Paediatric rheumatology: where are we going?

Filipa Oliveira Ramos[1]

ACTA REUMATOL PORT. 2014;39:296-297

In recent years all fields in rheumatology have had a great development and paediatric rheumatology is no exception. New breakthroughs in immunology, genetics and pharmacotherapeutics opened up new paths in research and clinical approach to juvenile rheumatic diseases. The increasing evidence that earlier therapeutic intervention improves long-term outcome for several juvenile rheumatic conditions, particularly in juvenile idiopathic arthritis (JIA), have highlighted the need for sensitive and specific imaging tools capable of identifying early changes, in order to determine which patients are at greatest risk of poor outcome and who need more aggressive treatment. This is one of the major objectives in the application of musculoskeletal ultrasound (MSK-US) in children but, in contrast to its widespread use in adults, experience with MSK-US in paediatric rheumatology is still limited.

In a report published in this issue of Acta Reumatológica Portuguesa (ARP), Dias JM et al describe the experience of a large Portuguese centre and the added value of MSK-US in the clinical assessment of pediatric rheumatic diseases[1]. This article is a retrospective study of 330 MSK-US exams, performed to 222 children with rheumatic inflammatory diseases. This study emphasizes that clinical evaluation does not seem to be specific enough for synovitis detection as MSK-US could exclude synovitis in nearly half (48.5%) of the children with the clinical diagnosis of arthritis and in two thirds of children with tender joints. Regarding tenosynovitis/tendinitis, there seems to be a remarkable discordance between clinical and MSK-US evaluation with most (61.5%) of the ultrasonographic diagnosis of tenosynovitis found in patients with no clinical signs or symptoms of this affection, which stresses the limitations of physical examination in children. Several other studies have shown the value of MSK-US, particularly in JIA, for multiple joint examining[2], for detecting cartilage and bone damage[3], for treatment monitoring and for evaluate disease remission[4]. Over the coming years an effort will be certainly made in order to standardize and define validated protocols and scores for the performance of MSK-US in children.

In addition to the development of imaging techniques in juvenile rheumatic diseases many other areas of paediatric rheumatology have had great advances. An example is the growing evidence for biomarkers and their utility to guide treatment in systemic JIA (such as S100A8/A9 and interleukin-18 [IL-18]) and the improved understanding of the mechanisms underlying chronic inflammation in severe JIA[5].

We are now in the era of post genomics revolution. Sequencing large parts of the genome has become more available and will certainly elucidate about the genetic component of many pediatric rheumatic diseases. Even for diseases that have a responsible gene well identified, like monogenic autoinflammatory syndromes, the etiopathogenesis is not clearly clarified. A study published in this ARP issue attempts to clarify the role of oxidative stress and oxidant/antioxidant imbalance in the persistent subclinical inflammation of familial mediterranean fever (FMF). The authors found in FMF patients, during attack-free periods, higher total thiols and lower advanced oxidative protein products, when compared with controls[6]. Other previous studies had demonstrated enhanced oxidative stress in the FMF patients[7] and oxidant/antioxidant parameters and anti-oxidant enzymes could have a future role at the evaluation of inflammation severity and subclinical inflammation in these patients. Additionally, studies on epigenetics will hopefully show factors that regulate gene expression of this and others autoinflammatory syndromes and will help to understand the variability of phenotypic expression and outcomes of these disorders.

