1.1 The synovial cytokine milieu shapes synovial pathotypes in rheumatoid arthritis patients via synovial fibroblast–T-cell interactions

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Introduction: Rheumatoid Arthritis (RA) is a chronic inflammatory disease, which is characterized by synovial inflammation resulting in bone and cartilage destruction. Crosstalk between activated fibroblast-like synoviocytes (FLS) and immune cells, such as CD4+ T cells, within the synovium might amplify synovial inflammation and joint destruction. In this study, the interaction profile of activated FLS and CD4+ T cells within an inflammatory setting and its consequence on synovial inflammation is elucidated.

Methods: To screen for factors that activate FLS in RA, isolated FLS were treated with different inflammatory cytokines and transcriptomic changes were measured with RNA-Seq. Fluorescence activated cell sorting (FACS) purified naïve CD4+ T-cells from the same patients were co-cultured with the cytokine pre-treated FLS. Automated fluorescence microscopy and downstream bioinformatic image analysis allowed visualization and quantification of cell-cell interactions. After co-culture T-cells were isolated and T-cell activation, proliferation and differentiation was determined by flow cytometry.

Results: To model the in vivo situation, FLS were pre-stimulated with different pro- and anti-inflammatory cytokines. RNA-seq revealed cytokine specific activation patterns of FLS. Correspondingly, we observed distinct CD4+ T-cells–FLS interaction profiles depending on the cytokine used for FLS activation. In line with distinct interaction profiles, specific patterns in CD4+ T cells activation, proliferation and differentiation of naïve T cells into CD62Lhigh CD45ROhigh memory T cells could be detected. Signatures of cytokine-stimulated FLS could be identified in transcriptomic data from synovial tissue samples.

Conclusion: Within this study, we highlight the role of FLS in orchestrating inflammation-associated synovial tissue remodeling and how cytokine induced CD4+ T cells–FLS interactions impact on T cell development.
studies to examine the value of STAT phosphorylation patterns guiding JAK inhibitor therapy are underway.

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1.3 Distinctive STAT activation patterns subgroup rheumatoid arthritis patients in active disease
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Introduction: In Rheumatoid Arthritis (RA) an imbalance of pro- and anti-inflammatory cytokines and the subsequent activation of the JAK/STAT pathway are hallmarks of disease pathogenesis and progression. Thus, many therapeutic approaches in RA target cytokines, their respective receptors or downstream signaling molecules. If chronically elevated cytokine levels in vivo, however, affect downstream cellular signaling is not measured.

Methods: Whole blood was drawn from 62 consecutive RA patients fulfilling the 2010 EULAR/ACR criteria (median + standard deviation, female ratio: 0.77, age: 64 ± 13 years). Nine healthy controls (HC, female ratio: 0.78, age: 48 ± 5 years) served as control group. Serum interferon gamma (IFNg), interleukin (IL)-6, -10, -12p70, -17A and tumor necrosis factor alpha (TNFα) concentrations were measured using a highly sensitive single molecule array (SIMOA). Assessment of phosphorylated (p)-STAT levels in granulocytes monocytes, B and T-cells was performed by flow cytometry. Geometric mean fluorescence intensities (gMFIs) of pSTAT1/3/5a,b/6 were used as indicators for JAK/STAT pathway activation of B cells. Unsupervised hierarchical clustering showed that 20/28 MDA RA patients shared a profile of increased cytokines. In contrast, 8/28 patients showed no increase in cytokine levels. pSTAT6 levels revealed that pSTAT1/3 and -6 levels in monocytes, granulocytes and T-cells were elevated in HCs but diminished in RA patients. Moreover, pSTAT6 levels of various leucocytes negatively correlated with cytokine levels. Stratification models of MDA RA patients identified 6 patients with low cytokine and pSTAT levels, 9 patients with high cytokine concentrations but no subsequent STAT activation and 11/28 high-profile patients with both elevated cytokine and pSTAT levels.

Conclusion: Here we describe a heterogeneity of serum cytokine milieu and downstream STAT activation in RA patients. We suggest that this observation might predict treatment success of JAK/STAT inhibitors, but further studies are needed for validation.

1.4 Deep immune phenotyping of SLE and RA by machine learning
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Introduction: Breakdown of self-tolerance is an important common mechanism in autoimmunity. Despite considerable clinical heterogeneity, many autoimmune diseases exhibit common immunological mechanisms leading to a breakdown of self-tolerance. Identification of unique and similar patterns across different autoimmune disease may help to understand their pathophysiology better. Establishing workflows for the multi-parameter deep immune phenotyping of T- and B-cells by unsupervised machine learning (ML) methods for feature extraction, cluster analysis and anomaly detection.

Methods: We use machine learning to identify common patterns and dissimilarities between type 1 diabetes (T1D, n = 69), rheumatoid arthritis (RA, n = 63), systemic lupus erythematosus (SLE, n = 38) and healthy controls (n = 69) samples based on multi-plex immune phenotyping. PBMCs were isolated from patients with T1D, RA, SLE, and controls. A flow cytometry-based approach was applied, and a traditional analysis was compared to a ML method implemented in R [1] and based on self-organizing maps. Our pipeline includes unsupervised pre-gating, normalization, FlowSOM clustering [2], and a statistical model (GLMM), to check for significant differential abundances of cell populations among the autoimmune conditions.

Results: After applying our automated workflow to one T cell panel we could identify 14 cell clusters present in all the samples. The GLMM test revealed a cluster with a significant difference (p = 0.035) and a trending one (p = 0.059) on the abundance across the different diseases. In particular, CD4apos T cells expressing high IL-7 receptor (CD127) levels and median amounts of CD15s but low CD25, CD161 and CD45RA are increased in SLE.

Conclusion: This unbiased, unsupervised ML workflow was able to identify canonical and novel clusters of T cells that are similar in RA, SLE and T1D. Additionally, a novel memory T cell population expressing CD15s was shown. This unsupervised analysis approach for large datasets enables the discovery of new immune cell populations complementing traditional workflows.

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1.5 Expression of co-stimulation maker CD19 on B cells is not altered by rituximab intake in patients suffering from systemic sclerosis
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Introduction: CD19 is a membrane glycoprotein interacting with different surface molecules like the B cell receptor (BCR) and is crucial for antigen-independent development as well as immunoglobulin-induced activation of B cells [1]. Alterations in this signalling pathway can incline autoantibody production and systemic autoimmunity in humans. Rituximab (RTX), a CD20 antagonist appears to be an effective candidate in the treatment of different autoimmune diseases that are partly driven by autoimmune B cells, such as systemic sclerosis (SSc) [2]. It has been specu-
lated that RTX might work not only by depleting B cells but also to down regulate activation markers, such as CD19. Thus, this study aimed to give an in-depth analysis of CD19 abundance and activation on B cells in SSc patients with and without RTX treatment.

Methods: Peripheral blood samples from 41 patients suffering from SSc (median ± standard deviation SD, age: 54.3 ± 13.9 years, female ratio: 0.8) and 45 age- and sex-matched healthy controls (HC) (age: 51.0 ± 13.9 years, female ratio: 0.8) were drawn and PBMCs were isolated on-site. We performed flow cytometry analysis on a standardized BD LSRfortessa platform to identify B cell (CD19+/CD20+) subpopulations. The geometric mean fluorescence intensity (gMFI) for CD19 in all B cell subtypes was extracted from the data set and used for further statistical analysis. Additionally, a quantitative flow cytometric bead-based assay (Quantibrite PE kit from Becton Dickinson) was used for the estimation of CD19 antibodies bound per cell.

Results: 3 SSc patients were in high disease activity at the time of blood drawal. 23 patients were under RTX therapy of whom 5 patients still displayed measurable B cells frequencies. Naive B cells made up the most abundant B cell population in SSc patients. The frequency of IgM+/IgD+/CD27– B cells was 67.9% ± 13.2 (mean ± SD), followed by class-switched memory B cells (IgM-/IgD+/CD27+, 10.5 ± 4.9), non-switched memory B cells (IgM+/IgD+/CD27+, 4.0 ± 3.6) and plasma blasts (0.3 ± 4.4). Pairwise Wilcoxon Tests (Bonferroni-corrected for multiple testing) showed significant differences (p < 0.001) between frequencies of naive B cells and all other cell types. In contrast, naive B cells displayed the second lowest CD19 gMFI levels (7601.0 ± 1912.0). Non-switched memory B cells in SSc patients showed the highest CD19 gMFI (10,620 ± 15,689.8), followed by class-switched B cells (9388 ± 3046.8). Plasma blasts displayed the lowest CD19 gMFI levels (4799.0 ± 4185.7). This trajectory in decreasing CD19 gMFI was found in both HCs and SSc patients. We saw a significant reduction in percentages of non-switch B cells and class-switched B cells in SSc patients compared to HCs (4.0 ± 3.6 vs 6.5 ± 4.2, p = 0.029, 10.5 ± 4.9 vs 13.2 ± 7.2 p = 0.04) but an increase in CD19 gMFI in nonswitched B cells (HC: 9204.5 ± 2116.8, p = 0.005). SSc patients under RTX treatment had significantly lower class-switched memory B cell frequencies compared to HCs p = 0.015. RTX did not affect CD19 gMFI or bound CD19 in SSc.

Conclusion: RTX treatment in SSc is not associated with downregulation of the co-stimulation marker CD19. Thus, the main effect of this drug is the reduction of B cells, especially class-switched memory B cells that might have a high capacity to activate other cells involved in the pathogenesis of SSc.

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2.1 Clinical, imaging and blood biomarkers to assess one-year progression risk in fibrotic interstitial lung diseases

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Introduction: We aimed to evaluate biomarkers derived from baseline patient characteristics, computed tomography (CT) and peripheral blood for prognosis of disease progression in fibrotic ILD patients.

Methods: Of 209 subsequent ILD-board patients enregistered, 142 had complete follow-up information and were classified fibrotic ILD as defined by presence of reticulation or honeycombing. Most patients had been diagnosed with autoimmune-associated ILD (24%), followed by idiopathic NSIP (21%) and IPF (16%). Using a standardized semi-quantitative CT evaluation, typical ILD findings like honeycombing or ground glass opacities were added up in 6 defined lung fields. Progression at one year was defined as relative loss of ≥10% in forced vital capacity, of ≥15% in diffusion capacity for carbon monoxide, death, or lung transplant. Two thirds of the patients were randomly assigned to a derivation cohort evaluated for the impact of age, sex, baseline lung function, CT finding scores and blood biomarkers on disease progression. Significant variables were included into a logistic regression model, its results were used to derive a progression risk score which was then applied to the patients.

