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Ultrasound advanced I & II

SP0075 ULTRASOUND AND MAGNETIC RESONANCE IMAGING FUSION OF IMAGES EVALUATION OF TENOSYNOVITIS – A PILOT STUDY ON A NEW IMAGING TECHNIQUE IN RHEUMATOID ARTHRITIS PATIENTS

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Background/Purpose: Image fusion is an advanced imaging technology, which enables fusion of ultrasound (US) and magnetic resonance imaging (MRI). This fusion gives for each US probe position an exact projection of the corresponding anatomical area on a previously obtained MR image, during a live US assessment. This study is the first to address image fusion of US and MRI tenosynovitis.
The aim of this study was to assess and compare US and MRI visualisation of tenosynovitis using image fusion technique.
Methods: Fifteen rheumatoid arthritis patients with US verified tenosynovitis in the wrist or hand had an MRI performed of the affected wrist or hand. A subsequent image fusion was performed, i.e. the MR images and a live US assessment of one tendon sheath were fused. In order to compare the two imaging modalities quantitatively, the area of the tendon and tendon sheath in the transverse axis was measured on US and MRI for each image fusion. Due to partial volume artefacts (voxel containing two different tissues and therefore possessing a signal average of tendon and tendon sheath) on MRI two measures were performed; area 1) the circumference of the black tendon, i.e. excluding voxels containing two types of tissue 2) the circumference of the grey line that surrounds the black tendon, i.e. including voxels containing two types of tissue. Tenosynovitis was assessed using the proposed OMERACT semi-quantitative scoring system for US and MRI. US scoring was therefore based on both grey scale and Doppler, whereas MRI scoring was based only on post-contrast tenosynovial enhancement, measured as distance from the tendon to end of the enhanced tendon sheath.
Results: The median circumference area of the tendons and tendon sheaths on US and MRI 1 and 2 were respectively 0.16 (25;75 pctl: 0.10;0.25), 0.9 (0.06–0.18) and 0.13 of (0.10;0.25) for the tendons and 0.18 (0.13–0.26), 0.27 (0.20–0.45) and 0.23 (0.16–0.40) for the tendon sheaths. Statistically significant differences were found for all measured areas between US and MRI, except for the US tendon area and the MRI tendon area 2 (Wilcoxon's test; p=0.47). Overall agreement between US and MRI tenosynovitis scoring systems was good (see table 1).
Conclusion: In conclusion, we found that US and MRI have good agreement for quantitative assessment of tendons and scoring of tenosynovitis, when comparing the two modalities using image fusion, if the partial volume artefacts on MRI are included in the measure.
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SP0076 HOW AND WHEN TO ASSESS THE CERVICAL FACET JOINTS + DEMO

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At any given time, 10% of the adult population will be affected by neck pain. Although similar in incidence to low back pain, its has less of a socio-economic impact and uncommonly progresses to neurologic deficit. Pain may result from degenerative, traumatic or inflammatory processes involving the diarthrodial facet (zygapophyseal) joints and/or the facet (medial branch of the dorsal dorsal rami) nerves. Although routinely evaluated by radiography, magnetic resonance imaging and computed tomography, high-resolution musculoskeletal ultrasound (MSKUS) imaging and guidance has become increasingly popular, particularly among pain management specialists, in the evaluation and treatment of these structures owing to its safety, portability, superior resolution and direct real-time visualization. This presentation will discuss the unique anatomy and sonoanatomy of the cervical spine and its innervation/vascularization with particular focus on the facet joints and nerves and the use of MSKUS in the evaluation and treatment of the facet joint/nerve with review of available evidence. Examination technique and sonoanatomic findings will be demonstrated.
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SP0077 HOW TO EVALUATE JOINTS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Ultrasound (US) has numerous advantages when used to examine joints in children compared to other imaging modalities. This include non-invasiveness, rapidity of performance, easy repeatability, high patient acceptability and lack of exposure to ionizing radiation. In addition, it does not require sedation for scanning in younger children. US is more sensitive than physical examination and may detect early disease that is not evident on physical examination. Lack of standardized precise definitions of grey scale (GS) and Power Doppler (PD) US findings in different age groups was the biggest limitation for its use. Additional difficulty is age dependent variability of normal sonoanatomy, due to maturation and ossification in children. That is why acquisition, interpretation and comparison of US images are completely different than in adults and had to be addressed specifically. All this may affect the validity of the technique, and without defined standardized examination technique, US can be a challenge in the childhood population. On the other hand, US as an imaging technique is considered to be examiner and equipment dependent. Studies resulting in good intra and inter-reader reliability and validity, based on specific definitions, are essential for its application as a diagnostic tool. Recently developed standardized image acquisition methodology, definitions of joint components in healthy children, as well as, definitions for synovitis components and its grading in GS and PD in children will be presented in details.
US allow precise and thorough visualization of inflammatory and destructive joint abnormalities, including synovial hyperplasia, joint effusion, cartilage damage, bone erosion, tenosynovitis and enthesopathy. In JIA ultrasound is considered particularly useful for its ability to detect subclinical synovitis and improve classification of JIA patients into the subtypes. Current evidences about application of ultrasound in JIA can improve definition of remission necessary to optimize treatment strategies. Due to peculiarities of US examination and image acquisition in children additional educational efforts among pediatric rheumatologists are required for expanding this imaging modality in daily practice.
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PsA: an integrated perspective

SP0078 CAN IMAGING BE A PREDICTOR OF PSORIATIC DISEASE?

