DOI: 10.1136/annrheumdis-2017-eular.4867

OP0184 IMSYC IMMUNOLOGIC SYNOVITIS SCORE: A NEW HISTOLOGICAL SCORE FOR DISCRIMINATING INFLAMMATORY AND NON-INFLAMMATORY ARTHRITIS

A. Najm[1,2], B. Le Goff[1,2], F. Blanchard[1], J. Amiaud[1], C. Charrier[1], V. Krenn[3]. *[1]Inserm UMR 957; [2]Rheumatology, Nantes University Hospital, Nantes, France; [3]MVZ-Zentrum für Histologie, Zytologie und Molekulare Diagnostik, Trier, Germany*

Background: General Synovitis score (GSS) has been developed by Krenn *et al.* in order to discriminate inflammatory arthritis (IA) and non-inflammatory arthritis (NIA) (1). This score assesses 3 major components of synovitis: lining layer hyperplasia, activation of resident cells (stroma) and inflammatory infiltrate. All components are graded semi-quantitatively from 0 to 3 and the total score is on 9. High-grade synovitis is highly associated with IA and is defined by a score upper than 5 with a sensitivity of 61.7% and a specificity of 96.1%. As immunohistochemistry (IHC) is frequently used to better characterize synovitis, we propose to create a new IMmunologic SYnovitis SCore (IMSYC) adding 5 components to the GSS: CD68, CD3, CD20, CD31 and Ki67 immunostaining.
Objectives: Our work aimed to evaluate the diagnostic performance of this new score including IHC, to define the best cut off for inflammatory arthritis recognition, and to compare its diagnostic performance with the GSS.
Methods: 53 synovial samples from patients were obtained during surgery (arthroplasty or synovectomy). All patients gave written consent prior surgery. Samples were cut and Hematoxylin and eosin stained. CD68, CD3, CD20, CD31 and KI67 Immunohistochemistry were performed. GSS was assessed for each slide and semi-quantitative 4 scale scores (0–3) were given for each immunostaining, in a blind manner. The score is calculated on 24 (GSS 0–9 points, and 0–3 score for each of the 5 immunostaining). A representative amount of slides was read by 2 observers with a good interobserver variability (spearman correlation coefficient of 0.95, $p<0.0005$). They then defined a consensual and reproducible scoring atlas.
Results: 53 patients were included. 25 were females (47,2%), mean age was 62.1 years [Standard deviation (SD) 13.2 years]. 36 had inflammatory arthritis reparsed as follows: 28 Rheumatoid arthritis (RA), 5 had Psoriatic arthritis, 3 had Undifferentiated arthritis. “Non inflammatory” arthritis group included 10 patients with Osteoarthritis and 7 with ligaments or meniscus injuries. Mean GSS was significantly higher in the IA group 5.70 [SD 0.321] vs.3.51 [SD 0.351]; $p<0.001$). Mean IMSYC was significantly superior in the IA group 14.94 [SD 0.747] vs. 8.50 [SD 0.639]; $p<0.001$). In univariate analysis by logistic regression, GSS (Odd Ratio (OR) 2.27; $p<0.001$), CD3 (OR 4.3; p=0.002), CD68 (OR 4.5; p=0.002), Ki67 (OR 11.8; $p<0.001$), and CD31 scores (OR 6.5; p=0.001) were significantly associated with IA, however CD20 score was not (OR 0.9; p=0.34). ROC curve analysis determined the score of 10.5 out of 24 as the best cut off for discrimination between IA and non-IA with a sensitivity of 74.3% and specificity of 100%. The area under ROC curves was statistically superior with IMSYC (0.93) compared to GSS (0.81) (p=0.05).
Conclusions: We hereby propose a new synovitis score including IHC. This score has a better sensitivity and specificity than the Global synovitis score for discrimination between IA and non-IA. Moreover, this score accurately describes synovial membrane immunophenotype and could therefore give a basis for tissue driven therapies in rheumatic diseases, especially in RA.
References:
[1] Krenn V et al. Synovitis score: discrimination between chronic low-grade and high-grade synovitis.Histopathology. 2006 Oct;49(4):358–64.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2547

