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Patients within joint inflammation: Area of interest for a rheumatologist

Joint pain is one of the most common reasons for patients to seek help from general practitioners in general and rheumatologists in particular. Fortunately, not all joint pains are inflammatory joint pain and do not need a rheumatology approach. On the other hand, atypical joint pain especially if associated with signs and symptoms of inflammation should rise "the red flag" indicating that this patient may benefit from early treatment to prevent irreversible joint damage and subsequent disability.

That was a philosophy to establish more specific criteria for early diagnosis of rheumatoid arthritis (RA). In line with an early diagnosis according to the European Alliance of Associations for Rheumatology (EULAR) recommendations, such a group of patients may benefit from early initiation of the proper treatment. In detail in the group of patients with swelling of at least one joint, with high parameters of inflammation (mainly high C-reactive protein or erythrocyte sedimentation rate) the treatment with methotrexate should be initiated as fast as possible even when the patient does not satisfy fully criteria for RA. In this issue, this problem was addressed by Kwiatkowska [1] who elegantly reviewed the up-to-date strategies to diagnose and treat RA. The complex approach to patients with RA is obviously not restricted to patients who potentially may have RA. Treatment of RA is still challenging both for the patients as well as for the treating physician. Rheumatoid arthritis has an unpredictable course, characterized by periods of remissions and high activity, therefore a tight approach to the patients is commonly indicated and the treatment even initiated early in the course of the disease should be monitored and adjusted when needed. Again, Kwiatkowska emphasized the need for proper disease monitoring with the use of available instruments such as DAS 28 and SDAI scales. Only such an approach may give precise insight into disease activity and provide the proper treatment for all patients. Treating to target strategy is a unique approach proposed many years ago by EULAR. It underlines that treatment alone is not enough to reach satisfactory outcomes, but disease activity should be frequently checked and treatment adjusted according to the patient's need and disease activity. With the advent of an era of biological disease-modifying anti-inflammatory drugs (DMARDs) and targeted synthetic DMARDs rheumatologists possess a strong weapon against the disease, which show to be efficacious and safe in patients with RA. Analysis of epidemiologic data however showed that these modern tools are underutilized in common practice. The real-world data showed for example, that methotrexate (MTX) compliance is very low and only approx. 40% of patients precisely followed physicians' recommendations. Moreover, due to limited oral absorption of MTX which reaches the plateau at the dose of 15 mg, higher oral MTX doses are often inefficacious, and patients never reach remissions and low disease activity. Therefore, it is advisable to switch patients to parenteral MTX when the target is not reached, or side effects are present. Moreover, the recent preliminary approach for treating RA proposed this year by EULAR accepts only a short course of glucocorticosteroids as a bridge therapy (when initiating or changing conventional synthetic

DMARDs) but they should be tapered and discontinued as fast as clinically feasible. In the other words, it is not acceptable to roll patients on steroids for a long time. Instead of this, it is advisable to switch patients early to biologics or targeted synthetic DMARDs when the target is not reached and poor prognostic factors are present. Moreover, concerns about Janus kinase (JAK) inhibitors' side effects, resulted that JAK inhibitors although still considered in the treatment but are not preferred over biological DMARDs.

Recent EULAR recommendations for the management of RA once again underlined the role of MTX in the treatment of patients with RA. However, in the setting of a real-world clinic sometimes MTX is contraindicated. If it is the case EULAR recommends starting leflunomide or sulfasalazine. At first glance, for many rheumatologists starting the treatment with sulfasalazine seems to be the preferred option, as the drug is believed to be safer than MTX. To address this question Osieleniec et al. [2] presented the case of sulfasalazine adverse event in the form of drug rash with eosinophilia and systemic symptoms (DRESS syndrome), neutropenic fever and severe nephrotic syndrome. The message from this case report strongly indicates that sulphasalazine is often responsible for mild adverse reactions (dyspeptic disorders, increased liver enzymes, decreased appetite, mild leucopenia), observed in approximately 25–50% of patients. This often leads to discontinuation of the treatment. Fortunately, severe adverse reactions are rare, however, when present they affect the haematological system (71%), liver (14%), skin (11%), and kidney (3%). The authors advise monitoring closely haematologic parameters as well as liver and kidney function tests before and after initiating the sulfasalazine treatment.