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Early detection of inflammatory joint diseases is very important to allow prompt initiation of effective therapies. Identifying patients with early arthritic disease can be challenging by conventional clinical, laboratory and radiographic methods, and more advanced imaging modalities such as computed tomography (CT), magnetic resonance imaging, ultrasonography (US) and various nuclear medicine techniques can provide additional information.
This talk describes the current knowledge on the value of different imaging modalities for 1) predicting development of psoriatic disease in undifferentiated patients 2) predicting development of psoriatic arthritis (PsA) in patients with psoriasis with and without musculoskeletal pain and 3) predicting the disease course in patients with PsA.
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SP0079 PATHOLOGIES ACROSS THE TISSUES IN PSA

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The psoriatic disease concept includes the skin disease psoriasis and joint disease psoriatic arthritis. Increasingly, prevalent comorbidities such as obesity and cardiovascular disease are considered to be an integral part of the psoriatic disease concept in many patients.
Within this disease concept, accumulating evidence indicates molecular and cellular cross talk between affected organs and tissues. Skin inflammation affects the bone; nail disease is associated with specific types of arthritis; inflammation links to cardiovascular disease; skin or joint disease may contribute to depression. Novel therapeutic strategies are reaching psoriatic disease patients as never before. Their global impact could be envisioned from a holistic perspective, optimizing the strategy chosen as determined by the active molecular and cellular network that triggers and sustains disease.
Thus, linking the joints with the skin and other organs involved is proposed as an entry point towards personalized medicine in a complex disease.
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Autoinflammatory diseases in children and adults

SP0080 RECURRENT EPISODES OF FEVER AND ARTHRITIS IN ADULT PATIENT

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Background: Familial Mediterranean Fever (FMF) is a relatively rare condition that belongs to the more recent group of autoinflammatory diseases (AIDs)[1]. It primarily affects patients with Mediterranean or Middle Eastern origins and its clinical setting includes short, recurrent episodes of fever, serositis, skin rash and a high risk of amyloidosis[2]. FMF is an autosomal recessive transmitted disease and several mutations of the Mediterranean fever gene (*MEFV*) on chromosome 16 have been identified[3]. Patients respond well to colchicine therapy or if necessary, biological therapy with anti-IL 1, IL6 or anti-TNF could be initiated[4]. Establishing the right diagnosis might raise difficulties for rheumatologists who are not fully accustomed to this condition.
Objectives: To evaluate the clinical course, specific features and treatment difficulties of a male patient diagnosed with FMF in adulthood, based on the description of a case report.
Methods: Case-description using patient's medical records and investigations.
Results: This is the case report of a 37-year old male patient currently admitted for right knee arthritis and high grade fever (39.1℃). His medical history dates back at age 16 when he presented in the Pediatric Department with recurrent episodes of prolonged fever (up to 40℃), diffuse abdominal pain together with myalgia, arthralgia accompanied by increased acute phase reactants; after various sources of infection and hematological malignancies were excluded, physicians noted positive low titer ANA (1/20) but normal complement fractions, absent lupus (LE) cells. Further medical investigations showed a negative rheumatoid factor, ACPA, negative antibodies' panel (dsDNA, Sm, Ro, U1-RNP) and absent cryoglobulins but a positive HLA B27. No signs of sacroiliitis were detected on the x-ray. Patients' repeated complaints of knee or ankle arthritis together with later finding of positive anti-Salmonella and anti-Shigella antibodies leaded to establishing the diagnosis of reactive arthritis. Due to symptoms' persistence and reoccurrence under non-steroidal anti-inflammatory drugs, he was prescribed high dose corticosteroids and sulfasalazine. At age 20 the patient presented with recurrent arthritis of the knees and ankles, fever (38.5℃) and abdominal pain with markedly elevated inflammatory markers. The abdominal ultrasound highlighted a splenomegaly and peritonitis. Colchicine treatment was initiated and his favorable response led to MEFV genetic testing that revealed a mutation of the 10.1 exon, thus confirming the diagnosis of FMF by fulfilling two major criteria of the Tel-Hashomer diagnostic set. Subsequently, he performed a gingival biopsy that excluded the presence of amyloid deposits. Patient's partial response to colchicine with repeated incomplete attacks of FMF and persistent inflammatory syndrome led to the initiation of biological therapy with Etanercept along with Sulfasalazine and glucocorticoids, due to temporary unavailability of an anti-IL1 agent. Patient's delay in diagnosis and longstanding corticosteroid therapy led to major articular consequences (bilateral aseptic osteonecrosis of the femoral head with requiring hip arthroplasty).
Conclusions: This case presentation depicts the hardships of setting the right diagnosis in a case of late onset FMF due to unusual geographical setting, absence of suggestive family history and heterogeneous clinical presentation together with possibilities in therapeutic approach if patients are non or partially responsive to traditional therapies. Furthermore it points out possible drug side effects and comorbidities that require the same quality medical care as the main rheumatic disease.
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Immunogenicity of biologics; myth or reality?