Results: In the derivation cohort, age, monocyte count ≥0.65G/L, honeycombing and traction bronchiectasis extent had significant impact. Multivariate analyses revealed the variables monocyte count ≥0.65G/L (1 point) and combined honeycombing or traction bronchiectasis score (0 vs. 1–4 (1 point) vs. 5–6 lung fields (2 points)) as significant, so these were used for score development. In the derivation cohort, resulting scores of 0, 1, 2 and 3 accounted for one-year progression rates of 20%, 25%, 46.9% and 88.9%, respectively. Similarly, in the validation cohort, progression at one year occurred in 0%, 23.8%, 53.9% and 62.5%, respectively, a score ≥2 showed 70.6% sensitivity and 67.9% specificity, receiver operating characteristic analysis for the scoring model had an area under the curve of 71.7%.

Conclusion: The extent of honeycombing and traction bronchiectasis, as well as elevated blood monocyte count predicted progression within one year in fibrotic ILD patients.

Abstracts

2 Klinische Studien und Präsentationen
2.2 Altered cellular immune response to vaccination against SARS-CoV-2 in patients with B-cell depleting therapy
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Introduction: B-cell depleting therapies result in diminished humoral immunity following vaccination against COVID-19, but our understanding on the impact on cellular immune responses is limited. Here, we performed a detailed analysis of cellular immunity following mRNA vaccination in patients receiving B-cell depleting therapy.

Methods: We analyzed T-cell responses in autoimmune patients treated with B-cell depleting therapy and healthy controls after mRNA vaccination against COVID-19. We isolated PBMCs and stimulated them with a peptide pool covering the spike protein in vitro. Reactive T-cells were determined by IFNγ ELISPOT assay and staining for effector cytokines by flow cytometry. Anti-SARS-CoV-2 spike receptor-binding domain antibody assays were performed to elucidate B-cell responses. To complement our cellular analysis, we performed immunophenotyping for T- and B-cell subsets.

Results: In this work, we show that SARS-CoV-2 vaccination using mRNA vaccines elicits cellular T-cell responses in patients under B-cell depleting therapy. Some facets of this immune response including TNFα production of CD4+ T-cells and GzmB production of CD8+ T-cells, however, are distinctly diminished in these patients. Consequently, it appears that the finely coordinated process of T-cell activation with a uniform involvement of CD4+ and CD8+ T-cells as seen in HCs is disturbed in autoimmune patients. In addition, we observed that immune cell composition does impact cellular immune responses as well as sustainability of anti-spike antibody titers, a fact that also holds true for healthy individuals.

Conclusion: Our data suggest disturbed cellular immunity following mRNA vaccination in patients treated with B-cell depleting therapy. Immune cell composition may be an important determinant for vaccination efficacy.

2.3 Identifying individuals at risk for Sjögren’s syndrome—The pre-Sjögren syndrome targeted immunology evaluation (PRESTIGE) study
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Introduction: Primary Sjögren’s Syndrome (pSS) is a chronic autoimmune disease. Symptoms range from sicca to systemic, potentially life-threatening organ damage. Little is known about the onset of the disease. Anti-Ro antibodies are described to develop before years to the first symptoms. In addition, first degree relatives of pSS patients have an increased risk of developing pSS. The aim of this study was to identify and follow-up individuals at risk for pSS in order to study symptoms and immune pathology before and at development of pSS.

Methods: In this ongoing long-term study individuals at risk for developing pSS but not fulfilling the ACR-EULAR classification criteria of pSS were included, defined as: (1.) Anti-SSA positive individuals (Anti-SSA +) without any sicca symptoms or diagnosis of an underlying systemic autoimmune disease; (2.) First degree relatives of patients (relatives) with an established diagnosis of pSS and typical autoantibodies (ANA ≥ 1:160 and/or anti-SSA + and/or rheumatoid factor +); (3.) Individuals with at least one feature of the ACR-EULAR classification criteria for pSS, but not fulfilling the criteria (incomplete). At baseline and at annual visits, demographic data, blood, saliva and urine samples were collected and stored. Salivary and lacrimal flow, salivary gland ultrasonography (SGUS), and patient-related outcome measures were analysed. A lip salivary gland biopsy was performed at baseline and upon development of symptoms suggestive of pSS. The primary endpoint was the development of definite pSS according to the ACR-EULAR classification criteria.

Results: After the first year of recruitment, 50 individuals (Anti-SSA+ n = 27, relatives n = 23, incomplete n = 2) were screened at baseline, of whom 28 were identified as individuals at risk for pSS and were included in the study. Twenty-two individuals were excluded from the study, most of whom were “relatives” with negative autoantibodies. Of these 28 individuals at risk, 89% were female (n = 25), they had a median age of 53 years (IQR: 19) and 57% (n = 16) had positive antinuclear antibodies. 86% were positive for anti-SSA and 14% were positive for anti-SSB. Decreased complement C3 and C4 were found in 18% and 4%, respectively. Serum IgG concentration was elevated in 29% of individuals. A reduction of lacrimal flow was found in 29% and stimulated whole salivary flow was reduced in 29%. The median of the ESSPRI was 1.6 (3.0). Eighteen percent of the investigated individuals had a pathological ultrasound [Hoeveier score median 4.5 (9.0)] and in 9% a focus score ≥ 1 [median 0.15 (0.57)] was found in the lip salivary gland biopsies. Four patients (14%) met the primary endpoint and were diagnosed with pSS within the first year.

Conclusion: The design of the PRESTIGE study allows us to follow individuals at risk for pSS and will help to unveil symptoms and immune pathology as pSS develops. We suggest to establish a larger international pre-pSS cohort to increase statistical power.

2.4 Humoral immune response in rituximab treated patients following SARS-CoV2 vaccination
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Introduction: Rituximab (RTX) is a monoclonal antibody targeting CD20 and is known as a cornerstone in the management of haematological disorders and various inflammatory rheumatic diseases. B cell depleting therapy with RTX has an influence on humoral immune response following vaccination. Recent studies are already addressing the effect of a SARS-CoV2-vaccination in patients on B-cell depleting therapies [1, 2]. The key question is as to whether RTX-treated patients can develop a humoral and T-cell-mediated immune response against SARS-CoV-2 following immunization.

Methods: The patient dataset was screened for patients under RTX treatment, were prioritized for mRNA immunization and enrolled. RTX treated patients (n = 17) were vaccinated with the mRNA-1273

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vaccine (Moderna) sequentially, the first dosage in March 2021 following the second in April 2021. Four weeks after the second vaccination, serum samples were obtained to screen for antibodies against the receptor-binding domain (RBD-Cut-off BAU/ml=15), in addition a FACS analysis was carried out and the peripheral CD19+ B cells were determined. The last dosage of RTX was administered 3–9 months before immunization. **Results:** All RTX treated patients (n = 17) showed a peripheral CD19+ B cell count of <0.1 x 10^9/l 4 weeks after the 2nd vaccination. There was a statistically significant correlation between the peripheral B cell count and SARS-CoV2 specific antibody levels <15 BAU/ml (Fig. 1). There were no detectable peripheral CD19+ B cells in patients with RBD antibody levels <15 BAU/ml (p = 0.028).

**Conclusion:** As confirmed in previous studies, in a cohort vaccinated with the mRNA-1273 vaccine, we could also show that patients without detectable CD19+ B cells did not develop specific SARS-CoV2 antibodies. Nevertheless, it is already known that RTX treated patients can build specific antibodies against SARS-CoV2 as soon as the peripheral CD19+ B cells partially repopulate, which should be investigated in more detail. **References**

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### 2.5 First symptoms at the onset of primary Sjögren’s syndrome—the patients’ perspective of a sneaky disease

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**Introduction:** The aim of this study was to investigate patients’ recollection of the first symptoms before diagnosis of PSS in qualitative interviews. The second aim was to verify and quantify these aspects in a representative cohort.

**Methods:** All PSS patients fulfilled the EULAR/ACR 2016 classification criteria. In the first part of the study, consecutive PSS patients were recruited for individual, semi-structured interviews. A discussion guide with five open-ended questions was developed to explore patients’ experiences on the onset of PSS. All interviews were audio-recorded and transcribed verbatim, and an inductive thematic data analysis was performed using MAXQDA software (VERBI, Berlin, Germany). In the second part, the identified aspects of the qualitative analysis were grouped to a checklist with ten items. Patients were asked to complete the checklist before their routine clinical assessment.

**Results:** One-hundred and thirty-four patients participated in the study. The qualitative part was completed by 31 PSS patients; 90.3% (n = 28) were female and patients had a mean disease duration of 6.9 years (±5.7(SD)) and a mean age of 58.1 years (±12.6). Four different major aspects emerged of how patients experienced the beginning and first symptoms of PSS: (1) sicca symptoms started after initial swelling of parotis and/or lymph nodes (2) “Classic” PSS symptoms (fatigue, pain, dryness): patients reported ed wandering joint pain before diagnosis with a long time apart from first symptoms until diagnosis. Patients described joint pain, chronic malaise, and fatigue over months. (3) Hormonal changes (e. g. after birth, hysterectomy) or infections before the onset of PSS symptoms. (4) Slowly progressing discomform due to sicca: patients reported a slow progression of symptoms with no initial recognition of sicca discomfort. In these patients recurrent dental problems and loss of teeth in the years prior to diagnosis was common. In the second part of the study, the four themes were verified in an independent cohort of 103 PSS patients. Patients were 59.9 ±13.7 years old and six patients were male. The main symptom before diagnosis was dryness (n = 77, 74.8%) with wandering joint pain (n = 51, 49.5%) and fatigue (n = 47, 45.6%). In 38.8% (n = 40), patients reported a swelling/inflammation of the parotid gland at the onset of disease.

**Conclusion:** We identified four themes describing the initial symptoms of PSS. Raising awareness of these symptoms among physicians and among the general public may allow earlier diagnosis of PSS.