OP0185 IMMUNOHISTOLOGIC STUDY OF SYNOVITIS FROM PATIENTS WITH UNDIFFERENTIATED ARTHRITIS WHO EVOLVED TO RHEUMATOID ARTRHITIS OR PSORIATIC ARTHRITIS AFTER FOLLOW-UP

A. Cuervo Aguilera, R. Celis, J. Ramírez, M.V. Hernández, V. Ruíz-Esquide, J. Inciarte-Mundo, R. Sanmartí, J.D. Cañete. *Rheumatology, Hospital Clínic Barcelona, Barcelona, Spain*

Background: Undifferentiated Arthritis (UA) is defined as an inflammatory oligo/poly arthritis that does not fulfil criteria for a definitive diagnosis.Delay in diagnosis and treatment leads to poor prognosis. Previous studies have found differences in the cellular infiltrate between the synovitis of Rheumatoid Arthritis (RA) and Spondyloarthritis, including psoriatic arthritis (PsA)
Objectives: To identify synovial biomarkers that may be useful to diagnose patients with early UA
Methods: Retrospective longitudinal study.Patients with UA followed in our Arthritis Unit,who underwent arthroscopy between 2000 and 2014.Synovial biopsy were stained by immunohistochemistry with the following antibodies:CD3 for T cells,CD20 for B cells,CD79 for B cells,CD138 for plasma cells,CD31 for vessels,CD68 for macrophages,CD15 for neutrophils,CD117 for mast cells and hsp47 for fibroblasts, and quantified by Digital Image Analysis (Olympus).The same antibodies were evaluated in RA and PsA control groups
Results: 55 UA and 78 controls were included.Table 1 shows the clinical, serological and demographic characteristics.Among patients with UA, 23 (42%) patients met criteria for RA and 32 (58%) for PsA during follow-up.Synovitis of patients with UA had higher macrophage (CD68+) density in total tissue (p=0.008) and sublining (SL) (p=0.012) than the control group.The UA that evolved to RA had a higher density of CD3 T lymphocytes than the control RA group (p=0.014). No differences were observed in cells of adaptive immunity (CD20 B lymphocytes, CD138 plasma cells), innate immunity (CD117 mast cells, CD15 neutrophils), vessels (CD31) between the 4 groups.The area (%) stained by anti-hsp47 (synovial fibroblasts) in SL was higher in the RA control group than in the PsA (p=0.003)

Table 1. Data are expressed as mean±SD

	UA n=55	UA-RA n=23	UA-PsA n=32	p	RA n=40	PsA n=38	p
Age (years)	47±13	51±13	44±12	0.058	60±12	54±13	0.065
Sex (male)n (%)	22 (40)	6 (26)	16 (50)	0.074	17 (43)	23 (61)	0.111
Disease duration (years)	3±4	3±2	3±4	0.114	3±6	2±2	0.851
Time of follow-up (years)	7±4	8±4	6±4	0.038	7±3	5±3	0.008
CRP (mg/dL)	2.7±3.9	2.4±1.9	3.0±4.9	0.189	3.8±3.2	3.0±3.8	0.102
DAS28 (ESR)	4.17±1.05	4,83±1,06	3,63±0,94	0.000	5,15±1,51	4,02±1,04	0.002
ACPA n (%)	4 (22)	4 (22)	0 (0)	0.000	30 (77)	0 (0)	0.000
RF n (%)	10 (7)	9 (41)	1 (3)	0.000	28 (70)	1 (3)	0.000
csDMARD n (%)	21 (41)	7 (35)	14 (45)	0.472	29 (73)	19 (50)	0.041
bDMARD n (%)	2 (4)	0 (0)	2 (6)	0.243	8 (20)	6 (16)	0.628
PDN n (%)	7 (13)	3 (14)	4 (13)	0.851	11 (28)	5 (13)	0.117