SP0081 THE T CELL RESPONSE TO THERAPEUTIC ANTIBODIES

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Therapeutic antibodies (TMabs) are part of the best successful therapeutic products of the last decades. They are currently used to treat many inflammatory diseases such as rheumatoid arthritis (RA) and bowel diseases and represent worldwide a market of several billions of dollars. However they have the major drawback to be potentially immunogenic and therefore might elicit anti-drug antibodies (ADA). ADA could dramatically reduce the efficacy of the drugs or might provoke allergic reactions. Because generally self-proteins are less immunogenic than foreign proteins, the sequence of therapeutic antibodies has been humanized. However humanization even at the highest level does not fully guarantee the lack of immune responses demonstrating the important need to know more about ADA response. Because T cells are known to initiate the ADA response, we are currently investigating the T cell response to immunogenic therapeutic antibodies. With the perspective of immunogenicity prediction, we quantified the number of very rare T cells specific for therapeutic antibodies in the blood of normal donors and found a good concordance between the number of T cells specific to them and their respective clinical immunogenicity level. We then identified the CD4 T cell epitopes of four immunogenic TMabs with different levels of humanization, namely the chimeric antibodies Infliximab (Ifx) and Rituximab (Rtx), the humanized antibody Natalizumab (Ntz) and the fully human Adalimumab (Adm). CD4 T lymphocytes were expanded by several weekly rounds of stimulation with autologous dendritic cells loaded with each of the investigated antibodies and the T cell specificity was assessed by IFNg ELISPOT using overlapping peptides encompassing the whole sequence of their variable parts. Nine epitopes were identified in the VL and VH chains of Rituximab and Infliximab. They overlap CDR or FR regions of both chimeric antibodies and some of them are shared by multiple donors. As inferred from binding experiments, T cell epitopes often exhibited a good affinity for HLA-DR molecules found in the responding donors. Nine CD4 T cell epitopes were found in the VH and VL parts of the humanized therapeutic antibody Natalizumab while the fully human antibody Adalimumab hosted 10 T cell epitopes. As a result, the number of T cell epitopes is very similar across the different therapeutic antibodies but their location is highly variable from one antibody to another one. Finally to assess the clinical relevance of the identified T cell epitopes, we evaluated the ability of Ifx and Rtx T cell epitopes to stimulate T cells of patients having developed ADA. Two third of the T cell epitopes identified from the healthy donors stimulated PBMCs from ADA+ patients and promoted the secretion of a diversity of cytokines. These data emphasize the predictive value of evaluating the T cell repertoire of healthy donors to anticipate and prevent immunogenicity of therapeutic antibodies. Together our data provide new insights on the origin of immunogenicity of chimeric, humanized and human therapeutic antibodies.
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SP0082 IMMUNOGENICITY OF BIOLOGICS IN INFLAMMATORY BOWEL DISEASES

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Anti-tumor necrosis factor-alpha and anti-integrin monoclonal antibodies show great benefits for inducing and maintaining remission, healing the mucosa and restoring the quality of life of patients with inflammatory bowel diseases. The therapeutic potential of these intrinsically powerful biologicals is tempered by a high variability in clinical response. Whereas primary non-response is defined as the lack of clinical response to treatment, assessed 8–12 weeks after initiation, secondary loss of response is defined as loss of clinical benefit after initially responding which can be attributed to disease-related or drug-related factors. Assays have been developed to determine the concentration of the therapeutic antibody in serum of the treated patient. The trough concentration is the concentration just before the next administration and for practical reasons therapeutic drug monitoring is mainly based on measurement of these trough concentrations. Several studies have reported correlations between through concentration of infliximab, adalimumab, golimumab, vedolizumab and clinical outcome. Optimal therapeutic windows have been defined for both infliximab and adalimumab. A panel of prospective studies in which dosage regimens are adapted in order to achieve target trough infliximab concentrations that correlate with beneficial therapeutic outcomes have been initiated.
Immunogenicity is the capability of biologicals to elicit an unwanted immune response that results in the formation of anti-drug antibodies. Anti-drug antibodies can be non-neutralizing or neutralizing. Non-neutralizing antibodies do not impair the drug-target interaction but may increase clearance of the drug resulting in lower serum concentrations. Neutralizing anti-drug antibodies compete with the target for the antigen-binding site and modulate directly the activity of the drug in addition to the enhanced clearance of the drug. A number of anti-drug antibody assays to quantify the immunogenicity of biologicals have been developed. Most of the assays quantify the total amount of anti-drug antibodies but comparing anti-drug antibody concentrations between different assays is hampered by the