### 2.6 Defining an acceptable state of quality of life in primary Sjögren’s syndrome

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**Introduction:** To define the threshold of an acceptable QoL state (AQLS) and the minimal detectable change (MDC) of the PSS-QoL.

**Methods:** Data of patients from the PSS registry fulfilling the 2016 ACR/EULAR classification criteria for PSS were analysed. Patients completed the PSS-Qol and ESPIRI (EULAR Sjögren’s syndrome patient-reported index), disease activity was assessed by the ESSDAI (EULAR Sjögren’s syndrome disease activity index) and an evaluator’s global assessment (EGA, scale from 0–10). Receiver operating characteristic curve analyses were used to estimate the AQLS based on patients’ assessment on the extent of HRQL. We selected the optimal cut-off of PSS-Qol by the maximal Youden index. At the follow-up visits after 12 months, patients assessed, whether their HRQL had changed. An anchoring method based on this evaluation was used to estimate the MDC of PSS-Qol. Furthermore, clinical data were compared in AQLS and non-AQLS groups.

**Results:** Data from 152 PSS patients were analysed which of 91.4% (n = 139) were female. The mean age was 59.6 ±12.3 years (± standard deviation) and the mean disease duration was 5.6 ±5.3 years. The AQLS estimate was defined as PSS-Qol ≤ 29.40% (n = 61) were categorized to be in AQLS. Although AQLS patients were significantly younger (56.9 ±11.3 years vs 61.5 ±11.4 years, p < 0.01) they had a longer disease duration (6.9 ±5.8 years vs. 4.7 ±4.7 years, p < 0.05) compared to non-AQLS patients. AQLS patients had a lower EGA (2 [0–5] vs 3 [0–7], p < 0.01 (median [range])), higher IgG (15.7 [7.7–33.8, range] vs 13.1 [6.5–38.1], p < 0.05) and higher rheumatoid-factor IgA (84 [0–500] vs 20 [0–500], p < 0.01). AQLS patients showed significantly lower burden of sicca (measured by ESPIRI and sicca VAS scores). The MDC for PSS-Qol was defined as 12.2 points. After one year, patients’ HRQL did not change in 83.3% and got worse 7.1%.

**Conclusion:** This study determined the AQLS and the minimal detectable change for HRQL. These results will help evaluating the HRQL of patients in clinical practice, as well as possible assistance designing future clinical trials. Patients in AQLS show lower dryness scores but higher immunological activity compared to non-AQLS patients. Longitudinal studies are needed to determine factors affecting patients’ HRQL in PSS.

### 2.7 Prediction of ineffectiveness of biological drugs using machine learning and explainable AI methods

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**Introduction:** Rheumatologists face the challenge of selecting the most effective drug from a variety of biologics taking into account several factors including laboratory values, patient history and demographic data. Machine learning models can help overcoming the complexity of this choice by providing both the probability of success and an explanation for this prediction at the individual patient level. For this purpose, we developed prediction models for 5 different biological drugs using machine learning methods based on patient data derived from the Austrian Biologics Registry (BioReg).
Methods: Data from 1397 patients with 2004 baseline visits and 22 variables with at least 100 treat to target (ttt)-courses per drug were used from the BioReg biologics registry. Starting from the first visit of the ttt-course, different machine learning algorithms were trained for all drugs to predict the risk of ineffectiveness for each biological drug within the first 26 weeks. 5-fold cross-validation and hyperparameter optimization methods were applied to generate the best models. Model quality was assessed using the area under the receiver operator characteristic (AUCROC). Using the Explainable AI method SHAP (SHapley Additive exPlanations; https://shap.readthedocs.io/en/latest/index.html) an approach from the mathematical field of game theory, the risk-reducing and risk-increasing factors were extracted.

Results: The best models per drug achieved an AUCROC-score of: Abatacept: 0.71 (95% CI 0.65–0.77), Adalimumab: 0.69 (95% CI 0.62–0.76), Certolizumab: 0.77 (95% CI 0.67–0.86), Etanercept: 0.69 (95% CI 0.53–0.85), Tocilizumab: 0.74 (95% CI 0.69–0.79). The 10 most predicting factors per drug were: (+: risk-increasing for high values, -: risk-decreasing for high values, 0: nearly neutral; or stated otherwise): Abatacept: VAS _GH_ (+), negative rheumatoid factor (risk-decreasing), age (+), ESR (+), BMI (–), intravenous administration (+), previous aTNF-therapy (+), TJC (–), DAS (–). Adalimumab: GC (+), CRP (–), VAS Ph (–), disease duration (–), HAQ (+), VAS _GH_ (+), age (0), ESR (0), SJC (–), negative rheumatoid factor (risk-increasing).

Certolizumab: dosage (–), previous aTNF-therapy (+), negative rheumatoid factor (risk-increasing), GC (+), age (+), BMI (–), other DMARDs (+), VAS _GH_ (+), SJC (–), HAQ (+). Etanercept: VAS _GH_ (+), VAS Ph (–), anti-CCP positive (+), MTX-Co-therapy (no cotherapy strongly increased the predicted risk, whereas MTX-cotherapy slightly decreased the risk), negative rheumatoid factor (risk-decreasing), GC (+), BMI (–), CRP (–), other DMARDs (–), male gender (+).

Tocilizumab: VAS Ph (+), SJC (–), VAS _GH_ (+), ESR (+), TJC (+), previous aTNF-therapy (+), intravenous administration (–), CRP (+), HAQ (+), BMI (–). Due to the low AUCROC-score (0.63 (95% CI 0.59–0.68)) Golimumab was excluded from further analysis with Explainable AI frameworks.

Conclusion: The results show that the ineffectiveness of some biological drugs can be predicted with promising accuracy, comparable to similar research in (pooled) aTNF therapy [1]. Interestingly, factors that decrease the risk of ineffectiveness for one biological drug are found to be risk-increasing for another, indicating highly complex interactions. Machine Learning can be of help in the decision-process by disentangling these relations.

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2.8 Abdominal aortic calcification in rheumatoid arthritis patients–Results from a large cross-sectional study

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Introduction: Abdominal aortic calcification (AAC) is an often overlooked, but common finding. Despite its predictive value for cardiovascular (CV) events it has received much less attention than the arteries in the coronary system or the carotid vessels. Little is known about AAC in RA patients. Our primary aim was to investigate the prevalence of AAC in RA patients in comparison to the general population.

Methods: We used the National Health and Nutrition Examination Survey (NHANES) data set, a large US cross-sectional study with a complex, multi-stage sampling design, which represents the non-institutionalized civilian resident population in the US. The 2013–2014 data set included measurement of AAC as well as data regarding RA status and comorbidities. Participants aged ≥40 years underwent dual-energy X-ray absorptiometry, including assessment of AAC. The presence of any calcification was accepted as presence of AAC.

Results: RA was associated with a higher prevalence of several CV risk factors: the odds ratio (OR) for arterial hypertension (HTN) was 2.83 (95% CI 1.77–4.52; p<0.001), for diabetes 2.11 (95% CI 1.39–3.20; p=0.001) and for current smoking 1.69 (1.19–2.40; p=0.006). In addition, RA patients had a higher OR for suffering from poverty (OR 2.08; 95% CI 1.35–3.19; p=0.002). Levels of total cholesterol, LDL cholesterol and triglycerides were comparable between the two groups. Chronic kidney disease (CKD) was more prevalent in the RA group and there was also a higher risk of albuminuria in RA patients (OR 1.94; 95% CI 1.18–3.20; p=0.013). In univariate analysis AAC tended to be more prevalent in RA patients (OR 1.64; 95% CI 0.97–2.77) with a borderline significance of p=0.06. After adjustment for potential confounders there was no independent association between RA and AAC (OR 1.23; 95% CI 0.71–2.10; p=0.43). HTN, age and smoking status remained significantly associated with AAC after adjustment.

Conclusion: While a number of traditional CV risk factors were more common in the RA group, RA itself was not independently associated with AA. It appears, that many of these risk factors already explain the presence of AAC in RA patients, more or less as some sort of summary measure of detrimental influences on the CV system. Therefore, the presence of AAC is a valuable piece of information in daily clinical practice and should prompt CV risk management also in RA patients.

2.9 Effectiveness of remote care interventions: a systematic review informing the 2022 EULAR points to consider for remote care in rheumatic and musculoskeletal diseases

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Introduction: To perform a systematic literature review (SLR) on different outcomes of remote care compared with face-to-face (F2F) care, its implementation into clinical practice and to identify drivers and barriers in order to inform a task force formulating the EULAR Points to Consider for remote care in rheumatic and musculoskeletal diseases (RMDs).

Methods: A search strategy was developed and run in Medline (PubMed), Embase and Cochrane Library. Two reviewers independently performed standardised data extraction, synthesis and risk of bias (RoB) assessment.