All the advances in the knowledge of the pathogenesis of autoinflammatory disorders have been changing the way they are approached and treated. However, apart from cryopyrin-associated periodic syndromes and FMF, therapy of autoinflammatory syndromes is based on small retrospective studies. A case series of

1 Department of Rheumatology, Centro Hospitalar Lisboa Norte, Hospital de Santa Maria, Lisbon Academic Medical Centre, Lisbon, Portugal

four patients with chronic recurrent multifocal osteomyelitis (CRMO) treated with bisphosphonates was published in ARP[8]. Treatment of chronic non-infectious osteomyelitis (CNO), the most common entity in autoinflammatory bone diseases, which in cases with extended multifocal involvement is also called CRMO, has been largely empiric. There are a few prospective studies of response to bisphosphonates in CRMO/ /CNO, but no randomized trials have been performed, primarily because of the rare nature of this disorder[9]. In fact this is a problem common to most pediatric rheumatic diseases as evidence based guidelines are sparse and treatment regimens differ between centers. In order to optimize diagnosis, management and long term complications of rheumatic diseases in children, patient's registries play a major role. Several national and international registries of many pediatric rheumatic diseases are ongoing and hopefully in the near future they might provide the answers to many of the knowledge gaps that still exist in this field. Reuma.pt is a good example of such an effort, constantly bringing original contributions[10] to unmet clinical needs.

CORRESPONDENCE TO
Filipa Oliveira Ramos
Rheumatology Department
Hospital de Santa Maria, CHLN
Av. Professor Egas Moniz
1649-035 Lisbon, Portugal
E-mail: filipa.o.ramos@gmail.com

REFERENCES

1. Dias JM; Costa MM; Canhão H, Saraiva F; Silva JAPd; Musculoskeletal ultrasound in Paediatric Rheumatology: a retrospective analysis. Acta Reum Port 2014;39:309-314.
2. Collado P, Naredo E, Calvo C, Gamir ML, Calvo I, García ML, Merino R, Graña J, Bustabab S, Garrido J; ECO-JIA Study Group.: Reduced joint assessment versus comprehensive assessment for ultrasound detection of synovitis in Juvenile Idiopathic Arthritis. Rheumatology 2013;52:1477-1484.
3. Collado Ramos P. Ultrasound imaging in juvenile idiopathic arthritis for the rheumatologist. Clin Exp Rheumatol. 2014 Jan-Feb;32(1 Suppl 80):S34-41.
4. Magni-Manzoni S1, Scirè CA, Ravelli A, Klersy C, Rossi S, Muratore V, Visconti C, Lanni S, Merli P, Montecucco C. Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis. Ann Rheum Dis. 2013 Feb;72(2):223-228.
5. Vastert S, Prakken B. Update on research and clinical translation on specific clinical areas: From bench to bedside: How insight in immune pathogenesis can lead to precision medicine of severe juvenile idiopathic arthritis.Best Pract Res Clin Rheumatol. 2014 Apr;28(2):229-246.
6. Sahin A, Erten S, Altunoglu A, Isikoglu S, Neselioglu S, Ergin M, Atalay H, Erel O. Comparison of serum oxidant and antioxidant parameters in familial Mediterranean fever patients with attack free period. Acta Reumatol Port 2014;39:316-321.
7. Guzel S1, Andican G, Seven A, Aslan M, Bolayirli M, Guzel EC, Hamuryudan V. Acute phase response and oxidative stress status in familial Mediterranean fever (FMF). Mod Rheumatol. 2012 Jun;22(3):431-417.
8. Ferraria N, Marques JG, Ramos F, Lopes G, Fonseca JE, Neves MC. Chronic recurrent multifocal osteomyelitis: case series of four patients treated with biphosphonates. Acta Reumatol Port. 2014 Jan-Mar;39(1):38-45.
9. Stern SM1, Ferguson PJ. Autoinflammatory bone diseases. Rheum Dis Clin North Am. 2013 Nov; 39 (4):735-749.
10. Mourão AF, Santos MJ, Melo-Gomes J, Martins FM, Costa JA, Ramos F, Brito I, Duarte C, Figueira R, Figueiredo G, Furtado C, Lopes A, Oliveira M, Rodrigues A, Salgado M, Sousa M, Branco JC, Fonseca JE, Canhão H. Using the juvenile arthritis disease activity score based on erythrocyte sedimentation rate or C-reactive protein level: results from the portuguese register. Arthritis Care Res (Hoboken). 2014 Apr;66(4):585-591.