Conclusions: This is the first immunohistological study of synovitis in a significant group of patients with UA who developed AR or PsA during follow-up. Although there are some differences between the UA and control groups in the density of CD68+ macrophages and lymphocytes T CD3+, these do not appear to be useful for an early diagnosis of UA. On the other hand, unlike the results of some previous studies, we not found differences between the cellular infiltrate (adaptive immunity, innate immunity or vessels) in patients with RA and PsA. The fact that some patients with UA were undergoing treatment prior to synovial biopsy and its retrospective character limit the results of this study
Acknowledgements: Financed: “Fondo de Investigación Sanitaria” (PI14/00785. JD Cañete) del Instituto de Salud Carlos III (ISCIII). Co-financed by BECA FER-2015. Premis “Emili Letang”, Hospital Clínic. BECA MSD-Sociedad Catalana de Reumatología
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4850

OP0186 TENOFOVIR, A NUCLEOSIDE ANALOG REVERSE TRANSCRIPTASE INHIBITOR FOR TREATMENT OF HIV, PROMOTES OSTEOCLAST DIFFERENTIATION AND BONE LOST IN VIVO IN A MECHANISM DEPENDING ON ATP RELEASE AND ADENOSINE, AND DIPYRIDAMOLE MAY BE A USEFUL TREATMENT TO REVERT THE EFFECTS

F.M. Conesa[1], P. Llamas[1], T. Wilder[2], P. Atencio[3], A. Cabello[3], M. Górgolas[3], B. Cronstein[2], R. Largo[1], G. Herrero-Beaumont[1], A. Mediero[1,2]. *[1]Joint and Bone Research Unit, Iis-Fundacion Jimenez Diaz, Madrid, Spain; [2]Division of Translational Medicine, Department of Medicine, NYU School of Medicine, New York, United States; [3]Internal Medicine Department, Iis-Fundacion Jimenez Diaz, Madrid, Spain*

Background: HIV infection devastates the immune system but also affects other tissues and organs Bone alterations have been observed in HIV disease for nearly two decades, in particular a higher risk of low bone mineral density (BMD) and fragility fractures. Treatment with Tenofovir alone or as part of HAART, leads to changes in bone catabolism markers and significant reductions in BMD in children and young adults. Tenofovir is taken up by cells and phosphorylatedand inhibits HIV-reverse transcriptase by mimicking AMP. We have recently found that Tenofovir inhibits Pannexin-1/Connexin-43-mediated ATP release from cells and decreases extracellular adenosine levels and fibrosis in murine models. Inhibition of osteoclast formation *via* adenosine A2A receptor stimulation or increasing local adenosine concentration stimulates new bone formation as well as rhBMP-2.
Objectives: As adenosine and ATP are key regulators of bone homeostasis, we determined whether Tenofovir directly affects bone by an adenosine- or ATP-dependent mechanism and if treatment with Dipyridamole, an agent that increases extracellular adenosine by blocking cellular adenosine uptake, may be a useful treatment to counteract Tenofovir effects.
Methods: M-CSF/RANKL-induced osteoclast (OC) was studied in primary murine bone marrow culture as the number of TRAP-positive cells after challenge with Tenofovir (1nM-100μM) alone or in combination with Dipyridamole (1nM-100μM). OC markers were measured by RT-PCR. Pannexin-1 and Connexin-43 expression were permanently knocked down by lentiviral infection with appropriate shRNA or scrambled shRNA and these cells were induced to differentiate into OC by RANKL. Male C57Bl/6 mice received Tenofovir 75mg/Kg/day alone or in combination with Dipyridamole 1mg/Kg/day for 4 weeks. Double labelling of bone with calcein/Alizarin Red to analized bone formation was performed and long bones prepared for microCT and histology.
Results: Tenofovir produced a dose-dependent increase in OC differentia-