Results: A total of 2240 references were identified. Forty-seven of them fulfilled the inclusion criteria. Remote monitoring (n=35) was most frequently studied, with telephone/video calls being the most common mode of delivery (n=30). Of the 34 studies investigating outcomes of remote care, the majority addressed efficacy and user perception; 34% and 21% of them, respectively, reported a superiority of remote care as compared with F2F care. Time and cost savings were reported as major benefits, technical aspects as major drawback in the 13 studies that investigated drivers and barriers of remote care. No study addressed remote care implementation. The main limitation of the studies identified was the heterogene-
Abstracts

Table 1 | Characteristics of the RA group and n-RA group

| Exposure variable | RA        | n-RA      | p      |
|-------------------|-----------|-----------|--------|
| Age (years)       | 57.5 (55.8–59.2) | 46.8 (46.0–47.7) | <0.001 |
| Female (%)        | 64.2 (55.7–71.9) | 51.3 (49.7–52.9) | 0.01   |
| AAC (%)           | 38.5 (25.6–53.2) | 27.7 (24.6–31.0) | 0.06   |
| BMI (kg/m²)       | 30.6 (29.5–31.7) | 29.0 (28.6–29.4) | 0.003  |
| RRsys (mmHg)      | 127.8 (125.3–130.4) | 121.4 (120.7–122.1) | <0.001 |
| RRdiast (mmHg)    | 69.6 (67.2–72.1) | 69.7 (68.9–70.5) | 0.94   |
| TC (mg/dl)        | 190.4 (184.3–196.5) | 189.2 (187.2–191.1) | 0.69   |
| LDL (mg/dl)       | 110.5 (103.4–117.5) | 111.1 (109.1–113.0) | 0.86   |
| Triglycerides (mg/dl) | 132.6 (105.2–160.0) | 120.0 (112.7–127.2) | 0.40   |

| Smoker (%)        | Never 45.7 (40.0–51.5) | 57.2 (54.3–60.0) | 0.02   |
|                   | Former 25.5 (17.0–36.3) | 23.5 (21.4–25.7) |       |
|                   | Present 28.8 (20.8–38.4) | 19.3 (17.2–21.6) |       |
| Diabetes (%)      | 18.2 (12.7–25.4) | 9.5 (8.6–10.6) | 0.001  |
| HTN (%)           | 67.2 (55.4–77.1) | 42.0 (40.2–43.8) | <0.001 |
| CKD (%)           | 6.3 (3.6–10.9) | 1.6 (1.3–2.1) | <0.001 |

| Albuminuria (%)   | A1 82.1 (73.0–88.7) | 89.9 (88.6–91.1) | 0.01   |
|                   | A2 14.8 (8.9–23.6) | 8.7 (7.7–9.9) |       |
|                   | A3 3.1 (1.4–6.6) | 1.4 (1.1–1.8) |       |
| Poverty-Index <1  | 25.8 (16.6–37.9) | 14.4 (11.6–17.6) | 0.002  |

Data are represented as proportions (categorical variables) or mean (quantitative variables) with 95% CI.

AAC: abdominal aortic calcification, HTN: arterial hypertension, BMI: body mass index, CKD: chronic kidney disease (defined as creatinine ≥ 1.5 mg/dl), RRsys: systolic blood pressure, RRdiast: diastolic blood pressure, TC: total cholesterol, LDL: low density lipoprotein cholesterol.

Poverty: Poverty was accepted to present if the “Ratio of family income to poverty” is < 1 (according to NHANES).

Table 2 | Multivariable logistic regression analysis for RA and presence of AAC

| Exposure variable | OR    | 95% CI     | p value |
|-------------------|-------|------------|---------|
| RA                | 1.23  | 0.71–2.10  | 0.43    |
| Age category      |       |            |         |
| 40–49             | 1     | –          | Ref.    |
| 50–59             | 1.64  | 1.07–2.53  | 0.03    |
| 60–69             | 2.37  | 1.52–3.69  | 0.001   |
| 70–80             | 8.30  | 5.20–13.27 | <0.001  |
| Smoking status    |       |            |         |
| Never             | 1     | –          | Ref.    |
| Former            | 1.56  | 1.17–2.07  | 0.005   |
| Current           | 2.28  | 1.43–3.65  | 0.002   |
| HTN               | 1.43  | 1.09–1.88  | 0.01    |
| Diabetes          | 1.03  | 0.78–1.36  | 0.80    |
| CKD               | 1.20  | 0.58–2.51  | 0.60    |
| Albuminuria       | 0.99  | 0.71–1.38  | 0.94    |

AAC: abdominal aortic calcification, HTN: arterial hypertension, CKD: chronic kidney disease (defined as creatinine ≥ 1.5 mg/dl), RA: rheumatoid arthritis.

Conclusion: Remote care leads to similar or better results compared with F2F treatment concerning efficacy, safety, adherence and user perception outcomes, with the limitation of heterogeneity and considerable RoB of the available studies.

2.10 Ultrasound based withdrawal of biologics in rheumatoid arthritis (RA-BioStop)

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Introduction: Discontinuation of biological (b)DMARDs may be considered in rheumatoid arthritis (RA) patients in persistent clinical remission[1]. Some earlier studies reported that baseline ultrasound may predict successful tapering or withdrawal of bDMARDs, while others found that ultrasound had little additional value over clinical parameters alone [2, 3]. The majority of these studies, however, were limited by small sample size, inadequate remission criteria and variable tapering regimens. The objective of this study was to test the hypothesis whether ultrasound-verified subclinical inflammation might predict a relapse in RA patients in stringent clinical remission who discontinue bDMARDs.

Methods: Prospective, phase IV clinical trial including RA patients in persistent clinical remission according to the ACR/EULAR criteria treat-
ed with a combination of conventional synthetic (cs)DMARD plus bDMARDs. Upon stopping the bDMARD, 9 study visits were conducted within 52 weeks. At each visit, patients underwent clinical examination and ultrasound of 14 joints. The primary hypothesis was that a Power Doppler (PD) score >0 predicted a relapse until week 16 after bDMARD cessation. Relapse was defined as change from remission to moderate/high disease activity according to the simplified disease activity index.

**Results:** Although 110 patients were required by the protocol, inclusion had to be stopped after reaching 38 (34.5%) due to insufficient recruitment. There were 9, 10 and 13 relapses between baseline and weeks 16, 24 and 52, respectively. Relapses till week 16 tended to be more common in patients without a relapse [mean 2.0 (±1.5), vs. 5.6 (±3.9), p = 0.647], respectively. There were trends towards a higher mean baseline PD score at baseline than in those without [9/30 (30.0%) vs. 0/7 (0%), p = 0.160]. Similar observations were made for weeks 24 [9/30 (30.0%) vs. 1/7 (14.3%), p = 0.647] and 52 [12/30 (40.0%) vs. 1/7 (14.3%), p = 0.383]. Kaplan-Meier plot indicates the relapse-free survival in patients with and without PD+ synovitis at baseline (Fig. 1). PD scores were higher at the time of relapse as compared to the preceding visits [mean difference in the PD score 3.2 (±4.5) points, p = 0.034]. PD scores were also higher at visits preceding a relapse [mean 5.6 (±3.9), n = 13] as compared to the mean PD score across all visits of patients without a relapse [mean 2.0 (±1.5), n = 24, p = 0.003, respectively]. There were trends towards a higher mean baseline PD score in patients who had a relapse between baseline and week 16 as compared to those who remained in remission (5.2 ± 5.8 vs. 2.3 ± 3.0, p = 0.079). Similar observations were made for relapses until weeks 24 and 52. No difference was observed comparing mean residual swollen or tender joint counts at baseline between patients with and without a relapse. There were 9 adverse events. All of them were mild to moderate.

**Conclusion:** In RA patients in strict clinical remission, PD assessment at baseline but not clinical joint count could help identify patients who will relapse after the cessation of a bDMARD. Due to insufficient recruitment and limited power of the present trial, however, no definitive conclusion can be made.

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**Fig. 1.2.10** Kaplan-Meier analysis of relapses according to presence or absence of Power Doppler (PD) synovitis at baseline

**2.11 ACR/EULAR remission criteria for rheumatoid arthritis—2022 revision**

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**Introduction:** More than 10 years ago ACR and EULAR endorsed provisional criteria to define remission in RA, both Boolean and index-based. However, the agreement between these two sets of criteria was moderate, especially if patient global assessment (PGA) was >1 (0–10). Recent studies indicated that a higher threshold for the PGA improved this agreement. We aimed to provide evidence for ACR and EULAR by externally validating a revision of the Boolean remission criteria using a higher PGA threshold and to validate the provisionally endorsed index-based criteria.

**Methods:** Data from 4 randomised trials of biologic disease modifying antirheumatic drugs (bDMARDs) vs. methotrexate (MTX) or placebo were utilised. We tested a higher proposed PGA (Visual Analogue Scale; 0–10) threshold of 2 (Boolean 2.0) vs. the original threshold of 1 (Boolean 1.0). We analysed agreement between the Boolean and index-based criteria (SDAI, CDAI). We further examined how fulfilling each remission definition at 6 months predicted good physical function (HAQ ≤0.5) and radiographic non-progression (predictive validity) at one year. The validity of a Boolean definition omitting the PGA (BooleanX) was also assessed.

**Results:** Data from 2048 trial participants, 1101 with early (disease duration 52 years) and 947 with established RA were included. The proportion of participants in remission at 6 months increased when using Boolean2.0 compared to Boolean1.0 from 14.8–20.6% in early RA and 4.2–6.0% in established RA (Fig. 1). Agreement between Boolean2.0 and the SDAI or CDAI remission criteria was better than for Boolean1.0, particularly in...
early disease (Table 1). Boolean2.0, SDAI and CDAI remission criteria had similar positive likelihood (LR+) ratios to predict radiographic non-progression and a HAQ of ≤0.5 (Table 2). The proportion of participants achieving both good radiographic and functional outcomes, were similar for all remission definitions, from 57–60% (Boolean 1.0, 2.0, pants achieving both good radiographic and functional outcomes, were index-based remission criteria with the addition of classifying more pa-

**Conclusion:** Using the Boolean2.0 definition increases the agreement with fully endorsed by

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### Table 1 | Agreement Rates (% concordantly classified) between different modified Boolean remission definitions with the index-based remission definitions. Provided for 6 months

|          | 6 months |          |          |
|----------|----------|----------|----------|
|          | Boolean1.0 | Boolean2.0 | BooleanX |
| **SDAI** | Early RA | Overall % concordantly classified | 93.4 | 95.9 | 90.8 |
|          | Established RA | Overall % concordantly classified | 98 | 98.2 | 94.6 |
| **CDAI** | Early RA | Overall % concordantly classified | 93.2 | 94.6 | 89.1 |
|          | Established RA | Overall % concordantly classified | 97.7 | 97.1 | 93.3 |

