Conclusion: The research shows that the most frequent symptoms among people with rheumatic diseases were depression and high levels of anxiety due to strong emotional stress. Psychological malaise caused direct effects in worsening the symptoms of rheumatic disease as well as other related effects, for example, insomnia. The forced isolation due to the lockdown has made people lack the social support that is fundamental for the psychological well-being especially for those suffering from some chronic pathology. Starting from the data collected, APMARR promptly activated a completely free psychological support service with 6 professional psychologists, two of them specialized in emergency psychology. The service is accessible online and is still going on for all who are not able to overcome the anxiety and fear related to the pandemic and its evolution. Thousands of accesses to the service have been measured to date.

References: S Mingolla¹, A Celano¹, M Santopietro²

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The origins of pain in RMDs

OP0083

INFECTIOUS AND AUTOINFLAMMATORY MODIC TYPE 1 CHANGES HAVE DIFFERENT PATHOMECHANISMS

I. Heggli^{1,2}, R. Schüpbach³, N. Herger^{1,2}, T. A. Schweizer⁴, A. Juengel^{1,2}, N. Farshad-Amacker⁵, M. Betz⁶, J. M. Spirig⁶, F. Wanivenhaus⁶, N. H. Ulrich⁶, F. Brunner², A. S. Zinkernagel⁴, M. Farshad⁶, O. Distler^{1,2}, S. Dudli^{1,2}. ¹Center of Experimental Rheumatology, Department of Rheumatology, University Hospital, University of Zurich, Zurich, Switzerland; ²Department of Physical Medicine and Rheumatology, Balgrist University Hospital, University of Zurich, Zurich, Switzerland; ³Unit of Clinical and Applied Research, Balgrist University Hospital, University of Zurich, Zurich, Switzerland; ⁴Department of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland; ⁵Department of Radiology, Balgrist University Hospital, University of Zurich, Zurich, Switzerland; ⁶Department of Orthopaedic Surgery, Balgrist University Hospital, University of Zurich, Zurich, Switzerland

Background: Modic type 1 changes (MC1) are vertebral bone marrow (BM) edema that associate with non-specific low back pain (LBP). Two etiologies have been described. In the infectious etiology the anaerobic aerotolerant *Cutibacterium acnes* (*C. acnes*) invades damaged intervertebral discs (IVDs) resulting in disc infection and endplate damage, which leads to the evocation of an immune response. In the autoinflammatory etiology disc and endplate damage lead to the exposure of immune privileged disc cells and matrix to leukocytes, thereby evoking an immune response in the BM. Different etiologies require different treatment strategies. However, it is unknown if etiology-specific pathological mechanisms exist.

Objectives: The aim of this study was to identify etiology-specific dysregulated pathways of MC1 and to perform in-depth analysis of immune cell populations of the autoinflammatory etiology.

Methods: BM aspirates and biopsies were obtained from LBP patients with MC1 undergoing spinal fusion. Aspirates/biopsies were taken prior screw insertion through the pedicle screw trajectory. From each patient, a MC1 and an intra-patient control aspiration/biopsy from the adjacent vertebral level was taken. If *C. acnes* in IVDs adjacent to MC1 were detected by anaerobic bacterial culture, patients were assigned to the infectious, otherwise to the autoinflammatory etiology.

Total RNA was isolated from aspirates and sequenced (Novaseq) (infectious n=3+3, autoinflammatory n=5+5). Genes were considered as differentially expressed (DEG) if p-value < 0.01 and log2fc > ± 0.5. Gene ontology (GO) enrichment was performed in R (Goseq), gene set enrichment analysis (GSEA) with GSEA software.

Changes in cell populations of the autoinflammatory etiology were analyzed with single cell RNA sequencing (scRNAseq): Control and MC1 biopsies (n=1+1) were digested, CD45⁺CD66b⁺ mononuclear cells isolated with fluorescence activated cell sorting (FACS), and 10000 cells were sequenced (10x Genomics). Seurat R toolkit was used for quality-control, clustering, and differential expression analysis.

Transcriptomic changes (n=5+5) of CD45⁺CD66b⁺ neutrophils isolated with flow cytometry from aspirates were analyzed as for total bulk RNAseq. Neutrophil activation (n=3+3) was measured as CD66b⁺ expression with flow cytometry. CD66b^{high} and CD66b^{low} fractions in MC1 and control neutrophils were compared with paired t-test.

Results: Comparing MC1 to control in total bulk RNAseq, 204 DEG in the autoinflammatory and 444 DEG in the infectious etiology were identified with only 67 shared genes (Fig. 1a). GO enrichment revealed "T-cell activation" (p = 2.50E-03) in the autoinflammatory and "complement activation, classical pathway" (p=1.1E-25) in the infectious etiology as top enriched upregulated biological processes (BP) (Fig. 1b). ScRNAseq of autoinflammatory MC1 showed an over-representation of T-cells (p= 1.00E-34, OR=1.54) and myelocytes (neutrophil progenitor cells) (p=4.00E-05, OR=2.27) indicating an increased demand of these cells (Fig. 1c). Bulk RNAseq analysis of neutrophils from the autoinflammatory etiology revealed an activated, pro-inflammatory phenotype (Fig. 1d), which was confirmed with more CD66b^{high} neutrophils in MC1 (+11.13 ± 2.71%, p=0.02) (Fig. 1e).

Figure 1. (a) Venn diagram of DEG from total bulk RNAseq (b) Top enriched upregulated BP of autoinflammatory (left) and infectious (right) etiology (c) Cell clustering of autoinflammatory MC1 BM (d) Enrichment of "inflammatory response" gene set in autoinflammatory MC1 neutrophils (e) Representative histogram of CD66b⁺ expression in MC1 and control neutrophils.

Conclusion: Autoinflammatory and infectious etiologies of MC1 have different pathological mechanisms. T-cell and neutrophil activation seem to be important in the autoinflammatory etiology. This has clinical implication as it could be explored for diagnostic approaches to distinguish the two MC1 etiologies and supports developing targeted treatments for both etiologies.

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OP0084

CENTRAL MECHANISMS TRAIT PREDICTS PERSISTENT KNEE OSTEOARTHRITIS PAIN AT 24-MONTHS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

S. Holden^{1,2,3}, D. McWilliams^{1,2,3}, S. Smith^{1,2,3}, D. Walsh^{1,2,3,4}. ¹University of Nottingham, Pain Centre Versus Arthritis, Nottingham, United Kingdom; ²University of Nottingham, NIHR Nottingham Biomedical Research Centre, Nottingham, United Kingdom; ³University of Nottingham, Division of Rheumatology, Orthopaedics and Dermatology, Nottingham, United Kingdom; ⁴Sherwood Forest Hospitals NHS Foundation Trust, Rheumatology, Mansfield, United Kingdom

Background: In the UK, 10% of men and 18% of women over the age of 60 suffer from symptomatic osteoarthritis (OA), and rising. OA knee pain can worsen without significant radiographic changes and pain remains a major problem for up to 20% of patients after total knee joint replacement. Chronic knee OA pain is