CAC≥400 vs. CAC<400)

Figure 1. Increasing CAC scores associated with higher cardiovascular event risk in RA