Upper table: Agreement with SDAI remission, lower table with CDAI remission

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### Table 2 | Percent of patients with a HAQ≤0.5, no increase in modified total Sharp Score (mTSS)/no radiographic progression, or both combined among those either fulfilling, or not fulfilling, the respective remission definition (Boolean1.0, Boolean2.0, BooleanX, SDAI-based, CDAI based definitions). Positive Likelihood ratios (LR+) for reaching the respective outcome at 12 months if remission is achieved at 6 months

| Criteria fulfilled | HAQ≤0.5 at 12 months | No increase in mTSS | Combined |
|--------------------|----------------------|---------------------|----------|
|                    | No       | Yes | LR+ | No | Yes | LR+ | No | Yes | LR+ |
| **Early RA**       |          |     |     |    |    |     |    |    |     |
| Boolean1.0         | 43.3     | 85.9 | 6.19 (4.0–9.5) | 65.6 | 78.5 | 1.76 (1.2–2.5) | 31.7 | 67.5 | 3.54 (2.6–4.8) |
| Boolean2.0         | 41.5     | 80.6 | 4.23 (3.1–5.7) | 64.4 | 79.3 | 1.85 (1.4–2.4) | 29.6 | 65.2 | 3.19 (2.5–4.1) |
| BooleanX           | 40.5     | 74.1 | 2.76 (2.3–3.3) | 63.1 | 79.5 | 1.86 (1.4–2.4) | 28.4 | 60.3 | 2.59 (2.1–3.2) |
| SDAI               | 41.4     | 83.3 | 3.88 (3.1–4.9) | 64.6 | 79.2 | 1.83 (1.2–2.5) | 29.7 | 66.7 | 3.41 (2.6–4.4) |
| CDAI               | 41.6     | 83.7 | 4.25 (3.4–5.4) | 64.8 | 78.9 | 1.81 (1.3–2.5) | 29.9 | 67 | 3.46 (2.7–4.5) |
| **Established RA** |          |     |     |    |    |     |    |    |     |
| Boolean1.0         | 29.2     | 72.5 | 5.86 (3.0–11.6) | 32.6 | 37.5 | 1.23 (0.7–2.3) | 12.1 | 22.5 | 2.02 (1.0–4.1) |
| Boolean2.0         | 28.7     | 68.4 | 4.19 (2.5–7.0) | 32.4 | 40.4 | 1.38 (0.8–2.3) | 11.8 | 24.6 | 2.27 (1.3–4.0) |
| BooleanX           | 28.1     | 57.9 | 2.42 (1.6–3.8) | 31.3 | 46.3 | 1.76 (1.2–2.6) | 11.6 | 21.1 | 1.86 (1.2–2.9) |
| SDAI               | 29       | 71.7 | 4.84 (2.7–8.5) | 32.6 | 37 | 1.2 (0.7–2.1) | 12 | 23.9 | 2.19 (1.1–4.2) |
| CDAI               | 28.7     | 76.1 | 4.84 (2.7–8.5) | 32.6 | 37 | 1.2 (0.7–2.1) | 11.8 | 28.3 | 2.74 (1.5–5.1) |
shown to be a valid tool for the evaluation of both cartilage change and bone erosions in RA. We aimed to formulate definitions including semi-quantitative scoring systems for assessing structural damage on US and to test the reliability of such systems in a web-based exercise.

**Methods:** A Delphi survey was prepared by an OMERACT US Working Group (USWG) task force based on a previously published systematic literature review [1] and circulated between members of the group, including statements on normal US appearance of joint components, scanning technique and new definitions and scoring systems for bone erosion and joint malalignment. After agreement was achieved (>75% of grades 4–5 on 1–5 Likert scale) on the statements, still images of metacarpophalangeal and interphalangeal joints 2–5 in RA patients and healthy controls were acquired by taskforce members of the. A dataset of 100 anonymized images, representing various grades of the 3 aspects of structural damage: bone erosions, cartilage change and joint malalignment were created and utilized in two rounds of a web-based exercise. Intra- and inter-reader reliability was almost perfect for bone erosion (kappa: 0.87) and cartilage change (kappa: 0.87) and substantial for malalignment (kappa of 0.72).

**Results:** Four Delphi rounds featuring 19 members were needed in order to reach agreement on a total of 9 statements. 4/12 statements were approved in the first, 2/6 in the second, 1/5 in the third and 2/2 in the fourth round. The final scoring systems and representative images are shown in Fig. 1. Twenty-two members participated in the web-based reliability exercise. The intra-reader reliability was almost perfect for bone erosion (kappa: 0.87) and cartilage change (kappa: 0.83) and substantial for malalignment (kappa of 0.72). The inter-reader reliability was almost perfect for bone erosion (kappa: 0.85), and substantial for cartilage change (kappa: 0.79) and malalignment (0.62).

**Conclusion:** In this first attempt to create a sonographic scoring system encompassing all aspects of structural damage, we demonstrate that US is a reliable tool for evaluating bone erosions, cartilage change and malalignment in the hand joints of patients with RA.

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**2.13 Tenderness and radiographic progression in rheumatoid arthritis and psoriatic arthritis**

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**Introduction:** In inflammatory arthritis swelling is regarded as a sign of synovitis and is associated with radiographic progression. The aim of this study was to assess the predictive value of tenderness in the absence of swelling with consideration of other potential risk factors for subsequent radiographic progression in rheumatoid arthritis (RA) and psoriatic arthritis (PsA).

**Methods:** Clinical and sonographic (greyscale and power Doppler (PD)) examination of 22 joints of the hand were performed in patients with RA and PsA. The impact of tenderness on progression after 2 years was analyzed in non-swollen joints for RA and PsA separately with multilevel mixed logistic regression calculating 3 models adjusting for age, sex, disease duration, PD baseline erosion and joint space narrowing (JSN), swollen joint count and seropositivity.

**Results:** We included 1063 joints in 55 RA patients and 352 joints in 18 PsA patients. In RA, tenderness was associated with radiographic progression even after adjustment (OR 1.85 (95%CI 1.01–3.27), p = 0.047), although the association of PD (OR 2.92 (95%CI 1.71–5.00), p < 0.001) and erosions (OR 4.74 (95%CI 2.44–9.23), p < 0.001) with subsequent structural damage was stronger. In PsA, we found a numerically positive association between tenderness and radiographic progression (OR 1.72 (95%CI 0.71–4.17), p = 0.23). In contrast, similarly to RA, erosions (OR 4.62 (95%CI 1.29–16.54), p = 0.019) and PD (OR 3.30 (95%CI 1.13–9.53), p = 0.029) had a marked effect on subsequent structural damage.

**Conclusion:** Our findings imply that—in contrast to PsA—tenderness in RA is associated with subsequent radiographic damage. In both diseases, ad-
ordinary risk factors, such as sonographic signs for synovitis and baseline radiographic damage are associated with radiographic progression.

3 Kindererheumatologie

3.1 Long-term data of children with chronic non-bacterial osteomyelitis (CNO)-Indicators for remission, disease activity and severe disease

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Introduction: To document the long-term course of CNO, to assess risk factors for severe disease course and to define remission criteria.

Methods: From 2015–2020 all patients with a confirmed diagnosis of CNO, who were registered in the NPRD during their first year of disease course and at least one follow-up visit, were included in this analysis.

Results: Additionally to the previously reported cross-sectional analysis of almost 800 CNO patients, a data set of 314 eligible patients including up to 5 years of follow-up visits was analysed. Selected patients' characteristics are described. The analysis of the location of the lesions showed that the distribution changed over the years. Whereas in the first year of disease course sites like vertebrae or mandible were inflamed (8% and 2% of all affected sites), these sites completely resolved over time, while other sites like pelvis or tibia (18%/20%) remained affected after 5 years. Initially, patients were mainly treated with non-steroidal anti-rheumatic drugs (NSAIDs). Inflammation of pelvis or femur at baseline posed an elevated risk to long term severe disease (OR 1.51/1.61, each p < 0.0001). Other risk factors for severe disease were raising numbers of lesions, elevated erythrocyte sedimentation rate and multifocal disease (defined as more than one lesion) in the beginning. The risk for arthritis increased with the initially higher number of lesions. Items defining remission best were PRDA 1, patient reported pain score and number of inflammatory bone lesions. The composite Childhood health assessment score (C-HAQ) and patient reported overall well-being did not correlate with inactive disease.

Conclusion: The NPRD long-term cohort documents a large number of children and adolescents with CNO. Most of the patients were treated effectively with non-steroidal anti-inflammatory drugs, second-line treatment in a limited number of patients are disease-modifying agents, steroids or bisphosphonates. An improvement of patient-, physician- and caregiver satisfaction was documented, suggesting CNO generally as benign disease with a modest number of complicated disease course. Remission defining items and risk factors for severe disease course were defined.

3.2 Osteoidosteom, auch bei Häftschmerzen eine wichtige Differentialdiagnose – ein Fallbericht

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Einleitung: Im Dezember 2019 wurde uns eine 13 Jahre alte Patientin mit Verdacht auf eine rheumatische Erkrankung zugewiesen.

Methoden: Das Mädchen klagte seit 9 Monaten über Schmerzen in der rechten Hüfte. Diese traten anfänglich nach sportlicher Aktivität auf, später auch nachts. Es wurde zunächst die Diagnose Coxalgie rechts mit Muskelansatzentzündung des Musculus Abductor longus gestellt. Einige Monate später wurde mittels Magnetresonanztomographie eine Partialruptur im Ansatzbereich der iliopsoasamnhe diagnose. Physiotherapie und die kurzfristige Einnahme von Ibuprofen und Paracetamol brachten kaum Besserung. Im November 2019 wurde neuheitlich eine MRT Untersuchung durchgeführt und die Patientin zu uns überwiesen.

Resultate: Bei der Untersuchung zeigten sich bei Beugung des rechten Hüftgelenks Schmerzen an der Innenseite des Oberschenkels proximal. Hier war auch ein deutscher Druckschmerz und ein Muskelhärterbiss. Weiters bestand eine deutliche Muskellatrophy des Musculus Glutea rechts und der Oberschenkelmuskulatur rechts. Laborbefunde waren alle unauffällig. In den von der Patientin mitgebrachten MRT-Bildern zeigte sich das typische Bild eines Osteoidosteoms. Es wurde eine CT-gezielte Radiofrequenzablation durchgeführt. Danach wurde die Patientin rasch beschwerdefrei.

Schlussfolgerungen: Das Osteoidosteom ist ein benigner, Knocheneralter geringer Größe, der von den Osteoplasten ausgeht und vor allem in der Corticalis der langen Röhrenknochen auftritt. Das Erkrankungsalter liegt meist zwischen dem elften und zwanzigsten Lebensjahr. Histologisch typisch ist eine nodusartige Struktur mit einem zellreichen, stark vaskularisierten Gewebe, umgeben von einer oft ausgedehnten Knochenkroste. Die typischen, meist nächtlichen Schmerzen sind durch die Prostaglandinproduktion der Tumorzellen bedingt. Nichtsteroidale Antirheumatika wirken meist schmerzlindernd. Ein Osteoidosteom kann spontan auftreten. Die Therapie ist eine CT-gezielte Radiofrequenzablation des Tumors. Die Diagnose eines Osteoidosteoms kann schwierig sein, da bei gelenknaher Lage eine reaktive Synovitis den diagnostischen Nidus klinisch und auch radiologisch maskieren kann.