Rheumatoid arthritis is a disease where the pathophysiological background has not been explained satisfactorily, and many genetic, epigenetic and environmental factors may play a role. Among many potential mechanisms responsible at least partially for the development of connective tissue disease in general and RA in particular recent advances in microbiology suggested the role of changes in the composition and function of the gut microbiome. This is a complicated microsystem of mutual interaction between bacteria localized in a gastrointestinal system with a plethora of metabolites, micromolecules and signalling pathways. As a result dysfunction of this system caused for example by antibiotics therapy, smoking and diet translated directly to a higher risk for the development of autoimmune response. Changes in gut microbiota are augmented by the increased permeability of antigens across the gut-blood barrier resulting in increased absorption of molecules commonly recognised as invaders by the immune system of the host. This phenomenon commonly referred to as "leaky gut" attracted the high attention of rheumatologists and immunologists as it may potentially act as a pathophysiological background for the development of several autoimmune diseases, such as inflammatory bowel disease, celiac disease, type 1 diabetes, multiple sclerosis, autoimmune hepatitis, systemic lupus erythematosus or RA [3]. In this review, Wąż et al. also emphasized that proper treatment of RA with the use of DMARDs may contribute to the restoration of proper composite and function of microbiota thus facilitating the achievement of treatment targets [3].

With the progress of imaging techniques and the implementation of magnetic resonance imaging (MRI) in the common rheumatological practice, it became evident that a large group of rheumatological conditions affecting the axial spine should not be recognized as one disease. With the use of MRI, it is now possible to diagnose patients with axial spine joint inflammation at the early stage of the disease. MRI can recognize the inflammation in the sacroiliac joint many years before X-ray changes are evident thus enabling an introduction of the proper treatment to stop the progression of the disease. For this form of sacroiliac joint involvement, the term non-radiographic spondyloarthritis (nr-axSpA) has been coined indicating that this group of diseases may represent a different clinical entity or simply be the initial stage of ankylosing spondylitis development. Following the progression of MRI and recognition of nr-axSpA as a new clinical entity, it has been shown that anti-TNF treatment can change the course of the disease and improve prognosis in nr-axSpA. Parallel to the introduction of TNFi, it was evident that interleukin-17 (IL-17) one of the most potent proinflammatory cytokines also plays a crucial role in the development and progression of spondyloarthritis. The discovery of the role of IL-17 in this condition resulted in the introduction of IL-17 inhibitors able to ameliorate the proinflammatory function of this cytokine. The role of IL-17 blockade has been recently

recognized by the national health system in Poland which translated directly to the implementation of IL-17 blockers into the therapeutic B.82 program. At the moment similar to the other European countries as well as the USA, Polish rheumatologists were given a new weapon against spondylarthritis. As far as it is not clear how to switch between available agents licensed in the Spa in case of their insufficiency. Sikorska et al. discussed this problem in detail suggesting possible scenarios [4]. A careful reading of this paper may help to choose the right treatment option for the given patients.

A multidisciplinary approach in the diagnosis and treatment of rheumatic conditions demands close cooperation between various specialists. It is especially true in connective tissue diseases. Although this group of disorders formally belongs to rheumatology, an organ-specific approach involving several specialists such as neurologists, haematologists, dermatologists and many others is of great importance. Of note is also the fact that advanced imaging techniques as well as complicated neurophysiological examinations become freely available to rheumatologists. In this issue, the current concepts on the role of clinical neurophysiology examinations in rheumatology have been presented. This technique is an especially valuable tool at the crossroads of neurology and rheumatology. This is widely used for the diagnosis of inflammatory myopathies as well as polyneuropathies commonly occurring in the course of connective tissue diseases. The results of neurophysiological examinations, however, should be interpreted with caution. Rheumatologists should possess essential knowledge of key elements of EMG records, conditions under which examination is performed and the influence of such factors as gender, age or style of life and their impact on the final shape of the EMG curve. In his review, Daroszewski et al. [5] addressed the most important elements of proper technique of neurophysiological examination and what is more important how to interpret findings in EMG examination. He provided concise and valuable guidelines on interpretation but also the limitations of these techniques.

We promised to create the journal as a mixture of valuable reviews giving up-to-date knowledge but also aimed to present interesting original reports in rheumatology. To fulfil this mission this issue contains a study on the analysis of deficits in knee flexion in children with cerebral palsy. The authors identified factors responsible for the proper range of motion of knee flexions such as extensor muscle tension, hip flexor movement or plantar flexors tension [6]. This study has practical implications as it simply may serve in the creation of a proper physiotherapy plan for children with cerebral palsy.

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