4 Rehabilitation

4.1 Rehabilitation bei SLE

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Einleitung: Obwohl Bewegung und Training (in Ergänzung zu Medikation) bei vielen rheumatischen Erkrankungen allgemein empfohlen werden, finden spezifische nicht-pharmakologische Therapiformen bei Patienten mit systemischem Lupus erythematoses (SLE) oft wenig Berücksichtigung bei der Erstellung des individuellen Behandlungsplans. Die EULAR hat in ihren Empfehlungen zur Behandlung des SLE im Jahr 2008 physische Aktivität, Gewichtskontrolle, Nikotinabusus als positive Lebensstilmodifikationen – insbesondere für Patienten mit erhöhtem kardiovaskulären Risiko – empfohlen, wobei die Evidenzlage diesbezüglich nach wie vor überschaubar ist. Es wird nachfolgend der Versuch unternommen, die bestehende Evidenz für nicht-pharmakologische Therapiformen bei SLE aufzuzeigen und mit einer Expertenmeinung aus österreichischarer Sicht zu verbinden.

Methoden: Suche in der PubMed mit den Schlagwörtern „lupus erythematosus“ AND „exercise OR rehabilitation“ ((„lupus vulgaris“ [MeSH Terms] OR([„lupus“ [All Fields] AND „vulgaris“ [All Fields]]) OR„lupus vulgaris“ [All
5 Sonstiges

5.1 Engraftment of NSG-DR4 mice with human mononuclear cells of rheumatoid arthritis patients induces arthritis

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Introduction: Emerging evidence supports an important role for T cells in the genesis of rheumatoid arthritis (RA). The pathogenesis of this incurable disease is still elusive. HLA class II genes however, such as HLA-DRB1*0401 (HLA-DR4), confer the strongest genetic risk and suggest involvement of CD4+ T cells. Existing mouse models mimic specific aspects of the disease but do not fully recapitulate the human immune system. Thereby current research is limited and would profit from a humanized mouse model. We aimed to identify arthritogenic cells by transferring HLA-DR4+ peripheral blood mononuclear cells (PBMC) of RA patients into NSG-DR4 mice. Thereby generating a novel mouse model with inflammatory joint disease, only triggered by the transfer of human immune cells

Methods: Humanized NSG-DR4 mice (NSG-AB6 Tg(HLA-DR4)) were generated by injecting PBMC of HLA-DR4 positive patients or controls. Engraftment within peripheral blood, bone marrow, skin, liver, and spleen was assessed comprehensively using multicolor flow cytometry. Development of RA was monitored by examination of the joints, followed by micro computed tomography analysis and histology. Joints were analyzed regarding pannus formation, bone erosions, cartilage damage, and human cell infiltration.

Results: Here, we show that DR4+ T cells of the peripheral blood of RA patients are capable of inducing an RA-like disease in NSG-DR4 mice. These mice recapitulate different hallmarks of the disease including immune cell infiltration, pannus formation, increased osteoclastogenesis, cartilage damage, and bone erosions. Compared to healthy controls, cells of RA patients are more likely to develop inflammatory joint disease in these mice (RA donor 70% vs. healthy control 20%, p = 0.00196). T-helper 1 (Th1) cells, dominated the human immune cell composition in humice, while regulatory T cells (Tregs) were diminished compared to donor PBMC composition. Transfer of in vitro Th1 polarized T cells increased arthritis incidence.

Conclusion: Arthritogenic cells found in the peripheral blood of RA patients are capable of inducing an RA-like disease in NSG-DR4 mice. This novel mouse model will allow to identify these cells on a patient-personalized level.
Abstracts

5.2 Felty-Syndrom – Fallbericht aus der Rheuma-Ambulanz St. Pölten

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Einleitung: Das Felty-Syndrom wurde im Jahr 1924 vom US-amerikanischen Arzt Augustus Roi Felty als eine Trias aus chronischer Arthritis, Splenomegalie und Leukopenie erstmals beschrieben. Auch fast 100 Jahre danach stellt dieses Krankheitsbild mitunter noch eine diagnostische und therapeutische Herausforderung dar. Dieser Fallbericht aus der Rheuma-Ambulanz St. Pölten veranschaulicht mögliche Probleme und gibt außerdem eine aktuelle Übersicht über einzelne Aspekte des Felty-Syndroms.

Methoden: Ein 42-jähriger Mann mit vorbekannter seropositiver rheumatoide Arthritis wurde zur Abklärung einer neu aufgetretenen Panzytopenie sowie multipler Hautulzerationen stationär aufgenommen. Zum Ausschluss einer malignen Ursache erfolgten eine Beckenkammbiopsie, eine Sonographie der Lymphknotenstationen sowie eine CT Thorax/Abdomen. Letztlich wurde die Diagnose eines Felty-Syndroms gestellt und eine Therapie mit Methotrexat in Woche 3 eingeleitet, welche kurz darauf (Woche 4) um Rituximab ergänzt wurde (1000 mg an Tag 1 und Tag 15). Begleitend erfolgte die Gabe von G-CSF und Prednisolon. Bei inadäquatem Ansprechen bzgl. Arthritis und Neutrophilenzahl war im Verlauf die Umstellung von Methotrexat auf Hydroxychloroquin geplant, welche aufgrund von Incompliance jedoch nicht möglich war. Die derzeitige Therapie besteht aus Rituximab, G-CSF und Prednisolon. Weitere Thera-

Abb. 1|5.1 a–d Hämoglobin-Gehalt (Hb), absolute Neutrophilenzahl (ANC), Thrombozyten (PLT) sowie C-reaktives Protein (CRP) im zeitlichen Verlauf (in Wochen, ab Beginn des ersten Krankenhausaufenthaltes). Der jeweilige untere Referenzwert für Hb, ANC, PLT bzw. der obere Referenzwert für CRP sind als orange horizontale Linien gekennzeichnet: Hb: 13.5 g/dL, ANC: 1.5 × 10^9/L, PLT: 150 × 10^9/L, CRP: 0.5 mg/dL. Abbildung D zeigt zusätzlich zum CRP-Verlauf die eingenommene Prednisolon-Dosis. Weiters sind folgende Ereignisse innerhalb der Diagramme gekennzeichnet: 1: Prednisolon-Steigerung auf 50 mg tgl. – nach 1 Woche; 2: Beginn mit Methotrexat p. o. (20 mg 1× wöchentlich) – nach 3 Wochen; 3: 1. Gabe Rituximab 1000 mg – nach 4 Wochen; 4: 2. Gabe Rituximab 1000 mg – nach 6 Wochen; 5: Umstellung auf Methotrexat s. c. (25 mg 1× wöchentlich) – nach 13 Wochen; 6: Fieberhafter Infekt mit CRP- und ANC-Anstieg – nach 16 Wochen; 7: ANC Abnahme aufgrund fehlender G-CSF Applikation bei Incompliance – nach 32 Wochen; 8: Beendigung von Methotrexat, Prednisolon-Reduktion auf 12.5 mg täglich, zweiter Zyklus Rituximab (1000 mg am Tag 1 sowie Tag 15) – nach 34 Wochen; 9: Ausdehnung des G-CSF Intervalls von einmal alle 5 Tage auf einmal wöchentlich – nach 50 Wochen

Abb. 2|5.1 a Hautulzerationen femoral links (a) sowie gluteal rechts (b) zum Aufnahmezeitpunkt
pieption (Splenektomie, Versuch mit JAK-Inhibitor) werden aktuell diskutiert. Der Patient ist weiterhin in unserer Ambulanz angebunden zur regelmäßigen klinischen und labordiagnostischen Verlaufskontrolle.

Resultate: Sowohl Anämie als auch Thrombopenie besserten sich bereits in den ersten Wochen (siehe Abb. 1), zur Aufrechterhaltung einer stabilen Neutrophilenzahl war aber bis Woche 7 eine zweitägliche G-CSF Gabe (Filgrastim 480 µg) notwendig. Auch die Prednisolon-Dosis konnte von initial 50 mg täglich nur langsam reduziert werden auf zuletzt 12.5 mg täglich in Woche 50. Die Hautulzerationen (siehe Abb. 2) heilten unter der immunsuppressiven Therapie vollständig ab. Die G-CSF Therapie wurde im betrachteten Zeitraum von 50 Wochen gut vertragen, derzeit erfolgt die Applikation einmal wöchentlich. In der initialen Beckenamputations war eine klonale T-Zellenpopulation nachweisbar, ohne jedoch die Kriterien einer T-LGL Leukämie zu erfüllen. DBzl: ist eine durchflusszytometrische Kontrolle im weiteren Verlauf geplant.

Schlussfolgerungen: Das Feltys-Syndrom ist ein seltener und mitunter schwer behandlbares Krankheitsbild. Zwar hat sich die Prognose durch den Einsatz von Methotrexat, Rituximab und G-CSF in den letzten Jahrzehnten deutlich verbessert, allerdings bedarf es in Zukunft, wie durch diesen Fallbericht verdeutlicht, weiterer Therapieoptionen. JAK-Inhibitoren zeigten eine Verbesserung der Neutropenie bei Patienten mit rheumatoider Arthritis und T-LGL-Leukämie. Da das Feltysyndrom pathogenetische Gemeinsamkeiten mit der T-LGL-Leukämie haben dürfte, könnten JAK-Inhibitoren eventuell auch in der Therapie des Feltys-Syndroms nützlich werden.

5.3 Innovation in rheumatology teaching–The RheumEscape room

Reisch M, Kickinger D, Sautner J, Bosch P, Puchner R, Dejaco C

Introduction: Over the years, methods in medical teaching have changed giving more emphasis on applied medicine, critical thinking and learner-centered activity. An Escape Room (ER) is a popular adventure game, where participants have to cooperate as a team to escape from a locked room by completing tasks and solving a series of puzzles. ERs can also be used in medical teaching as an entertaining way to acquire or refresh knowledge, to support critical thinking and team building as well as to improve communicative, technical and non-technical skills. We adapted this game design and created an ER in rheumatology with the objective to transfer a defined amount of knowledge in rheumatology to medical students and residents.

Methods: An educational ER in the field of rheumatology was developed and performed nine times with four to six medical students or residents per session. All groups had to complete the ER within 90 min including a briefing of 15 min. In the ER, the participants had to use their rheumatological knowledge, critical thinking and teamwork to unlock several puzzles on various rheumatological topics. The focus of the content was mainly on frequent diseases, common therapeutic problems and the implication of assessment tools. Afterwards, a didactic debriefing was done, giving a summary of all riddles and answering questions of the participants. To test the feasibility and effectiveness of this new teaching method, students and residents were asked to complete an anonymous feedback form with 15 questions. The answers of ten questions were rated on a 10-point Likert scale (0 = does not apply; 10 = totally applies). Furthermore, five questions were in a single (n = 4) or multiple-choice format (n = 1). Descriptive statistics were conducted to summarize the data.

Results: A total of 28 medical students and 19 residents completed the questionnaire. On a 10-point scale, the participants rated on average with 8.9 points [standard deviation 1.92; range 5–10] that they acquired new medical skills and with 8.9 points [standard deviation 1.92; range 5–10] that they enhanced their knowledge in rheumatology. All medical students and residents had the feeling, that they could participate actively in this game-based learning method. On average, they responded with 9.9 points [0.15; 9–10] that the ER was entertaining and 9.7 points [0.15; 9–10] that teambuilding was improved by the game. Furthermore, they gave a score of 9.7 points [0.15; 9–10] that they would recommend this learning method to a friend and a score of 9.9 points [0.14; 8–10] that they wanted to do a medical ER again.

Conclusion: A rheumatological ER is a unique complementary approach for medical education. It is a feasible and entertaining way of teaching, associated with a perceived increase in rheumatological knowledge, teambuilding and communication skills. Further studies assessing the level of competence before and after the ER are needed to ensure the learning success and to compare the rheumatological ER with other traditional teaching methods.

6 Fallstudien

6.1 Fallbericht einer Jugendlichen mit Takayasu Arteritis

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Einleitung: Dieser Fallbericht handelt von einer 15-jährigen Patientin, bei welcher seit ca. 2 Monaten rez. verschwommenes Sehen, vermehrter Schwindel mit Kollapsneigung sowie Kopfschmerzen und Sensibilitätsstörungen in den Extremitäten bestanden. Die linke Körperhälfte sei seit Beginn der Beschwerden vermehrt blass, eingeschränkt beweglich und leicht schmerzhaft, zusätzlich bestünden Hypäththesien, besonders bei Aktivität, ohne Krafteinbuße. Im Jänner 2020 erfolgte bei fragl. Halbseitensymptomatik die Vorstellung beim Kinderkardiologen, welcher mittels US eine schwere, beinahe komplette Stenose der Halsarterien feststellte. Acetylsalicylat wurde begonnen und eine MR-Angio organisiert, hier zeigten sich folgende Pathologien: Der Tr. brachiocephalicus, die rechten Aa. subclav. und carotis com. waren nicht darstellbar. Im Abgangsbereich der li. a. subclavia (ASS) zeigte sich eine höhergradige 15 mm lange Stenose. Nach dieser Stenose geht die sehr kaliberstarke li. a. vertebralis (AVS) ab, die nicht stenosiert ist. Die re. a. vertebr. ist retrograd perfundiert bis Höhe C5, dann weiter proximal verschlossen. Somit ist die AVS das einzige hirnversorgende Gefäß. Aufgrund dieses Befundes erfolgte die stationäre Aufnahme bei v.a. Takayasu Arteritis. In den immunol. Befunden zeigten sich ANA 1:160 nuklear, RSG 18/46 mm/h und ein Calprotectin von 15119 ng/ml. Es bestand eine deutliche RR-Differenz, mit normot. bzw. hypot. an den OEH und hypert. Werten an den UE. Es wurde sogleich mit einem Cortisonstoß begonnen und anschließend mit Prednisolon 1 mg/kg/d fortgesetzt. Zwei Tage darauf wurde die immunsupp. Therapie um den IL-6-Rezeptoranagonisten Tocilizumab (400 mg i.v.) erweitert. In der Dopplersonographie der Halsgefäße zeigte sich ein Verschluss der großen oberen Gefäße konsistent mit den Befunden des MRTs. Es wurde zur weiteren Diagnostik ein PET/MRT sowie ein CT der supraaortalen Gefäße durchgeführt, in welchen sich kein Nachweis einer floriden Arteritis zeigte. Im CT bestätigte sich ein vollständiger Verschluss der A. carotis int. bds., eine ausgeprägte Kollateralenbildung über die Halsmuskulaturgefäße mit Kontrastierung der cran. Gefäße über die beiden Aa. vertebr. Die rechte, proximal verschlossene A. vertebr. wird hierbei auf Höhe HWK6 über Kollateralen versorgt. Die kaliberkräftigeren AVS entspringt mit höchstgradiger kurzstreckiger Abgangstenose der ASS poststenotisch aus eben dieser. Somit ist die AVS das einzige hirnversorgende Gefäß. Ende Jänner erfolgte per Thorakotomie eine Anlage eines GoreTex-Graff (6 mm) von der Aorta ascend. auf die ASS um eine adäquate Versorgung des Gehirns.
zu gewährleisten, indem die langstreckige Stenose der ASS vor Abgang der AVS überbrückt wird. Postoperativ wurde niedrig dosiert Acetylsalicylat re-etabliert und mit einem ADP-Rezeptorantagonisten ergänzt, die immununsup. Therapie mit Tocilizumab wurde nach 3 i.v.-Gaben auf s.c. (162 mg zuerst wöchentlich, dann 2-wöchentlich) umgestellt. Prednisolon konnte ausgeschlichen werden.

Schlussfolgerungen: Zusammenfassend liegt bei der Patientin eine Takayasu Arteriitis mit Befall der von der Aorta abgehenden Halsgefäße und der linksseitigen A. subclavia vor, welche durch Arteriosklerose links, einem nicht messbaren Blutdruck des linken Arms und durch Sehstörungen und Schwindel auffiel. Die immununsuppressive Therapie und vor allem chirurgische Sanierung im Sinne der Schaffung eines Ascendens-Subclavia-AVS) gewährleistet und die Patientin vorerst vor neuropathologischen Komplikationen bewahren. Die Patientin steht lebenslang unter doppelter Plättchenhemmung mit Acetylsalicylsäure und Clopidogrel, ebenso ist eine langdauernde immunsuppressive Therapie (derzeit Tocilizumab 162 mg/2 Wochen) notwendig. Im weiteren Verlauf wurde zweimal (04/20, 03/22) eine Dilatation des Bypasses durchgeführt.

6.2 Sind IgG4 wirklich wichtig?
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Einleitung: Ein 62-jähriger Mann ohne Begleiterkrankungen kam mit Bauchschmerzen in die Notaufnahme. Die körperliche Untersuchung war unauffällig. Die Laborwerte sind in Tab. 1 aufgeführt. Die kontrastmittelverstärkte CT (Abb. 1a–d) zeigte eine Weichteilgewebsvermehrung um die thorakale und infrarenale Aorta (die den rechten Harnleiter umschloss und eine Hydronephrose verursachte); auch eine sklerosierende Pankreatitis (SP) wurde festgestellt. Das PET-CT zeigte, dass die periaortalen Veränderungen hypermetabolisch waren (SUVmax von 8). Die chirurgische Biopsie des perivasculären Gewebes zeigte ein entzündliches Infiltrat, bestehend aus Plasmazellen (PC), Lymphozyten und storiformer Fibrose (Abb. 1e–f). Diese Merkmale wurden als vereinbar mit einer idiopathischen fibroinflammatorischen Erkrankung angesehen, und es wurde mit Prednison 0,7 mg/kg/Tag begonnen. Der Patient wurde dann in unsere Klinik überwiesen. Aufgrund der Assoziation von retinalen Merkmalen mit dichtem lymphoplasmozytärem Infiltrat und storiformer Fibrose (etwa ein Fünftel IgG4-haltig erscheinen im GFR), d. h., etwa ein Fünftel IgG4-haltig erscheinen. Die Skalenbalken entsprechen 75 µm. Die Hämatoxylin-Eosin-Färbung (Abb. 1g–h) zeigt zahlreiche Plasmazellen (etwa 30/hpf), von denen bei der immunhistochemischen Analyse (Abb. 1i–k) etwa ein Fünftel IgG4-haltig erscheinen.
Ein seltsamer Fall von aseptischer Meningitis bei einer Patientin mit rheumatoider Arthritis

Zandonella Callegher S, Zampogna G, Weissteiner S, Bond M, Dejaco C

Einleitung: Wir berichten über den Fall einer 51-jährigen Frau mit seropositiver rheumatoider Arthritis (RA), die sechs Monate nach dem Beginn einer Therapie mit Adalimumab eine aseptische Meningitis entwickelte. Die Therapie wurde im Februar 2020 begonnen und führte nach 3 Monaten zu einer klinischen Remission. Im Oktober 2020 wurde die Patientin erstmals wegen Kopfschmerzen, Fieber und schmerzhaften, insbesondere tuberkulösen Meningitis erstmals in die neurologische Abteilung eingeliefert, weil sie zwei kurzzeitige Episoden einer plötzlichen, selbstlimitierten rechtsseitigen Parästhesie der rechten Körperhälfte erlitt. Die neurologische Untersuchung ergab keinen Hinweis auf ein infektiöses Geschehen oder eine Krebserkrankung. Aufgrund der diagnostischen Ungewissheit wurde eine pachy- als auch leptomeningeale Biopsie durchgeführt. Die präoperative MRT zeigte eine deutliche Progression der Meningitis mit diffuser meningealer Kontrastmittelanreicherung in der linken Hemisphäre. Die Histologie ergab in Folge eine chronische nekrotisierende granulomatose Pachy- und Leptomeningitis.

Die Polymerase-Kettenreaktion war negativ für Tuberkulose und andere Mykobakterien. Es wurde die Arbeitsdiagnose einer Anti-Tumor-Nekrosefaktor (TNF)-α-Therapie-assoziierten aseptischen Meningitis (TAAM) gestellt und Adalimumab wurde im November 2021 abgesetzt. Danach zeigte die MRT eine deutliche Verringerung der Kontrastmittelanreicherung. Einige Wochen später stellte die Patientin Adalimumab im November 2021 als Folge der Operation eingeleitet. Die durchgeführte Analyse ergab keinen Hinweis auf ein infektiöses Geschehen oder eine Krebserkrankung. Aufgrund der diagnostischen Ungewissheit wurde eine pachy- als auch leptomeningeale Biopsie durchgeführt. Die praoperative MRT zeigte eine deutliche Progression der Meningitis mit diffuser meningealer Kontrastmittelanreicherung in der linken Hemisphäre. Die Histologie ergab in Folge eine chronische nekrotisierende granulomatose Pachy- und Leptomeningitis.

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der Patient ungeschützten Geschlechtsverkehr. Aufgrund der Klinik und Anamnese wurde der Verdacht auf eine Affenpocken-Infektion gestellt. Die Diagnosesicherung der Affenpocken-Virus-Infektion erfolgte durch PCR Analyse (Polymerase-Kettenreaktion) von Proben aus zwei verschiedenen Hautläsionen – („cycle threshold“, CT-Wert 20 bzw. 21). Der Patient wurde bei milder Symptomatik in die Selbstisolation entlassen. Elf Tage später, am Ende der Quarantäne, zeigte sich das Exanthem und die Lymphadenopathie vollständig abgeklungen. Auffällig war eine neu aufgetretene ausgeprägte, schmerzhafte Schwellung des rechten Kniegelenkes. Der Patient wurde daraufhin an der Abteilung für Rheumatologie und Osteologie vorstellig. Laborchemisch fanden sich, bis auf ein leicht erhöhtes C-reactives Protein (CRP) von 18 mg/L, keine weiteren Auffälligkeiten. Die gesamte Rheumaserozologie war negativ. Die Arthrosenografie zeigte einen deutlichen Gelenkerguss rechts. Mittels Arthrozentese konnten 60 ml trübe Synovialflüssigkeit gewonnen werden. Die Analyse der Synovialflüssigkeit ergab das Bild einer unspezifischen Arthritis (Zellzahl 16.127/µl, 88,5 % mononuklearen Zellen (Lymphozyten), 11,5 % neutrophile Granulozyten). Eine ergänzende PCR Analyse des Punktats erbrachte einen positiven Nachweis des Affenpockenvirus (CT-Wert 27). Eine Magnetresonanztomographie (MRT) des rechten Kniegelenkes ergab neben einer Synovitis mit Resterguss ein ausgeprägtes Ödem des medialen Femurkondyls mit subchondraler Demarkationszone von 1 cm, dem Bild einer Osteomyelitis entsprechend. Eine symptomatische Therapie mit nichtsteroidalen Antirheumatika (NSAR) wurde etabliert. Darunter kam es innerhalb von drei Wochen zu einer deutlichen Verbesserung der Arthralgien und einem Rückgang der Gelenkschwellung.

Schlussfolgerungen: In der Literatur finden sich Nachweise des Affenpocken-Virus in Nasen-Rachen-Abstrichen, aus Haut- und Schleimhautläsionen, Sperma, Speichel, Urin, Stuhl und direkt aus Blutproben. Dies ist der erste dokumentierte direkte Virusnachweis aus Synovialflüssigkeit und stellt somit die erste Beschreibung einer Affenpocken-assoziierten akuten Arthritis dar. Viren sind, nach Bakterien, häufige Auslöser von infektiösen Arthritiden, jedoch ist das Auftreten einer viralen Osteomyelitis eine Rarität. Speziell bei Pockeninfektionen ist das Auftreten der sogenannten Osteomyelitis variolosa eine bekannte Komplikation und wird in der Literatur mit einer Prävalenz von 2–5 % der infizierten Kinder und 0,25–0,5 % aller mit Pocken infizierten PatientInnen angegeben. In Anbetracht der Tatsache, dass das Variola-Virus und das Affenpocken-Virus eng miteinander verwandt sind, beide aus der Familie der Orthopoxviren, kann eine virale Osteomyelitis als Ursache der Knochenaufzüchtungen im aktuellen Fall angenommen werden.

6.5 Pancreatitis-Panniculitis-Polyarthritis-Syndrome—a hidden diagnosis—case report

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Introduction: PPP—the combination of pancreatitis, panniculitis and polyarthritis is a rare, systemic syndrome that occurs in patients with acute or chronic pancreatitis or pancreatic malignancies. The early detection of this triad, especially in patients without any indicating abdominal symptoms, can avoid delays in specific diagnostic steps and therapy. A 50-year-old male patient presented with increasing joint pain and polyarthralgia in wrists and ankles for one week, impairing his ability to walk without additional aids for three days. The physical examination showed isolated nodules on the lower extremities on the extensor, as well as the flexor sides without any tenderness to pressure (Fig. 1), also the patient presented with multiple swollen joints (polyarthritis). Laboratory tests showed elevated pancreatic enzymes. Pancreatitis was assumed and verified by abdominal CT-scan, showing signs of chronic pancreatitis with concretions in the pancreatic duct. The diagnosis of panniculitis was confirmed by dermatological consultation. Concerning pancreatitis and panniculitis, the patient was hardly affected. In accordance to pre-existing literature, oral glucocorticoid therapy and NSAIDs failed to improve pain or polyarthralgia. Endosonography showed signs of chronic pancreatitis with calcifications, as well as acute inflammation of the pancreatic head. Subsequently ERCP was performed, the pancreatic duct was dilated, concretions were removed and a stent was implanted. Following ERCP, an instant decrease of pancreatic enzymes was observed, accompanied by a clear and sustained improvement of given polyarthritis.

Abb. 1|6.4 ▶ Knieschwellung (a), Haut Läsion (b), MRT des Knie mit subchondraler Demarkationszone und Erguss (c–e)

Fig. 1|6.5 ▶ Panniculitis of the lower limbs
Conclusion: The typical triad of clinical findings in mind, one should consider the PPP-syndrome in the context of acute or chronic pancreatitis. Panniculitis is often confused with erythema nodosum, which can lead to diagnostic delays and incorrect therapy. Regarding PPP, arthritis is usually chronic and responds poorly to NSAIDs or corticosteroids. A rare, but dreaded complication is a sudden increase in swelling of joints, leading to perforation and necrosis within a few days, requiring necrosectomy, incision, and debridement on all four limbs. All involved disciplines (gastroenterology, dermatology and rheumatology) should be familiar with this rare but severe condition. The prognosis depends on the extent of functional deficit of the extremities and the progression of pancreatitis.

Hinweis des Verlags. Der Verlag bleibt in Hinblick auf geografische Zuordnungen und Gebietsbezeichnungen in veröffentlichten Karten und Institutsadressen neutral.
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Buchbesprechung

Stephan Schindele, Grey Giddins, Philippe Bellemère
Arthroplasty in Hand Surgery
FESSH Instructional Course Book 2020

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Dieses Buch behandelt ein zentrales Thema in der Handchirurgie. Die Herausgeber und Autoren sind international anerkannte Spezialisten auf ihrem Fachgebiet.

Das Layout ist zeitgemäß. Die großzügigen und farbigen Abbildungen vermitteln zusammen mit dem Text didaktisch ausgezeichnet die Kapitelinhalte. Zeitgemäß wird ein Online-Zugang für das eBook vorgehalten.

Das Buch ist in 5 Abschnitte unterteilt. Zunächst wird die Anatomie des Handskeletts, speziell der Finger- und Handgelenke, abgehandelt. Martin Langer und Mitautoren haben in diesem Kapitel wieder ein Meisterwerk an hervorragenden zeichnerischen Perspektiven und Details präsentiert, die man in keinem anatomischen Atlas finden kann. Es folgt die Vorstellung der Grundlagen der Arthroplastik. Wichtige Aspekte, wie beispielsweise Implantat-Abrieb, Ermüdungsrissigkeit usw., werden dargelegt und vertieft das Verständnis für das Kunstgelenk an der Hand. Elisabeth Hagert und Susanne Reis arbeiten die Bedeutung der Propriozeption im Rahmen der Daumen- und Handgelenkarthroplastik auf. Der erste Abschnitt wird dann durch das Norwegische Prothesen-Register und die historische Entwicklung der Prothetik abgerundet. Der zweite Abschnitt beschäftigt sich mit den Finger- und Handgelenken. In diesem Zusammenhang werden sowohl die Silikon-Platzhalter als auch moderne Oberflächenersatz-Prothesen, sowie der vaskularisierte Zahnersatz für Fingergrund- und -mittelgelenken vorgestellt. In der nachfolgenden Sektion werden die Gelenkerkrankungen des Daumens mit den verschiedenen Therapieoptionen erfasst. Der vierte Abschnitt schildert die verschiedenen Strategien am Handgelenk, wobei verschiedene Prothesen aufgrund unterschiedlicher Indikationen systematisch abgehandelt werden. Zum Schluss werden die Therapiestrategien für das distale Radioulnargelenk vorgestellt.

Die einzelnen Abschnitte beginnen jeweils mit einer Übersicht über die Thematik, um dem Leser eine fundierte Einführung in diese hochspezifische Thematik zu ermöglichen. Das Buch überzeugt durch die systematische Gliederung. Das jeweilige Thema wird sorgfältig aufgearbeitet und die Autoren sind bemüht, die Inhalte trotz der Informationsmenge fokussiert vorzustellen. Die Kapitel sind strukturiert und logisch aufgebaut und basieren auf umfassenden und aktuellen Literaturverzeichnissen. Die Kapitel bestehen durch eindrückliche Abbildungen und Zeichnungen.

Die Essenz der meisten Kapitel findet man am Ende der jeweiligen Abschnitte. Hier werden äußerst wertvolle und relevante Informationen für den Leser zusammengefasst. Diese Abschnitte sind das Kondensat des jeweiligen Themas und der unverzichtbare Kern der Kapitel.

Dieses Werk besticht durch seine Vollständigkeit bei gleichzeitiger Fokussierung auf die wesentlichen Aspekte und ist damit eine unverzichtbare Bereicherung für den/die Handchirurgen/-in.

C. Spies (Bad Rappenau)